The use of linear quadrupoles in mass spectrometry as mass filters and ion guides is reviewed. Following a tutorial review of the principles of mass filter operation, methods of mass analysis are reviewed. Discussed are extensions of quadrupole mass filters to higher masses, scanning with frequency sweeps of the quadrupole waveform, operation in higher stability regions, and operation with rectangular or other periodic waveforms.

Two relatively new methods of mass analysis the use of “islands of stability” and “mass selective axial ejection” are then reviewed. The optimal electrode geometry for a quadrupole mass filter constructed with round rods is discussed. The use of collisional cooling in quadrupole ion guides is discussed along with ion guides that have axial fields. Finally, mass analysis with quadrupoles that have large distortions to the geometry and fields is discussed. An Appendix gives a brief tutorial review of definitions of electrical potentials and fields, as well as the units used in this article. © 2009 Wiley Periodicals, Inc., Mass Spec Rev 28:937–960, 2009

Keywords: linear; quadrupole; mass filter; resolution; stability; mass scans; quadrupole excitation; ion guide; axial fields; distorted fields; multipoles

I. INTRODUCTION

The linear quadrupole, originally developed for mass spectrometry by Paul and co-workers (Paul, Reinhard, & von Zahn, 1958), is widely used in many areas as a mass filter, an ion guide, or a linear ion trap. The history of the first 21 years of quadrupole devices has been given by Dawson (1976, Ch. 1). His classic book describing theory and applications of quadrupoles, both two-dimensional and three-dimensional, was published more than 30 years ago (Dawson, 1976). Since that time, there has been much progress in the development and use of quadrupoles in new ways. The book by March and Hughes (1989), while mostly concerned with three-dimensional ion traps, contains much useful information about the properties of ion motion in quadrupole fields that can be directly applied to two-dimensional linear quadrupoles. The use of quadrupoles as linear ion traps was reviewed by Douglas, Frank, and Mao (2005).

This article attempts to review the use of linear quadrupoles as mass analyzers and ion guides. Section II is a review of the equations of ion motion and stability regions. Section III describes the use of linear quadrupoles as mass analyzers with conventional and new methods of operation including the development of high mass range quadrupoles, scanning with frequency sweeps, operation in higher stability regions, and operation with rectangular waveforms. Two new methods of mass analysis the use of “islands of stability” and axial ejection are then reviewed. The optimal electrode geometry for a quadrupole mass filter constructed with round rods is discussed. The use of collisional cooling in quadrupole ion guides is discussed along with ion guides that have axial fields. Section IV discusses mass analysis with quadrupoles that have large distortions to the geometry and fields. An Appendix gives a brief review of definitions of electrical potentials and fields, as well as the units used in this article. Table 1 shows the units used in this article.

Many areas of quadrupole research could not be reviewed here. These include special applications of quadrupoles, development of hybrid instruments, novel electrode geometries, and micro-machined and miniature quadrupoles. Mathematical methods, such as matrix methods to calculate stability diagrams and boundaries, properties of solutions of the Mathieu equation, and mathematical methods for calculating ion motion in distorted fields are not covered. The patent literature is not generally included. Relevant publications up to June 2008 have been considered.

II. THE LINEAR QUADRUPOLE

A. The Quadrupole Potential

The electric potential of the linear quadrupole, \( \phi(x, y) \), is given by

\[
\phi(x, y) = \left( \frac{x^2 - y^2}{r_0^2} \right) \phi_0
\]

where \( x \) and \( y \) are Cartesian co-ordinates. This potential is produced by four parallel electrodes with hyperbolic shapes, as shown in Figure 1. The point \((x, y) = (0, 0)\) is the center of the quadrupole. The parameter \( r_0 \), called the “field radius,” is the distance from the center to an electrode. Balanced potentials are normally applied between the \( x \) and \( y \) electrodes, that is, a potential \( +\phi_0 \) is applied to the two electrodes in the \( x \) direction and a potential \( -\phi_0 \) is applied to the two electrodes in the \( y \) direction. In this case the potential at the center of the quadrupole is 0. It is readily verified that the potential of Equation (1) satisfies Laplace’s equation. In fact, for a two-dimensional potential where electric fields vary linearly with position (the simplest variation with position) Equation (1) can be derived from Laplace’s equation (Dawson, 1976, pp. 9–10).
TABLE 1. SI units used in this article

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>mass</td>
<td>kilograms</td>
</tr>
<tr>
<td>distance</td>
<td>meters</td>
</tr>
<tr>
<td>time</td>
<td>seconds</td>
</tr>
<tr>
<td>electric potential</td>
<td>volts</td>
</tr>
<tr>
<td>charge</td>
<td>Coulombs</td>
</tr>
<tr>
<td>force</td>
<td>Newtons</td>
</tr>
<tr>
<td>energy</td>
<td>Joules</td>
</tr>
<tr>
<td>electric field</td>
<td>volts/meter</td>
</tr>
</tbody>
</table>

If unbalanced voltages are applied to the x and y rods a quadrupole potential is still formed, but there is an axis potential. Suppose the magnitude of the voltage applied to the x rods is \( \phi_{0x} \) and to the y rods \( \phi_{0y} \). The potential can be written

\[
\phi(x, y) = \frac{\phi_{0x} + \phi_{0y}}{2} \left( \frac{x^2 - y^2}{r_0^2} \right) + \frac{\phi_{0x} - \phi_{0y}}{2}
\]

(2)

where \( (\phi_{0x} - \phi_{0y})/2 \) is the axis potential.

Round electrodes are often used to provide an approximate quadrupole field because it is less expensive to manufacture round rods with high precision. The optimum choice of the ratio of the radius of a round rod \( r \) to the field radius \( r_0 \) is discussed in Section IIIJ.

FIGURE 1. The quadrupole electrodes with applied potentials, showing equipotential lines. Reproduced from Du, Douglas, and Konenkov (1999a). Copyright the Royal Society of Chemistry.

B. Other Two-Dimensional Potentials

If a quadrupole does not have an ideal field with the potential given by Equation (1), the mathematical description of the potential is more complicated. The potential can be described as a superposition of two-dimensional multipole fields. The quadrupole potential is just one of the many possible solutions to Laplace’s equation in two dimensions. In general, the spatial part of any two-dimensional potential \( \Phi(r, \theta) \) can be written in polar co-ordinates \((r, \theta)\) as a sum of two-dimensional multipoles as follows:

\[
\Phi(r, \theta) = [(A \theta + B) (C \ln r + D)] + \sum_{N=1}^{\infty} \varphi_N(r, \theta)
\]

(3)

The terms \( \varphi_N(r, \theta) \) are referred to as “spatial harmonics” or “circular harmonics” (Smythe, 1939, p. 62) and are given in the most general form when \( N \geq 1 \) as

\[
\varphi_N(r, \theta) = (A_N \cos N\theta + B_N \sin N\theta) (C_N r^N + D_N r^{-N})
\]

(4)

For the field within a linear quadrupole only the terms in \( N \) contribute, so all \( D_N \) are zero and without loss of generality the spatial harmonics can be taken as

\[
\varphi_N(r, \theta) = \left( \frac{r}{r_0} \right)^N \cos N\theta
\]

(5)

In Cartesian coordinates, used in this review, a two-dimensional potential can be expanded in multipoles \( \phi_N(x, y) \) as

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

(6)

where \( A_N \) is the dimensionless amplitude of the two-dimensional multipole \( \phi_N(x, y) \). Each of the two-dimensional multipoles is also a solution to Laplace’s equation. The analytical form of a two-dimensional multipole can be calculated from

\[
\phi_N(x, y) = \text{Im}(x + iy)^N
\]

(7)

or

\[
\phi_N(x, y) = \text{Re}(x + iy)^N
\]

(8)

where \( \text{Im}(f(z)) \) is the imaginary part of the complex function \( f(z) \), \( \text{Re}(f(z)) \) is the real part of the complex function \( f(z) \), and \( z^2 = -1 \) (Smythe, 1939, p. 70; Feynmann, Leighton, & Sands, 1963). The set \( \text{Re}(x + iy)^N \) can be used without loss of generality. The term \( \phi_0 \) represents a potential that is independent of position, \( \phi_1 \) a dipole potential, \( \phi_2 \) a quadrupole potential (Eq. 1), \( \phi_3 \) a hexapole potential, \( \phi_4 \) an octopole potential, and so on.

Analytical forms of the two-dimensional multipoles have been given by Szylagyi (1988). The analytical forms of the first five multipoles are

\[
\phi_0 = \text{constant}
\]

(9)

\[
\phi_1(x, y) = \left( \frac{x}{r_0} \right)
\]

(10)

\[
\phi_2(x, y) = \left( \frac{x^2 - y^2}{r_0^2} \right)
\]

(11)
\[ \phi_3(x, y) = \left( \frac{x^3 - 3xy^2}{r_0^3} \right) \]  
\[ \phi_4(x, y) = \left( \frac{x^4 - 6x^2y^2 + y^4}{r_0^4} \right) \]  
\[ \phi_N(x, y) = \left( \frac{x^N - \frac{N}{2}x^{N-2}y^2 + \frac{N(N-2)}{8}x^{N-4}y^4}{r_0^N} \right) \]

The hexapole potential corresponds to the potential in a region between six rods, the octopole potential to the potential in the region between eight rods, and so on. The multipole \( \phi_N(x, y) \) gives the potential from an array of 2N electrodes with shapes given by

\[ \phi_N(x, y) = \pm 1 \]  

The electrode geometries and applied potentials producing these multipoles are shown by Szabo (1986).

**C. Equations of Motion and the Stability Diagram**

1. **Electric Fields in the x and y Directions**

For mass analysis, the potential applied to the quadrupole rods has both DC and time-varying parts, and is given by

\[ \phi_0(t) = U - V_{RF} \cos(\Omega t) \]  

where \( U \) is a DC voltage applied pole to ground, and \( V_{RF} \) is a zero to peak alternating voltage applied pole to ground. In this case the quadrupole potential is

\[ \Phi(x, y, t) = \left( \frac{x^2 - y^2}{r_0^2} \right) (U - V_{RF} \cos(\Omega t)) \]  

A typical operating frequency is approximately 1.0 MHz (\( \Omega = 2 \times \pi \times 1 \times 10^6 \text{s}^{-1} \)) which is a radio frequency (RF). Equation (16) has a periodic cosine variation of the potential with time. In fact, any periodic function may be used (see below).

Ion motion is determined by Newton’s law

\[ \vec{F} = m \frac{d\vec{v}}{dt} \]

where \( \vec{F} \) is the force on an ion, \( m \) is the mass of the ion, \( \vec{v} \) is the ion velocity, and \( t \) is the time. The force on a positive ion is

\[ \vec{F} = -ze \nabla \Phi(x, y, t) \]

where \( z \) is the number of charges on the ion. The electric field in the x direction is

\[ E_x = -\frac{\partial \Phi(x, y, t)}{\partial x} = -\frac{2x}{r_0^2} (U - V_{RF} \cos(\Omega t)) \]

and the electric field in the y direction is

\[ E_y = -\frac{\partial \Phi(x, y, t)}{\partial y} = -\frac{2y}{r_0^2} (U - V_{RF} \cos(\Omega t)) \]

The electric field in x depends only on x and the electric field in y depends only on y. The electric fields in the x and y directions are independent because the potential does not contain terms of the form \( x^n y^m \). As a result, ion motion in the x and y directions can be considered independently.

2. **Ion Motion and Stability in the x Direction**

The equation of ion motion for the x direction can be written as

\[ m \frac{d^2x}{dt^2} = -\frac{2ze}{r_0^2} \left( U - V_{RF} \cos(\Omega t) \right) \]

Introducing the variables

\[ \xi = \frac{\Omega t}{2}, \quad a_x = \frac{8zeU}{mr_0^2 \Omega^2}, \quad q_x = \frac{4zeV_{RF}}{mr_0^2 \Omega^2} \]

Equation (21) becomes

\[ \frac{d^2x}{d\xi^2} + (a_x - 2q_x \cos 2\xi)x = 0 \]

Equation (23) is the Mathieu equation (Emile Léonard Mathieu, 1835–1890). Ion motion consists of oscillations with combinations of many different frequencies. The angular frequencies of ion oscillation are given by

\[ \omega_n = (2n + \beta) \frac{\Omega}{2} \]

where \( n = 0, \pm 1, \pm 2 \ldots \) and \( \beta \) is a function of the \( a_x \) and \( q_x \) parameters.

Many of the methods of operating linear quadrupoles can be understood in terms of the stability of ion trajectories and stability diagrams. Solutions to the Mathieu equation are classified as “stable” or “unstable.” Ions oscillate in the x direction in a complex way.

A solution is “stable” if the amplitude of oscillation remains finite as \( t \to \infty \). Conversely, a solution is “unstable” if the amplitude of oscillation increases exponentially with time. In this case the ion will eventually have an oscillation amplitude equal to \( r_0 \) and will strike a rod. Examples of stable and unstable trajectories are given by Dawson (1976, p. 17). The stability of ion motion depends on the parameters \( a_x \) and \( q_x \). Combinations of \( a_x \) and \( q_x \) that give stable ion motion in the x direction are shown by the shaded regions labeled “stable x” in Figure 2.

3. **Ion Motion and Stability in the y Direction**

The equation of ion motion for the y direction is

\[ m \frac{d^2y}{dt^2} = -\frac{2ze}{r_0^2} \left( U - V_{RF} \cos(\Omega t) \right) \]

Equation (25) is similar to Equation (21), but differs in the sign of the right side (because of the different signs of the potential in \( x \) and \( y \), Eq. 1). Equation (25) can also be written as the Mathieu equation with the change of variables:

\[ \xi = \frac{\Omega t}{2}, \quad a_y = -\frac{8zeU}{mr_0^2 \Omega^2}, \quad q_y = -\frac{4zeV_{RF}}{mr_0^2 \Omega^2} \]
With these variables, the equation of motion for \( y \) becomes

\[
\frac{d^2 y}{dx^2} + \left( a_y - 2q_y \cos 2x \right) x = 0
\]  

(27)

The stability of ion motion in the \( y \) direction can be considered. Because Equation (27) is the same as Equation (23), the \( y \) motion will be stable if \( a_y \) and \( q_y \) have same values as those shown by the shaded regions labeled “stable \( y \)” in Figure 2 for \( a_x \) and \( q_x \).

4. Combined Stability for Ion Motion in the \( x \) and \( y \) Directions

What combinations of \( a_x, q_x \), and \( a_y, q_y \) make ion motion stable in both the \( x \) and \( y \) directions? The key is to note that

\[
a_y = -a_x, \quad q_y = -q_x
\]  

(28)

What values of \( a_x \) and \( q_x \) make the \( y \) motion stable? For the \( y \) motion to be stable the values of \( a_y \) and \( q_y \) must be in the shaded regions “stable \( y \)” of Figure 2. If \( a_x \) and \( q_x \) have the same magnitudes but with opposite sign, \( a_y \) and \( q_y \) will have these values. The stability diagram Figure 2 is symmetric about the \( a \) axis; replacing \( q_x \) by \(-q_x \) makes no difference. However, for the \( y \) motion to be stable when expressed in terms of the \( x \) parameters, the sign of \( a_x \) for the stable regions must be changed. This gives the regions in Figure 2 labeled “stable \( y \)” Regions where both the \( x \) and \( y \) motions are stable are called “combined stability regions” or simply “stability regions.” Eight stability regions can be found in Figure 2. In fact, there are an infinite number of stability regions. The \( a \) and \( q \) values of the tips of the first six regions have been given by Konenkov, Sudakov, and Douglas (2002). Almost all commercial mass filters use the stability region labeled “1” in Figure 2. Operation of quadrupole mass filters in other regions is reviewed in Section IIIC.

5. Hexapole and Octopole Fields

As discussed below, mass analysis takes advantage of the stability regions. Can stability diagrams be derived for other multipole rod sets, such as hexapoles or octopoles? The stability diagram of Figure 2 was derived by considering first the ion motion in the \( x \) direction and then the ion motion in the \( y \)
direction. Separate stability diagrams for each direction could be calculated because the ion motions in the $x$ and $y$ directions are independent. For a higher multipole such as a hexapole or octopole this is not possible. Consider the octopole. From Equation (13) the electric field in the $x$ direction is given by

$$E_x = -\left(\frac{4x^3 - 12xy^2}{r_0^2}\right)$$  \hspace{1cm} (29)

and the electric field in the $y$ direction by

$$E_y = -\left(\frac{-12x^2y + 4y^3}{r_0^2}\right)$$  \hspace{1cm} (30)

The electric field in $x$ depends on $y$, and the electric field in $y$ depends on $x$. Thus, the $x$ and $y$ motions are coupled and cannot be considered independently. No stability diagram can be derived. Stability boundaries are not well defined and become diffuse (Haag & Szabo, 1986; Gerlich, 1992). Thus, higher order multipole rod sets have not been used as mass filters.

**D. Acceptance and Emittance**

Not all combinations of initial position and initial radial velocity are transmitted at a given operating point ($a$, $q$), in the stability diagram. For a given RF phase, combinations of initial position ($x$, $y$) and radial velocity, $\dot{x} = dx/dt$, $\dot{y} = dy/dt$, that are transmitted, fall within ellipses in the $x$, $\dot{x}$ and the $y$, $\dot{y}$ planes (the “phase” planes) (Dawson, 1976, p. 32) as shown schematically in Figure 3. There are separate ellipses for the $x$ and $y$ directions. The area of an ellipse is the “acceptance” for that particular phase. The ellipses rotate about the origin of the phase plane at the RF frequency. The region where the ellipses overlap for all phases gives the acceptance in $x$ or $y$ for 100% transmission regardless of RF phase. The acceptance can also be described for 50% or some other value of transmission. The area of the acceptance ellipses scales as $r_0^2$ for each of the $x$ and $y$ directions, so that the combined acceptance in $x$ and $y$ is proportional to $r_0^4$.

The positions and radial velocities of ions from a source will occupy regions in the $x$, $\dot{x}$ and the $y$, $\dot{y}$ planes. In general, these positions will not form an ellipse. The areas of these regions are called the source emittance in $x$ and $y$. The transmission of a quadrupole will be determined by the overlap of the quadrupole acceptance and source emittance (Dawson, 1990). As the resolution of a quadrupole increases, the combined acceptance in $x$ and $y$ decreases with resolution ($R$) as $1/R$ (Dawson, 1980, 1990).

### III. MASS ANALYSIS WITH LINEAR QUADRUPOLES

#### A. Mass Analysis at the Tip of the First Stability Region

Figure 4 shows the first stability region. The boundaries correspond to the lines $\beta_3 = 0$, $\beta_1 = 1$, $\beta_0 = 0$, and $\beta_1 = 1$. Lines of constant $\beta_3$ and $\beta_0$ are within the stability region (“iso-beta lines”). At the tip of the region $\alpha_3 = 0.23699$ and $\alpha_2 = 0.70600$ (Dawson, 1976, p. 21). The stability boundaries when $\alpha_3 = 0$ are at $\alpha_2 = 0.000$ and $\alpha_2 = 0.908$.

Consider the positions on the stability diagram of three ions with masses (more accurately, mass-to-charge ratios) $m_1 < m_2 < m_3$ for fixed values of $U$ and $V_{RF}$. For mass analysis the values of $U$ and $V_{RF}$ are set so an ion, $m_3$ in this example, is just within the stability region at the tip of the stability diagram. For the same voltages heavier ions $m_1$ have lower $a$ and $q$ values, and lighter ions $m_2$ have greater $a$ and $q$ values. The ions lie on an “operating line” or “scan line.” Ions $m_2$ have stable motion within the quadrupole, and ions $m_1$ and $m_3$ have unstable motion. Comparison to Figure 2 shows $m_1$ has motion unstable in the $x$ direction, and $m_3$ has motion unstable in the $y$ direction. Thus, if an ion source is placed at the entrance of a quadrupole and a detector or some other device at the exit of the quadrupole, ions of mass $m_2$ will be transmitted and ions of other masses, $m_1$ and $m_3$, in this example, will become unstable, will collide with the electrodes of the quadrupole, and will not be transmitted. Thus the quadrupole acts as a “mass filter” for ions of mass $m_2$.

To transmit another mass the voltages $U$ and $V_{RF}$ are adjusted to place that mass at the tip of the stability region. If $U$ and $V_{RF}$ are scanned together with a constant ratio, ions of increasing mass will reach the tip of the stability region in order of their mass and will be transmitted sequentially to produce a mass spectrum. Scans by decreasing $U$ and $V_{RF}$ are also possible. Alternatively, the voltages $U$ and $V_{RF}$ can be switched so that the quadrupole transmits predetermined masses to provide “peak hopping” or single or multiple ion monitoring. The scanning is purely electronic and is amenable to computer control.

The mass resolution of a quadrupole can be changed by changing the ratio of DC ($U$) to RF voltage ($V_{RF}$) to change the slope of the scan line. Lower ratios provide lower mass resolution. If a quadrupole is operated with a constant ratio $U/V_{RF}$ the resolution will be constant across a mass scan. It is more common to operate a quadrupole so that the peak width is constant across a spectrum (e.g., to provide unit resolution.
FIGURE 4. The first stability region, showing an operating line. Reproduced from Moradian (2007).

Copyright A. Moradian.

across a spectrum). This can be done by changing the ratio \( U/V_{RF} \) with mass (Marchand & Marmet, 1964). The simplest, although somewhat approximate, method to do this for positive ions is to apply a constant negative DC voltage between the rods in addition to the positive DC voltage \( U \) which changes with mass.

In principle, the resolution can be increased without limit by placing ions closer to the tip of the stability region. In practice, at least two things limit the resolution—the residence time of ions in the quadrupole field and field imperfections in the quadrupoles. The effects of field imperfections are complex and not well understood and are discussed below. The effects of residence time are introduced here.

If ions do not spend a sufficiently long time in the quadrupole field they may be transmitted even though they have \( a_q \) values outside the stability region. The stability boundaries correspond to the amplitude of ion oscillation increasing exponentially and are for an infinitely long quadrupole (i.e., \( t \rightarrow \infty \)). If an ion which would otherwise be unstable reaches the end of the quadrupole before its amplitude of oscillation reaches \( r_0 \), it will be transmitted. When the mass resolution is limited by the ion residence time in the quadrupole, the resolution measured at half height, \( R_{1/2} \), is given by

\[
R_{1/2} = \frac{n_{RF}^2}{h} \tag{31}
\]

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 Paul, Reinhard, and von Zahn (1958) calculated \( h = 12.25 \). Austin, Holme, and Leck (1976) found \( h = 20 \). For this reason quadrupole mass filters, at least when operated in the first stability region, provide the highest mass resolution with low energy ions. High energy ions give poor resolution with tails on peaks, particularly the low mass side. If an ion beam has a distribution of energies with a high energy tail, the ions with high energies will not be well resolved and will produce peak broadening. Thus, quadrupoles benefit from ion beams that have both low energies and low energy spreads.

Equation (31) shows that the resolution of a quadrupole might be increased by running at a higher RF frequency. This, however, requires higher RF voltages for a given mass range. Manufacturers make choices between resolution, sensitivity, and mass range. Higher frequencies generally give higher resolution and somewhat higher sensitivity (because of the greater acceptance), but at the expense of lower mass range. Conversely, lower frequencies give higher mass range but at some expense of sensitivity and resolution. Where only a limited mass range is required, such as for inductively coupled plasma mass spectrometry (ICP-MS) (maximum \( m/z \) ca. 250), quadrupoles operated at frequencies of 2.0–3.0 MHz are commonly used. Another approach to increase \( n_{RF} \) is to use a longer quadrupole. Von Zahn (1962) used a quadrupole with a length of 5.82 m to obtain a resolution of several thousands with Xe\(^+ \) ions. Amad and Houk (1998, 2000) increased \( n_{RF} \) by reflecting ions to give multiple passes through a quadrupole. A resolution of \( R_{1/2} \approx 11,000 \) was obtained at \( m/z = 28 \).

B. Fringe Fields

The field of a quadrupole mass filter does not stop abruptly with its full value at the ends of the rods. At each end of the rods there are regions of length approximately \( r_0 \) both outside and inside the quadrupole where the field grows from 0 to its maximum value within the quadrupole. The “fringing fields” in this region can be defocusing. Consider an ion approaching the tip of the stability region of Figure 4 along the scan line. If the field grows linearly the ion will be in a region of unstable motion for the \( y \) direction and may be rejected before it reaches the mass filter (Dawson, 1980). The fringe field can change the acceptance of the quadrupole. The fringe field is not necessarily defocusing. The transmission depends on the number of RF cycles \( n_f \) that ions...
spend in the fringing field. There is an optimum transit time of \( n_f \approx 2 \) cycles which gives the maximum transmission with a quadrupole operated in the first stability region (Dawson, 1980).

In general, the fringing field is complex. Ion motion is no longer independent in the \( x, y, \) and \( z \) directions. Dawson (1980) proposed a linear model of the potential in the fringing field as follows:

\[
\phi(x, y, z) = \frac{(x^2 - y^2)z}{r_0^2}
\]

Hunter and McIntosh (1989) calculated numerically the fringing field of a quadrupole with an aperture plate at a distance \( d \) from the end of the rods and fit the fields to

\[
\phi(x, y, z) = \frac{x^2 - y^2}{r_0^2} f(z)
\]

with

\[
f(z) = 1 - \exp(-az - bz^2)
\]

where the distance \( z \) is measured from the aperture plate in units of \( r_0 \). Values of \( a \) and \( b \) were given for different distances of the end plate from the quadrupole. In a second article, McIntosh and Hunter (1989) calculated the effects of this more realistic fringe field model on the quadrupole acceptance. The defocusing effect of the fringing field can be eliminated with a delayed DC ramp, short RF-only quadrupole, which has some fraction of the main RF applied but no DC between the rods (Brubaker, 1968). The short quadrupole is sometimes called a “prefilter.” As an ion approaches the quadrupole it first experiences an RF field in which it is stable and then the DC is applied, but in such a way that the ion retains stable values of \( a \) and \( q \). The fringing field at the exit of a quadrupole can also be defocusing. If ions leaving the quadrupole enter a detector floated at a high potential the defocusing effects at the exit are overcome by the strong attractive field from the detector, and a delayed DC ramp is not used at the exit of the quadrupole.

C. Quadrupole Mass Filters for High Mass Ions

For mass analysis an ion is placed near the tip of the stability diagram where \( a = 0.23699 \) and \( q = 0.70600 \). For a quadrupole power supply with a maximum RF voltage output of \( V_{RF_{\max}} \) there will be a maximum value of the mass-to-charge ratio that can be mass analyzed, given by

\[
\frac{m}{z}_{max} = \frac{4eV_{RF_{\max}}}{0.70600\sqrt{\gamma\Omega^2}}
\]

For given rod size \( r_0 \), the maximum mass can be increased by lowering the operating frequency \( \Omega \). This was demonstrated for a 3D trap by Wuerker, Shelton, and Langmuir (1959) who trapped small (ca. 1 \( \mu \)m) particles of aluminum in a trap operated at 50 Hz. With a lower operating frequency the number of RF cycles that an ion spends in a quadrupole mass filter is reduced, so somewhat lower resolution can be expected. As well, because the acceptance of the quadrupole scales as \( \Omega^2 \), the sensitivity can be expected to be somewhat lower for a quadrupole operated at lower frequencies. Beuhler and Friedman (1982) described a quadrupole operated at 292 kHz with a maximum \( m/z \) of approximately 80,000, used to study cluster ions. Labastie and Doy (1988) described a quadrupole mass filter operated at 560 kHz, with a maximum mass range of 9,000, also used to study cluster ions. A resolution of approximately 80 was used, sufficient for the cluster experiments. With the development of electrospray ionization (ESI) there has been renewed interest in quadrupole mass filters with high mass ranges. Winger et al. (1993) described a quadrupole similar to that of Beuhler and Friedman (1982), operated at 292 kHz to give a maximum \( m/z \) of 45,000. The quadrupole was used to examine low charge states of protein ions and protein–protein complexes (Light-Wahl, Schwartz, & Smith, 1993, 1994). The resolution was surprisingly low, ca. 100, and there was a severe loss of sensitivity for ions with \( m/z < 500 \). Collings and Douglas (1997) described a quadrupole operated at 683 kHz with a mass range of 8,585. Unit resolution was possible at \( m/z = 5,000 \), and below \( m/z = 3,000 \) the sensitivity was comparable to the same system operated at 1.00 MHz with a mass range of 4,000, as expected from the slightly lower acceptance with the higher mass range quadrupole. High mass range quadrupoles have also been used with hybrid quadrupole time-of-flight (TOF) instruments. Sobott et al. (2002) described a system with a quadrupole with a calculated mass range of 32,000, used to study protein–protein complexes. A resolution of ca. 1,000 at \( m/z = 22,226 \) was demonstrated. Interestingly, to collisionally cool (see below) ions of large protein complexes requires a higher pressure in a quadrupole ion guide than is used for more highly charged protein ions or peptides (Chernusevich & Thomson, 2004).

D. Scanning with Frequency Sweeps

If the voltages \( U \) and \( V_{RF} \) are kept constant and the frequency of the quadrupole power supply is scanned, ions of different mass-to-charge ratio will reach the tip of the stability region and a mass spectrum can be produced. This was first demonstrated by Paul and Raether (1955) who swept the frequency of a quadrupole from 2.38 to 2.54 MHz to produce a mass spectrum of Rb isotopes (see also Paul, 1990). A quadrupole power supply capable of frequency scans was described by Mellor (1971). Marmet and Proulx (1982) described a frequency swept quadrupole that was intended to give greater stability than a conventional quadrupole with the electronics available then. A frequency scan from 500 to 350 kHz was used to produce a spectrum from \( m/z = 10 \) to 40 with better than unit resolution. A spectrum of Xe\(^+\) ions was demonstrated where the isotopic peaks were baseline resolved. Landais et al. (1998) described a quadrupole with a frequency that could be scanned from 0.4 to 1.1 MHz. Resolution of approximately 100–200 was obtained at \( m/z = 79–176 \). Nie et al. (2006) described a quadrupole with the frequency scanned from 100 to 500 kHz. The quadrupole was operated in the third stability region (see below) to improve resolution. The resolution with ions of cytochrome \( c \) was approximately 30–100. There are two potential difficulties with a frequency-swept quadrupole. First, at the lower frequency necessary for higher mass ions, resolution is limited by the number of RF cycles in the quadrupole. Second, because the acceptance of the quadrupole is proportional to the square of the frequency, as the quadrupole
scans to higher masses (i.e., to lower frequency) the sensitivity might be expected to decrease.

E. Operation in Other Stability Regions

Most commercial quadrupole systems operate in the first stability region. However, there have been several investigations of quadrupole operation in other stability regions with higher \(a\) and \(q\) values. In general, operation in higher stability regions provides higher resolution and the ability to obtain unit resolution with higher kinetic energy ions because the value of \(h\) in Equation (31) is considerably lower than with operation in the first region. Different authors use different notations for the stability regions. The notation used here is from Dawson (1976). Earlier reviews of operation in higher stability regions have been given by Konenkov and Kratenko (1991) and by Du, Douglas, and Konenkov (1999a).

1. The Second Stability Region

The second stability region, Figure 5, is centered at \(q = 7.547\) with a tip at \(a = 0.0295\). Values of \(\beta_x\) and \(\beta_y\) vary from 1 to 2 across the region. The width of the stability diagram at the base gives a resolution \(q/\Delta q\) of 114 for a quadrupole operated in RF-only mode. A quadrupole that requires \(V_{RF} = 5,000\) V to reach \(q = 7.7457\) requires only \(U = 20\) V to reach the tip of the region. A scan line that passes through the tip of the second region will also pass through the first region. When ions are transmitted at the center of the second region, ions of \(m/z\) 8.3 times greater or more are transmitted in the first region. Practical operation in the second region will require a second auxiliary mass analyzer to prevent transmission of ions in the first region. However, only very low resolution is required from the second analyzer.

Dawson and Bingqi (1984a, b) first studied this region and showed that considerably higher resolution is possible than with a quadrupole operated in the first region. The value of \(h\) in Equation (31) is lower in this region. A resolution of several thousands at \(m/z\) 44 and 129 was shown. With 300 eV ions, a resolution of ca. 1,500, sufficient to separate \(^{131}\text{Xe}^+\) from \(^{39}\text{F}^+\), was demonstrated. Dawson and Bingqi (1984a) calculated that in theory \(R = 180n^2_{RF}\) and measured \(R = 19n^2_{RF}\) (Dawson & Bingqi, 1984b). Titov (1998) calculated \(R = 24n^2_{RF}\). Du, Douglas, and Konenkov (1999a) measured \(R_{1/2} = 26n^2_{RF}\) and Konenkov and co-workers measured \(R_{1/2} = 24n^2_{RF}\) (Shagimuratov et al., 1990; Konenkov & Kratenko, 1991).

Because of the lower value of \(h\) compared to the first region, ions of higher energy can be mass analyzed with unit resolution in the second stability region. Hiroki, Kanenko, and Murakami (1995) showed resolution of 48 at \(m/z = 32\) with a quadrupole operated in the second region with no DC between the poles (i.e., \(a = 0\)) and an ion energy of 3,000 eV. Du, Douglas, and Konenkov (1999a) showed unit resolution at \(m/z = 39\) with 1,000 eV K\(^+\) ions.

Because of the higher RF voltages required for scanning in the second region, it may be most useful for mass analysis of relatively low \(m/z\) ions. Ying and Douglas (1996) and Du, Douglas, and Konenkov (1999a) discussed the possible advantages for ICP-MS. The ability to mass analyze high energy ion beams may reduce space charge problems, a source of non-spectroscopic interferences in ICP-MS. With low energy beams a resolution \(R_{1/2} \approx 5,000–9,000\) is sufficient in many cases to separate atomic ions from molecular ion interferences below \(m/z = 80\). Ying and Douglas (1996) demonstrated a resolution at half height of \(R_{1/2} = 5,000\) at \(m/z = 56\), sufficient to separate \(\text{ArO}^+\) from \(\text{Fe}^+\).

Low energy ions limit the maximum scan speed that can be achieved with a quadrupole. If the quadrupole mass setting changes before an ion passes through the quadrupole, the ion will not be transmitted. With high energy ion beams a quadrupole can, in principle, scan more quickly. For ICP-MS this will increase the number of elements that can be detected in a transient sample. Grimm, Clawson, and Short (1997) demonstrated the use of the second stability region to mass analyze ions with kinetic energies up to 1,000 eV for fast GC/MS scans. Scan rates of 1,000 scans/sec over 80 mass units were demonstrated.

The transmission with operation in the second region is expected to be considerably less than in the first region for two reasons: (1) the acceptance of the quadrupole is lower in the second region, and (2) the fringe fields are more defocusing. When a quadrupole is operated in the second region at a resolution of 10,000 the acceptance is approximately \(10^{-3}\) of the quadrupole operated in the first region at low resolution (Douglas & Konenkov, 1998). With operation at low resolution (114) in the second region, the fringing field can decrease the acceptance by three orders of magnitude if the ions spend too long in the fringing field (Dawson & Bingqi, 1984a; Douglas & Konenkov, 1998). However, these effects are not prohibitive. Ions can be tightly focused into the quadrupole so that the decrease in transmission between the first and second regions is less than calculated from the differences in acceptance (Douglas & Konenkov, 1998). The fringing fields do not defocus if the ion residence time is less than approximately 0.5 RF cycles (Dawson & Bingqi, 1984a; Douglas & Konenkov, 1998). Titov (1998) calculated a maximum in the transmission when \(n_f = 0.1\) for a quadrupole with a distorted field. These short times can be achieved by accelerating the ions in the fringe field and decelerating the ions in the quadrupole. A comparison between
an experimentally measured curve of transmission versus resolution and a curve calculated from the overlap of the source emittance with the quadrupole acceptance showed good agreement provided the emittance corresponded to the ions being tightly focused into the quadrupole (Douglas & Konenkov, 1998). Under these conditions the transmission at low resolution in the second region is approximately 10 times less than in the first region. Increasing the resolution to 5,000 causes another factor of 10 loss of transmission (Ying & Douglas, 1996).

Du, Douglas, and Konenkov (1999b) observed considerable structure on the peaks with a quadrupole operated in the second stability region at resolution of ca. 100–500 and ion energies of 20–100 eV. Two possible sources of the structure were considered: nonlinear resonances caused by field imperfections and ion collection effects. It was shown that the structure was caused by ion collection effects. Ions entering the quadrupole near the axis can be focused or defocused at the exit of the quadrupole. When defocused, the ions are collected less efficiently and a dip appears on the peak. It was shown that nonlinear resonances caused by hexapole and octopole fields cannot cause structure on a peak when the quadrupole is operated at a resolution greater than 800 because the resonance lines do not pass through the tip of the stability region. Similar observations of focusing effects were reported for a quadrupole operated in the third stability region (Du et al., 2000).

2. The Third Stability Region

The third stability region (Fig. 2) has a somewhat rectangular shape and is near \( a = 3, q = 3 \). The upper and lower tips are shown in Figure 6a and b, respectively. Values of \( \beta_x \) vary from 1 to 2 and \( \beta_y \) from 0 to 1. A scan line that passes through the center of the region gives a resolution of 22 (Dawson, 1974). Mass analysis is possible with scan lines that pass through the upper tip \((a, q) = (3.164, 3.234)\) or through the lower tip \((a, q) = (2.521, 2.815)\). Scan lines that pass through these tips do not pass through the first stability region and so a mass filter operated in the third region does not require any additional device to reject higher mass ions.

Operation of a mass filter in the third stability region can provide higher resolution than operation in the first stability region. Konenkov et al. (1990) first showed the separation of \( \text{CO}^+ \) from \( \text{N}_2^+ \) \((m/\Delta m = 2,500\) at \( m/z 28\)) (reproduced in the review of Konenkov and Kratenko, 1991), and separation of \( \text{Ar}^{3+}/\text{Ar}^{4+}\) from \( \text{Ne}^+ \) \((m/\Delta m = 177)\) and \( \text{D}_2\text{O}^+ \) \((m/\Delta m = 656)\). Shagimuratov et al. (1990) demonstrated baseline separation of isotopic peaks of \( \text{Kr}^{10+}/\text{Kr}^{11+} \) differing in mass by 0.5 Th. Konenkov, Silakov, and Mogilchenko (1991) demonstrated separation of \( \text{He}^+ \) from \( \text{D}_2^+ \) \((m/\Delta m = 157)\). Hiroki, Abe, and Murakami (1991) noted the resolution is higher than with operation in the first region and that the peaks have much less tailing, allowing the detection of a minor peak beside a major peak. Separation of \( \text{He}^+ \) from \( \text{D}_2^+ \) was demonstrated (Hiroki, Abe, & Murakami, 1992) and separation of \( \text{He}^+ \) from \( \text{HD}^+ \) \((m/\Delta m = 518)\) (Hiroki et al., 1994). Detection of \( \text{He}^+ \) in a large excess \((10^5)\) of \( \text{D}_2^+ \) was described (Hiroki, Abe, & Murakami, 1994a) and applied to leak detection (Hiroki, Abe & Murakami, 1996). In all these studies operation at the upper tip of the stability diagram was preferred because peaks had less tailing on the low mass side. Fringing fields of different lengths were investigated (Hiroki, Abe, & Murakami, 1994b) as well as use of a prefilter to improve sensitivity by a factor of 2 (Hiroki et al., 1995).

Du, Olney, and Douglas (1997) investigated the use of the third stability region for ICP-MS. Resolution of up to 4,000 was obtained at \( m/z = 59 (\text{Co}^{59+}) \) with operation at the upper tip, and ca. 1,000 with operation at the lower tip. These resolutions are not generally high enough to separate atomic ions from molecular ion interferences. However, at a resolution of ca. 600–1,000, readily obtained with operation at the upper tip, the peaks were found to be remarkably free of tails on the low and high mass...
sides compared to operation in the first stability region. An abundance sensitivity of greater than 10^7 less than 0.5 Th from the peak center was demonstrated at m/z 59. This lack of peak tails was also seen in later computer simulations of peak shapes by Turner, Taylor, and Gibson (2005), and Hogan and Taylor (2008).

Somewhat higher energy ions can be analyzed with operation in the third region. Hiroki, Abe, and Murakami (1994a) used peak shapes from computer simulations to calculate that at the upper tip \( R = 1.7n_{RF}^2 \) and at the lower tip \( R = 0.69n_{RF}^2 \). The same simulations showed \( R = n_{RF}^2/10.9 \) for the first region, in reasonable agreement with the calculation of Paul, Reinhard, and von Zahn (1958) which gave \( R = n_{RF}^2/12.25 \). Konenkov and co-workers found \( R = 0.7n_{RF}^2 \) (Konenkov et al., 1990; Konenkov & Kratenko, 1991). Dawson (1974) estimated that approximately five times fewer cycles were required than in the first region so \( R \approx 0.7n_{RF}^2 \). Titov (1998) calculated \( R = 1.4n_{RF}^2 \). Du, Douglas, and Konenkov (1999a) measured \( R_{1/2} = 1.0n_{RF}^2 \) for operation at the upper tip. These calculations and measurements suggest that ions of somewhat higher energy, a few tens of eV, might be mass analyzed with operation in the third region. Unit resolution with 63 eV Co^+ ions was shown by Du et al. (2000), and resolution of 275 with 120 eV Co^+ ions was demonstrated by Du and Douglas (1999).

Acceptance ellipses for the third region with operation at the upper and lower tips have been calculated by Dawson (1974), Konenkov, Mogilchenko, and Silakov (1992), Konenkov and Dowell (1997), Konenkov (1997), Titov (1998), and Du, Douglas, and Konenkov (1999a). The acceptance in the x direction is much greater than in the y direction. The combined acceptances (x and y) at the upper and lower tips are similar. Du, Douglas, and Konenkov (1999a) showed a calculated transmission versus resolution curve for a realistic emittance and an ion residence time in the fringe field of one RF cycle. Similar transmissions were calculated for operation at the upper and lower tips. In contrast, the experiments of Du, Olney, and Douglas (1997) showed remarkably different transmissions at the upper and lower tips. The differences between experiment and modeling remain unexplained, but may be related to the complex emittance of the “hollow” beam used in the experiments.

Du, Olney, and Douglas (1997) showed that peaks have remarkably little tailing provided ion energies remain low (<10 eV). With higher energy ions, peaks form tails. Hiroki, Abe, and Murakami (1994a) used computer simulations of peak shapes to show that, with operation at the upper tip, peaks tail on the high mass side but remain relatively sharp on the low mass side. Conversely, with operation at the lower tip, peaks tail on the low mass side but remain sharp on the high mass side. Du and Douglas (1999) demonstrated this with 120 eV Co^+ ions. Du and Douglas (1999) then described a tandem quadrupole mass analyzer that takes advantage of these peak shapes. Two quadrupole mass analyzers are operated in tandem, the first at the upper tip and the second at the lower tip and each at relatively low resolution. The quadrupoles scan together, with each eliminating tails on one side of the peak. The resulting peak is free of tails, even with relatively high energy (100 eV) ions. The sensitivity was found to be highest with the two quadrupoles placed ca. 2 mm apart with no intervening lens.

Several authors have considered the effects of the fringing field with operation in the third region. In comparison to the first stability region, fewer cycles in the fringing field give the optimum transmission. Konenkov (1993) showed that the transmission is highest if ions spend 1.2 cycles in the fringe field. Konenkov (1997) showed that with the optimum number of cycles in the fringe field, ca.1.2 at the upper and lower tips, the acceptance increased ca. 3 times over that with no fringing field so that, at a resolution of 100, the transmission was similar to that of a quadrupole operated in the first region. Konenkov and Dowell (1997) showed that the optimum residence times are about \( n_t = 1.0 \) with operation at the upper tip and \( n_t = 1.2 \) with operation at the lower tip. Titov (1998) calculated the optimum \( n_t \) at the upper tip is 1.3, and at the lower tip 1.2.

Hiroki, Abe, and Murakami (1994b) studied experimentally the effects of the inlet and outlet fringing field lengths by changing the separation between the quadrupole and a source and detector, and concluded short fringing fields were optimal. Hiroki et al. (1995) added a short RF-only quadrupole “prefilter,” with an RF voltage approximately 0.2 of that of the mass analyzing quadrupole, to a quadrupole operated at the center of the third region, and gained a factor of 2 in transmission. This was attributed to the ions remaining more stable in the y direction as they approached the quadrupole, although x motion was still unstable in the fringe field.

3. The Fourth Stability Region

The fourth stability region is shown in Figure 7. The \( q \) values on the \( a = 0 \) axis range from 21.298631 and 21.303174. At the tip \( a = 2.06 \times 10^{-3} \). The values of \( \beta_x \) and \( \beta_y \) vary from 2 to 3. When ions are transmitted in this region, ions with \( m/z \) 2.82 times greater are simultaneously transmitted in the second region, and ions with \( m/z \) 23.46 times greater or more are transmitted in the first region. With no DC applied to a quadrupole the width of the region gives a nominal resolution \( q/D_q \) of 4,700.

Chen, Collings, and Douglas (2000) investigated the ion optical properties of this region. With no DC applied between the rods a resolution of \( R_{1/2} = 13,900 \) was obtained with 40 eV ^39K^+ ions, as expected from the width of the stability region. When DC was added between the rods, the resolution did not increase. The resolution was found to vary approximately as \( R_{1/2} = 829n_{RF}^2 \), and it was calculated that unit resolution should be possible at \( m/z \) 39 with 10,000 eV ions. High resolution is possible with relatively high energy ions. A resolution of \( R_{1/2} = 5,000 \) was demonstrated with 750 eV ions and a resolution of \( R_{1/2} = 1,400 \) with 4,000 eV ions. The acceptance of the quadrupole was calculated for various residence times in the fringing field, and was found to drop severely for times of more than 0.3 RF cycles. The acceptance was calculated to be \( 10^{-2} \) to \( 10^{-4} \) of the acceptance of a quadrupole operated in the second region (depending on resolution). Measurements of the transmission in the fourth region were compared to measurements of the transmission in the second region when the quadrupole was operated at resolutions of 1,500–5,000. The transmission in the fourth region was two to three times less, because high ion energies (600–4,000 eV) could be used to increase the transmission in the fourth region.
F. Mass Filter Operation with Rectangular or Other Periodic Waveforms

Quadrupoles need not be operated with the sinusoidal waveform described by Equation (15). Any periodic waveform may be used. In this case, the equation of motion becomes

\[
\frac{d^2u}{dt^2} + \Psi(t)u = 0
\]

where \(u\) is \(x\) or \(y\) and \(\Psi(t)\) is any periodic function of time. This equation is known as the Hill equation (Dawson, 1976, p. 14).

Richards, Huey, and Hiller (1973) showed that a quadrupole mass filter can be operated with a periodic rectangular waveform, like that shown in Figure 8. They considered the case where \(|V_1| = |V_2|\). The claimed advantages are that more precise control of the waveform may be possible and, during the periods of constant voltage, the solutions to the equation of motion can be obtained analytically. Matrix methods (Pipes, 1953; Dawson, 1976, p. 83; Konenkov, Sudakov, & Douglas, 2002) can then be used to calculate the stability diagram, which differs somewhat from the more familiar diagrams of Figures 2 and 4. Provided the waveform has a net DC component on average, parameters \(a\) and \(q\), analogous to the Mathieu parameters, can be calculated and mass analysis is possible by placing an ion at the tip of a stability region. Richards, Huey, and Hiller showed that if the ratio \(\tau/T\) is set to 0.390, the stability region shrinks to a small region on the \(q\) axis and so mass analysis is possible with no DC component to the waveform. They demonstrated a resolution of up to 300 at \(m/z = 84\) (Kr\(^{+}\)). When operated with the waveform of Figure 8a, a quadrupole will have constant resolution over its mass scan. As discussed above quadrupoles are more often operated at constant peak width (often unit resolution). Richards (1977) show that with a rectangular waveform the resolution can be adjusted during a scan by changing the duty cycle \(\tau/T\).

Any periodic waveform can be used to operate a quadrupole. Richards, Huey, and Hiller (1973) also discussed the use of a trapezoidal waveform. More complex waveforms can be used, provided they are periodic. The stability diagrams for a variety of rectangular waveforms were described by Konenkov, Sudakov, and Douglas (2002). Sheretov (2000) derived properties of the
ion motion for a rectangular waveform and a harmonic waveform of the form \( \Phi(t) = U - V_{\text{RF}}(\cos \Omega t + k \cos \Omega q t) \), where \( j \) is an integer (usually 2 or 3). Sheretov et al. (2000) calculated stability diagrams for 3D traps and quadrupole mass filters operated with these waveforms, and described experimental investigations of the use of such waveforms with a quadrupole mass filter and three-dimensional ion traps. A quadrupole mass filter was operated with a rectangular waveform in two of the higher stability regions. Resolution matched that expected from the width of the stability regions and scan lines used. Sheretov and co-workers (Sheretov, 2002; Sheretov et al., 2002) later showed methods to calculate the properties of ion motion for any periodic waveform, including various rectangular and harmonic waveforms. In any real system, the rectangular waveform will have finite rise times and possibly ringing. Sudakov and Nikolaev (2002) showed that these distortions of the waveform make only minor changes to the stability diagram.

G. Mass Analysis with Islands of Stability

Another method of mass analysis takes advantages of “islands” of stability formed by quadrupole excitation. An auxiliary quadrupole excitation voltage with amplitude \( V \) and frequency \( \omega_{\text{aux}} \) is added, so that the quadrupole potential becomes

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

(37)

where \( \gamma \) is the phase of the excitation which can be taken as 0. The excitation is applied at a frequency which is a rational fraction of the main RF frequency, so that \( \omega_{\text{aux}} = n \Omega \) where \( n \) is an integer. The equations of motion become

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

(38)

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

(39)

where \( \xi, a, q \) and \( q' \) are as in Equation (22) and

\[
q' = \frac{4 \varepsilon \varepsilon' V'}{m \Omega^2 r_0^2} = q V' / V_{\text{RF}}
\]

(40)

The angular frequencies of oscillation in the quadrupole field are given by Equation (24). With quadrupole excitation, resonances are excited when

\[
\omega_{\text{aux}} = \left| \frac{l + \beta u}{K} \right| \Omega
\]

(41)

where \( u \) is x or y, \( K = 1, 2, 3, \ldots \) and \( l = 0, \pm 1, \pm 2, \pm 3, \ldots \) (Collings & Douglas, 2000; Sudakov et al., 2000). When \( n = Q/P \), the \( \beta \) values of the quadrupole resonances are determined by

\[
\frac{Q}{P} = \left| \frac{l + \beta u}{K} \right|
\]

(42)

The stability diagram forms \( P - 1 \) relatively strong resonance lines for the x and y motions. Bands of instability form in the stability region along lines with \( \beta_u \) values determined from Equation (42). Islands of stability are formed between the bands of instability.

Figure 9 shows, for example, the stability islands and bands of instability near the tip of the first stability region formed with \( n = 1/10 \) and \( q' = 0.0050 \). As the excitation amplitude \( q' \) increases, the width of the lines of instability increases. Mass analysis can be done with a scan line that passes through the tip of a stability island. The excitation parameters and scan line must be chosen so that the scan line does not pass through any other
islands. The upper or lower tip of an island can be used for mass analysis (e.g., island A in Fig. 9c).

The use of auxiliary excitation to improve peak shapes was first described by Devant et al. (1989). It was shown that addition of an auxiliary excitation waveform with frequency approximately $10^{-1}$ of the main quadrupole frequency and amplitude approximately $10^{-2}$ of the main quadrupole RF voltage could remove tails from peaks. However, this was not described in terms of bands of instability or islands of stability. The formation and use of islands of stability to improve peak shape was described by Miseki (1993) who again noted that islands can be used to remove tails on the low and high mass sides of a peak, and therefore improve the resolution. Konenkov et al. (2001) reported extensive calculations of island positions and described experiments with an ICP-MS system to map the island positions. The island positions and boundaries were calculated using a matrix method. For any values of $a$ and $q$ two ion trajectories, calculated over one period of the applied waveforms (PT where $T = 2\pi/\Omega$) can be used to determine if the ion motion is stable or unstable (Konenkov, Sudakov, & Douglas, 2002). Trajectories were calculated for a large number of $a$ and $q$ values and used to map the bands of instability and islands of stability. Measured island positions agreed well with the calculated positions. While the use of islands for mass analysis did not improve the limiting resolution of the quadrupole, the abundance sensitivity was improved from $10^6 - 10^7$ to $10^9 - 10^{10}$. Baranov, Konenkov, and Tanner (2001) described mass analysis with islands of stability with an ICP-MS system. They showed that use of an island prevented peak tails from forming when the ion energy in the quadrupole was increased from approximately 5 to 13–15 eV. The increased ion energy improved the sensitivity by approximately two times. Glebova and Konenkov (2002) modeled peak shapes and resolution with operation at the tip of island “A” (notation of Fig. 9). For a quadrupole constructed with round rods $(r_{R0} = 1.130)$, operation with an island with $q' = 0.012$ and $v = 9/10$ removed tails on the low mass side of a peak. This effect was not seen with an ideal quadrupole field, and it was concluded that use of an island of stability can improve peak shape for weakly distorted quadrupole fields.

Sheretov, Gurov, and Kolotilin (1999) considered the general case of periodic variations of the quadrupole operating parameters that produce parametric resonances and hence bands of instability in the stability diagram. They pointed out that bands of instability can be formed by modulating both the applied RF and DC together, or by modulating just the DC or just the RF amplitudes, and calculated that the number of RF cycles required in the field for a given resolution is decreased when an island of stability is used for mass analysis. Glebova and Konenkov (2002) compared conventional mass analysis with an ideal quadrupole field and mass analysis using an island of stability at a resolution of approximately 100, and concluded there were no advantages to using an island of stability. Later, however, Konenkov, Korolkov, and Machmudov (2005) used matrix methods to calculate island positions and boundaries, and ion trajectory calculations to determine peak shapes and resolution with mass analysis in islands. The effects of modulating the RF amplitude, and both the RF and DC amplitudes, were compared. Ideal fields were compared to results with a round rod set with ratio of rod diameter to field radius $r_{R0} = 1.13$. With amplitude modulation the resolution can be adjusted in three ways: (1) by changing the slope of the scan line at the upper or lower tip of an island, (2) by setting the scan line to pass through the center of an island and adjusting the modulation amplitude, or (3) by setting the scan line to pass through the center of an island and adjusting the modulation frequency. It was concluded that the preferred (and simplest) method is to fix the modulation amplitude and frequency and adjust the slope of the scan line. Modulation of the RF gave similar results to modulation of the RF and DC. Because modulation of the RF alone is simpler, it is preferred. With an ideal quadrupole field, amplitude modulation of the RF was found to remove peak tails at a resolution of 390 with 100 cycles of the field. This contrasts with the finding of Glebova and Konenkov (2002) that for an ideal field there are no benefits from using islands of stability, because the earlier study considered only low resolution (100). Konenkov, Korolkov, and Machmudov (2005) also found that use of islands removed peak tails in a quadrupole constructed with round rods. Finally, it was concluded that the number of RF cycles in the field required to reach a resolution of 400 was decreased from approximately 150 without modulation, to 75 with modulation of the RF amplitude.

H. Mass Analysis with Radial Ejection

If a quadrupole is used as a linear ion trap, ions may be ejected in order of their mass radially through a slot in a rod or rods to produce a mass spectrum. This can be done by scanning the trapping RF so that ions reach the stability boundary at $a = 0$, $q = 0.908$, or by applying dipole excitation between one of the rod pairs to excite ions for ejection (Schwartz, Senko, & Syka, 2002). This is not discussed in detail here because the method is used exclusively with trapped ions (reviewed by Douglas, Frank, & Mao, 2005).

I. Mass Analysis with Axial Ejection

A quadrupole mass filter may also be operated in RF-only mode for mass analysis. Ions of a broad range of mass-to-charge ratios are transmitted through the quadrupole. A stopping potential is applied to an electrode or electrodes at the quadrupole exit. Ions of a selected mass-to-charge ratio are excited in the radial directions. In the fringing field at the exit of the quadrupole the $x$ and $y$ motions are mixed with axial motion in the $z$ direction. Some of the increased energy in the radial direction is converted to axial kinetic energy so that the excited ions overcome the potential barrier and are transmitted to a detector. The original motivation for this work was to overcome the defocusing fringing fields at the entrance to a quadrupole mass filter operated conventionally with applied RF/DC voltages, to increase the acceptance over that of a conventional mass filter, and to overcome deleterious effects of field imperfections.

Brinkmann (1972) first described this concept. A quadrupole was operated in RF-only mode with a potential barrier at the exit. The quadrupole was scanned so that ions of increasing $m/z$ reached the stability limit at $q = 0.908$, where they gained kinetic energy in the radial directions. A resolution of more than 1,400 was obtained at $m/z = 500$, and the transmission was approximately 10 times greater than that of the same quadrupole.
operated conventionally. This work was extended by Holme and co-workers (Holme, 1976; Holme, Sayyid, & Leck, 1978) who reported that there is less dependence of the performance on mechanical imperfections, and less defocusing of ions at the quadrupole entrance. Yang and Leck (1982) extended the mass range to 600 and reported this mode of operation provided uniform transmission over the mass range, although with low resolution. They also reported a relative lack of susceptibility of the performance of the RF-only mass spectrometer to contamination and construction errors. Yang and Leck (1984) showed that the performance was only slightly affected by small spurious potentials applied to the rods, and that therefore an RF-only mass analyzer might be more suitable for use in a dirty vacuum system. Ross and Leck (1983) modified the collector assembly and reported the transmission depended less critically on operating parameters in comparison to conventional operation of the quadrupole, and that for a given transmission, the resolution was higher than with conventional operation. Dawson (1985) reported a detailed investigation of peak shapes, peak tailing, and resolution. The quadrupole was operated at various frequencies up to 3.0 MHz. The major finding was that reasonable peak shape and resolution were possible provided the ions spent sufficient time in the RF field. In all these studies there were difficulties with a continuum background caused by relatively high-velocity low q-value ions.

Hager (1999) reported operation of a quadrupole in RF-only mode with a greatly reduced continuum background. Ions formed by electrospray were collisionally cooled in a 20-cm long RF-only quadrupole operated at 7 mTorr, and then entered a 24-mm long RF-only quadrupole for mass analysis. Because it is the fringing fields that cause ions to gain energy in the axial direction when they are excited at \( q = 0.908 \), a very short quadrupole (24 mm) could be used. A stopping potential, typically 7 V above the rod offset of the quadrupole, was applied to an aperture lens at the exit of the quadrupole. The RF of the quadrupole was scanned to bring ions to the stability boundary at \( q = 0.908 \). The continuum background was reduced by applying unbalanced RF to the rods and \( \pm 3.0 \text{ V of DC} \) between the rods. It was found that applying some of the quadrupole RF voltage to the exit lens improved the transmission by nearly an order of magnitude. It is possible that the improved performance in this work derives partially from the collisional cooling of ions before they enter the quadrupole. This provides an ion source with smaller spatial and energy spreads than were used in prior studies (see below).

Hager (2002) later extended this work to a study with a triple-quadrupole mass spectrometer system. Precursor ions, mass selected in a first quadrupole (Q1), formed fragment ions in a quadrupole collision cell (Q2). The fragment ions could be trapped and accumulated in either Q2 (operated at \( 7 \times 10^{-3} \text{ Torr} \)) or a downstream quadrupole (Q3) (\( 3 \times 10^{-3} \text{ Torr} \)). For axial ejection ions were excited by auxiliary dipole or quadrupole fields. The trapping RF voltage was scanned to bring ions of different \( ml/z \) values into resonance with the excitation. Higher scan speed was possible with trapping of ions at the lower pressure in Q3. With ejection from Q2 a resolution of 6,000 at \( ml/z = 609 \) was possible with very slow scans (5 Th/sec), and a resolution of 1,000 was possible at 1,000 Th/sec. With ejection from Q3, resolution of 6,000 was possible at a scan speed of 100 Th/sec. Higher scan speeds gave lower resolution. The major advantage of this technique is that fragment ions can be accumulated in Q2 or Q3 operated as a linear trap to dramatically improve the sensitivity for tandem mass spectrometry. Hager (2002) reported an improvement in sensitivity of 16 times for MS/MS of reserpine ions in comparison to a conventional fragment ion scan with Q3. Hopfgartner, Hussel, and Zell (2003) reported a sensitivity improvement of 60 times for MS/MS analysis of drug metabolites.

Londry and Hager (2003) have used analytical and numerical calculations in a detailed investigation of forces on ions in the fringing field of a quadrupole used for axial ejection. The potential in this region consists of three parts: (1) the quadrupole RF potential which decreases towards the exit lens (the positive z direction), (2) the potential from the exit lens which decreases in the quadrupole, and (3) the potential from an auxiliary dipole excitation field. The decreasing quadrupole potential causes a net force (averaged over one RF cycle) towards the exit lens. This force increases in \( x \) and \( y \) as the square of the distance from the quadrupole center. The stopping potential on the exit lens produces a force in the opposite direction. At some point these two forces balance each other. Ions on the exit lens side of the balance point are ejected. Ions on the quadrupole side of the balance point are reflected back into the quadrupole. A map of the points where ions are reflected gives a cone shaped region near the quadrupole exit. Excitation of ions moves ions from regions near the quadrupole center, where they are reflected, to regions closer to the quadrupole rods where they are ejected.

\[ J. \text{ The Ratio } r/l_0 \]

While hyperbolic electrodes can produce the best approximation to a quadrupole field (aside from construction errors and the finite truncation of the electrodes), round rods are often used because they are easier to manufacture and mount to high precision. If the quadrupole electrodes have fourfold rotational symmetry, the symmetry of the potential requires that the amplitudes of higher multipoles are 0 except \( A_2, A_6, A_{10}, A_{14}, \ldots \) (Denison, 1971). Several authors have discussed the ratio of rod radius \( r \) to field radius \( r_0 \) that is optimum for a mass filter. With round rods, additional multipoles are added to the potential (Eq. 6). Dayton, Shoemaker, and Mozley (1954) showed that a ratio \( r/r_0 = 1.148 \) makes the amplitude of next highest multipole in the expansion, \( A_6 \), 0. Lee-Whiting and Yamazaki (1971) used conformal mapping to calculate the potential from four parallel rods and showed that \( A_6 = 0 \) when \( r/r_0 = 1.14511 \). Denison (1971) calculated the field of a quadrupole in a cylindrical housing of radius 3.44\( r_0 \) and found a ratio \( r/r_0 = 1.1468 \) makes \( A_6 = 0 \). Reuben et al. (1994, 1996) again used conformal mapping to determine the potential of a quadrupole in a grounded case and also found the ratio \( r/r_0 = 1.14511 \) makes \( A_6 = 0 \). This ratio was found to be independent of the radius of the case. The same ratio was calculated by Douglas et al. (1999).

In these studies it was assumed that the ratio \( r/r_0 \) that makes \( A_6 = 0 \) would produce the best mass filter. However, manufacturers did not necessarily use this ratio. It was shown in 1999 that a ratio that balances the effects of \( A_6 \) and \( A_{10} \) to decrease the effects of nonlinear resonances is preferred (Schulte, Shevchenko, & Radchik, 1999). A ratio \( r/r_0 = 1.10 \) was proposed...
to minimize losses from nonlinear resonances. Gibson and Taylor (2000) used trajectory calculations to simulate peak shapes for quadrupoles with hyperbolic and round rods with a ratio \( r/r_0 = 1.148 \) and found that the round rods produced tails on the peaks, especially on the low mass side. Gibson and Taylor (2001) subsequently investigated the effects of the ratio \( r/r_0 \) on the performance of a quadrupole and proposed that a ratio of 1.12\( r_0 \) to 1.13\( r_0 \) would give the highest resolution and transmission. Douglas and Konenkov (2002) used simulations to show that a ratio \( r/r_0 = 1.128–1.130 \) gives peak shapes and transmission similar to those of an ideal quadrupole field. When \( r/r_0 = 1.130 \), \( A_6 = 1.00 \times 10^{-3} \) and \( A_{10} = -2.44 \times 10^{-3} \). The \( A_6 \) and \( A_{10} \) terms have similar magnitudes but opposite signs and compensate for each other. The \( A_6 \) term shifts the pass band to low mass. The \( A_{10} \) term shifts the pass band to high mass. When both are present with the correct amplitude, the pass band corresponds to that of an ideal field. Thus, a ratio \( r/r_0 \) that makes \( A_6 = 0 \) does not produce the best mass filter. A ratio \( r/r_0 \approx 1.128 \) is preferred.

### K. Ion Guides

#### 1. Collisional Cooling and Focusing

As described above, to obtain high transmission with a quadrupole mass filter, it is desirable to match the emittance of the ion source to the acceptance of the quadrupole. As the resolution of the quadrupole increases, the acceptance decreases (as 1/R) for a quadrupole operated in the first stability region (Dawson, 1980, 1990). As mass spectrometry has pushed to higher mass for applications in life sciences, the demands for higher resolution and higher sensitivity have increased. The shape of the emittance from the source can be changed with an ion lens (Regenstreif, 1967; Dawson, 1980). For example, a nearly parallel beam with a spread of \( x \) positions but a small spread of radial velocities can be focused so it has a smaller spread of positions but a greater spread of radial velocities. However, there is a limit to using this to match a source to a mass analyzer. Liouville’s theorem (Joseph Liouville, 1809–1882) states that the area of the beam in phase space before and after an ion lens remains constant (Regenstreif, 1967; Dawson, 1980). Radial velocities can be traded for large radial positions, or vice versa, but an ion lens or a quadrupole ion guide cannot reduce the area in phase space occupied by the beam.

The use of RF ion guides, and particularly quadrupole ion guides, has provided a method to overcome this limitation. If a quadrupole is operated in RF-only mode, that is, with only RF between the rods, the Mathieu parameter \( a \) will be 0, ions of a broad range of \( m/v \) values will lie on the \( a = 0 \) axis and have stable trajectories in the quadrupole. The quadrupole can be used as an “ion guide” to transport ions from a source to an analyzer. Initially, it was believed that the pressure in the ion guide should be as low as possible to prevent losses of ions by scattering (see the review by Thomson, 1998). However, Douglas and French (1992) reported that the ion transmission through an ion guide and into a quadrupole mass filter increased as the pressure was increased from 5 \( \times 10^{-4} \) to 5 \( \times 10^{-2} \) Torr (see also Douglas & French, 1990). Collisions between ions and the gas in the ion guide cause the ions to move to the center of the ion guide and also to lose radial energy. Ions are “focused” to the center of the ion guide with a small spread of positions and small radial energies. Thus, the emittance of ions at the exit of the ion guide is less than at the entrance. At the same time the kinetic energy distributions of ions at the exit of the ion guide narrow to distributions with energies and energy spreads of approximately 1 eV per charge or less. The beam quality at the exit of the higher pressure ion guide is greatly improved for transmission into a downstream mass analyzer, particularly a quadrupole. Collisional focusing requires that the ions be injected into the ion guide with relatively low energies, ca. 10 eV/charge. At higher energies collisions cause ions to scatter or fragment. Subsequently, Xu et al. (1993) reported measurements of the transmission of \( O_2^+ \) ions through a hexapole ion guide with collisions with He. They noted the ions at the exit of the ion guide had energies and energy spreads of approximately 0.8 eV. Calculations of ion trajectories showed the ions moved to a region of approximately 0.5 mm in diameter at the center of the guide and therefore also showed collisional focusing. Collisional cooling of the ion beam in these experiments apparently overcomes Liouville’s theorem because the region occupied by the ions in phase space shrinks. However, Liouville’s theorem is not violated because the phase space of the gas molecules is not considered.

The use of collisional cooling or collisional focusing in ion guides was soon extended to ESI orthogonal injection TOF systems (Krutchnisky et al., 1998a) and vacuum MALDI orthogonal injection TOF systems (Krutchnisky et al., 1998b). With MALDI a nearly continuous beam of ions is obtained at the exit of the ion guide, and the properties of the ions are largely independent of the source parameters. The improvements for orthogonal injection TOF, higher sensitivity and higher resolution, have been described by Standing (2000). Ion guides with collisional cooling have since found widespread application in many areas such as ESI-FTICR (Jebanathirajah et al., 2005), ICP-MS (Tanner, Baranov, & Bandura, 2002), atmospheric pressure MALDI (Schneider, Lock, & Covey, 2005), and nuclear physics (see, for example, Nieminen et al., 2001; Kellerbauer et al., 2002). A complete review is beyond the scope of this article.

Collisional cooling and focusing have also found applications in tandem mass spectrometry. In triple-quadrupole mass spectrometers, mass selected precursor ions are fragmented by energetic collisions with gas in a quadrupole ion guide. If the ion guide is operated near single collision conditions the kinetic energies of fragment ions \( E_f \) are related approximately to the kinetic energies of the precursor ions \( E_p \) by

\[
E_f \approx \frac{m_f}{m_p} E_p
\]

Thus, the fragment ions have mass-dependent kinetic energies. To obtain high mass resolution in the downstream quadrupole mass analyzer Q3, it is desirable that the fragment ions have low kinetic energies within Q3 (Section IIIA). Ions can be slowed by increasing the rod offset potential of Q3. However, this requires knowing the kinetic energies of the fragments. The problem is that Equation (43) is only approximate. If the rod offset of Q3 is too low, the resolution is degraded; if too high, the ions are not transmitted. If the kinetic energies of the ions are measured, then the rod offset of Q3 can be set correctly to provide high

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**LINEAR QUADRUPOLES IN MS**

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**Mass Spectrometry Reviews DOI 10.1002/mas**

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951
transmission and resolution (Shushan et al., 1983) but this is not practical. In many applications, to avoid any loss of signal the rod offset of Q3 was commonly set equal to the rod offset of Q2. In this case fragment ions had relatively high kinetic energies in Q3 and the mass resolution was degraded. A solution to this problem was found when it was realized that collisional cooling could be applied to the fragment ions (Thomson et al., 1995). If the collision cell pressure is increased from ca. $5 \times 10^{-4}$ to ca. $5 \times 10^{-3}$ Torr (Ar), all fragment ions at the cell exit have kinetic energies of 1 eV or less. Thus improved mass resolution is possible in Q3 which can be operated with a fixed rod offset voltage, slightly below that of Q2. At the same time, because collisional cooling causes all ions to move to the center of Q2 with a reduced emittance, the transmission through Q3 increases greatly. The improvements to MS/MS spectra are dramatic and have been described by Thomson et al. (1995) and in more detail by Morris, Thibault, and Boyd (1994). The benefits of increased sensitivity and mass resolution are also seen where Q3 is replaced by a TOF system (Standing, 2000).

2. Ion Guides with Axial Fields

The use of collisional focusing in Q2 of triple quadrupoles provided an ion beam of greatly improved quality for Q3 but had one drawback. With pressures in the collision cell of $5 \times 10^{-3}$ Torr or greater, the transit time of the ions was increased and this caused problems with fast scans in some modes of operation. Suppose Q3 is set to a fixed product ion mass, and Q1 switches rapidly between two precursor masses, ions of mass $m_1$ which produce a fragment at the mass setting of Q3, and ions of mass $m_2$ which do not. When Q1 switches from $m_1$ to $m_2$, some of the fragments formed from $m_1$ are still draining from the collision cell and appear to have been formed from $m_2$. Thus, “crosstalk” problems were encountered with early versions of the high-pressure collision cell. A simple solution was to apply a voltage pulse to empty the collision cell between measurements. However, this did not address the slow transit of ions that also caused problems in precursor and neutral loss scan modes. A more complete solution was to apply a small axial field of the order of 1 V/m along the axis of the cell to cause the ions to drift more rapidly to the exit (Thomson, Jolliffe & Javahery, 1996; Thomson, 1998). Initially, this was done with a quadrupole with rods made of many segments. Each segment was given a different DC bias to provide a net axial field along the quadrupole. Many other methods of providing an axial field are possible (Thomson, Jolliffe, & Javahery, 1996; Thomson & Jolliffe, 1998). A system with conical shaped rods, which is both mechanically and electrically simple, has been described (Thomson, 1998; Loboda et al., 2000). The conical rods are arranged so that a first opposing pair of tapered rods have larger diameters at the entrance, and a second pair of rods have larger diameters at the exit. A DC potential difference is applied between the rod pairs. At any point along the quadrupole, the axis potential is determined by the larger rods. If a positive DC potential is applied to the first pair, and a negative DC potential to the second pair, the quadrupole axis potential will be positive at the entrance, zero at the center, and negative at the exit, so that an axial field is produced. Properties of a collision cell with an axial field produced this way were investigated in detail by Mansoori et al. (1998) who concluded that crosstalk problems were eliminated and at the same time, the benefits of collisional cooling were retained. An even simpler version that used cylindrical rods that are tilted with respect to the axis was eventually implemented in commercial systems. The DC applied between the rods limits the transmission of Q2 to a band pass. For triple-quadrupole structures where Q3 scans this is not a problem because the pass band can be scanned along with Q3 to transmit the ions of interest. For instruments where Q3 is replaced by a TOF system, the pass band becomes more of a problem. Loboda et al. (2000) described a method of adding an axial field by placing additional electrodes between the rods of Q2. The same potential is applied to all electrodes. The field on axis is determined by the spacing of the electrodes from the quadrupole center which varies along the length of the quadrupole. The pass band with this method can be up to 10 times that of the quadrupole with tapered rods. The use of quadrupole ion guides with axial fields has been extended to other applications such as the measurement of collision cross sections (Javahery & Thomson, 1997; Guo et al., 2005), the fragmentation of ions in an ESI-TOF system (Dodonov et al., 1997), improved scan speed and controlled ion molecule chemistry with an ICP-MS system (Bandura, Baranov, & Tanner, 2002), and an ion-molecule reactor with heating of ions (Guo, Siu, & Baranov, 2005). Most importantly, however, the use of collisional cooling to couple high-pressure sources to a quadrupole mass analyzer, and to improve the emittance of an ion beam from a collision cell, has contributed to the development of bench top mass spectrometers with sensitivity and resolution exceeding those of earlier much larger systems.

IV. LINEAR QUADRUPOLES WITH ADDED MULTIPOLe FIELDS

Most quadrupole mass filters are constructed with high precision to make the closest approximation to the desired field. It has long been argued that small construction errors can degrade the performance of a mass filter, although the effects of various errors have not been well described in the literature. Austin, Holme, and Leck (1976) concluded that to obtain a resolution of 900 required mechanical errors in general of less than $10^{-3}$. Titov (1995) calculated that a mechanical error of 10 $\mu$m in the rod diameters reduced the acceptance and hence the transmission by a factor of nearly 10. Taylor and Gibson (2008) used trajectory calculations of peak shapes to show that if the $y$ rod of a quadrupole (the rod with the negative DC with positive ions) is moved in by 0.005 $r_0$ (20 $\mu$m for a quadrupole with $r_0 = 4.0$ mm), the transmission decreases by ca. 2 times and structure is formed on a peak (nominal resolution 300–400). Dawson (1980) calculated the limiting resolution with various mechanical distortions, and stated “quadrupole rods are said to be manufactured to tolerances in radius of $10^{-3}$ cm and to parallelism of $10^{-4}$ cm.” As discussed, changing the ratio $r/r_0$ of a quadrupole with round rods from 1.12 to 1.13 significantly changes the peak shape and transmission. This corresponds to a change in rod radius of 40 $\mu$m for 4.0 mm radius rod.

The field of a quadrupole with distorted electrode geometries contains additional multipoles. Generally these have amplitudes $A_N$ which are $10^{-3}$ or less of $A_2$. For example, when an
linear quadrupole with an added octopole field has a potential of the form:

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

where \( A_2 \approx 1.0 \) and \( A_4 \) is the amplitude of the added octopole field. Sudakov and Douglas (2003) showed that an octopole field can be added to a linear quadrupole constructed with round rods by placing the two \( y \) rods closer to the central axis than the \( x \) rods. However, this method adds significant potential of other multipole terms. A preferred method is to make the radius of the \( y \) rods \( (R_y) \) greater than the radius of the \( x \) rods \( (R_x) \). This adds an octopole term and only low levels of other higher multipoles. An axis potential is formed, but this can be removed by unbalancing the RF and DC applied to the rods. The changes in rod radius are much greater than those caused by manufacturing tolerances. For example, to make \( A_4 = 0.026 \) requires \( R_y/R_x = 1.130 \), a difference of rod diameters of approximately 1.0 mm for a quadrupole with \( R_y = 4.0 \) mm. Figure 10 shows a photograph of a rod set with a 2.0% added octopole field \( (R_y/R_x = 1.220) \). A detailed description of trapped ion motion and fragmentation efficiencies of these rod sets used as linear ion traps has been given by Michaud et al. (2005). Given the discussion above, it would not be expected that such rod sets would be capable of conventional mass analysis.

Figure 10. A linear quadrupole with 2.0% added octopole field. The radius of the smaller rods is 4.50 mm and the radius of the larger rods is 5.49 mm. Reproduced from Ding, Konenkov, and Douglas (2003) with permission. Copyright John Wiley and Sons, Ltd. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
DOUGLAS

**FIGURE 11.** Peak shapes with mass analysis with a quadrupole with a 2.6% added octopole field with the positive DC applied to (a) the larger and (b) the smaller rods. Reproduced from Ding, Konenkov, and Douglas (2003) with permission. Copyright John Wiley and Sons, Ltd.

is consistent with the experimental observations, but does not explain why the boundaries become diffuse or sharp. Dawson (1980) estimated that, for a limiting resolution of 2,000, \( A_4 \) must be less than \( 3.5 \times 10^{-4} \). The results of Ding, Konenkov, and Douglas show that mass analysis is possible with values of \( A_4 \) nearly two orders of magnitude greater.

The use of islands of stability with quadrupoles with added octopole fields has also been studied for the cases \( a_x < 0 \). Konenkov et al. (2007) used trajectory calculations to determine island positions and peak shapes for quadrupoles that have added octopole fields of 2.0–4.0%. Rod sets that have only an added octopole field, and round rod sets with added octopole fields and multipoles up to \( N = 10 \) were modeled. Operation in the upper stability island at the tip with the greatest \( |a| \) gave resolution peak shape and transmission comparable to conventional operation with \( a > 0 \). In this case there is no advantage to using the island of stability. With the polarity of the applied DC reversed so \( a < 0 \), only low resolution and transmission are possible with conventional analysis. However, with \( a < 0 \) and use of the uppermost island operated at the tip with the lesser \( |a| \), the simulations showed that peak shapes and resolution similar to those with conventional operation with \( a > 0 \) are possible. These simulations were confirmed in experiments by Moradian and Douglas (2007). An island of stability was formed by using \( q = 0.020 \) and \( v = 9/10 \). These values are not necessarily optimum but were chosen to match the calculations of Konenkov et al. (2007). With a quadrupole with 2.0% added octopole field, measured positions of the island tips agreed well with the calculations of Konenkov et al. With \( a_x < 0 \) at least unit resolution was obtained at \( m/z = 609 \), sufficient to separate the isotopic peaks of ions of reserpine. Without the use of the island, under the same conditions, the peak was ca. 6 Th wide, and isotopic peaks could not be resolved. In this case use of the island overcomes the adverse effects of the added octopole field.

Mass analysis with mass selective axial ejection is also possible with quadrupoles with added octopole fields and was investigated by Moradian and Douglas (2008). Axial ejection at \( q = 0.908 \) with a quadrupole with 2.6% added octopole field gave only broad peaks with low resolution, both with ions flowing continuously through the quadrupole and with trapped ions. The low resolution was attributed to changes in the \( x \) and \( y \) stability boundaries. When \( a = 0 \), the \( x \) stability boundary is at \( q = 0.908 \), but the \( y \) boundary moves out to \( q \approx 0.931 \). It was proposed that between these \( q \) values, ions excited in \( x \) lead to excitation in \( y \) where the motion is stable, possibly delaying ion ejection.

Axial ejection of trapped ions was investigated with a quadrupole with 2.0% added octopole field, with ions excited by dipole excitation in the \( x \) or \( y \) directions, quadrupole excitation, or simultaneous dipole excitation in the \( x \) and \( y \) directions. With a linear quadrupole with added multipole fields, the resolution and scan speed possible depend on the scan direction, as with 3D traps (Makarov, 1996). Best resolution and sensitivity were obtained with forward scans from low to high mass, dipole excitation applied to the smaller rods, and ion excitation and ejection at high \( q \) (0.80). Ejection efficiencies were similar to those obtained with a conventional quadrupole and decreased from approximately 60% at a scan speed of 15 Th/sec to approximately 1% at 4,000 Th/sec.

### B. Linear Quadrupoles with Added Hexapole Fields

A linear quadrupole may also be constructed with an added hexapole field with the potential given by

\[
\Phi(x, y, t) = \left( A_2 \frac{x^2 - y^2}{r_0^2} + A_3 \frac{x^3 - 3xy^2}{r_0^3} \right) \times (U - Y_{\text{RF}} \cos \Omega t)
\]

(45)
where $A_j$ is the amplitude of the hexapole field. The properties of quadrupoles with added hexapole fields have been modeled in detail by Konenkov et al. (2006). It was shown that a hexapole field can be added to a quadrupole constructed with round rods by rotating the two $y$ rods through an angle $\theta$ towards an $x$ rod. With round rods, other multipoles are added to the potential, especially an octopole term. Geometries that produce nominal hexapole fields of 4%, 8%, and 12% were described. Rotating the $y$ rods towards an $x$ rod moves the field center closer to the $x$ rod.

Mass analysis was modeled by running many trajectories with a thermal distribution of speeds (300 K) and a Gaussian distribution of positions in $x$ and $y$ with a standard deviation $\sigma = 0.002r_0$. Quadrupoles with added hexapole fields and no other multipoles were modeled first. These can be constructed with electrodes that have the shapes given by

$$A_2 \left( \frac{x^2 - y^2}{r_0^2} \right) + A_3 \left( \frac{x^3 - 3xy^2}{r_0^3} \right) = \pm c \quad (46)$$

where $c$ is a constant. With a quadrupole with a 2% added hexapole field, and no other higher multipoles, a resolution of ca. 1,130 can be obtained with positive ions. The peak shape and transmission are similar to those with a pure quadrupole field, provided the positive DC is applied to the $x$ rods so the Mathieu parameter $a > 0$. If the polarity of the DC is reversed so $a < 0$, only very low resolution and poor peak shape are obtained. Increasing the amplitude of the hexapole field causes the peak to broaden because of changes to the stability diagram, although resolution of several hundreds could be obtained with quadrupoles with 8% and 12% added hexapole fields.

Mass analysis with quadrupoles with added hexapole fields of 2–12%, constructed with round rods, was then modeled. Multipoles up to $N = 10$ were included. Poor resolution and peaks with considerable structure were obtained, showing that the higher multipoles strongly affected the transmission and resolution. It was shown that the octopole term that is added is largely responsible for the poor performance. The octopole term can be removed by making both $x$ rods greater in diameter than the $y$ rods so that $A_4 = 0$. Modeling the transmission and resolution with these rod sets showed greatly improved transmission and resolution. Resolution of $R_{1/2} \approx 700–800$ was calculated for quadrupoles with 8–12% added hexapole field, and resolution of 1,400 for a quadrupole with 6% added hexapole. At low and high resolution, peaks were free of structure. However, at intermediate resolution peaks showed some structure.

The stability diagram was calculated for a quadrupole with 2% hexapole and no other multipoles, and round-rod quadrupoles with 2–12% added hexapole fields. With $a > 0$, the boundaries remained sharp. Increasing $A_3$ causes the $x$ stability boundary to move out towards larger $q$ values. With $a < 0$, only a diffuse region of stability with low transmission was seen, consistent with the low resolution and transmission seen in simulations of mass analysis when $a < 0$.

Preliminary experimental tests of mass analysis with quadrupoles with added hexapole fields have appeared (Zhao et al., 2007; Xiao, Zhao, & Douglas, 2008). Conventional mass analysis, mass analysis with islands of stability, and mass analysis with axial ejection have been tested. Figure 12 shows

![Figure 12](image-url)

**Figure 12.** Mass analysis with a quadrupole with a 4.0% added hexapole field and unequal diameter rods $R_x = r_0 = 4.500$ mm, $R_y = 5.279$ mm. a: Conventional mass analysis with the positive DC applied to the $x$ rods, $R_{1/2} = 2.070$, relative sensitivity $9 \times 10^4$ ions/sec. b: Mass analysis with an island of stability with $r = 1/20$ and $q' = 0.002$, $R_{1/2} = 2.170$, relative sensitivity $2.8 \times 10^4$ ions/sec. c: Mass selective axial ejection with dipole excitation between the $x$ rods at $q = 0.72$, $R_{1/2} = 2.250$, ejection efficiency 2%. 

Mass Spectrometry Reviews DOI 10.1002/mas
peak shapes obtained with a rod set with 4% added hexapole field and rod diameters chosen to make \( A_4 = 0 \). With conventional mass analysis, Figure 12a, the resolution is \( R_{1/2} \approx 2000 \), but there are tails on the peaks. With an island of stability and at similar resolution, Figure 12b, the tails of the peaks are removed. The transmission is approximately five times lower than that of a conventional quadrupole operated at the same resolution. With axial ejection of trapped ions, Figure 12c, peak shapes and resolution comparable to those obtained with axial ejection from a conventional round-rod quadrupole are possible.

These results show that mass analysis with rod sets with large geometric and field distortions is sometimes possible. The use of islands of stability can in some cases overcome the effects of both small and large field distortions. It appears that our understanding of the effects of field distortions is incomplete. Dawson (1976) concluded that “There remains, therefore, a great deal of scope for further advance in design, performance and applications, building upon the established technological foundation . . .”. This statement, subsequently proven correct, would seem to be equally valid in 2009.

ACKNOWLEDGMENTS

This work was supported by the Natural Sciences and Engineering Research Council of Canada and MDS-Analytical Technologies through an Industrial Research Chair.

V. APPENDIX: ELECTRIC POTENTIALS AND FIELDS: UNITS

This appendix gives a brief review of definitions of electrical potentials and fields, as well as the units used in this article. More detail can be found in text books on electromagnetic theory (Smythe, 1939; Kip, 1969). In linear quadrupoles, as well as many other devices for manipulating ions, electric potentials are applied to electrodes to produce forces on ions. The force \( \mathbf{f} \) on an ion at a point in space with Cartesian co-ordinates \((x, y, z)\) is given by

\[
\mathbf{f}(x, y, z) = Q \cdot \mathbf{E}(x, y, z) \tag{A.1}
\]

where \( Q \) is the charge of the ion and \( \mathbf{E}(x, y, z) \) is the electric field at that point. The electric field at a point is the force per unit charge. Force and electric field are vectors; they have both magnitude and direction. In a Cartesian co-ordinate system they have components along the \( x, y, \) and \( z \) axes, \( f_x, f_y, f_z \), and \( E_x, E_y, \) and \( E_z \), respectively.

If a charged particle is moved from a position \( s_1 \) to a position \( s_2 \) through an electric field, the mechanical work done on the particle is

\[
w = - \int_{s_1}^{s_2} \mathbf{f} \cdot d\mathbf{l} \tag{A.2}
\]

The work done per unit charge is the change in electrical potential \( \Delta \Phi(x, y, z) \) between the points \( s_1 \) and \( s_2 \) so that

\[
\Delta \Phi = - \int_{s_1}^{s_2} \mathbf{E} \cdot d\mathbf{l} \tag{A.3}
\]

It follows that the components of the electric field are given by

\[
E_x = -\frac{\partial \Phi(x, y, z)}{\partial x} \tag{A.4}
\]
\[
E_y = -\frac{\partial \Phi(x, y, z)}{\partial y} \tag{A.5}
\]
\[
E_z = -\frac{\partial \Phi(x, y, z)}{\partial z} \tag{A.6}
\]

Equations (4)–(6) can be written as

\[
\mathbf{E} = -\nabla \Phi(x, y, z) \tag{A.7}
\]

where the gradient operator, \( \nabla \), is given by

\[
\nabla = \frac{\partial}{\partial x} \hat{i} + \frac{\partial}{\partial y} \hat{j} + \frac{\partial}{\partial z} \hat{k} \tag{A.8}
\]

where \( \hat{i}, \hat{j}, \) and \( \hat{k} \) are unit vectors in the \( x, y, \) and \( z \) directions, respectively. In free space where there are no charges, such as the region between the electrodes of a quadrupole mass filter, \( \mathbf{E} \) must satisfy

\[
\nabla \cdot \mathbf{E} = 0 \tag{A.9}
\]

or equivalently

\[
\frac{\partial E_x}{\partial x} + \frac{\partial E_y}{\partial y} + \frac{\partial E_z}{\partial z} = 0 \tag{A.10}
\]

It follows from Equations (A.10) and (A.7) that:

\[
\nabla^2 \Phi(x, y, z) = 0 \tag{A.11}
\]

or equivalently

\[
\frac{\partial^2 \Phi(x, y, z)}{\partial x^2} + \frac{\partial^2 \Phi(x, y, z)}{\partial y^2} + \frac{\partial^2 \Phi(x, y, z)}{\partial z^2} = 0 \tag{A.12}
\]

Equation (A.12) is known as Laplace’s equation (Pierre Simon Laplace, 1749–1824).

A. Units

This article uses SI units. Mass is in kilograms, distance in meters, time in seconds, force in newtons. The unit of electrical potential is the volt (the practical unit). Because electric field is force per unit charge, it has units of newton per coulomb. However, because electric field is also derivative of potential with position, it also has units of volts per meter. These units are summarized in Table 1.

In these units, if a charge of 1 C is moved through a potential difference of 1 V, the change in potential energy of the charge is 1 J. If a charge of 1 C is at a point where the field is 1 V/m, the force on the charge is 1 N. If a charge on an electron or proton of \( 1 \times 10^{-19} \) C is moved through a potential difference of 1 V, the change in potential energy is \( QAV = 1.6 \times 10^{-19} \text{ J} \). This unit of energy is called the electron volt.
REFERENCES


