Mass Analysis with Quadrupoles with Added Multipole Fields

by

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Abstract

Conventional mass analysis, mass analysis with islands of stability, and mass selective axial ejection were investigated using linear quadrupoles with added hexapole fields. Experiments agree with computer simulations. When the resolving dc is applied, so that the Mathieu parameter $\alpha > 0$, conventional mass analysis is possible. However, the transmission and resolution are low, and there is peak structure. When $\alpha < 0$, only very low resolution (80) and transmission are seen. With both $\alpha > 0$ and $\alpha < 0$, the use of islands of stability for mass analysis greatly improves peak shape, resolution, and in some cases, transmission.

Mass selective axial ejection (MSAE), has also been investigated with linear quadrupoles with added hexapole fields. Trapped ions were ejected using dipole excitation with various ejection parameters: ejection $q$, excitation amplitude, excitation between the $x$ or $y$ rods, scan speed and scan direction. At high ejection $q$ ($q = 0.73$), excellent peak shapes and resolution up to 4500 were obtained. Scan speeds up to 4000 Th/s were possible. The optimal combination of specific rod set, scan direction, and dipole excitation rod pair was determined. MSAE at lower ejection $q$ was also investigated and found to give lower resolution and spurious peaks on the low mass side of the peaks.

Simulations were used to investigate mass analysis in islands of stability with linear quadrupoles with added octopole or hexapole fields. With both $\alpha > 0$ and $\alpha < 0$, the best resolution and peak shape are obtained with operation at the upper tip of the uppermost island formed with the auxiliary excitation. The improvement of resolution and peak shape with $\alpha < 0$, confirms that the use of islands generally can provide a method for mass analysis when added multipole fields otherwise prevent mass analysis.
The possibility of operating conventional quadrupole as a mass filter and ion trap as Q3 in a triple quadrupole system is limited because of its low fragmentation efficiency at low pressure. Quadrupoles with added multipoles give greater fragmentation efficiency at $1 \times 10^{-4}$ Torr. The experiments and simulations here suggest that quadrupoles with added hexapole fields might be good candidates where Q3 must be operated as both a trap and mass filter.
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**List of Symbols and Abbreviations**

- rf: Radio frequency
- dc: Direct current
- 3D: Three dimensional
- ESI: Electrospray ionization
- MALDI: Matrix assisted laser desorption ionization
- P: Integer
- Q: Integer
- $R_{1/2}$: Resolution at half peak height
- LIT: Linear ion trap
- FTICR: Fourier transform ion cyclotron resonance
- LC: Liquid chromatography
- MS: Mass spectrometry
- TOF: Time of flight
- MS/MS: Mass spectrometry/mass spectrometry
- 2D: Two dimensional
- RIT: Rectilinear ion trap
- MSAE: Mass elective axial ejection
- Q0: Quadrupole ion guide
- Q1: First quadrupole
- Q2: Collision cell
- Q3: Third quadrupole
- DAC: Digital to analog converter
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>MCS</td>
<td>Multichannel scaler</td>
</tr>
<tr>
<td>CEM</td>
<td>Channel electron multiplier</td>
</tr>
<tr>
<td>QPS</td>
<td>Quadrupole power supply</td>
</tr>
<tr>
<td>cps</td>
<td>Counts per second</td>
</tr>
<tr>
<td>$U$</td>
<td>Direct current voltage</td>
</tr>
<tr>
<td>$V_{rf}$</td>
<td>Radio frequency voltage</td>
</tr>
<tr>
<td>$V'$</td>
<td>Excitation voltage amplitude</td>
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<td>$x,y$</td>
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<td>$\omega_n$</td>
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<td>$a,q$</td>
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<td>Mathieu parameter for quadrupole excitation</td>
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<td>Mass to charge ratio</td>
</tr>
<tr>
<td>$n$</td>
<td>Number of rf cycles</td>
</tr>
<tr>
<td>$h$</td>
<td>Constant for each stability region</td>
</tr>
<tr>
<td>$d$</td>
<td>Distance from the end of the rods</td>
</tr>
</tbody>
</table>
$\omega_{ex}$  
Excitation frequency  

$A_N$  
Dimensionless amplitude of the electric potential multipole N  

$r_{\text{norm}}$  
Normalization radius  

$\text{Re}[f(\zeta)]$  
Real part of the complex function $f(\zeta)$  

$R_y, R_x$  
Radius of $y$-pole and $x$-pole rod pairs  

$\omega_0$  
Secular frequency  

$\Delta \omega$  
Frequency shift  

$\Phi(x, y, t)$  
Time dependent two-dimensional potential  

$\alpha$  
Parameter in the nonlinear differential equation  

$\beta_u$  
Parameter in the solution of the Mathieu equation  

with $u = x$ or $y$.  

$\gamma$  
Phase of the auxiliary quadrupole excitation voltage  

$\zeta$  
Complex variable $\zeta = x + iy$  

$\lambda$  
$U/V_{rf}$  

$\xi$  
$\xi = \Omega t/2$  

$\nu$  
Ratio of excitation frequency to trapping frequency  

$\varphi(t)$  
Time dependent potential applied to an electrode  

$\varphi_N(x, y)$  
Two dimensional multipole of order $N$  

CID  
Collision-induced dissociation  

CAD  
Collisionally activated dissociation  

$K$  
Order of the perturbation theory
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Foremost, I would like to express my deep and sincere gratitude to my advisor Dr. Don Douglas for the continuous support of my Ph.D study and research, for his enthusiasm in research, immense knowledge in mass spectrometry and endless patience to explain things clearly and simply. His guidance helped me in all the time of research, paper preparation and writing of this thesis.

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The project was initiated by Dr. Douglas. Also Dr. Douglas contributed greatly to the design of the project, research details and editing of the manuscript. Dr. Zhao gave valuable suggestions for determining the optimized experimental configurations. My major contributions are:

- Literature survey
- Identification and design of the research project
- Data acquisition
- Data analysis including data selection, organization of the results and explanation of the observations
- Preparing the manuscripts including drafting/editing the papers and providing the figures and tables
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The project was initiated by Dr. Douglas. Also Dr. Douglas contributed greatly to the design of the project, research details and editing of the two manuscripts. Dr. Konenkov developed the simulation software. Dr. Zhao conducted part of the simulation and preparation of the manuscript. My major contributions are:

- literature survey
- running simulations of stability diagrams and islands of stabilities
- Analyzing the data including data reduction, organization of the results and explanation of the observations
- Preparing parts of the manuscripts including editing the papers and providing the figures and tables
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The project was initiated by Dr. Douglas. Also Dr. Douglas contributed greatly to the design of the project, research details and editing of the two manuscripts. Dr. Zhao acquired part of the data and prepared the manuscript. My major contributions are:

- literature survey
- Contribute to the designing and identification of the research projects
- Analyzing the data including data reduction, results organization of the results and explanation of the observations
- Preparing part of the manuscripts including drafting/editing the papers and providing the figures and tables
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- Contribute to the designing and identification of the research projects
- Analyzing the data including data reduction, results organization of the results and explanation of the observations
- Preparing part of the manuscripts including drafting/editing the papers and providing the figures and tables
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The project was initiated by Dr. Douglas. Also Dr. Douglas contributed greatly to the design of the project, research details and editing of the manuscript. Dr. Zhao gave valuable suggestions for determining the optimized experimental configurations. My major contributions are:

- literature survey
- Identification and design of the research projects
- Analyzing the data including data reduction, results organization of the results and explanation of the observations
- Preparing parts of the manuscripts including editing the papers and providing the figures and tables
1 Introduction
The history of mass spectrometry (MS) began with J. J. Thomson’s studies on the composition of cathode rays. In 1907, Thomson constructed the first mass spectrometer for the determination of the mass-to-charge \((m/z)\) ratios of ions [1]. In this instrument, ions generated in a discharge tube were passed through electric and magnetic fields. Deflection of ions was measured by placing a photographic plate in their path. Thomson's measurement of the mass to charge ratio of cathode rays was the first example of mass spectrometry. Later in 1918, Arthur Jeffrey Dempster designed a mass spectrometer in which ions were dispersed by mass and focused by velocity [2]. The velocity-focusing device improved MS resolving power by an order of magnitude over the resolution Thomson had been able to achieve. The quadrupole mass filter, which proved to be ideal for coupling to a GC, was first reported by the group of Wolfgang Paul [3, 4], who shared the 1989 Nobel Prize in Physics for his work on ion trapping. His research showed that ions with different mass to charge \((m/z)\) ratios could be separated by a quadrupole electric field (comprising radio-frequency [rf] and direct-current [dc] components). Another instrument that Paul originated was the quadrupole ion trap, which can trap and mass-analyze ions using a three-dimensional (3D) quadrupolar rf electric field. An ion trap system was first introduced commercially in 1984 by Finnigan as a mass selective GC detector based on technology developed by Finnigan research scientist George C. Stafford and coworkers [5]. Today, ion trap instruments serve not only as GC detectors but also as Liquid Chromatography (LC) -MS detectors and stand-alone mass spectrometers.

New soft ionization techniques, developed over the last 25 years, such as electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI) have made it possible to mass analyze large biomolecules using various types of mass spectrometers. The combination of the new soft ionization methods with collision induced dissociation (CID), also called
“collisionally activated dissociation (CAD)” led to great improvement in the performance of the tandem mass spectrometry, also known as MS/MS. Tandem mass spectrometry involves multiple steps of mass analysis, with some form of fragmentation occurring between the stages. For example, a precursor ion is mass-selected (isolated) and then fragmented by CID/CAD, followed by mass analysis of the resulting product ions. Tandem mass spectrometry is highly informative about the structures of both the precursor ions and fragmentation products. The progress of experimental methodology and refinements in instrumentation have led to great improvements in resolution, sensitivity, mass range and mass accuracy. After 100 years of development and several Nobel Prizes awarded for related research, mass spectrometry is now a widely employed technique and a large family of instruments has been developed. It has become one of the most important complex instruments used in many fields of science in the twentieth century.
1.1 Theory and Background of Quadrupole Mass Spectrometry

1.1.1 The Linear Quadrupole as a Mass Filter

The basic theory of quadrupoles is well described in Dawson’s book [6]. Two- and three-dimensional (2D and 3D) ion traps are based on the same basic principles. In a review, Douglas not only discusses the traditional use of linear quadrupole mass analyzers and ion guides, and also introduces recent developments and new methods of using quadrupoles [7].

The linear quadrupole mass filter consists of four parallel-rod electrodes. Ideally, each electrode should be hyperbolic, but cylindrical rods are often used, due to ease of manufacturing. The effects of the imperfections introduced to the pure quadrupole field by using the round rods can be minimized by adjusting the ratio of rod radius, \( r \), to field radius, \( r_0 \) [7-9]. Connecting opposite pairs of rods and applying rf and dc potentials between the pairs creates the quadrupole field. Figure 1.1 is a schematic diagram of a quadrupole mass filter.
The electric potential of an ideal linear quadrupole, $\Phi(x, y, t)$, is given by

$$\Phi(x, y, t) = \left(\frac{x^2 - y^2}{r_0^2}\right) \varphi(t)$$  \hspace{1cm} (1.1)

where $x$ and $y$ are Cartesian coordinates orthogonal to a central axis, $r_0$ is the distance from the central axis to an electrode and $\pm \varphi(t)$ is the voltage applied between the electrodes and ground. For mass analysis, the applied pole to ground voltage has both dc ($U$) and rf ($V_{rf}$) components, and is given by

$$\varphi(t) = (U - V_{rf} \cos \Omega t)$$  \hspace{1cm} (1.2)
Here, $\Omega$ is the angular frequency of the rf voltage. For an operating frequency of 1.0 MHz, $\Omega = 2 \times \pi \times 1 \times 10^6$ s$^{-1}$.

In a quadrupole field, the equation of ion motion in each direction can be written as

$$m \frac{d^2 x}{dt^2} = -\frac{2ze}{r_0^2} \left( U - V_{rf} \cos \Omega t \right) \quad (1.3)$$

$$m \frac{d^2 y}{dt^2} = \frac{2ze}{r_0^2} \left( U - V_{rf} \cos \Omega t \right) \quad (1.4)$$

where $z$ is the number of charges on an ion, $e$ is the electron charge, $m$ is the ion mass and $t$ is time. As a result, ion motion in the $x$ and $y$ directions are independent. Equations (1.3) and (1.4) can also be written as the Mathieu equation by defining the variables

$$\xi = \frac{\Omega t}{2} \quad (1.5)$$

$$a_x = -a_y = \frac{8zeU}{m\Omega^2 r_0^2} \quad q_x = -q_y = \frac{4zeV_{rf}}{m\Omega^2 r_0^2} \quad (1.6)$$

With these variables, the equations of motion for $x$ and $y$ become

$$\frac{d^2 x}{d\xi^2} + (a_x - 2q_x \cos 2\xi)x = 0 \quad (1.7)$$

$$\frac{d^2 y}{d\xi^2} - (a_y - 2q_y \cos 2\xi)y = 0 \quad (1.8)$$

Equations (1.7) and (1.8) have the form of a Mathieu equation [6, 10].
The properties of the Mathieu equation are well established. The solution is presented here only to give an understanding of ion trajectories

\[ u (\xi) = \alpha' e^{\mu \xi} \sum_{n=-\infty}^{\infty} C_{2n} e^{2\mu n \xi} + \alpha'' e^{-\mu \xi} \sum_{n=-\infty}^{\infty} C_{2n} e^{-2\mu n \xi} \quad (1.9) \]

where \( u = x \) or \( y \), and \( \alpha' \) and \( \alpha'' \) are integration constants depending on the initial conditions, \( u_0 \) (initial position) and \( \dot{u}_0 \) (initial velocity in \( x \) or \( y \)). The \( C_{2n} \) coefficients are factors that describe the amplitudes of ion motion and depend only on \( a \) and \( q \). The other constant, \( \mu \), which can be expressed as \( \mu = \alpha + i\beta \), is also only determined by \( a \) and \( q \). As a result, the nature of the ion motion is determined by \( a \) and \( q \) regardless of the initial conditions. The solutions of the Mathieu equation, which depend on the term \( \mu \), are classified as stable or unstable. The solutions are stable and periodic, only if \( \mu = i\beta \) and \( \beta \) is not a integer number. Unstable solutions arise when \( \mu \) is real and not zero, or complex, or if \( \mu = im \), with \( m \) being an integer. If an ion source is placed at the entrance of a quadrupole and a detector or other apparatus at the exit of the quadrupole, with stable solutions, ions oscillate in the \( xy \) plane with amplitudes that are smaller than \( r_0 \), and can pass through the quadrupole field without hitting the rods. With \( \mu = i\beta \), equation (1.8) becomes

\[ u (\xi) = A \sum_{n=-\infty}^{\infty} C_{2n} \cos(2n + \beta)\xi + B \sum_{n=-\infty}^{\infty} C_{2n} \sin(2n + \beta)\xi \quad (1.10) \]

The constants \( A \) and \( B \) depend upon the initial conditions and can be written as \( A = \alpha' + \alpha'' \) and \( B = i(\alpha' + \alpha'') \). The parameter \( \beta \) is a function of \( a \) and \( q \). The relationship between \( \beta \) and \( (a, q) \) is determined by a continued fraction and can be expressed as
\[ \beta^2 = a + \frac{q^2}{(2 + \beta)^2 - a - \frac{q^2}{(4 + \beta)^2 - a - \frac{q^2}{(6 + \beta)^2 - a - \cdots}}} + a \]
\[ \quad + \frac{q^2}{(\beta - 2)^2 - a - \frac{q^2}{(\beta - 4)^2 - a - \frac{q^2}{(\beta - 6)^2 - a - \cdots}}} \quad (1.11) \]

When \( q \leq 0.4 \), equation (1.10) can be simplified to

\[ \beta = [a + \frac{q^2}{2}]^{1/2} \quad (1.12) \]

An ion oscillates in a quadrupole field with a “secular” frequency (\( \omega_0 \), the lowest frequency) and a number of higher-order frequencies given by

\[ \omega_n = (2n + \beta) \frac{\Omega}{2}, \quad n = 0, \pm 1, \pm 2, \ldots \quad (1.13) \]

As a result, \( \omega_0 \) in a quadrupole field is

\[ \omega_0 = \frac{\beta \Omega}{2} \approx \frac{q \Omega}{\sqrt{8}} \quad (1.14) \]

when \( a = 0 \). Ions with the same \( \beta \) values have the same frequencies. The region of the stable and bounded solutions for the Mathieu equation in either the x or y direction can be constructed as stability diagrams for x and y, respectively, as shown in [6]. Figure 1.2 shows the first stability region. This is formed by the overlapping regions of the two separate stability diagrams for x and y. Ion motion in the regions outside the stability boundaries is unstable. The iso-\( \beta \) lines within the stable region correspond to the set of \((a, q)\) points which have the same values of \( \beta \).
Along these lines, ions will have the same frequency components of oscillation for \( x \) or \( y \) but may have radically different trajectories. There are an infinite number of stability regions, but the first stability region is used most often.

![Figure 1.2](image)

Figure 1.2 The first stability region of a linear quadrupole field. The distance \( d_0 \) refers to the distance of the central point of the stable region from the origin; the distance \( d \) is the width of the stable region measured along the scan line. The mass resolution \( = \frac{d_0}{d} \).

### 1.1.2 Conventional Mass Analysis with Linear Quadrupoles

In a quadrupole mass filter, with fixed \( r_0, \Omega, U \) and \( V_{rf} \), ions with the same \( m/z \) ratio have the same \( a \) and \( q \) values, and are located at one operating point in the stability diagram. Ions are generated by an ion source placed at the entrance of a quadrupole ion guide, transmitted to a mass filter and then detected by a detector or other apparatus at the exit of the quadrupole. Since the ratio \( a/q = 2U/V_{rf} \) does not depend on \( m \), the values of \( U \) and \( V \) are chosen so that
ions with different masses are transmitted in order of increasing $m/z$ ratio and reach a detector, producing a mass spectrum. The operating points for all ions lie on the same line of constant $a/q$, the so-called scan line (Figure 1.2). The resolution of a quadrupole can be adjusted by changing the ratio of $U/V_{rf}$. Increasing the ratio will place the scan line closer to the tip of the stability region, thus increasing the mass resolution. In theory the resolution is calculated from the stability diagram as shown in Figure 1.2 and it could be infinite as the scan line approaches the tip of the stability region. Only if a quadrupole analyzer has unlimited length and produces a pure quadrupole field will the resolution be unlimited. In practice, however, the resolution is limited by the length of the analyzer and the purity of the quadrupole field. Resolution is defined as $R_{1/2} = (m/z)/(\Delta m/z)_{1/2}$, where $(\Delta m/z)_{1/2}$ is the width at half height of a measured peak. Considering the length of a real quadrupole, the resolution measured at half height is given by

$$R_{1/2} = \frac{n_{rf}^2}{h}$$

(1.15)

where $n_{rf}$ is the number of rf cycles an ion spends in the quadrupole field, and $h$ is a constant.

For operation in the first stability region Austin, Holme, and Leck found that $h = 20$ [11]. As a result, the resolution of a quadrupole can be increased by running at a higher rf frequency, but this may also lower the mass range.

For some applications, quadrupoles are used as ion guides. In this case, no dc voltage is applied between the pole pairs ($U = 0$). As a result, the Mathieu parameter $a$ will be 0. With fixed $V_{rf}$ and $\Omega$, ions of a broad range of $m/z$ values will have stable trajectories in the quadrupole. Thus, operation with only rf allows the largest possible range of ions with different $m/z$ ratios to pass through the quadrupole.
1.2 Linear Quadrupole Ion Traps

1.2.1 Linear Ion Traps

A linear ion trap can be formed by applying stopping potentials to electrodes at the entrance and exit of a linear quadrupole, which is usually operated with rf-only voltages. Ions are confined radially by the rf fields, and axially by the stopping potentials.

In 1969, Church reported two ion traps derived from the linear quadrupole, the storage-ring ion trap and the “racetrack” storage ring [12]. The electrodes of a rf–only quadrupole mass filter were made into circular shapes to make the storage-ring trap. The study showed that at a pressure of $2 \times 10^{-10}$ Torr, the ion trap could confine $\text{H}^+$ and $\text{^3He}^+$ ions up to 8 minutes [12]. Linear ion traps have been used to study ion/molecule reactions [13, 14]. In related work, Watson [15] reported that it is possible to increase the ejection efficiency and selectivity of the primary reaction products of the precursor primary ions by ejecting ions through an ion trap, so that these ions can be distinguished from cluster ions and secondary product ions. In that study, a mixture of $\text{Fe(CO)}_n^+$ ions ($n = 0-5$, m/z 54-196) were confined (0.5 ms) in a rf-only collision cell of a tandem quadrupole mass spectrometer. Use of an optimized auxiliary rf field allowed almost complete rejection of the $^{56}\text{Fe}^+$ ion with no intensity distortion of other $\text{Fe(CO)}_n^+$ ions, and with only a slight intensity decrease of the $^{54}\text{Fe}^+$ ion. The result indicated that $^{56}\text{Fe}^+$ ion didn’t form cluster ions and secondary product ions.

Compared to 3D traps, linear ion traps have several advantages [16, 17]. They have higher injection efficiencies than 3D traps, because there is no quadrupole field along the z-axis. The larger storage volume relative to 3D traps allows linear trap to traps store more ions with
reduced space charge effects. Instead of point focusing as with a 3D trap, ions are focused along the axis of the quadrupole.

Linear ion traps provide a method to couple continuous ion sources with other mass analyzers such as 3D traps [18-20], Fourier Transform Ion Cyclotron Resonance (FTICR) [21], time of flight (TOF) mass analyzers [22, 23], and Orbitrap mass analyzers [24, 25]. It has shown that the duty cycle improves significantly when a linear trap is used to pre-concentrate analyte ions and remove unwanted ions prior to MS analysis in the 3D trap [20]. Collings et al. described a system combining a linear ion trap and a TOF, where the linear ion trap was used to isolate analyte ions which can subsequently be fragmented by applying auxiliary dipole excitation at the resonant frequency of the ions [23]. With the proper pressure and excitation amplitude, the mass resolution was increased by a factor of 3 [23]. As with 3D ion traps, a linear ion trap can be used to improve the duty cycle of an FTICR mass analyzer [21, 26]. Recently, linear ion traps have been used to couple ESI to Orbitrap mass analyzers [25]. Ions from ESI are admitted via rf-only multipole ion guides into the linear trap, and then are delivered by a transferring octopole into a curved rf-only quadrupole named a “C-trap”. The C-trap is biased by a few volts relative to the linear trap in order to trap and accumulate ions before injecting ions into the Orbitrap mass analyzer. Ions are collisionally cooled and focused along the curved axis of the C-trap, and extracted by changing the voltages applied to the C-trap and ion optics in front of the Orbitrap. Nominal mass resolution of 60 000 and high-accuracy mass measurements within 5 ppm are possible with the hybrid instrument in LC/MS mode.

Linear quadrupole ion traps have also been developed as stand-alone mass analyzers [7, 17, 27, 28]. Besides the traditional linear quadrupole, other novel linear ion traps have also been
developed, such as the rectilinear trap [29] and the ion trap array mass analyzer [30]. The rectilinear ion trap (RIT) introduced by Cooks and co-workers [29] has the increased trapping capacity of linear ion traps but with simpler construction than cylindrical ion traps (CIT) [31, 32]. The simplest version of an RIT consists of two pairs (x and y) of rectangular electrodes supplied with rf potentials, and a pair of z electrodes to which only a dc voltage is applied. The rf signal applied forms a trapping field in the xy plane. The trapping potential along the z axis is generated by the dc voltages. The rf field in the xy plane close to the center of the RIT trap is approximately a quadrupole field. The RIT can be operated as a linear quadrupole ion trap. The demonstrated capabilities of the RIT include tandem mass spectrometry, a mass resolution in excess of 1000, and a mass/charge range of 0-650 Th [29].

More recently, an ion trap array mass analyzer (ITA) has been designed, constructed and evaluated in Ding’s group at Fudan University [30]. The ITA is constructed with six planar electrodes: two end-cap electrodes for applying dc voltages, two boundary electrodes that are grounded during experiments, and two central ion trap electrodes for applying the rf voltage. The central electrodes were fabricated as several identical rectangular electric strips, and there is a gap between any two adjacent rectangular electric strips. The two central ion trap electrodes were placed symmetrically to those on the opposite plate. The six planar electrodes can be perpendicularly mounted together to form a closed space. The ITA has small size and very low cost. A preliminary mass spectrum has been recorded with one of the ion trap channels, and it shows a mass resolution of over 1000 at \( m/z = 391 \) with a scan speed of 358 Th/s [30].
1.2.2 Fringing Fields

In practice, in a linear quadrupole the ideal quadrupole field is interrupted at the entrance and exit of the rods. The fields in these two regions are referred to as fringing fields [6]. In a fringing field region, ion motion in the $x$, $y$ and $z$ directions are coupled. The complexity of the fringing fields makes it difficult to study the ion motion in these regions. Dawson proposed a linear model of the potential in the fringing field [6]. Later, Hunter and McIntosh suggested a more realistic model using an exponential function [33].

Brubaker described two qualitative results for the effects of the entrance fringing fields on the amplitudes of ion motion [34]. Short fringing fields give low amplitudes of ion oscillation which may increase the transmission. Long fringing fields give more rf cycles which result in larger amplitudes of oscillation. As a result, ions will be defocused in the fringing field. Several modifications have been done to the ion entrance fields to avoid the fringing field. A successful example is called a “delayed dc ramp”, developed by Brubaker [34]. In this device, a short rf-only quadrupole has some fraction of the main rf applied but no dc between the rods. Ions approaching the quadrupole are first stabilized in the rf field before the dc is applied. Thus ions entering the quadrupole field have stable $a$ and $q$ values. The fringing field at the exit of a quadrupole can also be defocusing, but the defocusing effects can by overcome by the strong attractive field from a detector. In addition, the fringing field at the exit presents opportunities for different method of mass analysis, such as axial ejection, which will be discussed in Section 1.2.5.
1.2.3 Ion Excitation: Dipole and Quadrupole Excitation

Ion motion in a quadrupole field, with the frequencies expressed by equation (1.13) can be excited with either dipole excitation or quadrupole excitation. The amplitude of the excitation voltage is several orders of magnitude lower than the amplitude of the main rf voltage. Dipole excitation can be performed by applying a small auxiliary voltage at a frequency of the ion motion between one pair of quadrupole rods. For quadrupole excitation, the auxiliary voltage is applied to all four rods. The quadrupole excitation can be applied to the electrodes with [35] or without external electronics [36]. With sufficient excitation voltages applied to the rods, either dipole or quadrupole excitation can be used to eject an ion of a selected mass to charge ratio from a quadrupole trap. To eject ions of different m/z values, the frequency of the voltage is fixed at a value corresponding to an ion resonant frequency at a given q as in equation (1.13) and the main rf is scanned, while in a second method the excitation frequency is scanned at a fixed trapping rf voltage. Resonant excitation of ions has been used for ion isolation, fragmentation and mass-selective ejection at different q values in quadrupole ion traps. Ion isolation can be done by applying multiple frequencies as a broadband waveform with a notch in frequency space. The notch includes frequencies that are close to the resonant frequency of an ion to be isolated. As a result, all ions that have frequencies of motion matching the applied frequencies are ejected leaving ion of one m/z isolated [16].

1.2.4 Mass Selective Radial Ejection with a Linear Quadrupole Ion Trap

Mass analysis can be performed by ejecting ions radially through a slot cut in a quadrupole rod or rod pairs. Ions are ejected radially by scanning the trapping rf so that ions reach the stability boundary at $a = 0$ and $q = 0.908$, or by applying dipole excitation between
the \( x \) rods to excite ions for ejection. A linear ion trap mass spectrometer using mass selective instability with resonance ejection was constructed and evaluated by Schwartz et al. [17]. The instrument is based on ideas previously described by Bier and Syka [37]. The quadrupole was built with hyperbolic rods, which were cut into three sections lengthwise and placed adjacent to each other to avoid the exit fringing field. For radial ejection, a slot was cut through the center of one rod. The imperfections introduced to the field by the slot were compensated for by shifting the cut rod and the one opposite it outwards 0.75 mm beyond their normal positions. Ions were confined radially in the central rod set by the rf voltage and by dc voltages on the two end sections. Resonant excitation was used for isolation, fragmentation and mass analysis. For ion isolation, unwanted ions are ejected resonantly with a broadband waveform with frequencies of 5-500 kHz. The target ions are isolated at a notch of the waveform where the frequency corresponds to the ejection \( q = 0.83 \). A frequency corresponding to an activation \( q \) of 0.25–0.35 was chosen for MS/MS. The ion capacity or space charge limit of this linear ion trap mass spectrometer was more than ten times greater than those of a 3D ion trap [17]. Sensitivity was also increased because of the enhancement of the injection efficiency [17].

### 1.2.5 Mass Selective Axial Ejection (MSAE) with Linear Quadrupole Ion Traps

There is at least one major problem associated with mass selective radial ejection with linear quadrupole ion traps. Cutting slots in the rods introduces field imperfections. The imperfection of the quadrupole field may cause ions to eject at different \( q \) values, which leads to lower resolution and poor peak shapes. Hager described methods of mass selective axial ejection from rf-only linear ion traps to avoid these problems [27, 28, 38-41]. The idea of performing mass analysis with rf-only quadrupoles without resolving dc applied between the rods was first
described by Brinkmann [42]. An rf-only quadrupole was operated as a high-pass filter with a potential barrier at the exit. The increased radial energy of ions with \( q \) value closes to the stability boundary (\( q = 0.908 \)) is converted to axial energy by the exit fringing field. Ions with sufficient radial energy that have been brought to the boundary by scanning the amplitude of the rf voltage are ejected. With this technique, Brinkmann was able to obtain a spectrum with resolution of more than 1400 at \( m/z = 500 \) and transmission 10 times higher than produced with the same instrument operated conventionally. Holmes and co-workers found that rf-only quadrupole ion traps can tolerate greater mechanical imperfections [43, 44].

Using a similar principle, Hager developed a new method for mass analysis with a linear quadrupole [38]. Ions formed by ESI were first collisionally cooled in an rf - only quadrupole ion guide and then injected into a 24-mm long rf - only quadrupole for mass analysis. A stopping potential of a few volts above the rod offset was applied to an exit lens. Ions were ejected at \( q = 0.908 \) as described by Brinkmann [42]. It was found that applying some of the trapping rf voltage to the exit lens, having a low resolving dc voltage between the rods, and auxiliary rf voltages in phase with trapping rf on the rods gives rise to improved signal-to-background levels [38].

The work was later extended by Hager [27] with a triple – quadrupole mass spectrometer as shown in Figure 1.3. Ions are generated by ESI, pass through an aperture in a curtain plate, orifice and a skimmer into an rf-only ion guide Q0 (7×10^{-3} Torr, N\(_2\)). A quadrupole, Q1, collision cell with a linear quadrupole ion guide q2 (4×10^{-4} Torr, N\(_2\)) and third quadrupole Q3 (3×10^{-5} Torr) are located after Q0 and separated by apertures. Both the collision cell q2 and Q3 were tested as linear ion traps. Stopping potentials are applied accordingly to aperture plates at the ends of the quadrupoles to trap ions. For axial ejection, ions were excited at their resonant
frequencies with auxiliary dipole or quadrupole rf voltages (fixed frequency). Resonantly excited ions gain axial energy in the exit fringing field and overcome the stopping potential at the trap exit. Ions can be ejected by fixing the excitation frequency and scanning the trapping rf voltage. This way, ions of different \( m/z \) values come into resonance with the excitation and are ejected.

With q2 as the ion trap, axial ejection could produce spectra with resolution \( R_{1/2} \) of 1000 with a scan speed of 1000 Th/s at \( m/z \) 609. With slow scans (5 Th/s), a resolution of 6000 at \( m/z \) 609 could be obtained. With ejection from Q3, resolution of 6000 could be obtained at a much higher scan speed (100 Th/s) due to the lower pressure in this trap. For MS/MS, ions were fragmented in q2 and then trapped and axially ejected from Q3. Accumulating fragment ions in Q3 increases the ion intensity and improves the signal-to-noise ratio. Compared to the conventional triple quadrupole MS/MS scan with the same instrument, the sensitivity obtained with axial ejection was 16 times higher [27].
Mass selective axial ejection was adopted for use in fields such as, drug discovery [45] and proteomics [46]. Hopfgartner and co-workers used several pharmaceutical compounds to evaluate a triple quadrupole LC/MS/MS system with MSAE. In the system q2 is the collision cell and Q3 is the ion trap. Experimental procedures described by Hager [27] for MS/MS were employed. Fragment ions trapped in Q3 were ejected by axial ejection. The sensitivity of MS/MS was 60 times higher than that obtained by conventional MS/MS with the same instrument.

Leblanc et al. showed that the combination of the very selective triple quadrupole-based tandem mass spectrometry (MS/MS) scans with the very sensitive ion trap MSAE product ion scans allows rapid identification of peptides at low concentrations [46]. One of the common problems with analyzing unseparated peptide mixtures is the presence of chemical noise from singly charged ions. The chemical noise often obscures the multiply charged peptide signals, especially at low peptide concentrations. The study used a triple quadrupole mass spectrometer as shown in Figure 1.3. The ion trap is first used to isolated desired precursor ions from the
unwanted single-charged ions, and then switched to a mass filter mode to scan the fragment ions of the precursor ion to produce a mass spectrum. The precursor ion selection is accomplished by flowing ions through Q1, thus contaminant species can be removed from the ion beam before the desired ions enter the ion trap. Fragments are generated in MS/MS scans via ion acceleration between Q1 and a pressurized q2. The ability to conduct a variety of ion processing steps prior to or concurrent with performing a mass scan improved the duty cycle significantly. The ability also made it possible to isolate the multiple-charged ions from unwanted single-charged ions. As a consequence, MSAE with q2 and Q3 operated as traps provided additional selectivity in MS/MS.
1.3 Quadrupoles with Added Multipoles

1.3.1 Multipole Potentials

With field distortions the potential of the linear quadrupole is no longer given by equation [1.1]. Instead the field is described as a superposition of multipoles, $\phi_N[16, 47]$ given by

$$\Phi(x, y, t) = \varphi(t) \sum_{N=0}^{\infty} A_N \phi_N(x, y)$$  \hspace{1cm} (1.16)

where $A_N$ is the dimensionless amplitude of the multipole $\phi_N(x, y)$. The terms $\phi_N(x, y)$ can be derived from

$$\phi_N(x, y) = Re \left( \frac{x + iy}{r_0} \right)^N$$  \hspace{1cm} (1.17)

where $Re[f(\zeta)]$ means the real part of the complex function $f(\zeta), \zeta = x + iy, i^2 = -1$ and $r_0$ is a scaling factor. Szilágyi [48] gave detailed analytical expressions for the multipoles in Cartesian coordinates. The term $\phi_0(x, y) = 1$ represents a constant potential independent of $x$ and $y$. A linear dipole potential is represented by $\phi_1(x, y)$. The terms $\phi_2(x, y), \phi_3(x, y)$ and $\phi_4(x, y)$ represent a quadrupole potential, a hexapole potential and an octopole potential respectively. In quadrupoles, non-linear higher order fields refer to the electric field components higher than those from $\phi_2(x, y)$ and are called as higher multipoles. From equation 1.17, the potentials of the dipole ($N = 1$), quadrupole ($N = 2$) and the first few higher order multipoles ($N = 3$ and $4$) can be written as

Dipole potential

$$\phi_1(x, y) = x/r_0$$  \hspace{1cm} (1.18)
Quadrupole potential

$$\phi_2(x,y) = \frac{x^2 - y^2}{r_0^2}$$  \hspace{1cm} (1.19)

Hexapole potential

$$\phi_3(x,y) = \frac{x^3 - 3xy^2}{r_0^3}$$  \hspace{1cm} (1.20)

Octopole potential

$$\phi_4(x,y) = \frac{x^4 - 6x^2y^2 + y^4}{r_0^4}$$  \hspace{1cm} (1.21)

The potential of a linear quadrupole with an added multipole, as a result will be presented as the sum of equation (1.19) and the term of the corresponding multipole. For example, The potential of a linear quadrupole with an added hexapole and no other multipoles then is given by

$$\Phi(x, y, t) = \left[ A_2 \left( \frac{x^2 - y^2}{r_0^2} \right) + A_3 \left( \frac{x^3 - 3xy^2}{r_0^3} \right) \right] \varphi(t)$$  \hspace{1cm} (1.22)

where $A_2$ and $A_3$ are the dimensionless amplitudes of the quadrupole and hexapole field, and $\pm \varphi(t)$ is the voltage applied to the electrodes.

1.3.2 Higher Order Fields in Linear Ion Traps

In practice, it is impossible to build an ion trap with a quadrupole without any field imperfection. Field imperfections can be introduced by the truncation of the electrodes, substitution of round rods for hyperbolic rods, the cutting of slots in the rods for ion ejection, and
construction tolerances [49]. In the past, such field imperfections were regarded as disadvantages for performing mass analysis with 2D quadrupole mass filters. Field imperfections can decrease resolution [11], lower transmission [50, 51] and degrade peak shapes [51].

During recent years, however, studies have shown that there are benefits to adding weak multipole fields to ion trap mass spectrometers. It has been demonstrated that the tandem mass spectrometry fragmentation efficiency of a linear quadrupole trap is improved by adding higher multipoles to the potential [16, 47, 52, 53].

The amplitudes of the higher multipole fields introduced by construction mechanical errors are usually very small, about $10^{-3}$ or less of the quadrupole term. Douglas and co-workers have described quadrupoles that have much higher amplitude multipoles [47, 52, 55, 56]. The multipoles with higher amplitudes were added to round-rod quadrupole by deliberate modification of the electrode geometries. Linear quadrupoles with added octopole fields [47, 52, 55, 57-61] and hexapole [54, 56, 62-66] fields have been designed, constructed and evaluated for mass analysis.

### 1.3.3 Quadrupoles with Added Hexapole Fields

A linear quadrupole with an added hexapole field has a potential of the form

$$
\Phi(x, y, t) = A_2 \left( \frac{x^2 - y^2}{r_0^2} \right) + A_3 \left( \frac{x^3 - 3xy^2}{r_0^3} \right) (U - V_{rf} \cos \Omega t) \quad (1.23)
$$

Where $A_2$ and $A_3$ are the dimensionless amplitudes of the quadrupole and hexapole fields, respectively, $A_2 \approx 1$, $r_0/\sqrt{A_2}$ is the distance from the center of the quadrupole to a $y$ electrode
when \( x = 0 \). The voltages \( U, V_{r f} \) and frequency \( \Omega \) are defined as in equation (1.2). Konenkov et al. have simulated mass analysis with quadrupoles with added hexapole fields [54]. The study shows that a hexapole field can be added to a quadrupole constructed with round rods by rotating the two \( y \) rods towards an \( x \) rod through an angle \( \theta \). The amplitude of the added hexapole field, \( A_3 \), is approximately proportional to \( \theta \) [54]. Other multipoles are added to the potential. The proportion of the other multipoles, especially the amplitude of the octopole field, depends on the ratio of the radius of the \( x \) rods (\( R_x \)) to the radius of the \( y \) rods (\( R_y \)). When \( R_x = R_y \), the multipole potential has a significant octopole term. If \( R_x > R_y \), the octopole term can be minimized, and the amplitude of the hexapole field will be the greatest of the other higher multipoles fields other than the quadrupole field. Rotating the \( y \) rods towards an \( x \) rod moves the field center closer to the \( x \) rod.

Six rod sets with added hexapole fields of 4%, 8% and 12% (i.e. \( A_3/A_2 = 0.04, 0.08 \) and 0.12) were constructed. Three of the rod sets, labeled 4A, 8A and 12A, have added hexapole fields of 4%, 8% and 12% respectively, and have the radius of the \( x \) rods, \( R_x \), equal to the radius of the \( y \) rods, \( R_y \). This arrangement produces a quadrupole field that has an added hexapole component and other higher multipoles, especially a significant octopole term. Three other rod sets, labeled 4B, 8B and 12B, have added hexapole fields of 4%, 8% and 12% respectively, and have the radius of the \( x \) rods greater than the radius of the \( y \) rods (\( R_x > R_y \)), to produce a quadrupole field that has an added hexapole component and a minimized octopole field (\( A_4 \approx 0 \)) [54]. The ratio \( R_x/r_0 \) to make \( A_4 \approx 0 \) depends on the rotation angle and is thus different for rod sets 4B, 8B and 12B. Figure 1.4 shows the coordinate system used including the rotation angle. The rods are equidistant from the central axis and all rod sets have \( r_0 = 4.5 \) mm. All quadrupoles
are 20.0 cm long. Table 1.1 shows the dimensions and values of $x_0$ of the rod sets. All rod sets contain additional higher multipole fields, although with lower amplitudes than the hexapole field. Table 1.2 shows the multipole amplitudes. Figure 1.5 shows a photograph of a round rod quadrupole with a 12% added hexapole field with no significant octopole field. The percentage of the hexapole here indicates the ratio of the hexapole amplitude $A_3$ to the quadrupole amplitude $A_2$, i.e. $(A_3/A_2) \times 100\%$. Despite the large field distortions, it is found that conventional mass analysis [63], mass selective axial ejection [62, Chapter 6] and mass analysis with islands of stability [65, 66] (described in detail in section 1.4) are possible with these rod sets. In some cases, the spectra produced by these rod sets are surprisingly good, with high resolution ($R_{1/2} \approx 2000$) and smooth peaks. In addition, higher fragmentation efficiencies and faster fragmentation with auxiliary excitation at low pressure have been observed with these rod sets [53].

Figure 1.4 Electrode geometry for adding a hexapole field by rotating two $y$ rods through an angle $\theta$ toward an $x$ rod.
Table 1.1 Geometries and dimensions of the quadrupoles with added hexapole fields.

<table>
<thead>
<tr>
<th>Rod Set</th>
<th>% $A_3$</th>
<th>$\theta$ [degrees]</th>
<th>$R_x$ [mm]</th>
<th>$R_y$ [mm]</th>
<th>$x_0$ [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A</td>
<td>4</td>
<td>2.56</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8A</td>
<td>8</td>
<td>5.13</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12A</td>
<td>12</td>
<td>7.69</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>4B</td>
<td>4</td>
<td>2.56</td>
<td>5.2425</td>
<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8B</td>
<td>8</td>
<td>5.13</td>
<td>5.4945</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12B</td>
<td>12</td>
<td>7.69</td>
<td>5.9378</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>conventional</td>
<td>0</td>
<td>0</td>
<td>4.690</td>
<td>4.690</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1.2 Multipole amplitudes of the quadrupoles with added hexapole fields.

<table>
<thead>
<tr>
<th></th>
<th>4A</th>
<th>4B</th>
<th>8A</th>
<th>8B</th>
<th>12A</th>
<th>12B</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_0$</td>
<td>-0.00022</td>
<td>0.00119</td>
<td>-0.00088</td>
<td>0.00514</td>
<td>-0.00198</td>
<td>0.01143</td>
</tr>
<tr>
<td>$A_1$</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>$A_2$</td>
<td>1.0035</td>
<td>1.00401</td>
<td>1.00497</td>
<td>1.00719</td>
<td>1.00745</td>
<td>1.01232</td>
</tr>
<tr>
<td>$A_3$</td>
<td>0.03871</td>
<td>0.03973</td>
<td>0.07981</td>
<td>0.07990</td>
<td>0.12020</td>
<td>0.12052</td>
</tr>
<tr>
<td>$A_4$</td>
<td>0.00143</td>
<td>0.00009</td>
<td>0.00592</td>
<td>-0.00002</td>
<td>0.013386</td>
<td>0.00000</td>
</tr>
<tr>
<td>$A_5$</td>
<td>-0.00712</td>
<td>-0.00723</td>
<td>-0.01398</td>
<td>-0.01495</td>
<td>-0.02025</td>
<td>-0.02353</td>
</tr>
<tr>
<td>$A_6$</td>
<td>-0.00010</td>
<td>-0.00153</td>
<td>-0.00329</td>
<td>-0.00564</td>
<td>-0.007063</td>
<td>-0.01254</td>
</tr>
<tr>
<td>$A_7$</td>
<td>-0.00121</td>
<td>-0.00125</td>
<td>-0.00277</td>
<td>-0.00308</td>
<td>-0.00501</td>
<td>-0.006051</td>
</tr>
<tr>
<td>$A_8$</td>
<td>-0.00008</td>
<td>-0.00012</td>
<td>-0.000349</td>
<td>-0.00052</td>
<td>-0.00094</td>
<td>-0.00126</td>
</tr>
<tr>
<td>$A_9$</td>
<td>0.00006</td>
<td>0.00007</td>
<td>0.00012</td>
<td>0.00023</td>
<td>0.00017</td>
<td>0.00058</td>
</tr>
<tr>
<td>$A_{10}$</td>
<td>-0.00242</td>
<td>-0.00227</td>
<td>-0.00230</td>
<td>-0.00227</td>
<td>-0.00208</td>
<td>-0.00187</td>
</tr>
</tbody>
</table>
Figure 1.5 Photograph of a round-rod quadrupole with a 12% added hexapole field. The distance from the central axis to the rods is $r_0 = 4.50$ mm, rotation angle $\theta = 7.69^\circ$, $R_y = 5.1692$ mm and $R_x = 5.9378$ mm. Since $R_x > R_y$, the octopole term is minimized.

### 1.3.4 Quadrupoles with Added Octopole Fields

A linear quadrupole with an added octopole field has a potential of the form

$$
\Phi(x, y, t) = \left[ A_2 \left( \frac{x^2 - y^2}{r_0^2} \right) + A_4 \left( \frac{x^4 - 6x^2y^2 + y^4}{r_0^4} \right) \right] \left( U - V_{rf} \cos \Omega t \right) \quad (1.24)
$$

where $A_2$ and $A_4$ are the dimensionless amplitudes of the quadrupole and octopole fields, respectively, and $A_2 \approx 1$. Two methods have been described to add an octopole field to a quadrupole [47]: 1. Placing the two $y$ rods closer to the central axis than the $x$ rods; 2. Making the radius of the $y$ rods ($R_y$) greater than the radius of the $x$ rods ($R_x$). The second method is preferred because the first method adds other multipole terms to the quadrupole with significant amplitudes. Both simulations and experiments show that a quadrupole with an added octopole field can be used for conventional mass analysis [57], mass selective axial ejection [59] and mass...
analysis with islands of stability [58, 61] (described in detail in section 1.4). High fragmentation efficiencies with excitation with trapped ions have also been observed with a rod set with a 4% added octopole field (i.e. $A_4/A_2 = 0.04$) [52].
1.4 Islands of Stability

When an auxiliary quadrupole excitation waveform is applied to a quadrupole, ions that have oscillation frequencies that are resonant with the excitation are ejected from the quadrupole. Bands of instability are formed, and the stability diagram splits into "islands" of stability. The changes to the stability conditions of ions and modifications of the stability diagram by the excitation have been discussed in detail [35, 67-70].

With auxiliary quadrupole excitation, the quadrupole potential becomes

\[
\Phi(x, y, t) = \left( \frac{x^2 - y^2}{r_0^2} \right) \left( U - V_{rf} \cos \Omega t - V' \cos(\omega_{ex} t - \gamma) \right) \]

where \( U \) is the dc potential applied to the electrodes, \( V_{rf} \) and \( \Omega \) are the amplitude and angular frequency of the main rf voltage, \( V' \), \( \omega_{ex} \) and \( \gamma \) are the amplitude, angular frequency and phase of the auxiliary quadrupole excitation voltage, and \( t \) is time.

When the ratio of the quadrupole excitation frequency (\( \omega_{ex} \)) to the main rf frequency (\( \Omega \)) is chosen to be

\[
\nu = \frac{\omega_{ex}}{\Omega} = \frac{Q}{P} \]

where \( Q \) and \( P \) are integers, the equations of ion motion can be written

\[
\frac{d^2x}{d\xi^2} + (a - 2q \cos 2\xi - 2q' \cos 2\nu \xi)x = 0 \]

(1.27)
\[
\frac{d^2 y}{d\xi^2} - (a - 2q \cos 2\xi - 2q' \cos 2\nu\xi)y = 0
\]  
(1.28)

where $\xi$, $a$ and $q$ are defined in equations (1.5) and (1.6), and

\[
q' = \frac{4zeV'_{rf}}{m\Omega^2 r_0^2} = q \frac{V'_{rf}}{V_{rf}}
\]  
(1.29)

The angular frequencies of oscillation in the quadrupole field are given by equation (1.13). With quadrupole excitation, resonances are excited when

\[
\omega_{ex} = |l + \beta_u| \frac{\Omega}{K}
\]  
(1.30)

where $u$ is $x$ or $y$, $K = 1, 2, 3...$ and $l = 0, \pm 1, \pm 2, \pm 3...$ [33, 70].

With $= Q/P$, the stability diagram has relatively strong resonance lines for the $x$ and $y$ motions with $\beta_u$ values determined by

\[
\frac{Q}{P} = \frac{|l + \beta_u|}{K}
\]  
(1.31)

The unstable points form bands of instability along iso-$\beta$ lines for the $x$ and $y$ directions, with $\beta_u$ values given by equation (1.31). As a result the first stability region in the plane splits into islands of stability. Theoretically $P - 1$ unstable bands will be formed, but in practice the number of bands observed is usually less.
1.4.1 Mass Analysis Using Islands of Stability

The tips of islands can be used to perform mass analysis. Figure 1.6 shows calculated stability boundaries of an ideal quadrupole field, the stability boundary for 1% transmission in the field of a linear quadrupole with a 2% added hexapole field, and islands of stability formed with quadrupole excitation for a linear quadrupole with a 2% hexapole field and no other multipoles. The upper and lower tips of island A and upper tip of island B can be used, in principle, to perform mass analysis. Mass analysis can be done with a scan line that passes through the tip of a stability island. It is important, however, to choose the correct excitation parameters and slope of the scan line, so that the scan line does not simultaneously pass through more than one island. Previous studies have shown that mass analysis with islands can improve peak shapes by removing tails on peaks [67, 69, 70].
Figure 1.6 (1) Calculated stability boundaries for a pure quadrupole field, and (2) stability boundary for 1% transmission in the field of a linear quadrupole with a 2% added hexapole field and no other multipoles for $\alpha > 0$; A, B, C, and D are islands of stability with auxiliary quadrupole excitation (excitation voltage $V'/V = 0.029$, excitation frequency $\omega_{ex} = 0.9\Omega$).
1.5 Overview of the Thesis

Linear quadrupoles with added hexapole [54, 57, 71] fields were constructed and their performance, both as mass filters [63] and as ion traps with MSAE [62] is evaluated. These rod sets were originally built because it was expected [54] that they would give greater fragmentation yields with excitation of trapped ions for MS/MS at low pressure ($\leq 1 \times 10^{-4}$ Torr). Simulations have also shown that mass analysis may also be possible with linear quadrupoles with added hexapole fields [54]. The properties of these rod sets make them good candidates for the Q3 quadrupole in a MS/MS system, where Q3 is used to trap ions. In general, in a triple quadruple system the pressure in Q3 is less than $1 \times 10^{-4}$ Torr. The fragmentation efficiency with a conventional quadrupole at such a low pressure is low. As a result, the possibility of operating conventional quadrupole as a mass filter and ion trap in Q3 is limited. If quadrupoles with added hexapole fields not only can perform mass analysis with unit resolution, and can be used as ion traps with improved fragmentation efficiency at low pressure, then in principle these rod sets can replace conventional rod set used as Q3 in an MS/MS system. When they are operated as ion traps, ions can be fragmented in the trap and then mass analyzed by axial ejection. However, the hexapole fields introduced in these rod sets are large compared to the fields of a quadrupole due to construction errors. The mass analyses spectra predicted by the simulations with these rods may not be realized in experiments. The main goal of the work described in this thesis is to evaluate whether linear quadrupoles with added hexapole fields can be used as Q3 in a MS/MS system for either mass analysis or operated as an ion trap with mass selective axial ejection.
At the beginning of the project, some effort was put into the simulation of the islands of stability with quadrupoles with added octopole fields. A computer program written by Dr. Konenkov was used for the simulation. The results were later used for another project [58] involving the investigation of the properties of linear quadrupoles with added octopole fields. Chapter 2, which describes the simulations, has been published [60]. The simulation methods also apply to quadrupoles with added hexapole or other higher order multipole fields. As a result, this work provides a better understanding of how islands of stability are formed in such fields. Chapter 3 describes experimental results with mass analysis with quadrupoles with added hexapole fields. This work has been published [63]. Chapters 4 and 5 describe mass analysis using islands of stability with quadrupoles with added hexapole fields. This work has also been published [65, 66]. Chapter 6 describes mass selective axial ejection with dipole excitation of trapped ions from quadrupoles with added hexapole fields. This work described in this chapter will be submitted for publication. Chapter 7 is a summary with suggestions for future work.
1.6 References


53. Granot, O.; Douglas, D. J. In *Proceedings 55th ASMS Conference on Mass Spectrometry and*
Allied Topics, Indianapolis, IN, 2007.


2 Mass Analysis in Islands of Stability with Linear Quadrupoles with Added Octopole Fields*

* A version of this chapter has been published.
2.1 Introduction

Linear quadrupole ion traps are finding increasing use in mass spectrometry [1]. Ions can be stored for tandem mass spectrometry [2, 3] or confined and manipulated before injection into other mass analyzers, such as time-of flight [4, 5] Paul trap [6], ion cyclotron resonance [7, 8] or electrostatic ("Orbitrap") [9, 10] analyzers.

As with three-dimensional Paul traps [11], the addition of field distortions to a linear quadrupole ion trap can improve MS/MS efficiency [12-14] or give faster ejection of ions at a stability boundary [15, 16]. The field distortions are described mathematically by the addition of higher spatial harmonics or multipole fields to the quadrupole field. Methods to add octopole [14, 17] or hexapole [18, 19] fields to linear quadrupoles have been described.

In some applications [3], it is desirable that a linear trap used for MS/MS be capable of mass analysis. Various methods of mass analysis with linear quadrupoles have been described. Conventionally, dc and rf potentials can be applied between the rod pairs [20] to place ions to be mass analyzed at a tip of a stability region. The addition of higher multipoles to the field has in the past, been expected to degrade the performance of a linear quadrupole operated as a mass filter in this way [21, 22]. Nevertheless it has been found that linear quadrupoles with added octopole [23] and hexapole fields [18] can in fact be operated as mass analyzers, provided the dc voltage is applied to the electrodes with the correct magnitude and polarity. Ions can also be mass analyzed in a linear quadrupole by radial ejection through slots in the rods [2]. Alternatively, axial ejection can be used for mass analysis with a linear quadrupole, either with or without trapping of ions. Ions within the quadrupole are excited by dipole or quadrupole excitation, gain sufficient kinetic energy to overcome a potential barrier at the quadrupole exit,
and are ejected [3, 24, 25]. Preliminary experiments show that this method can be used for mass analysis with a linear quadrupole that has an added octopole field [26].

For mass analysis, linear quadrupoles can also be operated with "islands" of stability formed either by auxiliary quadrupole excitation [27-29] or by amplitude modulation of the rf voltage [30]. In a mass filter with a pure quadrupole field, the potential, $\Phi(x, y, t)$, is

$$
\Phi(x, y, t) = \left( \frac{x^2 - y^2}{r_0^2} \right) \varphi(t) \tag{2.1}
$$

where $x$ and $y$ are Cartesian coordinates, and $r_0$, the field radius, is the distance from the centre to an x or y electrode. With quadrupole excitation, the time dependent potential applied to the electrodes, $\pm \varphi(t)$, is given by

$$
\varphi(t) = U - V_{rf} \cos \Omega t - V' \cos \omega_{ex} t \tag{2.2}
$$

Where $U$ is the dc potential applied from an electrode to ground, $V_{rf}$ the amplitude of the main rf voltage with angular frequency $\Omega$ applied from pole to ground, and $V'$ is the amplitude of the quadrupole excitation voltage with angular frequency $\omega_{ex}$. With no damping, motion of an ion in the potential of equations (2.1) and (2.2) is determined by

$$
\frac{d^2 x}{d\xi^2} + (a - 2q \cos 2\xi - 2q' \cos 2\nu\xi)x = 0 \tag{2.3}
$$

$$
\frac{d^2 y}{d\xi^2} + (a - 2q \cos 2\xi - 2q' \cos 2\nu\xi)y = 0 \tag{2.4}
$$

where the dimensionless parameters are defined as
\[ \xi = \frac{\Omega t}{2}; \quad a = \frac{8zeU}{m\Omega^2r_0^2}; \quad q = \frac{4zeV_{rf}}{m\Omega^2r_0^2} \]

\[ \nu = \frac{\omega_{ex}}{\Omega}; \quad q' = \frac{4zeV'_{rf}}{m\Omega^2r_0^2} = \frac{V'_{rf}}{V_{rf}} \] (2.5)

And \( m \) is the ion mass, \( e \) is the electron charge and \( z \) is the number of charges on the ion.

The angular frequencies of ion oscillation in a quadrupole field, \( \omega_u \) are given by

\[ \omega_u = (2n + \beta_u) \frac{\Omega}{2} \] (2.6)

Where \( u \) is \( x \) or \( y \), \( \beta_u \) is a function of the \( a \) and \( q \) parameters and \( n = 0, \pm 1, \pm 2, \ldots \). With quadrupole excitation, resonances are excited when

\[ \omega_{ex} = \frac{|l + \beta_u|\Omega}{K} \] (2.7)

where \( K = 1, 2, 3 \ldots \) [31] and \( l = 0, \pm 1, \pm 2, \pm 3 \ldots \)

If \( \nu = \frac{Q}{P} \) where \( Q \) and \( P \) are integers, the \( \beta \) values of the quadrupole resonances are determined by

\[ \frac{Q}{P} = \frac{|l + \beta_u|}{K} \] (2.8)

Near the tip of the stability diagram, where \( \beta_x \approx 1 \) and \( \beta_y \approx 0 \), the strongest resonances occur for the \( x \) motion with \( \beta_x = \frac{Q}{P} \) (\( l = 0 \) and \( K = 1 \) in equation (2.8)) and for the \( y \) motion with \( \beta_y \approx 1 - \frac{Q}{P} \) (\( l = -1 \) and \( K = 1 \) in equation (2.8)). The stability diagram forms bands of
instability along iso-β lines, with β_u values given by equation (2.8). Islands of stability are formed between the bands of instability [27- 30]. Ions of a particular mass to charge ratio (m/z) can be mass analyzed by adjusting the applied rf and dc voltages to place ions at the tip of an island. Ions of other mass to charge ratios lie outside the stability island and are not transmitted. A mass scan is performed by changing the rf to dc voltages with a constant ratio U/V_{rf} to bring ions of different m/z ratios to the tip of the stability island. As with conventional mass analysis, the resolution can be adjusted by changing the ratio U/V_{rf}.

In principle, islands of stability provide an alternate method for mass analysis with linear quadrupoles with added multipoles. The potential in a quadrupole with an added octopole field and no other multipoles, is given by

$$\Phi(x, y, t) = \left[ A_2 \left( \frac{x^2 - y^2}{r_0^2} \right) + A_4 \left( \frac{x^4 - 6x^2y^2 + y^4}{r_0^4} \right) \right] \varphi(t) \quad (2.9)$$

where $A_2$ and $A_4$ are the dimensionless amplitudes of the quadrupole and octopole terms respectively. With quadrupole excitation, $\varphi(t)$ is given by equation 2.1. (For the potential of equation (2.9), the distance from the center to an $x$ electrode is approximately $\frac{r_0}{\sqrt{A_2}} \left( 1 - \frac{A_4}{2A_2^2} \right)$ and to a $y$ electrode approximately $\frac{r_0}{\sqrt{A_2}} \left( 1 + \frac{A_4}{2A_2^2} \right)$. With an added octopole field, and with $U > 0$ ($\alpha > 0$ in equation (2.5)), the boundaries of the stability diagram without excitation are like those of a pure quadrupole field, and are well defined, so that conventional mass analysis is possible. Conversely, when $U > 0$ ($\alpha > 0$ the stability boundaries move outwards relative to the boundaries with a pure quadrupole field, become diffuse, and conventional mass analysis is not possible [23].
Here, computer simulations are used to calculate in more detail the stability boundaries for quadrupoles with $A_4 = 0.020$, 0.026, and 0.040, for the two cases $U > 0$ and $U < 0$, both for the case where the field contains quadrupole and octopole terms only (equation (2.9)) and also for the case where the field is created by rod sets with round rods and therefore contains higher multipoles [17]. The positions of the stability islands which are of potential use for mass analysis are calculated. With $U > 0$, the stability boundaries are like those of a pure quadrupole field, regardless of the value of $A_4$. The island positions and boundaries depend on the amplitude $A_4$. With $U < 0$, the stability boundaries move outwards and the positions and boundaries of stability islands again depend on the amplitude $A_4$. Provided the correct tip of an island is used, mass analysis in a stability island is possible when $U > 0$ and, also when $U < 0$ where conventional mass analysis without an island is not possible. Comparable peak shapes and resolution are found in both cases, and these are nearly the same as the same quadrupole operated without excitation and $a > 0$. Thus the use of an island of stability allows mass analysis under conditions where the added octopole field otherwise prevents conventional mass analysis.
2.2 Experimental Section

In a linear quadrupole with field distortions or added higher multipoles, the potential is given by

\[ \Phi(x, y, t) = \varphi(t) \sum_{N=0}^{\infty} A_N \phi_N(x, y) \]  

(2.10)

where \( A_N \) is the dimensionless amplitude of a multipole \( \phi_N(x, y) \), and \( \varphi(t) \) is determined by the time dependent voltage applied to the electrodes. If the potential contains only quadrupole and octopole terms, \( \Phi(x, y, t) \) is given by equation (2.9). (This potential can be produced by electrodes with exact shapes calculated from \( \Phi(x, y) = \pm 1 \) with \( \Phi(x, y) \) given by the spatial dependence of equation (2.9)). A quadrupole with an added octopole field can be constructed with round rods equally spaced from a central axis at a distance \( r_0 \), and with the radius of the \( y \) rods, \( R_y \), greater than the radius of the \( x \) rods, \( R_x \) [17]. In this case, the \( x \) direction is the direction of the smaller rods, and \( A_4 > 0 \). This co-ordinate system is used here. The use of round rods contributes additional higher multipoles to the potential [17]. The properties of round rod sets with nominal 2\% to 4\% added octopole fields are being investigated experimentally in this lab [12, 23]. The amplitudes of the multipoles of these round rod sets, calculated as in [32], and the relative rod radii are shown in Table 2.1. These are referred to as rod sets with "2, 2.6 and 4\%" added octopole fields, although the exact values of \( A_4 \) used are given in Table 2.1. Mass analysis with these rod sets is modeled in this study. Unless otherwise stated, multipoles up to \( N = 10 \) were included in all the calculations for the round-rod sets.
When $U > 0$ and $a > 0$, an island is formed in the upper part of the stability diagram and it is convenient to refer to the "upper" and "lower tips" of the island. When $U < 0$ and $a < 0$, references to the upper and "lower" tips of the island can be confusing, and we refer to the tips with the greater and lesser magnitudes of $a$.

Table 2.1 Multipole amplitudes for the round rod sets investigated. In all cases $R_x = r_0$. The multipoles for rod sets with 2.0 and 2.6% added octopole fields were calculated including a grounded case of radius $4r_0$.

<table>
<thead>
<tr>
<th>$A_N$</th>
<th>2% octopole</th>
<th>2.6% octopole</th>
<th>4.0% octopole</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R_y/R_x = 1.220$</td>
<td>$R_y/R_x = 1.304$</td>
<td>$R_y/R_x = 1.516$</td>
</tr>
<tr>
<td>$A_2$</td>
<td>0.99941489</td>
<td>1.00149121</td>
<td>1.00558276</td>
</tr>
<tr>
<td>$A_4$</td>
<td>0.01957926</td>
<td>0.02592904</td>
<td>0.03988935</td>
</tr>
<tr>
<td>$A_6$</td>
<td>0.00327973</td>
<td>0.00119149</td>
<td>-0.0029836</td>
</tr>
<tr>
<td>$A_8$</td>
<td>0.00086596</td>
<td>0.00095967</td>
<td>0.00085715</td>
</tr>
<tr>
<td>$A_{10}$</td>
<td>-0.000234434</td>
<td>-0.00235790</td>
<td>-0.00232151</td>
</tr>
</tbody>
</table>

2.2.1 Peak Shapes and Boundary Calculations

Stability boundaries and peak shapes were calculated as described previously [18, 33]. Ion trajectories were run to determine if ions have stable or unstable motion for given values of the $a$ and $q$ parameters. Initial spatial positions were selected from Gaussian distributions in $x$ and $y$ with standard deviations $\sigma_x/r_0 = 0.002$. Initial velocities were selected for an ion of mass 390
Da, with a thermal distribution with temperature $T = 300 K$. With quadrupole frequency $f = 1.0 \times 10^6$ Hz and $r_0 = 5 \times 10^{-3}$ m, this gives a dimensionless velocity dispersion [18] of

$$\sigma_v = \sqrt{\frac{2 k_B T}{m}} \frac{m}{\pi r_0 f} = 0.007$$

(where $k_B$ is Boltzmann's constant). Twenty initial rf phases uniformly distributed between 0 and $2\pi$ were used. For the calculation of stability boundaries and island positions, $a$ was fixed and $q$ was systematically varied to produce a curve of transmission vs. $q$.

For the boundaries without quadrupole excitation $q'$ was set to zero. Values of $a$ and $q$ giving 1% transmission were taken as stability boundaries. For peak shape calculations, the variation of transmission with $q$ was determined as $a$ and $q$ were varied systematically along a scan line with slope

$$\frac{a}{q} = 2 \lambda = \frac{2U}{V_{rf}}$$

(2.11)

In all calculations, ions spent 150 rf cycles in the field, $q$ was varied in step sizes typically of 0.0002 to 0.0004, and 4000-6000 trajectories were run for given $a$ and $q$ values. Reported resolutions, $R_{1/2}$, are calculated from peak full widths at half maximum, $q/\Delta q$. All calculations with quadrupole excitation were done for $\nu = 9/10$ (as in [27, 29]) and $q' = 0.020$. No fringing fields were included in the calculations.

The calculations give the boundaries of islands or stability diagrams where the transmission is 1%. Because the initial conditions are selected randomly, there is a statistical uncertainty in the calculated transmission. If the number of trajectories run at a point $(a, q)$ is $N$, and the number of ions transmitted is $N_t$, the transmission is $N_t/N$ and the uncertainty in the transmission is $\sqrt{N_t}/N$. Peaks with low transmission therefore have a "noisy" appearance.
2.3 Results and Discussion

2.3.1 Peak Shapes with Conventional Mass Analysis

In [23] peak shapes were calculated for a quadrupole with a 2.0% added octopole field and no other multipoles. For direct comparison to the peaks shapes and stability boundaries with islands calculated below, peak shapes and boundaries without excitation were calculated for round rod sets with 2%, 2.6%, and 4% added octopole fields, including all the multipoles up to $N = 10$, and with the ion source model described above. Figure 2.1a shows peak shapes for a round rod set with 2.6% added octopole field with the positive dc applied to the smaller rods so that $\alpha > 0$. The resolutions of the peaks are from 384 to 705. Figure 2.1b shows peak shapes for the same rod set but with the negative dc applied to the smaller rods so $\alpha < 0$. For a given transmission the resolution is lower, and there are tails on the high mass sides of the peaks. For example at a transmission of 0.026 the resolution is 238 compared to a resolution of 705 with a transmission of 0.032 in Figure 2.1a. These results are qualitatively consistent with the experimental and calculated peak shapes of [23]. With $\alpha > 0$, peak shape and resolution comparable to those of a quadrupole with no added octopole field, are possible. With the polarity of the dc reversed ($\alpha < 0$), poor peak shape and resolution are obtained; the added octopole field prevents conventional mass analysis because the stability boundaries become diffuse [23].
Figure 2.1 Peak shapes for four values of $\lambda$ for a round-rod set with 2.6% added octopole field without additional quadrupole excitation ($q' = 0$) with (a) $\alpha > 0$ and (b) $\alpha < 0$. 
2.3.2 Islands and Stability Boundaries

The stability boundaries and island positions were compared for rod sets that have quadrupole and octopole terms only (i.e. only $A_4 \neq 0$ and $A_2 \neq 0$ (equation 2.9)) and for round rod sets with 2%, 2.6%, and 4% added octopole fields. For example, for the quadrupole with 2.6% octopole, a quadrupole with same values of $A_2$ and $A_4$ (Table 2.1) but with all the other multipole amplitudes, $A_N$, set to zero was simulated. These calculations show that the higher multipoles added by the use of round rods do not substantially change the island positions or stability boundaries. This differs from the case of quadrupoles with added hexapole fields, where the higher multipoles cause small shifts of the stability boundaries [18].

The effect of the polarity of the dc voltage applied to the quadrupole electrodes, i.e. the sign of $a$, was investigated for round rod sets with 2%, 2.6%, and 4% added octopole fields. Figure 2.2 shows the calculated stability boundaries and islands of stability for a round-rod set with 2.6% octopole field. The islands are labeled as in [27]. With $a > 0$, Figure 2.2a, and without excitation, the $x$ and $y$ boundaries of the stability diagram are nearly identical to the boundaries with a pure quadrupole field. In this case the added octopole field does not cause significant changes to the stability diagram. The island boundaries however, differ from those with a pure quadrupole field (see below). In principle, these islands can be used for mass analysis.

Figure 2.2b shows the case with $a < 0$. There are significant changes to the islands and stability boundaries. The boundaries without excitation move outwards to greater $a$, $q$ values and become diffuse. Because the boundaries move outwards, greater values of $\lambda$ are required for mass analysis at a given resolution. The islands A, B and C have boundaries ($|a|$, $q$) similar to those with $a > 0$. The boundaries of island D change substantially and move out towards the
inner boundaries of islands B and C. Thus the "gaps" between island D and islands B and C become smaller. Because the stability boundaries without excitation move outwards, island A now appears within these boundaries, although it has $|a|, q$ values similar to the case with $a > 0$.

Figure 2a
Figure 2b

Figure 2.2 Stability boundaries ($q' = 0.00$) and islands of stability ($q' = 0.02, \nu = 9/10$) for a quadrupole with 2.6% added octopole field with (a) $\alpha > 0$ and (b) $\alpha < 0$. 
For comparison, the stability boundaries and islands of round rod sets with added octopole fields of 2%, 2.6%, and 4% are shown in Figure 2.3. With \( \alpha > 0 \), the stability boundaries without excitation for these rod sets were found to be nearly identical, and like those of a quadrupole with a pure quadrupole field (Figure 2.2a). With \( \alpha < 0 \), the stability boundaries without excitation depend on the amplitude \( A_4 \). Both with \( \alpha > 0 \) and \( \alpha < 0 \), the boundaries and positions of the islands depend on the amplitude \( A_4 \). The greatest changes with \( A_4 \) occur with \( \alpha < 0 \).

Figure 2.3a shows islands of stability with \( \alpha < 0 \) for round rod sets with 2% and 2.6% added octopole fields. Also shown are stability boundaries without excitation for rod sets with 0, 2, 2.6 and 4% added octopole fields. As \( A_4 \) increases, the \( x \) stability boundary moves outwards. The \( y \) stability boundary also moves outwards, but to a lesser extent. Island A has nearly the same position for values of \( A_4 \) of 2.0-4.0% (see below). Islands B and C have similar positions, although the boundaries change slightly with \( A_4 \). The largest changes with \( A_4 \) occur for island D. The right boundary moves outwards with increasing \( A_4 \). With a 4.0% added octopole field, the boundary between island D and C cannot be detected in these calculations and therefore the islands with 4% added octopole are not shown in Figure 2.3a. As \( A_4 \) increases, the left boundary of island D, also moves outwards but to a lesser extent.
Figure 2.3 (a) Stability boundaries ($q' = 0.00$) and islands of stability ($q' = 0.020$ and $\nu = 9/10$) for quadrupoles with 2, 2.6 and 4% added octopole fields constructed with round rods, $a < 0$. (b) Island A for quadrupoles with 0.0 (ideal quadrupole, solid line boundaries of the shaded area) 0.15, 2, 2.6 and 4% added octopole fields, with $a > 0$ and $a < 0$. 
Figure 2.3b shows the stability islands A both for $a > 0$ and $a < 0$ for quadrupoles with 0.15, 2, 2.6 and 4% added octopole fields. Also shown, by the shaded area within solid lines, is the stability island for a pure quadrupole field. The overlapping area of the stability islands for $\pm a$ is the island with no added octopole field. With $a > 0$ the two upper boundaries of island A (the boundaries with greater $a$, $q$ values nearly coincide with those of a pure quadrupole. The two lower boundaries, labeled (2) and (4) in the figure, which are formed by the resonant excitation band, move away from the island of a pure quadrupole. With $a < 0$, the lower boundaries in the figure, which are formed by the resonant excitation band, remain nearly the same as those of a pure quadrupole, and the upper boundaries, labeled (1) and (3), move outwards. The boundaries of island A for $A_4=0.02$, 0.026 and 0.04 are very similar. The island for $A_4=0.0015$ show boundaries intermediate between those of $A_4=0$ and $A_4=0.020$.

A scan line with $\lambda=0.17005$ passes through the upper tip (greater $|a|$) of island A with $a > 0$ and a scan line with $\lambda=0.16765$ passes through the tip with the lesser $|a|$ with $a < 0$. These two tips, which correspond to boundaries that are relatively unperturbed by the addition of the octopole field, provide the highest resolution and best peak shapes as described below.

The $x$ and $y$ stability boundaries without excitation ($q' = 0$) with $a < 0$ (Figure 2.3a) show unequal shifts for $0.02 < A_4 < 0.04$. To investigate this further, the $q$ values of the $x$ and $y$ stability boundaries, with $a = 0.240$ were calculated for round rod sets with added octopole fields in the range $0 < A_4 < 0.04$. The results are shown in Figure 2.4a. It is seen that the shifts are nonlinear with $A_4$, with the $y$ boundary showing greater shifts for $A_4 < 0.01$ and the $x$ boundary showing greater shifts for $A_4 > 0.01$. The average shift is nearly linearly proportional to $A_4$ and the data are symmetric about this line.
The island boundaries in Figure 2.3b also show unequal shifts with different values of $A_4$ and for $\pm \alpha$. To further investigate how the islands move with $0 \leq A_4 \leq 0.04$, the values of $q$ of the boundary of island $A$ were calculated for $\alpha = +0.2352, +0.2360, -0.2412, -0.2400$, with the results shown in Figure 2.4b. Values of $A_4 < 0.005$ cause significant shifts in the boundary, while for $0 \leq A_4 \leq 0.04$ any additional shifts are small.

![Figure 2.4a](image_url)
Figure 2.4b

Figure 2.4 (a) Magnitudes of the shifts of the values of $q$ of the positions of the $x$ and $y$ stability boundaries, from those of an ideal quadrupole, calculated at $a = 0.2400$, vs. $A_4$ for rod sets constructed with round rods with $a < 0$. (b) Shifts of the positions of the stability boundaries (1) to (4) of island A vs. $A_4$ with both $a > 0$ and $a < 0$. 
2.3.3 Mass Analysis in Islands of Stability

Figure 2.5a shows peak shapes with $a > 0$ with mass analysis at the upper tip (greater $|a|$) of island A with values of $\lambda$ from 0.16980 to 0.17005. The peaks have resolutions of 380 to 744. These values of $\lambda$ give scan lines which pass outside the conventional stability region (where, at the tip, $\lambda = 0.16784$). Good peak shape and resolution are obtained. The peaks are free of tails.

Figure 2.5b shows peak shapes with mass analysis at the lower tip (lesser $|a|$) of island A with $a > 0$. Here, for a given transmission the resolution is relatively poor. For example at a transmission of about 0.04, $R_{1/2} = 275$, whereas with operation at the upper tip $R_{1/2} = 540$, for the same transmission. When $\lambda$ is decreased from 0.16655 to 0.16645 in an effort to increase the resolution, the nominal resolution decreases from 382 to 293. As well, the peaks have tails on the high mass side and undesirable structure. Clearly with $a > 0$ the upper tip of island A gives superior mass analysis.

Figure 2.6a shows peak shapes for mass analysis in island A with $a < 0$ at the tip with the greater $|a|$. For a given transmission, the resolution is relatively low (e.g. at a transmission of 0.022, $R_{1/2} = 245$ compared to $R_{1/2} = 540$ in Figure 2.5b) and structure appears on the peaks.
Figure 2.5 Peak shapes for mass analysis in island A for a rod set with 2.6% added octopole field and \( \alpha > 0 \) at (a) the upper tip (the tip with greater \(|\alpha|\)) and (b) the lower tip (the tip with lesser \(|\alpha|\)).
Figure 2.6 Peak shapes for mass analysis in island A for a rod set with 2.6% added octopole field and \( a < 0 \) at (a) the tip with the greater \( |a| \) and (b) the tip with the lesser \( |a| \).
Figure 2.6b shows peak shapes for mass analysis in island A with $a < 0$ at the tip with the lesser $|a|$. The peak shape, transmission and resolution are improved compared to operation at the tip with the greater $|a|$. The peaks have resolution from 380 to 767, are free of structure and do not tail on the high or low mass side. The peaks are comparable to those with conventional mass analysis with $a > 0$ and no excitation applied. Thus this island allows mass analysis when the added octopole otherwise prevents mass analysis. Calculated peak shapes and transmission for operation in island A with quadrupoles with $A_4 = 0.02$ and $A_4 = 0.04$ are very similar (data not shown).

Figure 2.7 shows peak shapes at $R_{1/2} \approx 700$ for (a) a quadrupole with a pure quadrupole field, (b) a quadrupole with 2.6% octopole and round rods operated with $a > 0$ at the tip of the stability diagram with no excitation (c) a quadrupole with 2.6% octopole and round rods operated with $a < 0$ at the tip of island A with the greater $|a|$, and (d) a quadrupole with 2.6% octopole field and round rods with $a < 0$ operated at the tip of island A with the lesser $|a|$. It is seen that with the rod set with 2.6% added octopole, operation at the preferred tips of island A gives peak shapes and transmissions similar to that of the same quadrupole operated at the tip of the stability island with no excitation. Thus, with $a < 0$, the use of the island of stability provides resolution and transmission similar to that with $a > 0$. However all the peaks for the quadrupole with 2.6% added octopole have transmission that is lower than that of a pure quadrupole field by a factor of about 25. Experiments comparing the transmission vs. resolution of a round rod quadrupole with a 2.0% added octopole field to a conventional rod set constructed with round rods, did not show this large difference in transmission [23]. The rod set with added octopole showed lower transmission than the conventional rod set, but only for resolutions greater than about 1500. The transmission of mass analyzing quadrupoles with added multipoles,
and the dependence of the transmission on the source characteristics require additional investigation. Preliminary results here show that the fringing fields at the entrance to a quadrupole with an added octopole field can increase the transmission by about a factor of ten to give transmission comparable to that to a conventional round rod quadrupole [19].

Figure 2.7 Peak shapes comparison of (a) an ideal quadrupole, resolution 802, (b) a round-rod quadrupole with 2.6% octopole field operated at the tip of the stability boundary without excitation \( q' = 0.00 \) with \( \alpha > 0 \), resolution 720, (c) a round-rod quadrupole with 2.6% octopole field operated at the tip of island A with greater \( |\alpha| \) \( (q' = 0.020 \text{ and } \nu = 9/10) \) with \( \alpha > 0 \), resolution 861, (d) a round rod quadrupole with 2.6% octopole field operated at the tip of island A with the lesser \( |\alpha| \) \( (q' = 0.20 \text{ and } \nu = 9/10) \) with \( \alpha < 0 \), resolution 782. The scale for the transmission of the ideal quadrupole is on the right.
2.4 Conclusions

The results here show that the best resolution and peak shape are obtained with operation at the peak of island A with the greater $|a|$ with $a > 0$ and the lesser $|a|$ with $a < 0$. Similar results were obtained for operation in island A with quadrupoles with 2 and 4% added octopole fields. Because the islands are essentially in the same position for these other values of $A_4$, scan lines with a given $\lambda$ give nearly the same resolution and transmission. With the negative dc applied to the smaller rods so that $a < 0$, the added octopole prevents conventional mass analysis. Nevertheless, by operating at the tip of island A with the lesser $|a|$, mass analysis with resolution, transmission and peak shape similar to that with $a > 0$ is possible. Further work is required to determine if the use of islands generally can provide a method for mass analysis when added multipoles otherwise prevent mass analysis.
2.5 References


3 Quadrupole Mass Filters with Added Hexapole Fields*

* A version of this chapter has been published.
3.1 Introduction

Mass analysis with linear quadrupoles can be done by scanning direct-current (dc) and radio-frequency (rf) voltages applied between rod pairs to place the working point of ions at the tip of a stability region [8], by mass selective radial ejection [22], by mass selective axial ejection [23, 24] and by using islands of stability [19-4]. Linear quadrupoles used as mass filters are usually constructed to high precision to avoid field distortions, described by the addition of higher multipoles to the electric potential. Linear quadrupoles can also be used as two-dimensional (2D) ion traps [12]. Higher order fields in 3D ion traps increase ion fragmentation efficiency for tandem mass spectrometry (MS/MS) experiments [25, 26] and can give higher resolution in ion ejection [27, 28]. Douglas and co-workers discussed how these benefits can also apply to linear quadrupole ion traps [29, 30]. Thus, methods to add octopole [13, 31] or hexapole[17, 32] fields in the range of 2–12% to linear quadrupoles have been described. Such quadrupoles have much greater field distortions than those normally attributed to manufacturing tolerances or construction errors.

With field distortions, the potential in a linear quadrupole, \( \Phi(x, y, t) \), is described as a superposition of multipoles, \( \phi_N(x, y) \), given by

\[
\Phi(x, y, t) = \varphi(t) \sum_{N=0}^{\infty} A_N \phi_N(x, y) \tag{3.1}
\]

where \( A_N \) is the dimensionless amplitude of the multipole \( \phi_N(x, y) \), and \( \varphi(t) \) is a time dependent potential applied to the electrodes. The terms \( \phi_N(x, y) \) can be derived from

\[
\phi_N(x, y) = \text{Re} \left( \frac{x + iy}{r_0} \right)^N \tag{3.2}
\]

Where \( \text{Re}[f(\xi)] \) means the real part of the complex function \( f(\xi) \), \( \xi = x + iy \), \( i^2 = -1 \) and \( r_0 \) is the field radius of the quadrupole. For example, the potential of a linear quadrupole with an
added hexapole field and no other multipoles can be described as

$$
\Phi(x, y, t) = \left[ A_2 \left( \frac{(x^2-y^2)}{r_0^2} \right) + A_3 \left( \frac{(x^3-3xy^2)}{r_0^3} \right) \right] \phi(t) \quad (3.3)
$$

where $A_2$ and $A_3$ are the dimensionless amplitudes of the quadrupole and hexapole fields, respectively, $A_2 \approx 1$, $r_0/\sqrt{A_2}$ is the distance from the center of the quadrupole to a y electrode when $x = 0$, and $\pm \phi(t)$ is given by

$$
\phi(t) = (U - V_{rf} \cos \Omega t) \quad (3.4)
$$

Where $U$ is a dc voltage, $V_{rf}$ is an rf voltage, and $\Omega$ is the angular frequency of the rf voltage. Quadrupole operation is usually described in terms of two Mathieu parameters, $a$ and $q$, given by

$$
a = a_x = -a_y = \frac{8zeU}{m\Omega^2r_0^2} \quad q_x = -q_y = \frac{4zeV_{rf}}{m\Omega^2r_0^2} \quad (3.5)
$$

where $z$ is number of charges on an ion, $e$ is the electron charge, and $m$ is the ion mass.

Linear quadrupoles with added octopole [13, 31] fields have been constructed and tested, both as mass filters [33, 18] and ion traps [30, 34]. These rod sets were originally built because it was expected [16], and later shown [15], that they would give greater fragmentation yields with excitation of trapped ions for MS/MS. Subsequently it was found that quadrupoles with added octopole fields of 2% to 4% (i.e. $A_4/A_2 = 0.02 - 0.04$) can be used for mass analysis, either conventionally with applied rf and dc [33], with axial ejection [34] or with islands of stability [19, 18]. The addition of a hexapole field can also increase fragmentation efficiency for MS/MS [14, 18]. Simulations have shown that mass analysis may also be possible with linear quadrupoles with added hexapole fields [17]. To investigate this, linear quadrupole rod sets that have added hexapole components of 4, 8 and 12% (i.e. $A_3/A_2 = 0.04, 0.08$ and 0.12) have been designed and constructed [14]. Preliminary experiments have shown that some of these
quadrupoles can be used for conventional mass analysis [14].

In this work we have measured transmission, resolution and peak shapes of quadrupole mass filters that have added hexapole fields. The quadrupoles were operated conventionally by scanning applied rf and dc voltages to place the working point of ions at the tip of the first stability region. Six rod sets have been tested; three with added hexapole fields of 4%, 8% and 12% with equal diameter rods, and three with added hexapole fields of 4%, 8% and 12% with the x rods greater in diameter than the y rods, to remove an added octopole field [17]. With the positive resolving dc applied to the y rods, so that the Mathieu parameter \( a_x < 0 \), only low resolution (10-100) and low transmission are possible. With the polarity reversed, so \( a_x > 0 \), much higher resolution and transmission are possible. Increasing the magnitude of the added hexapole field decreases the limiting resolution. The rod sets with 4%, 8% and 12% added hexapole fields and unequal diameter rods have limiting resolutions of about 2000, 1500, and 850, respectively, while the rod sets with the same added hexapole fields and equal diameter rods have limiting resolutions of about 1900, 400, and 200 respectively. Thus, removing the added octopole field improves performance, as seen in previous computer simulations [17]. For a given scan line slope, \( U/V_{rf} \), the resolution decreases as the amplitude of the added hexapole field increases. These results are consistent with changes to the stability diagrams, calculated here. With \( a_x > 0 \), adding a hexapole field causes the x stability boundary to move out, with all rod sets. With \( a_x < 0 \), the boundaries become diffuse and the tip of the stability diagram becomes rounded, limiting resolution to ca. 10-100. With \( a_x > 0 \), in some cases structure is formed on the peaks at low and intermediate resolution, but not at high resolution. Where comparisons are possible, the rod sets with added hexapole fields have transmission 10-300 times less than a conventional quadrupole rod set. Thus these rod sets are less useful for mass analysis than
conventional quadrupoles. Nevertheless it is surprising that resolution of 1000 or more is possible with at least some rod sets with such highly distorted fields.
3.2 Methods

3.2.1 Rod Sets

Six rod sets with added hexapole fields of 4%, 8% and 12% were constructed with round rods. To add the hexapole field, the two \( y \) rods were rotated towards an \( x \) rod through an angle \( \theta \) (see Figure 4 of reference 18 for the coordinate system used including the rotation angle, and Figure 2 of reference 24 for a photograph of a rod set with a 12% added hexapole field). The amplitude of the added hexapole field, \( A_3 \), is approximately proportional to \( \theta \) [17]. The rods are equidistant from the central axis and all rod sets have \( r_0 = 4.5 \) mm. Three of the rod sets, labeled 4A, 8A and 12A, have added hexapole fields of 4%, 8% and 12% respectively, and have the radius of the \( x \) rods, \( R_x \), equal to the radius of the \( y \) rods, \( R_y \). This arrangement produces a quadrupole field that has an added hexapole component and other higher multipoles, especially a significant octopole term. Three other rod sets, labeled 4B, 8B and 12B, have added hexapole fields of 4%, 8% and 12% respectively, and have the radius of the \( x \) rods greater than the radius of the \( y \) rods (\( R_x > R_y \)), to produce a quadrupole field that has an added hexapole component and a minimized octopole field (\( A_4 \approx 0 \)) [17]. The ratio \( R_x/r_0 \) to make \( A_4 \approx 0 \) depends on the rotation angle and is thus different for rod sets 4B, 8B and 12B. Computer simulations have shown that removing the octopole field improves the resolution and peak shapes of the rod sets used as mass filters [17]. In some experiments a conventional round-rod quadrupole with \( r_0 = 4.17 \) mm, and \( R_x/r_0 = R_y/r_0 = 1.1247 \) was also used. All quadrupoles were 20.0 cm long. When a hexapole field is added, the center of the field is shifted a distance \( x_0 \) off axis and a dipole potential with amplitude \( A_1 \) is added [18]. Simulations, with an ion beam with a diameter of about 0.002\( r_0 \), show that injecting the ions at the field center instead of at the geometric center of the rod sets improves transmission [17]. Table 3.1 shows the dimensions and values of \( x_0 \) of the rod sets. The
multipole compositions of the rod sets are given in ref [35].

Table 3.1 Geometries and dimensions of the rod sets used.

<table>
<thead>
<tr>
<th>Rod Set</th>
<th>% $A_3$</th>
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<th>$R_y$ [mm]</th>
<th>$x_0$ [mm]</th>
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<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8A</td>
<td>8</td>
<td>5.13</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12A</td>
<td>12</td>
<td>7.69</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>4B</td>
<td>4</td>
<td>2.56</td>
<td>5.2425</td>
<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8B</td>
<td>8</td>
<td>5.13</td>
<td>5.4945</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12B</td>
<td>12</td>
<td>7.69</td>
<td>5.9378</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>conventional</td>
<td>0</td>
<td>0</td>
<td>4.690</td>
<td>4.690</td>
<td>0</td>
</tr>
</tbody>
</table>

3.2.2 Mass Spectrometer System

Experiments were performed with a system constructed in house [34]. Ions formed by electrospray ionization (ESI) pass through a 1.5 mm diameter aperture in a "curtain plate", through a dry N$_2$ curtain gas, and enter a vacuum system through a 0.125 mm diameter orifice in the tip of a cone. Ions then pass through a 20 cm long quadrupole ion guide, Q0, (4.6×10$^{-3}$ Torr, N$_2$) where they are collisionally cooled to energies and energy spreads of a few eV, confirmed with stopping curves. Ions then pass through a 3.0 mm diameter aperture in an "inter-quadrupole" lens (Q0/Q1 lens) and enter the mass-analyzing quadrupole, Q1, in a chamber pumped to 1.6×10$^{-5}$ Torr. There are two lenses after Q1, each with a 9.0 mm diameter aperture. The first, "exit lens 1", is covered with a 50×50 wires per inch mesh, with a plain weave pattern, with 0.001 inch diameter wire. The second, "exit lens 2", has an open aperture. The distances from the end of Q1 to exit lens 1 and 2 are 3.5 mm and 8.5 mm, respectively. Ion counting is used for ion detection. Mass spectra were acquired by co-adding 100-500 scans with a step size
of 0.1 Th. Transmission values are reported as (counts/s) × 100. The quadrupole power supply (Sciex API III, Concord, ON, Canada) frequency is 1.0 MHz.

Protonated ions of reserpine ($m/z$ 609) were used to investigate the peak shapes of all the quadrupoles. In some cases, the monoisotopic ions (CsI)$_2$Cs$^+$ ($m/z$ 652.5) were used. Operating voltages are listed in Table 3.2. Two different sets of voltages were used. Set 2 had higher voltages applied to the orifice, inter-quadrupole lens (Q0/Q1), offsets of Q0 and Q1, and exit lens 1, than set 1. Higher transmission, higher resolution and better peak shapes were obtained with the voltages in set 2 with all rod sets except rod set 4B, which used the voltages listed in set 1. With set 1, the ion energy at the inter-quadrupole lens is about 34 eV; with set 2, about 18 eV. The energy at this point controls the time ions spend in the entrance fringing field of Q1, and thus differences in peak shape, resolution and transmission between set 1 and set 2 may be due to fringing field effects.

All experiments used conventional mass analysis i.e. with rf and dc voltages applied between the quadrupole rod pairs to place the working point of ions near the tip of the first stability region. The resolution was adjusted by changing the ratio $U/V_{rf}$. Experimental resolution is reported as $R_{1/2} = (m/z)/\Delta(m/z)_{1/2}$ where $\Delta(m/z)_{1/2}$ is the peak width at half height. With peaks that are split or have structure, or when isotopic peaks overlap, we refer to this as the "nominal resolution". In most experiments the positive dc of the quadrupole supply was connected to the $x$ rods (unshifted rods) and the negative dc to the $y$ rods (shifted rods) to give the Mathieu parameter $a_x > 0$ [17]. In some experiments the polarity was reversed to give $a_x < 0$. 
Table 3.2 Operating voltages (V).

<table>
<thead>
<tr>
<th></th>
<th>Set 1</th>
<th>Set 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sprayer</td>
<td>+4300</td>
<td>+4300</td>
</tr>
<tr>
<td>Curtain Plate</td>
<td>+500</td>
<td>+500</td>
</tr>
<tr>
<td>Orifice</td>
<td>+20</td>
<td>+120</td>
</tr>
<tr>
<td>Q0 dc offset</td>
<td>+4</td>
<td>+110</td>
</tr>
<tr>
<td>Q0/Q1 inter-quad lens</td>
<td>-30</td>
<td>+92</td>
</tr>
<tr>
<td>Q1 dc offset</td>
<td>+2.3</td>
<td>+108</td>
</tr>
<tr>
<td>Exit lens 1</td>
<td>-20</td>
<td>-30</td>
</tr>
<tr>
<td>Exit lens 2</td>
<td>-150</td>
<td>-150</td>
</tr>
</tbody>
</table>

3.2.3 Solutions and Reagents

Reserpine (Sigma, St. Louis, MO, USA) was 50 μM in glacial acetic acid (99.99%, Fisher Scientific, Nepean, ON, Canada) / methanol/deionized water (0.006:1:1); CsI (Sigma, St. Louis, MO, USA) was 0.01 M in acetonitrile (Fisher Scientific, Nepean, ON, Canada)/deionized water (9:1). All solutions were infused into the ESI source at 1 μL/min. Nitrogen, UHP-grade, manufacturer's stated purity 99.999%, was from Praxair Vancouver, BC, Canada.

3.2.4 Calculations of Stability Boundaries

Stability boundaries were calculated as in ref [17] with the following parameters: spatial spreads of the ion beam in the x and y directions, \( \sigma_x = \sigma_y = 0.002r_0 \); thermal transverse velocities of the ion beam with \( T^\circ = 300 \text{ K} \) to give \( \sigma_v = 0.007 \); 150 rf cycles in the field, and no fringing fields. All multipoles up to \( N = 10 \) were included. Values of \( a \) and \( q \) giving 1% transmission were taken as the stability boundaries.
3.3 Results and Discussion

3.3.1 Mass Analysis with Quadrupoles with Unequal Diameter Rods

Figure 3.1 shows mass spectra of reserpine ions with rod sets 4B (a-c), 8B (d-f) and 12B (g-i). The amplitude of the added hexapole field increases down each column. Each row shows peak shapes obtained with a given rod set with resolution settings increasing from left to right. The highest resolution that could be obtained with each rod set, and the corresponding peak shapes are shown in the right column. With rod set 4B (Fig. 3.1c), the isotopic peaks are almost baseline resolved with a limiting resolution of 2070, the highest of all the rod sets. The limiting resolution of rod set 8B is about 1500 (Fig. 3.1f). The isotopic peaks are separated but not baseline resolved because of low and high mass tails on the peaks. The highest resolution obtained with rod set 12B is about 850 (Fig. 3.1i). With rod set 12B, the isotopic peaks are only just resolved. Figures 3.1c, 1f, 1i show that increasing the amplitude of the added hexapole field lowers the limiting resolution. In each column of Figure 3.1, the resolution settings of the quadrupole were nearly the same. For a given resolution setting, the peaks broaden and the resolution decreases as \( A_3 \) increases, because increasing the amplitude \( A_3 \) shifts the stability boundary outwards [17].
Figure 3.1 Mass spectra of reserpine ions with rod sets 4B (a-c), 8B (d-f) and 12B (g-i). The amplitudes of the added hexapole fields increase down each column. Each row shows the peak shapes from a given rod set with resolution settings increasing from left to right.
Figure 3.2 Peak shapes with (CsI)2Cs+ (m/z 652.5) with (A) rod set 4B, at nominal resolutions of (a) 1610 (b) 870 (c) 383 (d) 352 and (e) 611; (B) rod set 8B at nominal resolutions of (a) 1380 (b) 830 (c) 798 and (d) 177; and (C) rod set 12B with nominal resolutions of (a) 1170 (b) 1070 (c) 538 and (d) 271.
3.3.2 Peak Tails

Low mass tails on the peaks generally decrease the resolution of the B rod sets. This is most evident in Figure 3.1c. The tails are less obvious in spectra having lower resolution and broader peaks, because the isotopic peaks overlap (e.g. Fig. 3.1b, 3.1e and 3.1h). The monoisotopic ions $(CsI)_2Cs^+$ were used to investigate peak shapes in more detail because the resolution and peak shape are not affected by overlap of isotopic peaks.

Figure 3.2(A) shows peak shapes with $(CsI)_2Cs^+$ ions obtained with rod set 4B. Spectra from a to e were obtained with decreasing resolution settings. Spectrum a has the highest resolution setting to give $R_{1/2} = 1610$. The low mass tail in spectrum a (expanded in the inset) is apparent but does not substantially affect the resolution at half height. With lower resolution settings, the nominal resolutions at half height are 870 (b), 383 (c) and 352 (d). As the resolution decreases, the tail increases in intensity to form additional structure on the peak. Spectrum e has a nominal resolution of 611 because at half height the width is determined by the narrow part of the peak on the low mass side. At still lower resolution settings these features eventually merge to give a single peak with $R_{1/2} < 200$.

Figures 3.2(B) and 2(C) show peak shapes with $(CsI)_2Cs^+$ ions with rod sets 8B and 12B, respectively. In each Figure, spectra from a to d were obtained with decreasing resolution settings. At their highest resolution in these spectra, rod sets 8B (Fig. 3.2(B) spectrum a) and 12B (Fig. 3.2(C) spectrum a) (expanded in the insets) both show peak tails. Unlike rod set 4B, no additional structure is observed on the peaks at intermediate resolution with rod sets 8B (Fig. 3.2(B) spectra b and c) and 12B (Fig. 3.2(C) spectra b and c). At low resolution ($R_{1/2} < 300$), rod set 8B (Fig. 3.2(B) spectrum d) shows structure on the peak, similar to rod set 4B (Fig. 3.2(A) spectrum e). Rod set 12B (Fig. 3.2(C) spectrum d) operated at low resolution shows no
pronounced structure on the peak.

Computer simulations of peak shapes with rod sets with 2-12% added hexapole fields and $A_4 \approx 0$ did not show structure at low ($R_{1/2} \approx 35-100$) and high ($R_{1/2} \approx 700-1400$) resolution. At intermediate resolution (ca. 500), simulation of a rod set with $A_3 = 0.1016$ and $A_4 \approx 0$ gave structure similar to that of Figures 3.2A and 3.2B [17]. In these experiments the radius of the aperture in the entrance lens (1.5 mm or 0.33$r_0$) gives a much greater range of initial $x$ and $y$ positions (0.33$r_0$) than used in the simulations (typically 0.002$r_0$). Thus only qualitative agreement between these experiments and the simulations might be expected.

3.3.3 Mass Analysis with Rod Sets with Equal Diameter Rods

Figure 3.3 shows mass spectra of reserpine ions with rod sets 4A (a-c), 8A (d-f) and 12A (g-i). As in Fig. 3.1 the amplitude of the added hexapole field increases down each column, and each row shows spectra obtained from a given rod set with resolution settings increasing from left to right. The right column shows the highest resolution that could be obtained with each rod set. Rod set 4A has a limiting resolution of about 1900 (Fig. 3.3c), the highest of these three rod sets. At this resolution the peaks are relatively free from tails. Rod set 8A has a nominal limiting resolution of about 400 (Fig. 3.3f). The isotopic peaks are just barely resolved. With rod set 12A, the highest resolution is nominally about 200, with overlapping isotopic peaks (Fig. 3.3i). Figure 3 also shows that as the amplitude of the hexapole field increases, the limiting resolutions of the rod sets decrease. Figures 3.3b, 3e, 3h show three spectra obtained with the same resolution setting. As the amplitude of the hexapole field increases the resolution decreases. This is consistent with changes to the boundaries of the stability diagram, discussed below.
Comparison of the spectra of the A and B rod sets shows that the rod sets with unequal
diameter rods generally can give higher resolution than the rod sets with equal diameter rods. Of
the A rod sets, only 4A gives well separated isotopic peaks (Fig. 3.3c). However when rod set
4A is operated at low resolution, the peaks split into two broad peaks (Fig. 3.3a). The cause of
this requires further investigation. Rod set 8A can only just resolve the isotopic peaks, and, with
rod set 12A, only broad peaks can be obtained at any resolution setting. In contrast, both rod sets
4B and 8B, operated at high resolution, can resolve the isotopic peaks of reserpine, and rod set
12B can almost resolve the isotopic peaks. However, with rod sets 4B and 8B operated at
intermediate (Fig. 3.2(A) spectra b-d) or low resolution (Fig. 3.2(A) spectrum e and Fig. 3.2(B)
spectrum d), there is structure on the peaks.
Figure 3.3 Mass spectra of reserpine ions with rod sets 4A (a-c), 8A (d-f) and 12A (g-i). The amplitudes of the added hexapole fields increase down each column. Each row shows the peak shapes from a given rod set with resolution settings increasing from left to right.
Figure 3.4 Peak shapes with reserpine ions with the positive resolving dc applied to the y rods with (a) rod set 4A, (b) rod set 8A, (c) rod set 12A, (d) rod set 4B, (e) rod set 8B, (f) rod set 12B.

3.3.4 Spectra with $\alpha_x < 0$ and Stability Diagrams

Figure 3.4 shows peak shapes and the highest resolution possible with all six rod sets, with the positive resolving dc applied to the y rods so that the Mathieu parameter $\alpha_x < 0$. Only very low resolution ($R_{1/2} < 100$) and low transmission are possible. Simulations show that the low resolution can be explained by changes to the stability diagrams of these rod sets.

Previously, stability boundaries were calculated for quadrupoles with added hexapole fields, with unequal diameter rods so that $A_4 \approx 0$ (the B rod sets), with $\alpha_x > 0$, and $A_3 = 0.02 - 0.12$, and including the other higher multipoles up to $N = 10$ [17]. Adding a hexapole field causes the
$\beta_x = 1$ stability boundary (the right boundary) to shift to greater $q$ values for a given $a$ value, but the boundaries remain sharp [17]. Stability boundaries have now been calculated for the A rod sets with $a_x > 0$ and are shown in Fig. 3.5, along with the boundaries of an ideal quadrupole field. With the A rod sets, adding a hexapole field also causes the $\beta_x = 1$ stability boundary to shift to greater $q$ values for a given $a$. The shift increases with increasing $A_3$ and the boundaries remain sharp. The shifts, $\Delta q$, for a given $A_3$ with the A rod sets are about 0.6 of the shifts with the B rod sets. These shifts cause the resolution to decrease for a given scan line slope $U/V_{rf}$ as $A_3$ increases, as seen in the experiments (Fig. 3.3).

Figure 3.5 Calculated stability boundaries with an ideal quadrupole field and with rod sets with added hexapole fields of 4%, 8% and 12% with equal diameter rods with $a_x > 0$. $\star$, ideal quadrupole field; $\blacktriangle$, rod set 4A; $\blacksquare$, rod set 8A; $\bullet$, rod set 12A. The left boundaries with an ideal quadrupole field and with rod sets 4A and 8A nearly coincide.
Calculated stability boundaries for all six rod sets and an ideal quadrupole field with $\alpha_x < 0$ are shown in Fig. 3.6. With $\alpha_x < 0$ the boundaries become diffuse. The $\beta_x = 0$ stability boundary (the left boundary) shifts to greater $q$ values for a given $a$ value, or, for a given $q$, shifts to lower $a$ values. The shift increases with increasing $A_3$. The $\beta_y = 1$ stability boundary (the right boundary) shows more complex behavior. Near the tip of the modified stability diagram, for a given $a$ value, the boundary shifts to lower $q$ values. At lower values of $a$, the boundary shifts to greater $q$ values. While the boundaries of the A and B rod sets are similar, for a given amplitude of added hexapole field, the B rod sets show shifts that are ca. 10% greater than shifts with the A rod sets. The net effect of these shifts is that the tip of the stability diagram moves to lower values of $a$. Increasing $A_3$ causes greater shifts in the tip position. The tip is near $|a| = 0.235$ with 4% added hexapole field, near $|a| = 0.233$ with 8% added hexapole field, and near $|a| = 0.232$ with 12% added hexapole field.

The low resolution with the A rod sets can be attributed to two changes to the stability diagram. First, the boundaries become diffuse, so there are no longer sharp sides on the peaks. Second, the tip of the stability region becomes rounded, so only low resolution is possible. For example the widths $q/\Delta q$ with 4%, 8%, and 12% added hexapole fields, measured at $a=0.2345$, 0.2325 and 0.2315, respectively, are 204, 84, and 92, respectively, in qualitative agreement with the $R_{1/2}$ values of Figure 3.4.
Figure 3.6 Calculated stability boundaries with an ideal quadrupole field and of the A and B rod sets with $a_x < 0$. ★, ideal quadrupole field; ▲, rod set 4A; ∆, rod set 4B; ■, rod set 8A; □, rod set 8B; ●, rod set 12A; ○, rod set 12B.
3.3.5 Transmission vs. Resolution Curves with Reserpine Ions

Figure 3.7 shows transmission (T) vs. \( R_{1/2} \) curves measured with reserpine ions for the A and B rod sets, as well as for a conventional rod set. The results are summarized in Table 3.3 The limiting resolutions of all rod sets are lower than that of the conventional rod set, and the limiting resolutions decrease with increasing amplitude of the added hexapole field. At all \( R_{1/2} \), all rod sets with add hexapole fields have much lower transmission than the conventional rod set, except for rod set 4B (Fig. 3.7a curve 2) at \( R_{1/2} < 300 \).

Figure 3.7 Transmission (T) vs. resolution (\( R_{1/2} \)) with reserpine ions. With rod set 4B (curve 2), 8B (curve 3) and 12B (curve 4). (b) With rod sets 4A (curve 5), 8A (curve 6) and 12A (curve 7). In both (a) and (b) curve (1) was obtained with a conventional mass filter.
Table 3.3 Limiting resolutions and transmission at various resolutions of the conventional rod set and rod sets A and B.

<table>
<thead>
<tr>
<th>Rod Set</th>
<th>Limiting resolution ( (R_{1/2}) )</th>
<th>Transmission at ( R_{1/2} = 1000 )</th>
<th>Transmission at ( R_{1/2} = 900 )</th>
<th>Transmission at ( R_{1/2} = 400 )</th>
<th>Transmission at ( R_{1/2} = 200 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional</td>
<td>2400</td>
<td>( 1.5 \times 10^7 )</td>
<td>( 2.0 \times 10^7 )</td>
<td>( 8.0 \times 10^7 )</td>
<td>( 9.0 \times 10^7 )</td>
</tr>
<tr>
<td>4B</td>
<td>2000</td>
<td>( 7.0 \times 10^5 )</td>
<td>( 8.0 \times 10^5 )</td>
<td>( 3.0 \times 10^6 )</td>
<td>( \sim 7.0 \times 10^7 )</td>
</tr>
<tr>
<td>8B</td>
<td>1500</td>
<td>( 1.0 \times 10^5 )</td>
<td>( 2.0 \times 10^5 )</td>
<td>( 5.0 \times 10^5 )</td>
<td>( 2.0 \times 10^6 )</td>
</tr>
<tr>
<td>12B</td>
<td>850</td>
<td>---</td>
<td>( 1.5 \times 10^4 )</td>
<td>( 1.0 \times 10^5 )</td>
<td>( 1.0 \times 10^6 )</td>
</tr>
<tr>
<td>4A</td>
<td>1900</td>
<td>( 1.0 \times 10^6 )</td>
<td>( 1.0 \times 10^6 )</td>
<td>---</td>
<td>( 1.0 \times 10^7 )</td>
</tr>
<tr>
<td>8A</td>
<td>400</td>
<td>---</td>
<td>---</td>
<td>( 1.0 \times 10^5 )</td>
<td>( 2.0 \times 10^6 )</td>
</tr>
<tr>
<td>12A</td>
<td>200</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>( 1.0 \times 10^5 )</td>
</tr>
</tbody>
</table>

Curves (2, 3 and 4) in Fig. 3.7a show \( T \) vs. \( R_{1/2} \) curves with rod sets 4B, 8B and 12B respectively. As shown in Table 3.3 and Fig. 3.1, the limiting resolutions of rod sets 4B, 8B and 12B are about 2000, 1500 and 850 respectively. At \( R_{1/2} = 1000 \), the transmissions of rod sets 4B and 8B are about 20 and 150 times less than that of the conventional mass filter. At \( R_{1/2} = 750 \), the transmissions of rod set 12B is about 300 times less than that of the conventional mass filter. At resolutions between 300 and 1000, the transmissions decrease with increasing amplitude of the hexapole field. The slopes of the curves in this range are similar. At \( R_{1/2} < 300 \), the transmission of rod set 4B approaches that of the conventional rod set, and the transmission of rod sets 8B and 12B are similar and about 50 times less than the conventional rod set.

Curves (5, 6 and 7) in Fig. 3.7b show \( T \) vs. \( R_{1/2} \) curves with rod sets 4A, 8A and 12A respectively. The limiting \( R_{1/2} \) of rod sets 4A, 8A and 12A are about 1900, 400 and 200. At \( R_{1/2} = 1000 \), the transmission of rod set 4A is about 20 times less than that of the conventional
mass filter. The $T$ vs. $R_{1/2}$ curve of rod set 4A cannot be plotted for resolutions between 100 and 600. Here the spectra all have badly split peaks, such as is shown in Fig. 3.3a. In the region with $R_{1/2} = 200 - 400$, the transmissions of rod sets 8A and 12A decrease dramatically. The transmission of rod set 12A decreases most rapidly. At $R_{1/2} < 200$, the transmission of rod set 12A becomes higher than that of rod set 8A. Both have much lower transmission than the conventional rod set.

The experiments show that the B rod sets have higher limiting resolutions than the A rod sets. For example, the limiting resolution of rod set 8B (1500) is almost 4 times greater than that of rod set 8A (400). The difference between the limiting resolution of rod set 4A (1900) and 4B (2000) is much smaller, but at $R_{1/2} = 2000$, rod set 4B has about 7 times higher transmission than rod set 4A. Thus, minimizing the octopole field improves the performance, as observed in computer simulations [17].
3.4 Conclusion

Because of the relatively low transmission, limited resolution and peak structure problems, these rod sets are less useful for conventional mass analysis, in comparison to a conventional rod set. Nevertheless, given the highly distorted fields, it is surprising that at least some of the rod sets can give resolution of 1000 or more. As discussed, these rod sets were originally developed for and found to improve fragmentation efficiency of trapped ions [29]. With trapped ions, mass analysis is possible with mass selective axial ejection, in which case these rod sets give much higher resolution and peaks free of structure (e.g. $R_{1/2} \approx 1800$ with rod set 12A) [16]. Use of islands of stability for mass analysis with these rod sets also greatly improves peak shape, resolution, and in some cases, transmission [35]. Thus, despite their limited performance with conventional mass analysis, quadrupoles with added hexapole fields may find future applications.
3.5 References


4 Mass Analysis with Islands of Stability with Linear Quadrupoles Incorporating Higher Order Multipole Fields*  

4.1 Introduction

Linear quadrupoles can be operated as either radio frequency (rf) only ion guides for ion transport, mass filters [1-4] or ion traps [5]. As with 3D Paul traps [6], adding higher order multipole fields either dc [7] or rf [8] to a linear quadrupole can improve MS/MS fragmentation efficiency. In some instruments, a quadrupole operated as a linear ion trap (such as Q3 in a triple quadrupole mass spectrometer) must also be capable of mass analysis [9].

In general, the potential of a linear quadrupole with field distortions can be written as [10]

\[
\Phi(x, y, t) = Re \left[ \sum_{N=0}^{\infty} A_N \left( \frac{x + iy}{r_0} \right)^N \right] \varphi(t) \tag{4.1}
\]

where \(x\) and \(y\) are Cartesian coordinates, \(r_0\) represents the distance from the central axis to an electrode for an ideal quadrupole and otherwise is a normalization factor, \(Re[f(x + iy)]\) is the real part of the complex function \(f(x + iy)\), \(i^2 = -1\), \(A_N\) is the dimensionless amplitude of a multipole \((2N\)-pole\), and \(\varphi(t)\) is a time-dependent voltage applied to the electrodes. An ideal linear quadrupole has \(A_2 = 1\) and all other multipoles zero. A practical linear quadrupole usually has \(A_2 \approx 1\), and other higher order multipole amplitudes in the range \(10^{-5}\) to \(10^{-3}\) [2-4].

Methods of adding an octopole field of 2-4% [11], i.e. \(A_4/A_2 = 0.02-0.04\), and a hexapole field [12] of up to 12% \((A_3/A_2 \leq 0.12\) to linear quadrupoles constructed from round rods have been described. A hexapole field is added by rotating the two \(y\) rods towards an \(x\) rod through a small angle \(\theta\). The amplitude of the hexapole, \(A_3\), is approximately proportional to \(\theta\). This method also adds other higher multipoles, including an octopole field [12].
Addition of these field distortions might be expected to deteriorate conventional mass analysis, done by scanning the applied direct current (dc) and radio frequency (rf) voltages so that ions cross the tip of the first stability diagram [1]. Nevertheless, mass analysis with quadrupoles with added octopole [13] or hexapole [14] fields has been found to be possible in some cases, provided the positive dc is applied to the x rods so that the Mathieu parameter $\alpha$, (equation (4.5) below) is positive for positive ions.

For mass analysis, linear quadrupoles can also be operated with islands of stability [4, 15-20]. Islands of stability, separated by bands of instability, are formed in a stability region when auxiliary quadrupole excitation with a properly chosen frequency and amplitude is added to the quadrupole. Islands can also be formed by amplitude modulation of the main rf voltage, the dc voltage, or both the rf and the dc voltages [19]. Tips of the stability islands are potential candidates for mass analysis.

Previously, mass analysis with islands has been used to correct for minor field distortions. Miseki [15] described the use of islands to correct for manufacturing tolerances and errors and showed it can be used to remove tails on peaks. Konenkov et al. [16], showed that use of islands can remove tails on peaks, but with "a high precision quadrupole". Baranov et al. [17] also showed that the use of islands removes peak tails to improve abundance sensitivity, but with a commercial quadrupole designed to have minimal field distortions. Glebova and Konenkov [18] modelled the use of islands for "quadrupoles that have weak field distortions". They compared an ideal quadrupole field to the field of a quadrupole constructed with round rods instead of hyperbolic rods. The round rod set had multipole amplitudes $A_2 = 1.00176$, $A_6 = 1.00 \times 10^{-3}$, and $A_{12} = -2.44 \times 10^{-3}$. They too showed that use of islands removes tails on the low mass side of the
peak. For the same round-rod quadrupole, Konenkov et al. [19] showed that not only did the use of islands removed peak tails, but also the number of rf cycles required to reach a resolution of 400 was decreased from approximately 150 without islands to 75. In all these papers, islands were used to correct for minor field distortions, with $A_N/A_2 \approx 10^{-3}$.

We have found that the use of islands of stability can in some cases overcome the much greater field distortions of quadrupoles that have added octopole or hexapole fields. Computer simulations [20] and then experiments [21] showed that with quadrupoles with an added octopole field of 2-4%, use of an island allows mass analysis when the positive dc is applied to the $y$ rods. Without use of an island, only low resolution and transmission are possible. Zhao et al. showed that with quadrupoles that have added hexapole fields of 4-12%, use of a stability island greatly improves peak shape, resolution and in some cases transmission [22]. With added hexapole fields of 8 and 12%, the islands used were very narrow, and only a limited range of resolution could be explored. With quadrupoles with 4% added hexapole fields, islands similar to those of a conventional quadrupole can be performed, and the resolution can be adjusted over a considerable range by adjusting the slope of the scan line.

In this work we report more detailed experimental investigations of mass analysis using islands of stability with three linear quadrupoles. Two of these quadrupoles have 4% added hexapole fields. The first, quadrupole 4A, has equal diameter rods. The second, quadrupole 4B, has $x$ rods greater in diameter than the $y$ rods to remove an octopole field. The third quadrupole is a conventional design with round rods, but apparently has been slightly damaged. With quadrupoles 4A and 4B with the positive resolving dc applied to the $y$ rods, so that the Mathieu parameter $a < 0$, conventional operation gives only low resolution mass spectra. It is possible to
increase the resolution by a factor of 10 or more with the use of islands. With the dc reversed, so that $a > 0$, when quadrupole 4A is operated normally, i.e. without islands, peak shapes similar to that of a conventional quadrupole can be obtained at resolutions higher than 850, but peaks tail slightly on the high mass side. At resolutions lower than 850, split peaks are observed. When quadrupole 4B is operated without islands, although resolution up to 2000 is possible, low mass tails are observed at higher resolution and structure is formed on the peaks at intermediate resolution. When quadrupoles 4A and 4B are operated with mass analysis using an island of stability, peaks free of structure and without tails are formed, and, with some operating conditions, the transmission is increased. For the conventional round-rod quadrupole, mass analysis with islands increases the limiting resolution from 2500 to 4360. At a resolution of 2500, the transmission is increased by about two orders of magnitude.
4.2 Methods

4.2.1 Islands of Stability Theory

With auxiliary quadrupole excitation, the time dependent voltage applied to a quadrupole is

$$\varphi(t) = U - V_{\text{rf}} \cos(\Omega t - \phi_0) - V' \cos(\omega_{\text{ex}} t)$$  \hspace{1cm} (4.2)$$

where $U$ is a dc potential applied to the electrodes, $V_{\text{rf}}$, $\Omega$, and $\phi_0$ are the amplitude, angular frequency, and initial phase of the main rf voltage, $V'$ is the amplitude of the quadrupole excitation voltage with angular frequency $\omega_{\text{ex}}$, and $t$ is time. The equations of ion motion for the $x$ and $y$ directions for an ion of mass $m$ can be written as

$$\frac{d^2x}{d\xi^2} + (a - 2q \cos[2(\xi - \xi_0)] - 2q' \cos(2\nu\xi)) \left( x + \frac{r_0^2}{2} \frac{\partial}{\partial x} \text{Re} \left[ \sum_{n=2}^{\infty} \frac{A_n}{A_2} \left( \frac{x + iy}{r_0} \right)^n \right] \right) = 0 \hspace{1cm} (4.3)$$

$$\frac{d^2y}{d\xi^2} + (a - 2q \cos[2(\xi - \xi_0)] - 2q' \cos(2\nu\xi)) \left( y + \frac{r_0^2}{2} \frac{\partial}{\partial y} \text{Re} \left[ \sum_{n=2}^{\infty} \frac{A_n}{A_2} \left( \frac{x + iy}{r_0} \right)^n \right] \right) = 0 \hspace{1cm} (4.4)$$

where the dimensionless parameters are defined as

$$\xi = \frac{\Omega}{2} \; ; \; \xi_0 = \frac{\phi_0}{2}$$

$$a = \frac{8zeUA_2}{m\Omega^2r_0^2} ; q = \frac{4zeV_{\text{rf}}A_2}{m\Omega^2r_0^2}$$

$$\nu = \frac{\omega_{\text{ex}}}{\Omega} ; q' = \frac{4zeV'A_2}{m\Omega^2r_0^2} = q \frac{V'}{V_{\text{rf}}} \hspace{1cm} (4.5)$$

Where $z$ is the number of charges on the ion and $e$ is the electron charge. Note $q'$ is a measure of the quadrupole excitation strength. For a quadrupole with added higher order multipoles, the excitation field contains multipoles other than the quadrupole term. This is reflected in the summation terms in equations (4.3) and (4.4).

When the ratio of the quadrupole excitation frequency to the main rf frequency is chosen to be
\[ v = \frac{\omega_{ex}}{\Omega} = \frac{Q}{P} \]  

(4.6)

where \( Q \) and \( P \) are integers with no common divisors except for 1, the common period of the main rf voltage and quadrupole excitation voltage is \( \xi = P\pi \). For the special case of an ideal quadrupole \( (A_2 = 1 \text{ and all other multipole amplitudes zero}) \), equations (3.3) and (3.4) become Hill equations [23-25] because the coefficients are periodic in \( \xi \). To determine the stability of the solutions of equations (3.3) and (3.4) the matrix method is particularly advantageous. Details of the matrix method applied to the solutions of Hill equation can be found in [23], and applications to rf quadrupoles are in [24].

When \( v = Q/P \), the unstable points form bands of instability along iso-lines for the and directions. As a result the first stability region in \((a, q)\) the plane splits into islands of stability. The maximum possible number of unstable bands in each of the \( x \) and \( y \) directions is \( P - 1 \). The number of bands observed is usually less. The width of each band depends on the excitation voltage and frequency. With the addition of nonlinear multipole fields to a quadrupole field, the matrix method is no longer strictly applicable to the calculation of stability, because equations (3.3) and (3.4) have nonlinear terms and are no longer Hill equations. For example, theory and experiments show that with quadrupole excitation in linear quadrupoles with added octopole fields, the \( x \) and \( y \) frequencies differ slightly, so the island boundaries will not exactly match those calculated for a pure quadrupole field [26]. However, it has been found by simulations [20] and experiments [16, 17, 21] that the overall trend of island formation is still the same for quadrupoles incorporating weak higher order multipoles.
4.2.2 Operation with Islands of Stability

The positions of the stability islands and the widths of the unstable bands separating the stability islands are determined by the excitation frequency \( (\nu) \) and strength \( (q') \). The tips of stability islands can be used for mass analysis provided the scan line crosses only one island. The slope of a scan line is defined as

\[
\lambda = \frac{a}{2q} = \frac{U}{V_{rf}}
\]

Experimentally, for a given quadrupole excitation frequency, the excitation amplitude \( V' \) and the scan line slope \( \lambda \) are varied until a scan line can be found to cross the tip of one stability island only.

Figure 4.1 shows stability islands calculated with \( P = 20 \) and \( P = 30 \) (\( \nu = 1/20 \) and \( \nu = 1/30 \)). Scan lines with slopes \( \lambda = U/V_{rf} \) are also shown. With increasing \( P \) the left most stable bands become very narrow strips as shown by the dotted lines in Figure 4.1. The transmission in these narrow islands is very low so that the uppermost islands formed inside the stability boundary can be used for mass analysis, such as the island crossed by the scan lines \( \lambda = 0.165 \) in Figure 1(a) and \( \lambda = 0.166 \) in Figure 1(b). The islands are named A, B, C, and D, as illustrated in Figure 1(a). Because these islands use different excitation conditions, \( \nu \) and \( q' \), they cannot be compared directly to the islands with the same labels, used by others [16].

Experimentally we have used two methods to change the mass resolution. The first is to adjust the scan line slope near the tip of an island. The second is to adjust the quadrupole excitation frequency and amplitude to make narrow islands. In this second case the width of the island determines the mass resolution.
Figure 4.1 The first stability region without quadrupole excitation of an ideal quadrupole, shown by the solid triangle, and the stability islands formed with (a) $\nu = 1/20$, $q' = 0.006$; (b) $\nu = 1/20$, $q' = 0.003$. The uppermost four islands that might be used for mass analysis are labeled A, B, C, and D. The very narrow strip at the left cannot be used for mass analysis and therefore is not named.
4.3 Experimental Section

4.3.1 Apparatus

Experiments were performed with a single quadrupole mass spectrometer system described previously [13, 21]. Ions generated by electrospray pass through an aperture in a curtain plate, a curtain gas, an orifice (0.125 mm in diameter), and enter a quadrupole ion guide (Q0, 4.6 mTorr) where they are collisionally cooled to energy spreads of a few eV, then pass through an entrance lens (3.0 mm aperture diameter) and enter a differentially pumped mass analyzing quadrupole (Q1, 1.2×10⁻⁵ Torr). The mass analyzing quadrupole Q1 can be either a conventional quadrupole or one of two quadrupoles with added hexapole fields. Ions leaving Q1 pass through a mesh covered exit lens and a second exit lens. Both exit lenses have 9 mm diameter apertures. A channel electron multiplier is used for ion counting.

The quadrupole power supply (Sciex API III, Concord, ON, Canada) is operated at 1.0 MHz. Auxiliary quadrupole excitation, generated by a function generator (DS345, Stanford Research Systems, Sunnyvale, CA, USA) is added to the main rf voltage with a circuit described previously [21] which allows both the dc and rf voltages from the quadrupole power supply to be applied to the quadrupole electrodes. For all the measurements here, the positive dc was applied to the rods, unless otherwise stated. The quadrupole excitation and the main rf quadrupole power supply are not phase locked.

Typical voltage settings are sprayer +4.3 kV, curtain plate +500 V, orifice 160 V, Q0 dc offset +110 V, inter-quadrupole lens Q0/Q1 +92 V, Q1 dc offset 107 V, first exit lens -30 V, and second exit lens -150 V. The transmissions given are 100 × the ion count rate at a given m/z, because one hundred scans were summed to give a spectrum. Resolution is defined as \( R_{1/2} = (m/z)/\Delta(m/z)_{1/2} \), where \( \Delta(m/z)_{1/2} \) is taken as the full width at half maximum of a peak. With
reserpine ions, the resolutions given are calculated at $m/z = 609$. A scan step size of 0.1 Th was used to obtain the mass spectra presented here, unless otherwise stated.

4.3.2 Quadrupoles

Linear quadrupole rod sets with 4% added hexapole fields with $r_0 = 4.5$ mm were constructed by rotating the two $y$ rods of a quadrupole towards an $x$ rod through an angle, $\theta$, of 2.56°. Rod set 4A has equal diameter rods. Rod set 4B has the $x$ rods greater in diameter than the $y$ rods to remove an added octopole field [12]. The diameters of the electrodes, and the amplitudes of multipoles up to $A_{10}$ for these quadrupoles, calculated in a coordinate system centered at the field center [12], are listed in Table 4.1. The third quadrupole is a conventional round rod quadrupole with $r_0 = 4.17$ mm and a rod radius $R = 1.125r_0$. All the quadrupoles have a length of 200 mm.

4.3.3 Reagents

Reserpine (50 µM), (Sigma, St. Louis, MO, USA), was prepared in 50% methanol /50% deionized water/0.3% acetic acid. Methanol, acetonitrile, and acetic acid were from Fisher Scientific (Nepean, ON, Canada). Glacial acetic acid was from Aldrich (Oakville, ON, Canada). UHP-grade nitrogen, used as the curtain gas, was from Praxair (Vancouver, BC, Canada).
Table 4.1 The dimensionless amplitudes of the multipoles for quadrupoles with 4% added hexapole fields, $R_y/r_0 = 1.1487$, $r_0 = 4.5$ mm.

<table>
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<tr>
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<th>4B</th>
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<tr>
<td>$A_3/A_2$</td>
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<td>0.04</td>
</tr>
<tr>
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<td>1.014</td>
</tr>
<tr>
<td>$\theta$</td>
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<td>0.001193</td>
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<td>0.000000</td>
</tr>
<tr>
<td>$A_2$</td>
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<td>1.004006</td>
</tr>
<tr>
<td>$A_3$</td>
<td>0.039715</td>
<td>0.039730</td>
</tr>
<tr>
<td>$A_4$</td>
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<td>0.000084</td>
</tr>
<tr>
<td>$A_5$</td>
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</tr>
<tr>
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</tr>
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</tr>
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</tr>
<tr>
<td>$A_{10}$</td>
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<td>-0.002419</td>
</tr>
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4.4 Results and Discussion

4.4.1 Quadrupoles with 4% Added Hexapole Fields

Conventional mass analysis with quadrupoles 4A and 4B is possible [14, 22], provided that the positive dc is applied to the \( x \) rods, so that the Mathieu parameter \( a > 0 \). Quadrupole 4A gives peak shapes similar to those of a conventional round-rod quadrupole at resolutions from about 850 to 1800. At resolutions lower than 850, peak splitting is observed. With quadrupole 4B, resolution up to 2000 is possible, but there is a low mass tail at higher resolution and peak structure at intermediate resolution.

4.4.2 High Excitation Frequencies

Stability islands can be formed with different excitation frequencies. Both high (\( \nu \approx 1 \)) and low excitation frequencies (\( \nu \leq 1/10 \)) were investigated. With \( \nu = 9/10 \), there can be a maximum of nine unstable bands along the iso-\( \beta \) lines for motion in each of the \( x \) and \( y \) directions [25].

The left column of Figure 4.2, i.e. Figures 4.2(a) to 4.2(d), shows peak shapes obtained with quadrupole 4A with conventional mass analysis and with operation with islands of stability. Figure 4.2(a) shows the peak shape with \( R_{1/2} = 1720 \), obtained with conventional operation. This is close to the highest resolution obtained with this rod set. There is minor tailing on the high mass sides of the peaks. Figures 4.2(b) to 4.2(d) show peak shapes with the same quadrupole with mass analysis with islands of stability formed with three different excitation frequencies. These peaks have resolutions, \( R_{1/2} = 2140, 2140, \) and \( 1920 \), respectively, all higher than that obtained with conventional mass analysis, Figure 4.2(a).
With excitation frequencies of $v = 19/20$ as in Figure 4.2(c) and $v = 21/20$ as in 2(d), the tails on the high mass side are removed and consequently the isotopic peaks are baseline resolved. The transmission with $v = 9/10$ in Figure 4.2(b) is comparable to that with conventional mass analysis with this rod set. For excitation frequencies of $v = 19/20$ and $v = 21/20$, the transmission is reduced by a factor of ca. $\times 4$. This is likely a result of the smaller stability islands under these excitation frequencies, as discussed below for low frequency excitation.

The right column of Figure 4.2, i.e. Figures 4.2(e) to 4.2(h), shows peak shapes obtained with quadrupole 4B with conventional mass analysis and with mass analysis with operation in islands of stability. The pairs of Figures in each row of Figure 4.2 were obtained with the same operating conditions. The minor difference in the excitation amplitudes for the two spectra of each pair is the result of their being taken two years apart. Figure 4.2(e) shows the peak shape with a resolution of $R_{1/2} = 1560$ obtained without auxiliary quadrupole excitation. There are unacceptable tails on the low mass sides of the peaks. With mass analysis with islands of stability Figures 4.2(f), 4.2(g), and 4.2(h) the resolution is increased to $R_{1/2} = 1820, 2450$ and 2350 respectively. Transmissions are increased by factors of ca. $f$ 26 $(g) 1.6$, and $(h) 3.2$ when compared to that obtained with conventional operation (Figure 4.2(e)). With mass analysis in islands of stability, in all cases the tails on the lower mass sides are removed. For excitation frequencies $(g) v = 19/20$ and $(h) v = 21/20$, the isotopic peaks are baseline resolved.
Figure 4.2 Mass spectra of protonated reserpine ions with quadrupoles 4A (left column) and 4B (right column). Quadrupole 4A: (a) conventional mass analysis, transmission \(1.51 \times 10^5\); (b) operation at the upper tip of island A, \(v = 9/10, q' \approx 0.028\), transmission \(1.29 \times 10^5\); (c) upper tip of island A, \(v = 19/20, q' \approx 0.018\), transmission \(4.11 \times 10^4\); (d) upper tip of island B, \(v = 21/20, q' \approx 0.013\), transmission \(4.10 \times 10^4\). Quadrupole 4B: (e) conventional mass analysis, transmission \(1.2 \times 10^4\); (f) upper tip of island A, \(v = 9/10, q' \approx 0.030\), transmission \(3.19 \times 10^5\); (g) upper tip of island A, \(v = 19/20, q' \approx 0.021\), transmission \(1.92 \times 10^4\); (h) upper tip of island B, \(v = 21/20, q' \approx 0.010, 3.8 \times 10^4\).
### 4.4.3 Low Excitation Frequencies

Low excitation frequencies, \( \nu = 3/40, 1/20, \) and \( 1/30, (75 \text{ kHz}, 50 \text{ kHz}, 33.3 \text{ kHz} \) respectively), were investigated. Some of the spectra are shown in Figure 4.3. With these frequencies peak tails are also eliminated and the isotopic peaks are baseline resolved. The left column of Figure 4.3, i.e. Figures 4.3(a) to (d), shows spectra obtained with quadrupole 4A. In comparison to conventional mass analysis with the same quadrupole (Fig. 4.2(a)), the spectra obtained with islands with frequencies (a) \( \nu = 1/10, (b) \nu = 1/15, \) (c) \( \nu = 1/20, \) and (d) \( \nu = 1/30 \) all have peaks free of structure and tailing, and are baseline resolved. The resolutions are \( R_{1/2} = 1740, 1940, 1960, \) and \( 2580 \) at \( \nu = 1/10, 1/15, 1/20 \) and \( 1/30, \) respectively. In addition, the transmission is changed by (a) \( \times 2, \) (b) \( \times 1/7 \) (c) \( \times 1, \) and (d) \( \times 1.4 \) compared to Figure 4.2(a).

The right column of Figure 4.3, i.e. Figures 4.3(e) to (h), shows mass spectra obtained with quadrupole 4B with mass analysis with islands of stability formed with the same low excitation frequencies used for quadrupole 4A. The pairs of Figures in each row of Figure 4.3 were obtained with the same \( \nu \) and \( q'. \) In comparison with conventional mass analysis with the same quadrupole (Fig. 4.2(e)), all the spectra obtained with mass analysis in islands of stability for frequencies (e) \( \nu = 1/10, \) (f) \( \nu = 1/15, \) (g) \( \nu = 1/20, \) and (h) \( \nu = 1/30 \) are baseline resolved and the tails on the low mass sides are removed. Higher resolutions are obtained for \( \nu = 1/20 \) \( (R_{1/2} = 2720) \) and \( \nu = 1/30 \) \( (R_{1/2} = 2950) \). In addition, increases in transmission of 4(e) \( \times 12 \) 4(f) \( \times 2.6 \) , 4(g) \( \times 17, \) and 4(h) \( \times 14 \) were observed in comparison with Figure 4.2(e).
Rod set 4B also produced considerable structure on the peaks when operated at low to intermediate resolutions of 300 to 1200. It was found that when the island formed with \( \nu = 1/10 \), \( q' \approx 0.012 \) was used for mass analysis, all structure at low and intermediate resolution was removed, and the transmission increased by up to a factor of ten (data not shown). There was slight tailing on the high mass sides of the peaks.

The mass spectra of Figure 4.2 and Figure 4.3 show that mass analysis with islands of stability removes peak structure and tails on peaks caused by the higher order multipoles added to the potential of quadrupoles 4A and 4B. Comparison of the results with high and low frequencies shows that low frequency excitation tends to give higher resolution, especially when \( \nu < 1/10 \). To obtain a mass spectrum with the same or higher resolution, the required excitation strength \( q' \) is much lower with low frequency excitation than with high frequency excitation. For example with quadrupole 4B, with excitation at \( \nu = 9/10 \) (900 kHz), \( q' \approx 0.030 \) is needed for the spectrum in Figure 4.2(f) (resolution \( R_{1/2} = 1820 \), high mass tails), while for excitation at \( \nu = 1/30 \) (33.3 kHz), \( q' \approx 0.003 \) only is needed to obtain the spectrum in Figure 4.3(h) (resolution \( R_{1/2} = 2950 \), no tails).
Figure 4.3 Mass spectra of protonated reserpine ions with quadrupoles 4A (left column) and 4B (right column) obtained with mass analysis with islands of stability operated at the uppermost island. Quadrupole 4A: (a) \( \nu = 1/10, q' \approx 0.011, 3.06 \times 10^5 \); (b) \( \nu = 1/15, q' \approx 0.008, \) transmission \( 2.26 \times 10^4 \); (c) \( \nu = 1/20, q' \approx 0.006, \) transmission \( 1.34 \times 10^5 \); (d) \( \nu = 1/30, q' \approx 0.003, \) transmission \( 1.05 \times 10^5 \). Quadrupole 4B: (e) \( \nu = 1/10, q' \approx 0.011, \) transmission \( 1.34 \times 10^5 \); (f) \( \nu = 1/15, q' \approx 0.008, \) transmission \( 3.11 \times 10^4 \); (g) excitation
\( \nu = 1/20, q' \approx 0.009, \) transmission \( 1.98 \times 10^5; \) (d) upper tip of island B, \( \nu = 1/30, q' \approx 0.003, \) transmission \( 1.68 \times 10^5. \)

### 4.4.4 Transmission vs. Resolution

With conventional mass analysis, quadrupoles 4A and 4B gave lower transmission over the range of achievable resolutions in comparison to a conventional quadrupole operated under the same conditions. As shown above, it is possible to improve peak shape, resolution, and, in some cases, transmission, when quadrupoles 4A and 4B are operated in islands of stability. When the size of an island is relatively large, e.g. those formed at an excitation frequency of \( \nu = 9/10, \) the overall transmission tends to be higher while the improvements in the peak shape and resolution are less than that in the case of a smaller/narrower island formed at a low excitation frequency, e.g. \( \nu = 1/30. \) When a smaller/ narrower island is used, however, only a limited range of resolution can be achieved by adjusting the slope of a scan line.

In order to illustrate the general trend of transmission versus resolution of quadrupoles 4A and 4B when operated with islands, in comparison to conventional mass analysis, a compromise between the size of an island and the attainable resolutions has to be made. We choose an excitation frequency of \( \nu = 1/10 \) and excitation strength of \( q' \approx 0.012. \) With these conditions, Figure 4.4 shows the ion transmission versus resolution for a conventional quadrupole with conventional mass analysis, and quadrupoles 4A (in Figure 4.4(a)) and 4B (in Figure 4.4(b)) operated at the upper and lower tips of island A, and the upper tip of island B. With conventional mass analysis and mass analysis using the stability island with \( \nu = 1/10 \) and \( q' = 0.012, \) the transmission of these quadrupoles with added hexapole fields is lower than that of a conventional quadrupole. For instance,
at a resolution of 1000, the transmission at the upper tip of island B of quadrupole 4B is 7 times lower than that of a conventional quadrupole. The transmission of both quadrupoles 4A and 4B operated with islands are comparable to those without islands. This result, and the experimental observation of increased transmission under some conditions with mass analysis using islands of stability, suggests the use of islands is not the reason for the lower transmission, at least with these operating conditions.

Figure 4.4 Transmission versus resolution for a conventional quadrupole and quadrupoles with added 4% hexapole fields (a) 4A (b) 4B. Curve 1, the conventional quadrupole operated without stability islands. Curve 2, open triangles, quadrupoles 4A or 4B operated without islands. Curves 3, 4, 5, solid symbols, quadrupole 4A or 4B operated at the upper and lower tips of island A and upper tip of island B, as labeled. The islands are formed with $\nu = \frac{1}{10} \text{ (100 kHz)}$ and $q' \approx 0.012$. The resolution was changed by varying the slopes of the scan lines.
The effect of stability island size on the ion transmission was also investigated. Experimentally, it is observed that for a given quadrupole at a fixed excitation frequency, the island size decreases with increasing excitation strength. We also observe that as the size of an island decreases, the transmission decreases. When a scan line crosses the widest part of an island, the transmission is highest. For example, for quadrupole 4A at an excitation frequency of \( \nu = 1/10 \), the highest transmission in island A is reduced from \( 3.09 \times 10^7 \) (corresponding to \( R_{1/2} = 150 \)) to \( 2.05 \times 10^6 \) (corresponding to \( R_{1/2} = 300 \)) when the excitation strength is changed from \( q' \approx 0.011 \) to \( q' \approx 0.018 \). Note for each of these two excitation amplitudes, the slope of the scan line is chosen to give the highest ion transmission in each case. These slopes differ. This result is consistent with the computer simulations of island formation with an ideal quadrupole field, reported in [18].
4.4.5 Quadrupoles with a 4% Added Hexapole Field with $\alpha < 0$

With the positive resolving dc applied to the two shifted $y$-rods, so that the Mathieu parameter $\alpha < 0$, conventional mass analysis with quadrupoles 4A and 4B gives only low resolution. As shown in Figure 4.5(a), the mass spectrum of quadrupole 4A has a resolution of about 80; while in Figure 4.5(c), the mass spectrum of quadrupole 4B has a resolution of 84. Attempts to increase the resolution by increasing the slope of the scan line resulted only in losses of signal, with no increases in resolution. In both cases the stability boundaries are not well defined. This is reflected in the existence of small broad peaks on both the high and low mass sides adjacent to the main peaks. For both quadrupoles, mass analysis with islands of stability can greatly improve the resolution. Figure 4.5(b) shows a mass spectrum obtained with quadrupole 4A operated at the upper tip of island A. The islands are formed with $\nu = 1/20$ and $q' \approx 0.012$. The resolution is $R_{1/2} = 1180$, about 15 times higher than that of the mass spectrum in Figure 4.5(a); while the transmission in Figure 4.5(b) is only marginally lower than Figure 4.5(a). Figure 4.5(d) shows a mass spectrum obtained with quadrupole 4B operated at the upper tip of island A, formed with $\nu = 1/20$ and $q' \approx 0.009$. The resolution is about $R_{1/2} = 840$, 10 times greater than with conventional analysis (Figure 4.7(c)). However, in this case the transmission is 6 times lower than that with conventional operation, Figure 4.5(c). Thus with rod sets 4A and 4B, when $\alpha < 0$, the use of an island of stability helps to overcome the adverse effects of the added multipole fields, as was seen with a quadrupole with an added octopole field [20, 21].

Mass analysis with $\alpha < 0$ and islands of stability formed with other excitation frequencies, $\nu = 9/10, 19/20, 21/20, 1/10, 1/15, 3/40$ and $1/30$, was also investigated.
Although the resolution in each case was increased, compared to the resolution with conventional analysis, none gave resolution or transmission higher than those seen in Figures 4.5(b) and (d).

![Mass spectra of protonated reserpine ions with quadrupoles 4A and 4B](image)

Figure 4.5 Mass spectra of protonated reserpine ions with quadrupoles 4A (left column) and 4B (right column) obtained with mass analysis with islands of stability operated at the upper tip of island A. The positive resolving dc is applied to the $y$-rods so that the Mathieu parameter $\alpha < 0$. Quadrupole 4A: (a) conventional mass analysis, transmission $5.02 \times 10^4$; the scan step size is 0.5 Th; (b) $\nu = 1/20$, $q' \approx 0.012$, transmission $4.09 \times 10^4$. Quadrupole 4B: (c) conventional mass analysis, transmission $1.31 \times 10^5$; the scan step size is 0.5 Th; (d) $\nu = 1/20$, $q' \approx 0.009$, transmission $2.21 \times 10^4$. 

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**4.4.6 Conventional Round Rod Quadrupole**

The conventional quadrupole used here has a limiting resolution of about 2500. The quadrupole apparently has been slightly damaged. At a resolution of $R_{1/2} = 1000$, the transmission is about 1/17 of that at resolutions less than about 200; at $R_{1/2} = 1000$, the transmission is about 1/100 of that at low resolutions. The effects of mass analysis with an island of stability were investigated for this quadrupole. The results are shown in Figure 4.8. The use of a stability island greatly improves the transmission at resolutions above 500, as evidenced by curves 2, 3, and 4 in Figure 4.8. With $\nu = 9/10$ and $q' \approx 0.004$ (curve 4), the transmission remains constant up to at least $R_{1/2} \approx 1000$. At $R_{1/2} = 2000$ the transmission is still more than half of that at $R_{1/2} = 200$. Resolutions $R_{1/2} > 3000$ were also possible. At $R_{1/2} = 2500$, mass analysis in islands of stability increased the transmission by up to two orders of magnitude in comparison with that obtained without islands.

With other excitation conditions, $\nu = 1/10$ and $q' \approx 0.011$, a mass spectrum with a resolution of $R_{1/2} = 4360$ was obtained, indicating that the limiting resolution can be increased by using an island of stability. At this resolution, the transmission is about 1/220 of that at low resolutions, about the same as that obtained by mass analysis without stability with the same quadrupole at its limiting resolution of 2500. In addition to the improvements in transmission, mass analysis in islands of stability with this quadrupole gives sharper peaks at the baseline in contrast to the mild tails of the peaks obtained with the same quadrupole with conventional mass analysis without stability islands, consistent with [16].
Figure 4.6 Transmission versus resolution for a conventional quadrupole. Curve 1, mass analysis without stability islands; Curves 2, 3, and 4, mass analysis at the upper tip of island A formed with $\nu = 1/10$ and $q' \approx 0.007$ for line 2, $\nu = 1/15$ and $q' \approx 0.003$ for line 3 and, $\nu = 9/10$ and $q' \approx 0.009$ for line 4. The resolution was changed by varying the slopes of the scan lines.
4.5 Summary

Mass analysis using islands of stability was investigated for linear quadrupoles with 4%, 8% and 12% added hexapole fields constructed from equal and unequal diameter rods. With $a > 0$, both high and low frequency excitation produce stability islands in which improved resolution, peak shape, and transmission are possible. Resolutions up to 3000 were obtained. With $a < 0$, an increase of a factor of 10 or more in resolution is possible with mass analysis using islands of stability. A conventional quadrupole also showed improved performance when operated with islands of stability. Apparently the stability boundaries formed by quadrupole excitation are more suited to mass analysis than the conventional boundaries when quadrupoles have distorted fields. It appears that the use of islands of stability generally provides an improved method of mass analysis for quadrupoles with field distortions. In future, this may allow the use of quadrupoles with at least some lower mechanical tolerances and hence lower cost.
4.6 References


5 Overcoming Field Imperfections of Quadrupole Mass Filters with Mass Analysis in Islands of Stability*

* A version of this chapter has been published.
5.1 Introduction

Linear quadrupoles are widely used in mass spectrometry as ion guides [1, 2], linear ion traps [1], and mass filters [2]. For mass analysis, a linear quadrupole can be operated conventionally with dc and radiofrequency (rf) voltages applied between the rod pairs [3], with axial ejection of ions [4, 5], or with mass analysis with islands of stability [6-10]. For mass analysis with islands of stability, auxiliary quadrupole or other parametric excitation is added to the quadrupole field. Ions that are resonant with the excitation are ejected from the quadrupole. A stability region splits into bands of instability and islands of stability [6-10]. The tip of an island of stability can be used for mass analysis just as conventional mass analysis uses the tip of a stability region.

The literature emphasizes the need to construct quadrupole mass filters to high precision to minimize field distortions [11-14]. With field distortions the quadrupole does not have a pure quadrupole field, and the potential $\Phi(x, y, t)$, is described by a superposition of multipoles or spatial harmonics, $\phi_N$,

$$
\Phi(x, y, t) = \varphi(t) \sum_{N=0}^{\infty} A_N \phi_N(x, y)
$$

where $A_N$ is the dimensionless amplitude of the multipole $\phi_N(x, y)$ and $\varphi(t)$ is an applied time-dependent potential. It has been believed that the amplitudes of multipoles with $N > 2$ (the quadrupole term) should be less than about $10^{-3}$. This generally requires constructing rod sets to micron tolerances [12,14]. Field imperfections can cause
structure or tails on peaks, limit the resolution, and decrease the transmission of a quadrupole mass filter.

In some cases it is desirable to add higher multipoles to the field of a linear quadrupole. If the quadrupole is used as a linear trap, ions of a given \( m/z \) can be isolated and then excited at their resonant frequencies in the presence of gas to cause fragmentation. In the excitation process there is a competition between ion ejection and ion fragmentation. The addition of higher multipoles causes the frequency of ion oscillation to change with oscillation amplitude. As ions are excited, their oscillation frequencies shift, and their motion becomes out of phase with the excitation. The net effect is that it is more difficult to eject ions from the trap and fragmentation efficiencies can be increased [15-17]. Michaud et al. [15] have shown that a linear quadrupole with a 4\% added octopole field (i.e. \( A_4/A_2 = 0.04 \)) can give substantially higher fragmentation yields than a conventional quadrupole, particularly at pressures less than about 10\(^{-4}\) Torr (N2).

An octopole field can be added to a linear quadrupole by making one rod pair greater in diameter than the other rod pair, while keeping the rods equally spaced from the central axis [18]. Ding et al. investigated the use of linear quadrupoles with added octopole fields of 2.0 and 2.6\% for conventional mass analysis [19]. The mechanical distortions of the rods were much greater than usually attributed to manufacturing or construction errors. For example the ratios of the radii of the \( x \) and \( y \) rods, \( R_x \) and \( R_y \) respectively, to the field radius, \( r_0 \), for the quadrupole with 2.6\% added octopole field were \( R_x/r_0 = 1.000 \) and \( R_y/r_0 = 1.300 \); for the field radius \( r_0 = 4.50 \) mm, the \( y \) rods
were 2.30 mm greater in diameter than the $x$ rods. Nevertheless conventional mass analysis was possible provided the positive resolving dc was applied to the smaller rod pair, to give a Mathieu parameter $a > 0$. If the positive dc was applied to the larger rods, only very low resolution and poor transmission were possible. The added octopole field prevents conventional mass analysis in this case. However computer modeling [8] and experiments [10] have shown that with the use of an island of stability, even with $a < 0$, peak shape and resolution comparable to those obtained when $a > 0$ were possible. Thus use of an island of stability for mass analysis overcomes the deleterious effects of the added octopole field.

It is expected that the fragmentation efficiency of ions can also be increased by addition of a hexapole field to a linear quadrupole. To investigate this, we have constructed quadrupoles with added hexapole fields of 4% to 12% (i.e. $A_3/A_2 = 0.04$-$0.12$). The hexapole field is added by rotating the two $y$ rods toward a $x$ rod [20]. Other higher multipoles are also added to the potential, notably an octopole field, which can be removed by making the $x$ rods larger in diameter than the $y$ rods [20]. These rod sets have severely distorted quadrupole fields, with a mix of both even and odd higher harmonics. They allow us to evaluate the performance of rod sets with strong geometric and field distortions as mass filters. Six rod sets are used in this work: three with hexapole fields of 4%, 8% and 12% constructed with equal diameter rods, and three with hexapole fields of 4%, 8% and 12% with unequal diameter rods to minimize the octopole field. Computer simulations suggest that removing the octopole field improves resolution, transmission and peak shape with conventional mass analysis [20]. We show that with conventional mass analysis the transmission, resolution and peak shapes are relatively
poor in comparison to a conventional rod set. However, the use of islands of stability dramatically improves the resolution and peak shape, and in some cases ion transmission, suggesting that mass analysis with islands stability may provide a method to overcome a wide range of field imperfections in linear quadrupole mass filters.
5.2 Experimental Section

5.2.1 Island Formation

Islands of stability are formed by applying auxiliary quadrupole excitation so that in equation (5.1)

\[ \varphi(t) = U - V_{rf} \cos \Omega t - V' \cos(\omega_{ex} t - \gamma) \] (5.2)

Where \( \Omega \) is the angular frequency of the main rf voltage applied between rod pairs, \( V_{rf} \) is the zero to peak rf amplitude applied pole to ground, \( V' \) is the amplitude of the auxiliary excitation voltage, \( \omega_{ex} \) is the angular frequency of the excitation voltage, \( \gamma \) is the phase of the excitation, taken to be zero in what follows, and \( t \) is time. The ion motion can be described in terms of the following parameters

\[ a = \frac{8zeU}{m\Omega^2 r_0^2} ; \quad q = \frac{4zeV_{rf}}{m\Omega^2 r_0^2} ; \quad q' = \frac{4zeV'A_2}{m\Omega^2 r_0^2} = q \frac{V'}{V_{rf}} \] (5.3)

Where \( e \) is the electron charge, \( z \) is the number of charges on an ion, \( m \) is the ion mass, and \( r_0 \) is the field radius of the quadrupole. The parameters \( a \) and \( q \) are the well known Mathieu parameters used to define the stability regions of a linear quadrupole [3].

With quadrupole excitation, ions are excited when the excitation frequency is

\[ \omega_{ex} = |l + \beta_u| \frac{\Omega}{K} \] (5.4)

Where \( u \) is \( x \) or \( y \), \( \beta_u \) is determined by \( a \) and \( q \) [3], \( K = 1, 2, 3 \ldots \) and

\( l = 0, \pm 1, \pm 2, \pm 3 \ldots [21,22] \) To form islands, the excitation frequency is applied at a
rational fraction of the main quadrupole frequency so \( \omega_{ex} = \nu \Omega \), with \( \nu = Q/P \) where \( Q \) and \( P \) are integers. Ions that are resonant with the excitation are ejected from the quadrupole and the stability region splits into \( P - 1 \) bands of instability for the \( x \) and for the \( y \) motion to form "islands" of stability [6-10, 23].

In this work we use relatively low values of \( \nu \). As an example, the bands of instability and islands of stability of the first stability region, calculated as in reference [8], with \( \nu = 1/15, q' = 0.010 \) and with \( \nu = 3/40, q' = 0.020 \) are shown in Figures 5.1a and 5.1b respectively. Scan lines with slopes \( \lambda = U/V \) are also shown. With these operating conditions an island of stability can be so narrow that ions are not transmitted. The left most band of stability in Figure 5.1b is one such example.

![Figure 5.1](image_url)

Figure 5.1 The first stability region (the triangle in solid lines) and the stability islands (shaded regions) of an ideal quadrupole for excitation frequencies (a) \( \nu = 1/15, q' = 0.010 \); (b) \( \nu = 3/40, q' = 0.020 \).
5.2.2 Rod Sets

The geometries of the six quadrupole rod sets used are shown in Table 5.1. Nominal hexapole fields of 4%, 8% and 12% were added by rotating the y rods toward an x rod through angles $\theta$ of 2.56°, 5.13°, and 7.69° respectively. The field radius, $r_0$, of the quadrupoles with added hexapole fields was 4.50 mm. The rod sets 4A, 8A and 12A have equal diameter x and y rods with radii $R_x = R_y = 1.1487r_0$, and the rod sets 4B, 8B and 12B have x rods greater in diameter than the y rods to minimize the octopole field [20]. In comparison to a conventional round-rod quadrupole, these rod sets have very distorted geometries. Figure 5.2 shows a photograph of rod set 12B. A conventional round-rod quadrupole rod set (Sciex, Concord, ON, Canada) with $r_0 = 4.17$ mm, and ratio of rod radius to field radius $r/r_0 = 1.247$ was also used for comparison. All the quadrupoles are 200 mm long.

All rod sets contain additional higher multipole fields, although with lower amplitudes than the hexapole field. Table 5.2 shows the multipole amplitudes. With an added hexapole field, the centre of the field is shifted a distance $x_0$ toward an x rod by 0.0702 to 0.2102 mm ($1.56x10^{-2} r_0$ to $4.67x10^{-2} r_0$) [20]. This shift is small compared the aperture in the entrance lens (1.5 mm radius, $0.33r_0$). The rod sets were mounted in cylindrical cases with the field center at the center of the case. The multipole amplitudes of Table 5.2 were calculated in a co-ordinate system centered at the field center [20].
Table 5.1 Geometries and dimensions of the rod sets used.

<table>
<thead>
<tr>
<th>Set</th>
<th>% $A_3$</th>
<th>$\theta$ (degrees)</th>
<th>$R_x$ (mm)</th>
<th>$R_y$ (mm)</th>
<th>$x_0$(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A</td>
<td>4</td>
<td>2.56</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8A</td>
<td>8</td>
<td>5.13</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12A</td>
<td>12</td>
<td>7.69</td>
<td>5.1692</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>4B</td>
<td>4</td>
<td>2.56</td>
<td>5.2425</td>
<td>5.1692</td>
<td>0.0702</td>
</tr>
<tr>
<td>8B</td>
<td>8</td>
<td>5.13</td>
<td>5.4945</td>
<td>5.1692</td>
<td>0.1409</td>
</tr>
<tr>
<td>12B</td>
<td>12</td>
<td>7.69</td>
<td>5.9378</td>
<td>5.1692</td>
<td>0.2102</td>
</tr>
<tr>
<td>conventional</td>
<td>0</td>
<td>0</td>
<td>4.690</td>
<td>4.690</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 5.2 Photograph of quadrupole rod set 12B with a 12% added hexapole field, $r_0 = 4.50$ mm, a rotation angle $\theta = 7.69^\circ$, $R_y = 5.1692$ mm and $R_x = 5.937$ mm.
Table 5.2 Multipole amplitudes of the rod sets.

<table>
<thead>
<tr>
<th></th>
<th>4A</th>
<th>4B</th>
<th>8A</th>
<th>8B</th>
<th>12A</th>
<th>12B</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_0$</td>
<td>-0.00022</td>
<td>0.00119</td>
<td>-0.00088</td>
<td>0.00514</td>
<td>-0.00198</td>
<td>0.01143</td>
</tr>
<tr>
<td>$A_1$</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>$A_2$</td>
<td>1.0035</td>
<td>1.00401</td>
<td>1.00497</td>
<td>1.00719</td>
<td>1.00745</td>
<td>1.01232</td>
</tr>
<tr>
<td>$A_3$</td>
<td>0.03871</td>
<td>0.03973</td>
<td>0.07981</td>
<td>0.07990</td>
<td>0.12020</td>
<td>0.12052</td>
</tr>
<tr>
<td>$A_4$</td>
<td>0.00147</td>
<td>0.00009</td>
<td>0.00592</td>
<td>-0.00002</td>
<td>0.013386</td>
<td>0.00000</td>
</tr>
<tr>
<td>$A_5$</td>
<td>-0.00712</td>
<td>-0.00723</td>
<td>-0.01398</td>
<td>-0.01495</td>
<td>-0.02025</td>
<td>-0.02353</td>
</tr>
<tr>
<td>$A_6$</td>
<td>-0.00010</td>
<td>-0.00153</td>
<td>-0.00329</td>
<td>-0.00564</td>
<td>-0.007063</td>
<td>-0.01254</td>
</tr>
<tr>
<td>$A_7$</td>
<td>-0.00121</td>
<td>-0.00125</td>
<td>-0.00277</td>
<td>-0.00308</td>
<td>-0.00501</td>
<td>-0.006051</td>
</tr>
<tr>
<td>$A_8$</td>
<td>-0.00008</td>
<td>-0.00012</td>
<td>-0.000349</td>
<td>-0.00052</td>
<td>-0.00094</td>
<td>-0.00126</td>
</tr>
<tr>
<td>$A_9$</td>
<td>0.00006</td>
<td>0.00007</td>
<td>0.00012</td>
<td>0.00023</td>
<td>0.00017</td>
<td>0.00058</td>
</tr>
<tr>
<td>$A_{10}$</td>
<td>-0.00242</td>
<td>-0.00227</td>
<td>-0.00230</td>
<td>-0.00227</td>
<td>-0.00208</td>
<td>-0.00187</td>
</tr>
</tbody>
</table>

5.2.3 Apparatus

All experiments were done with an electrospray single quadrupole system described previously [10]. Ions formed by electrospray (+4.3 kV) pass through an aperture in a curtain plate (+500 V), a dry nitrogen curtain gas (UHP grade, Praxair, Vancouver), and then through a 0.12 mm diameter orifice (+160 V) into a chamber containing a quadrupole ion guide Q0 (rod offset +110 V) operated at 4.6x10^{-3} Torr (N2). Short rf only rods were not used at the entrance to the mass filter.. Ions leaving Q0 pass through a
3.0 mm diameter aperture in an entrance lens (+92 V) and enter the quadrupole mass filter, Q1 (rod offset +107 V, $1.2 \times 10^{-5}$ 1.2 Torr). Ion counting is used for ion detection.

The quadrupole power supply (Sciex API3, Sciex, Concord, Ontario) was operated at 1.00 MHz. The auxiliary quadrupole excitation voltage, generated by a function generator (SRS DS345, Stanford Research Systems, Sunnyvale, CA) was added to the main rf voltage with a circuit that allowed the application of both the dc and rf voltages of the main quadrupole power supply to the quadrupole [10]. The main quadrupole rf and the excitation were not phase locked and the phase difference between the main rf and excitation could not be adjusted.

Reserpine (Sigma, St. Louis, MO) was 50 M in 50% methanol/50% water/0.3% acetic acid. Methanol and acetic acid were from Fisher Scientific (Nepean, ON). Acetic acid was from Aldrich (Oakville, ON).
5.3 Results and Discussion

5.3.1 T vs. R with Quadrupoles with a 8% and 12% Added Hexapole Field

Figure 5.3 shows peak shapes obtained with conventional mass analysis of protonated reserpine ions with all six rod sets. For these spectra, the positive resolving dc was applied to the x rods. If the positive dc is applied to the y rods, only very low resolution (ca. 100) is possible and the transmission is very low, as seen in computer simulations [20]. As the amplitude of the hexapole increases from 4% to 8% and 12% the resolution decreases. Rod sets 4A and 4B give the highest resolution. The rod set 4B, however, shows tails on the low mass sides of the peaks. These were not seen in computer simulations, possibly because of the much smaller spatial spread of the ions used in the simulation (0.002r₀ in the simulations; 0.33r₀ in the experiments) The transmissions of rod sets 4A and 4B are about 8 and 80 times lower, respectively, than a conventional rod set operated at the same resolution. With the rod sets with 8% and 12% hexapole fields and equal diameter rods (8A, 12A) the best resolution obtained is relatively low. The nominal resolutions at half height are about 370 and 200 respectively, although this includes contributions from the isotopic peaks which are not resolved. The transmission of rod sets 8A and 12A at these low resolutions is 100 to 1000 less than a conventional rod set. The rod sets with unequal diameter rods give higher resolution, about 1560, 1740 and 920 at half height for the rod sets with 4%, 8% and 12% hexapole fields respectively. The isotopic peaks can be resolved. This is in accord with computer simulations that show that removing the octopole field improves peak shapes at low and high resolution, although there is still structure on the peaks at intermediate resolution [20]. With rod set 8B the isotopic peaks are resolved, but there are unacceptably long tails on both the low
and high mass sides of the peak. The transmission is about 1.4 times less than a
conventional rod set operated at this resolution. With rod set 12B, the isotopic peaks can
just be resolved. The transmission of the rod sets is about 250 times less than a
conventional quadrupole. A full description of conventional mass analysis with these
quadrupoles with added hexapole fields of 4% - 12% is in preparation [24].

Figure 5.3 Conventional mass analysis (i.e. without islands of stability) for linear
quadrupoles (a) 4A, 4% hexapole with equal diameter rods, transmission $1.12 \times 10^5$; (b)
8A, 8% hexapole with equal diameter rods, transmission $7.74 \times 10^5$; (c) 12A, 12%
hexapole with equal diameter rods, transmission $9.56 \times 10^4$; (d) 4B, 4% hexapole with
unequal diameter rods, transmission $1.2 \times 10^4$; (e) 8B, 8% hexapole with unequal diameter
rods, transmission $3.68 \times 10^5$; (f) 12B, 12% hexapole with unequal diameter rods, transmission $7.93 \times 10^4$.

Figure 5.4 shows the peak shapes and resolution obtained with these rod sets when operated in islands of stability, again with the positive resolving dc applied to the $x$ rods. The resolution, peak shapes and, in some cases the transmission, are greatly improved. In all cases higher resolution and peaks free of tailing on the low and high mass sides are obtained. With rod sets 4A and 4B the transmission is about the same or slightly higher ($\times 1.4$ to $\times 2$) than a conventional rod set operated at this resolution. With rod sets 8A the transmission is about 8 times less, and with rod set 8B about equal to that of a conventional rod set operated at these resolutions. These increases in sensitivity are accompanied by improvements in resolution and peak shape. With rod sets 12A and 12B the use of islands decreases sensitivity, but this is accompanied by dramatic increases in resolution. The transmission of rod sets 12A and 12B under these conditions is about 100 to 1000 times less than a conventional rod set. Apparently for these two rod sets the use of islands is not sufficient to give transmission similar to a conventional rod set. Nevertheless, the use of islands allows relatively high resolution and good peak shape despite the severely distorted geometries (Figure 5.2) and fields of these rod sets.

With our conventional rod set, the limiting resolution is about 2500. The use of islands with rod sets 4A and 4B can give resolution higher than this. Figure 5.5 shows resolutions of 2500 and 2950 obtained with rod sets 4A and 4B respectively. The higher resolution with rod set 4A was obtained by increasing $q'$ the slope of the scan line, and with rod set 4B by lowering the excitation frequency from 50 kHz to 33.33 kHz. The
transmission is about 5 times less than the same rod sets operated at the lower resolutions in Figure 5.4. Comparisons of transmission to our conventional rod set are not possible because it cannot produce this resolution.

Figure 5.4 Mass analysis in islands of stability for linear quadrupoles (a) 4A, 4% hexapole with equal diameter rods, $\nu = 1/30, q' \approx 0.003$, transmission $5.56 \times 10^5$; (b) 8A, 8% hexapole with equal diameter rods, $\nu = 1/15, q' \approx 0.009$, transmission $1.18 \times 10^5$; (c) 12A, 12% hexapole with equal diameter rods, $\nu = 3/40, q' \approx 0.028$, transmission $1.07 \times 10^4$; (d) 4B, 4% hexapole with unequal diameter rods, $\nu = 1/20, q' \approx 0.009$, transmission $8.15 \times 10^5$; (e) 8B, 8% hexapole with unequal diameter rods, $\nu = 1/15, q' \approx 0.012$, transmission $1.52 \times 10^5$; (f) 12B, 12% hexapole with unequal diameter rods, $\nu = 3/40, q' \approx 0.017$, transmission $1.02 \times 10^4$. 
The peaks in Figure 5.4 were obtained after the optimum excitation frequency and amplitude were found. The optimum frequency and excitation amplitude depend on the rod set used. Generally, lower excitation frequencies $\nu = 1/15$ and 3/40 were found to give higher resolution than higher excitation frequencies such as $\nu = 9/10$. (Frequencies tested gave $\nu = 1/30, 1/20, 1/15, 3/40, 1/10, 0.90, 0.95, 1.05$.) It is not clear which island gives these spectra. These spectra were obtained by lowering the slope of the scan line until peaks were obtained. With these low excitation frequencies, islands and bands of instability are similar to those of Figure 5.1. The island is a very narrow band of stability. For this reason only small changes in resolution were possible by changing the slope of the scan line. Scans over a broad mass range showed that the scan line did not pass through any other islands or regions of stability.

Figure 5.5 Resolution of 2580 and 2950 obtained with rod sets 4A and 4B with operation in an island of stability. The transmission is (a) $1.05 \times 10^5$ and (b) $1.68 \times 10^5$. 
5.4 Summary

Future improvements in transmission might be obtained by phase locking the excitation to the quadrupole rf at the optimum phase, or by forming islands by modulation of the resolving the dc, the rf or both the dc and rf of the quadrupole [7], or by using rectangular wave forms with amplitude modulation. Previous work has noted that use of islands of stability can be useful to overcome minor field imperfections such as the use of round rods instead of hyperbolic rods [7, 9]. The results here show that despite the very large field distortions of these quadrupoles, peak shape and resolution, and in some cases ion transmission, like that of a quadrupole mass filter with much lower field distortions are possible. This suggests that mass analysis with islands of stability may find use for correcting for a broad range of field distortions in quadrupole mass filters.
5.5 References


6 Mass Selective Axial ion Ejection from Linear Quadrupoles with Added Hexapole Fields*
6.1 Introduction

Linear quadrupoles are widely used as two-dimensional (2D) linear ion traps [1, 2, 3]. For use as an ion trap, radio frequency (rf) only voltages are applied between the rod pairs and stopping potentials are applied to electrodes at the ends of the rods. Compared to three dimensional (3D) traps, linear ion traps have reduced space charge effects due to the increased ion storage volume and higher ion injection efficiencies [1, 2].

Both mass selective radial [2] and mass selective axial ejection (MSAE) [3, 4] can be used for mass analysis of ions confined in a linear trap. For MSAE, ions are resonantly excited in the radial direction. The rf fringing fields at the quadrupole exit couple the $x$ and $y$ motions to the axial motion. Ions gain kinetic energy in the axial direction, overcome the stopping potential barrier and are ejected in the axial direction [3, 4]. The trapping rf voltage can be scanned to bring ions of different mass to charge ratios into resonance with the excitation, to produce a mass spectrum. Resolution can be improved by applying a small resolving dc voltage between the rods and a fraction of the trapping rf to the exit lens [4].

Distorting the field of a 3D quadrupole trap increases ion fragmentation efficiency for tandem mass spectrometry (MS/MS) experiments [5, 6] and can give higher resolution in ion ejection [7- 9]. The same benefits might be expected to apply to linear quadrupole ion traps. The distorted field has higher multipoles added to the potential. Methods of adding octopole [10, 11] and hexapole [12, 13] fields to a linear quadrupole have been described. Addition of octopole [14] and hexapole fields [15] has been shown to increase fragmentation efficiency in linear quadrupole traps.
Douglas and co-workers have investigated mass analysis with linear quadrupoles with added octopole fields operated as conventional mass filters [16], as mass filters with mass analysis in islands of stability [17], and as ion traps with MSAE [18]. With mass selective axial ejection a resolution of several thousand and scan speeds of at least 2000 Th/s were possible [18].

Mass analysis with linear quadrupoles with added hexapole fields has also been investigated. Linear quadrupole rod sets that have added hexapole components of 4, 8 and 12% (i.e. $A_3/A_2=0.04, 0.08$ and $0.12$) have been designed and constructed [13, 19, 20, Chapter 1]. The potential in a linear quadrupole with field distortions, especially with an added hexapole field and no other multipoles has been described in detail in [12, 13, 19]. It has been found that quadrupoles with added hexapole fields can be used for mass analysis, either operated conventionally [12, 21], or with islands of stability [20, 22]. A preliminary study of MSAE with linear quadrupoles with added hexapole fields has been reported [22]. MSAE show that some of these rod sets can produce resolutions of several thousand with scan speeds up to 4000 Th/s with MSAE [22]. In addition, the addition of a hexapole field can increase fragmentation efficiency for MS/MS [15].

In this work, we investigate axial ejection as a method of mass analysis of ions confined in a linear quadrupole trap that has an added hexapole field. The improved fragmentation efficiency of these rod sets makes them potential candidates as ion traps for performing MS/MS at low pressure. Mass analysis of the fragment ions requires MSAE.
Comparisons are made between axial ejection with quadrupoles with 4%, 8% and 12% added hexapole fields. The effects of trapping ions at different $q$ values, excitation voltage, excitation between $x$ or $y$ rods, scan direction, and quadrupole dc applied between the rods have been investigated. The highest scan speeds and resolution are obtained with excitation and ejection at high $q$ (0.73). Resolution up to $R_{1/2} = 4500$ is possible in some cases. The effects of scan speed were investigated and a resolution at half height of about 1800 is possible at scans speed up to 4000 Th/s with some of the rod sets. The oscillation frequencies of ions shift with oscillation amplitudes because of the added hexapole fields. These shifts may play a role in determining the optimal operating conditions for MSAE with these rod sets.
6.2 Experimental methods.

6.2.1 Mass Spectrometer System

The system, timing diagram and methods of acquiring spectra have been described previously [18]. Ions formed by electrospray pass through a dry N$_2$ curtain gas, a 0.125 mm diameter ion sampling orifice, a quadrupole ion guide Q0 ($8 \times 10^{-3}$ Torr, N$_2$), an interquadrupole aperture lens (3.0 mm diameter aperture) and enter a quadrupole Q1 ($3 \times 10^{-5}$ Torr), operated as an ion trap. For axial ejection experiments, a low resolving dc voltage (7.0 V pole to ground) was applied between the rods. Operating voltages for conventional mass analysis are shown in Table 6.1a. Conventional mass analysis was always done prior to axial ejection, to record the rf voltages corresponding to $m/z = 609, q = 0.706$. For MSAE, the voltages on Q0/Q1 lens and Exit lens 1 are switched between trapping values and ejection values as shown in Table 6.1b. The other voltages remain the same as shown in Table 6.1a.

Table 6.1 Operating voltages (V).

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>b</th>
</tr>
</thead>
<tbody>
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<td>+4300</td>
<td></td>
</tr>
<tr>
<td>Curtain Plate</td>
<td>+500</td>
<td></td>
</tr>
<tr>
<td>Orifice</td>
<td>+20</td>
<td></td>
</tr>
<tr>
<td>Q0 dc offset</td>
<td>+4</td>
<td></td>
</tr>
<tr>
<td>Q0/Q1 lens</td>
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<td></td>
</tr>
<tr>
<td>Q1 dc offset</td>
<td>+2.3</td>
<td></td>
</tr>
<tr>
<td>Exit lens 1</td>
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<td></td>
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<tr>
<td>Exit lens 2</td>
<td>-150</td>
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</tbody>
</table>
6.2.2 Injection and Ejection q Values

Ions were injected into the linear trap at \( q \approx 0.40 \). Ion ejection used dipole excitation at several frequencies, but mostly 300 kHz corresponding to a Mathieu stability parameter of \( q \approx 0.73 \) (quadrupole power supply frequency 1.0 MHz). Frequencies of 410 kHz, 150 kHz and 75 kHz were also used, corresponding to ejection q values of 0.87, 0.41 and 0.21 respectively. All excitation voltages \( (V_{ex}) \) are reported as zero to peak, pole to ground.

6.2.3 Rod Sets

Six rod sets, with added hexapole fields, described previously in Chapter 1 and in [12, 20, 21] were used. Three, labelled 4A, 8A and 12A had added hexapole fields of 4\%, 8\% and 12\% and equal diameter rods. Three others labelled 4B, 8B and 12B had added hexapole fields of 4\%, 8\% and 12\% and \( x \) rods greater in diameter than the \( y \) rods in order to remove and added octopole field [12]. All had the rods equally spaced 4.50 mm from the central axis and were 200 mm long.

6.2.4 Data Acquisition

Resolution is reported as \( R_{1/2} = (m/z)/\Delta(m/z)_{1/2} \) where \( (\Delta m/z)_{1/2} \) is the peak width at half height. If isotopic peaks are not resolved or if there is structure on the peaks, we refer to this as "nominal resolution". The total numbers of trapped ions are measured for calculating ejection efficiencies, the ratio of the number of axially ejected ions to the number of trapped ions. The total numbers of trapped ions in the linear ion trap was measured as described in [18].
6.2.5 Solutions and Reagents

Reserpine (Sigma, St. Louis, MO, USA) was 50 µM in glacial acetic acid/methanol/deionized water (0.006:1:1). Methanol and 99.99% glacial acetic acid were from Fisher Scientific, Nepean, ON, Canada. Nitrogen (UHP-grade, manufacturer’s stated purity 99.999%) was from Praxair (Vancouver, BC, Canada). All solutions were infused into the ESI source at a flow rate of 1 µl/min.
6.3 Results and Discussion

6.3.1 Axial Ion Ejection at Boundaries without Trapping

First experiments investigated ejection at the stability boundary near $q = 0.908$, without dipole excitation and without trapping. With MSAE, resolution generally decreases with increasing scan speed [3] but even at the low scan speed of 40 Th/s, only nominal resolutions less than about 300 were possible as shown in Figure 6.1a for rod sets 4A and 4B. All the other rod sets also gave low resolution. The spectra in Figure 6.1 were obtained with a portion (~23%) of the main drive rf applying on the exit lens 1 and about 7 V of resolving dc adding to the rods. Hager [3] found that the resolution and peak shapes were improved rf applied to the exit lens and resolving dc on the rods. With the same operating conditions, but without added rf and the small resolving dc voltage, the resolution was even lower than shown in Figure 6.1a.

The low resolution may be a result of changes to the stability boundaries caused by adding the hexapole fields. With a conventional rod set, as the operating point of ions approaches the $(a = 0, \ q = 0.908)$ boundary, ion motion becomes unstable in the $x$ and $y$ directions simultaneously. However, the $x$ and $y$ boundaries with quadrupoles with added hexapole fields differ near $q = 0.908$. Calculated stability boundaries of the quadrupoles with 4% added hexapole fields, are shown in Figure 6.1b. With rod set 4A (boundary 2), the points of intersection of the $x$ and $y$ stability boundaries with the $a = 0$ axis differ. Extrapolation of the $y$ stability boundary to $a = 0$ (the dashed line in Figure 6.1b) shows that the $x$ boundary is at $q = 0.9125$; the $y$ boundary is at $q = 0.9138$. Dipole excitation of ions in $x$ near $q = 0.9125$ may lead to excitation in $y$ where the ions
are still stable, leading to delayed ejection of some ions. A similar effect was seen with a quadrupole with a 2.6% added octopole field [18].

With rod set 4B (boundary 1), the $x$ and $y$ boundaries have the same $q$ value at $a = 0$. However the boundary is at $q = 0.913$, higher than the $q$ value of an ideal quadrupole ($q = 0.908$). The shifts of the boundaries compared to the boundaries of an ideal quadrupole may lead to low resolution.

Figure 6.1 (a) Peak shapes of reserpine ions with rod sets 4A and 4B ejected at the stability boundary without dipole excitation. (b) Calculated stability boundaries near $q = 0.908$ with quadrupoles with 4% added hexapole fields. Boundary 1 is for rod set 4B and boundary 2 is for rod set 4A.
MSAE experiments were then done with dipole excitation applied between the \( x \) or \( y \) rods to eject ions at \( q \) values of 0.21, 0.41, 0.73 and 0.87. With a conventional rod set, and with rod sets with added octopole fields, ejection at higher \( q \) values (up to 0.80 or more) gives higher resolution [17]. With all rod sets, increasing the ejection \( q \) from 0.20 to 0.73, gave higher resolution. However, with all six rod sets, ejection at \( q \approx 0.88 \), gave lower resolution and broad continuum baselines. The poor performance with \( q \approx 0.88 \) may also be caused by the distortion of the stability boundaries [12, 13, 18]. All subsequent experiments ejection were done with ejection at \( q = 0.73 \).

### 6.3.2 MSAE with All Six Rod Sets at the Limiting Scan Speeds with Dipole Excitation Applied Between the \( x \) Rods with Forward and Reverse Scans

With MSAE, the resolution generally decreases with increasing scan speed [3]. Here we call the highest scan speed that gives \( R_{1/2} = 1800 \) the "limiting scan speed". The limiting scan speeds with forward and reverse scans and with dipole excitation between the \( x \) or \( y \) rods were determined for each rod set as follows. Spectra were recorded at scan speeds from 45 Th/s to 4500 Th/s. The scan speeds giving \( R_{1/2} = 1800 \) were then interpolated from plots of \( R_{1/2} \) vs. scan speed. The limiting scan speeds are shown in Table 6.2, along with the scan directions and excitation directions. Table 6.2a and 6.2b show the limiting scan speeds with excitation between the \( x \) and \( y \) rods respectively. The first three rows show the limiting scan speeds of the A rod sets and the last three rows show the limiting scan speeds of the B rod sets. Where no limiting scan speed is shown, it was not possible to achieve \( R_{1/2} = 1800 \) at any scan speed.
With excitation between the $x$ rods and forward scans, all A rod sets have limiting scan speeds greater than 800 Th/s, with the highest scan speed possible with rod set 8A. However, with reverse scans and excitation in $x$, the limiting speeds are much lower. Only rod set 4A gives a limiting scan speed of more than 200 Th/s with reverse scans. With rod sets 8A and 12A, the highest resolutions are 1500 and 1200 respectively at a scan speed of 45 Th/s. Thus no limiting scan speeds for rod sets 8A and 12A are listed in the Table 6.2.

With the B rod sets, the differences among the limiting scan speeds obtained with different scan directions are not as great as with the A rod sets. Especially with rod set 4B, the limiting scan speeds with forward and reverse scans are almost the same. With rod sets 8B and 12B, the limiting scan speeds with reverse scans are greater than with forward scans. Rod set 4B gives highest limiting scan speed (840 Th/s) of the B rod sets, about half the limiting scan speed obtained with rod set 8A.
Table 6.2 The highest scan speeds of each rod set giving $R_{1/2} = 1800$ with ejection at $q \approx 0.73$. The excitation direction and scan direction are listed.

<table>
<thead>
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<th>DE</th>
<th>Forward (F) or Reverse (R)</th>
<th>Speed (Th/s)</th>
</tr>
</thead>
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<td>x F</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>240</td>
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<tr>
<td>8A</td>
<td>x F</td>
<td>1600</td>
</tr>
<tr>
<td></td>
<td>R ---</td>
<td></td>
</tr>
<tr>
<td>12A</td>
<td>x F</td>
<td>870</td>
</tr>
<tr>
<td></td>
<td>R ---</td>
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<tr>
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<td></td>
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<td>8B</td>
<td>x F</td>
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<td></td>
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<td>x F</td>
<td>400</td>
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<tr>
<td></td>
<td>R 810</td>
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<table>
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<th>Forward (F) or Reverse (R)</th>
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<tr>
<td></td>
<td>R 40</td>
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</tr>
<tr>
<td>8A</td>
<td>y F</td>
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<tr>
<td></td>
<td>R 590</td>
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</tr>
<tr>
<td></td>
<td>R 290</td>
<td></td>
</tr>
<tr>
<td>4B</td>
<td>y F</td>
<td>460</td>
</tr>
<tr>
<td></td>
<td>R 270</td>
<td></td>
</tr>
<tr>
<td>8B</td>
<td>y F</td>
<td>260</td>
</tr>
<tr>
<td></td>
<td>R 300</td>
<td></td>
</tr>
<tr>
<td>12B</td>
<td>y F</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>R 80</td>
<td></td>
</tr>
</tbody>
</table>
6.3.3 MSAE with All Six Rod Sets at the Limiting Scan Speeds with Dipole Excitation

Applied Between the y Rods with Forward and Reverse Scans

Table 6.2b shows that the limiting scan speed of the A rod sets with excitation between the y rods is always less than with excitation between the x rods. The highest limiting scan speed is produced by rod set 8A (900 Th/s). Forward scans always give higher limiting scan speeds than reverse scans. However, the limiting scan speeds with the B rod sets do not show such a clear trend. With rod set 4B, forward scans produce the higher limiting scan speed. With both rod sets 8B and 12B, higher limiting scan speeds are obtained with reverse scans.

6.3.4 MSAE with Six Rod Sets at with a Scan Speed of 2000 Th/s and Dipole Excitation Between the x Rods

For a given scan speed, excitation rod pair, and scan direction, different resolution is obtained with each of the rod sets. Figure 6.2 shows spectra obtained with ejection at \( q \approx 0.73 \) and a scan speed of 2000 Th/s with DE between the x rods with all six rod sets. The amplitude of added hexapole field increases down each column. Spectra in each column have the same scan direction, forward or reverse scan. The first and second columns show spectra with the A rod sets, and the third and fourth columns shown spectra with the B rod sets.

With the A rod sets and excitation applied between the x rods, forward scans gave similar resolution (\( \geq 1500 \)) and peak shapes regardless of the amplitude of the added hexapole field (Figure 6.2a, b, c). With reverse scans, as shown in the second column, the resolutions are lower. The isotopic peaks are not baseline resolved with rod sets 4A (Figure 6.2d) and 8A (Figure 6.2e). With rod set 12A (Figure 6.2f) isotopic peaks
are nearly baseline resolved. Thus, with the A rod sets at this scan speed (~2000 Th/s), forward scans with excitation between the x rods are preferred.

With the B rod sets, excitation between the x rods and forward scans, as shown in the third column, only rod set 4B can produce a spectrum with well resolved isotopic peaks and a resolution of 1730 (Figure 6.2g). With rod set 8B (Figure 6.2h), a spurious peak appears at $m/z = 608$. With rod set 12B (Figure 6.2i), the isotopic peaks are barely separated. Resolutions of both rod sets 8B and 12B are lower than 1000.

With reverse scans (Figure 6.2j, k, l) all the B rod sets give spectra with resolved isotopic peaks. However, with rod set 4B (Figure 6.2j), the isotope ratios are incorrect. With rod sets 8B (Figure 6.2k) and 12B (Figure 6.2l), there are spurious peaks on the low mass side. The resolution with rod sets 8B and 12B with reverse scans is greater than with forward scans. Thus, at this scan speed, forward scans give the best performance with rod set 4B, and reverse scans with rod sets 8B and 12B. However reverse scans with ejection at $q = 0.73$ are not useful for producing spectra of ions of a broad mass range, because only a limited mass range of ions with q values between about 0.72 and 0.9 can be stored and ejected.

Comparing the A and B rod sets, it is clear that with dipole excitation between the x rods, MSAE with the A rod sets and forward scans consistently produces spectra with good peak shapes and resolution $\geq 1500$ at this scan speed (~2000 Th/s).
Figure 6.2 Spectra obtained with the A and B rod sets with scan speeds of 2000 Th/s, excitation between the $x$ rods and with ejection at $q = 0.73$. The amplitude of the added hexapole field increases down each column. The two left columns show the spectra with the A rod sets. The two right columns show the spectra with the B rod sets. Spectra with forward and reverse scans are shown in alternate columns.
6.3.5 MSAE with the A Rod Sets with Forward Scans and Dipole Excitation between x Rods at $q \approx 0.73$, but with Different Scan Speeds

Figure 6.3 shows spectra produced by the A rod sets with forward scans and excitation between the $x$ rods, at different scan speeds. The amplitude of the added hexapole field increases down each column. Spectra in each column have nearly the same scan speed, with the scan speeds increasing from 44 Th/s to 450 Th/s, 1100 Th/s and 4000 Th/s from left to right. The spectra of the A rod sets at scan speeds of 2000 Th/s are shown in Figure 6.2. Resolution generally decreases as scan speed increases, as seen with conventional rod sets [3] and rod sets that have added octopole fields [18]. Rod set 4A produced the highest resolution ($R_{1/2} = 4500$) at 44 Th/s (Fig 6.3a). Both rod sets 8A (Figure 6.3b) and 12A (Figure 6.3c) also produced resolution of more than 2500 at low scan speeds. The A rod sets produce spectra with good peak shape and resolution of at least 1500 at all scan speeds up to 4000 Th/s.
Figure 6.3 Spectra with rod sets 4A, 8A and 12A with forward scans, excitation applied between the $x$ rods and ejection at $q \approx 0.73$.

The amplitude of the added hexapole field increases down each column. Spectra in each column have the same scan speed, with the scan speeds increasing from left to the right. The scan speeds are about 44 Th/s, 450 Th/s, 1100 Th/s and 4000 Th/s in the first, second, third and fourth columns respectively.
6.3.6 The Effect of the Frequency Shifts

The superior performance of the A rod sets over the B rod sets may be related to the frequency shifts. It has been shown that with added octopole fields the oscillation frequencies of ions shift with oscillation amplitudes [14, 18, 23]. The frequency shifts can affect the resolution depending on the scan direction. If the shifts are to higher frequencies with increasing oscillation amplitude, with forward scans, the shifts drive the ions faster towards the frequency of the driving rf. As a result, the ions are ejected faster and the mass resolution is improved [9, 18, 23]. Similarly, the hexapole fields added to these rod sets also cause the oscillation frequencies of ions to shift with oscillation amplitude. However, the higher multipoles of these rod sets consist not only of a hexapole field [24], but other multipole fields, and, especially for the rod sets with equal diameter rods, a significant octopole field. As a result, the frequency shifts are not caused only by the added hexapole fields [24]. The frequency shifts in these rod sets are complex because many multipoles must be considered. No simple conclusion follows. The frequency shifts considering all multipole components will be part of future work.

6.3.7 MSAE with Ejection at \( q \approx 0.41 \)

MSAE was tested with all the rod sets with ejection at \( q = 0.41 \). Figure 6.4 and Figure 6.5 show spectra obtained with the A and B rod sets with scan speeds of 40 Th/s. The amplitude of the added hexapole field increases down each column. Spectra in each column have the same scan direction. The first and second columns show spectra with dipole excitation between the \( x \) rods and forward and reverse scans respectively. The third and fourth columns show spectra with dipole excitation between the \( y \) rods and
forward and reverse scans respectively. This low scan speed was used because at higher speeds isotopic peaks cannot be resolved.

For the A rod sets, even at 40 Th/s there are two major problems. First the intensity ratios of the isotopic peaks are incorrect in some cases (Figure 6.4a, b, d, e). Second there are spurious peaks in some of the spectra (Figure 6.4b, h, k). With a scan speed of 300 Th/s, spurious peaks are observed with all the A rod sets (data not shown). Some of the spectra in Figure 6.4 however still show well separated isotopic peaks and high resolution. The highest resolution is $R_{1/2} = 2960$ (Figure 6.4j), obtained with rod set 4A with excitation between the $y$ rods and forward scans. Similar resolution and peak shape are obtained with both forward and reverse scans (Figure 6.4g and 6.4j). With 4A superior peak shapes are obtained with excitation in $y$ rather than in $x$ (Figure 6.4a, d). With rod set 8A, the highest resolution obtained is with dipole excitation between the $y$ rods and a reverse scan (Figure 6.4k). Resolution and intensity ratios of the isotopic peaks and peak shapes are improved with rod set 8A with excitation in $y$ (Figure 6.4h, k)) compared to excitation in $x$ (Figure 6.4b, e). However, spurious peaks are observed with DE between the $y$ rods. Spectra produced by rod set 12A all have good peak shapes regardless of the scan direction and excitation direction. Generally with the A rod sets with $q_{eject} = 0.41$, dipole excitation between the $y$ rods is preferred.

At 40 Th/s, spectra obtained with the B rod sets (Figure 6.5) show fewer problems than with the A rod sets. Spurious peaks are only observed with rod set 12B (Figure 6.5f and l). With a scan speed of 300 Th/s, spurious peaks are observed with all the B rod sets (data not shown). Incorrect ratios of the isotopic peak intensities are observed (Figure 6.5a, d, h, k, l). The highest resolution is $R_{1/2} = 4630$ (Figure 6.5h), obtained with rod set...
8B with excitation between the \( y \) rods and forward scans. Rod set 8B also produces good peak shapes and high resolution \( R_{1/2} = 2110 \) with excitation between the \( y \) rods and reverse scans (Figure 6.5h). With both rod sets 4B and 12B, peak shapes obtained with excitation in \( y \) are better than those with excitation in \( x \). As a result, dipole excitation between the \( y \) rods is preferred with the B rod sets with \( q_{\text{eject}} = 0.41 \).

Even though some of the rod sets produce high resolution (Figure 6.4g, Figure 6.5h), none of the rod sets produce good peak shape and high resolution with ejection at \( q = 0.41 \) with higher scan speeds (\( \geq 300 \) Th/s). Axial ejection experiments were also done with rod sets 12A and 8B with ejection at \( q = 0.21 \). Even with a scan speed as low as 40 Th/s, the isotopic peaks are barely resolved. Only dipole excitation between the \( y \) rods with reverse scans gave spectra with separate isotopic peaks at 40 Th/s. With \( q_{\text{eject}} = 0.41 \) and 0.21, dipole excitation between \( y \) rods is preferred.
Figure 6.4 Peak shapes with reserpine ions with forward and reverse scans at 40 Th/s with rod sets 4A, 8A and 12A, ejection at $q = 0.41$, and forward and reverse scans.
Figure 6.5 Peak shapes with reserpine ions with forward and reverse scans at 40 Th/s with rod sets 4B, 8B and 12B, ejection at $q = 0.41$, and forward and reverse scans.
6.3.8 Ejection Efficiency

Ejection efficiency determines the sensitivity of MSAE. The excitation amplitude, scan speed and voltage on the exit lens affect the ejection efficiency. In general, higher scan speed requires higher excitation amplitude, and a higher exit lens barrier is required to obtain better resolution. At a given scan speed, the ejection efficiency can be improved by decreasing the exit lens barrier, but at the cost of lower resolution. In practice, the exit lens barrier was optimized to obtain the highest resolution with minimal loss in sensitivity [25]. Table 6.3 shows the ejection efficiencies of all the A and B rod sets with the optimal exit lens barriers with ejection at \( q \approx 0.73 \). Where no ejection efficiency is shown, it is not possible to obtain ejection efficiency higher than 0.5%, so that spectra were not recorded. Regardless of the scan direction and dipole excitation rod pair, the ejection efficiency decreases as the scan speed increases. The results are consistent with the previous studies with a rod set with a 2.0% added octopole field [18] and a conventional rod set [25].
Table 6.3 Ejection efficiencies (%) with the system optimized for the highest resolution at each scan speed.

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<th>1000</th>
<th>2000</th>
<th>4000</th>
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<tbody>
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<td></td>
<td></td>
<td>Dipole Excitations</td>
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<td></td>
<td></td>
<td></td>
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<td>( x )</td>
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<tr>
<td></td>
<td></td>
<td>( y )</td>
<td>11</td>
<td>1.8</td>
<td>1.2</td>
<td>0.9</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>( x )</td>
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<td>3.3</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>( y )</td>
<td>3.1</td>
<td>2.0</td>
<td>0.8</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4B</td>
<td>F</td>
<td>( x )</td>
<td>19</td>
<td>10</td>
<td>3.6</td>
<td>3.2</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>14</td>
<td>7.6</td>
<td>3.5</td>
<td>1.2</td>
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</tr>
<tr>
<td></td>
<td>R</td>
<td>( x )</td>
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6.4 Summary

Mass selective axial ejection with quadrupoles with 4%, 8% and 12% added hexapole fields with different modes of excitation are compared. The specific combination of rod set, scan direction and dipole excitation setting can greatly affect the resolution and peak shape. With optimized operating conditions mass selective axial ejection is possible with a resolution of several thousand and scan speeds of up to 4000 Th/s. Thus these rod set can be used as rf/dc mass filters, demonstrate higher fragmentation efficiency in MS/MS experiments, and can perform MSAE with high resolutions and scan speeds. Further investigation of the effects of frequency shifts on MSAE with these rod sets is required.
6.5 References


7 Summary
Linear quadrupoles, one type of mass analyzer, are widely used in many scientific instruments, such as GC-MS, LTQ ("linear trap quadrupole") and tandem mass spectrometry, as mass filters, linear ion traps or ion guides. Linear quadrupole ion traps have the advantages of larger storage capacity and higher injection efficiency in comparison to 3D ion traps [1, 2].

The benefits of introducing higher order multipoles to the potential of a 3D trap have been well studied [3-7]. Douglas and co-workers were the first to investigate linear quadrupoles with significant added hexapole and octopole fields [8-11].

Usually, in a triple quadrupole instrument, Q2 is used as a collision cell to fragment ions, and Q3 is used as a mass filter. If Q3 can also be used as an ion trap, so that ions can be further fragmented, more information about the precursor ions can be obtained. In fact, the idea has been adopted in the Q-trap mass spectrometer from AB Sciex. The Q-trap instruments combine a fully functional triple quadrupole and ion trap mass spectrometer within the same platform. The Q3 in the Q-trap system can be operated as either an rf/dc mass filter or a linear ion trap with mass selective axial ejection. The fragmentation efficiency of conventional quadrupoles is low at low pressure ($1 \times 10^{-5}$ Torr) [11], but in order to operate a conventional quadrupole as a mass filter in Q3, the pressure has to be lower than $10^{-5}$ Torr. As a result, the possibility of operating conventional quadrupoles as mass filters and ion traps in Q3 of a Q-trap is limited. We are interested in evaluating the performance of mass analysis, such as resolution, peak shape and transmission, of linear quadrupoles with added multipoles because these rod sets give greater fragmentation efficiency than conventional quadrupoles at low pressure. Simulations show that mass analysis with rod sets with large geometric and field
distortions is sometimes possible [12 -15]. Previous studies [8, 13, 16, 17] have evaluated the performance of mass analysis using linear quadrupoles with added octopole fields and found that they give greater fragmentation yields of trapped ions [11]. Subsequently, it was found that quadrupoles with added octopole fields of 2% to 4% can be used for mass analysis, either conventionally with applied rf and dc [13], with axial ejection [17], or with islands of stability [14, 16]. The work described in this thesis aims to further our understanding of the effects of adding significant higher multipoles by evaluating the performance of mass analysis of linear quadrupoles with different added multipole fields as mass filters and ion traps.

This work is a systematic investigation of the performance of linear quadrupoles with added hexapole fields. Experiments with conventional mass analysis and mass analysis with islands of stabilities with quadrupoles with added hexapole fields agree with simulations [15, 18, 19]. The results show with the correct operating parameters that mass analysis with some of these rod sets can produce resolution comparable to that of a conventional rod set. However, overall these rod sets are less useful as mass filters, because of the low resolution and transmission compared to those of a conventional rod set. The resolution, peak shape and transmission can be improved significantly when islands of stability are used for mass analysis for both $a > 0$ and $a < 0$. The islands of stability can be used to overcome the effects of both small and large field distortions. The experiments and simulations suggest that quadrupoles with added hexapole fields can be used for conventional mass analysis as mass filters with applied rf and dc and islands of stability.
Mass analyzing fragment ions requires MSAE when a quadrupole is used as an ion trap as Q3 in a Q-trap system. As a result, MSAE has been used to evaluate the performance of quadrupoles with added multipoles as linear ion traps. MSAE experiments were performed with dipole excitation to eject ions at \( q = 0.73 \). Comparisons are made between axial ejection with quadrupoles with 4%, 8% and 12% added hexapole fields. The effects of varying several operation conditions, including \( q \) value, excitation voltage, excitation applied to the \( x \) or \( y \) rods, and scan direction, have been investigated. With optimized operating conditions, resolution up to \( R_{1/2} = 4500 \) is possible in some cases. The effects of scan speed were investigated and a resolution at half height of about 1800 is possible at scan speeds of up to 4000 Th/s [20] with some of the rod sets. These rod sets also show improved fragmentation efficiency compared to a conventional quadrupole at low pressure [21]. The experiments and simulations suggest that these rod sets might be good candidates for operation both as traps and mass filters, and might replace conventional rod sets used as Q3 in a Q-Trap instrument.

The major contribution of this thesis is that it presents and evaluates the benefits and disadvantages of introducing hexapole fields to linear quadrupoles. It shows that both conventional mass analysis and MSAE are possible with such distorted rod sets. Conventional mass analysis with islands of stability is carefully studied. The results show that the islands of stability can be used to overcome the effects of field distortions. MSAE with these rod sets show that linear quadrupoles with added multipole fields have the potential to be excellent ion traps providing high fragmentation efficiency, as well as high resolution and good peak shapes at high scan speeds for mass analysis.
Comparison can be also made between the results obtained with linear quadrupoles with added hexapole fields in this study and with linear quadrupoles with added octopole fields in previous studies [13, 16, 17]. Both studies indicate that adding higher multipole fields to linear quadrupoles can be used to make novel linear ion traps. Even though adding higher multipole fields is not in favor of conventional mass analysis, so that the rod sets are less useful as mass filters than conventional quadrupoles, quadrupoles with added higher multipole fields are still good candidates for ion traps, and islands of stability can be used to overcome the disadvantages of these rod sets as mass filters. In addition, the studies show that adding odd order multipole fields, such as the hexapole field, might be less beneficial than adding even order multipole fields, such as the octopole field. In addition, it is more difficult to predict the direction and degree of the frequency shifts of linear quadrupoles with added odd order multipole fields, due to the disturbance of the symmetry of the quadrupole fields.

In general, the thesis contributes to the overall understanding of how higher order multipole fields affect the performance of mass analysis with linear quadrupoles with added multipole fields. It also provides possible solutions, such as islands of stability, to overcome the disadvantages brought by adding multipole fields.

However, the solutions may not be easily adopted. For example, in order to use islands of stability for mass analysis, it is important to optimize the frequency and amplitude of the auxiliary quadrupole fields, so that well defined islands of stability with suitable size can be created. In our experiments, in order to obtain high mass resolution with islands of stability, the frequency and amplitude of the auxiliary quadrupole voltage were adjusted to make narrow islands. Comparison of the results with high and low
frequencies shows that low frequency excitation tends to give higher resolution. To obtain a mass spectrum with the same or higher resolution, the required excitation strength has to be much lower for a low frequency excitation than a high frequency excitation. In addition, we also observe that as the size of an island decreases, the transmission decreases. As a result, in order to obtain both good resolution and transmission with mass analysis with islands of stability, different combinations of frequency and amplitude have to be tested to optimize the operating conditions.

In addition, even though significant knowledge was obtained about the effects of added multipoles on the performance of a linear quadrupole as a mass analyzer, a prediction of the optimal multipole components for the best fragmentation efficiency and mass analysis result is not yet possible.

In the future, the concept of using islands of stability to perform mass analysis could be applied to performing mass analysis with the 3rd stability region. The frequency shifts caused by adding higher multipoles could be predicted by simulation. This would lead to the optimization of the operation conditions for MSAE. More research is also needed to explore additional methods of utilizing the benefits of adding higher multipoles to a linear quadrupole to develop a novel quadruple ion trap instrument.
7.1 References


