Laser desorption analyses in trapped ion mass spectrometry systems
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Citation for published version (APA):
van Rooij, G. J. (1999). Laser desorption analyses in trapped ion mass spectrometry systems.

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Theory and Operating Principles

The results described in this thesis were obtained with two different mass spectrometers: a Fourier Transform Ion Cyclotron Resonance Mass Spectrometer and a Quadrupole Ion Trap Mass Spectrometer. This chapter deals with the theoretical concepts, the layout of the instruments, and the experimental procedures for both techniques.

2.1 Introduction

In FTICR-MS and ITMS, ions are confined in a trap by the joint effect of an approximately quadrupolar electrostatic potential and a second force provided by either a static magnetic field (FTICR-MS) or a quadrupolar rf electric potential (ITMS). In both techniques, the motion of the ions inside the trap is modulated to determine the ion’s mass-to-charge ratios. This chapter discusses some theoretical aspects of the ion motion in the two types of ion traps that are useful to understand the experimental techniques. These discussions are heavily based on the excellent book of Marshall and Verdun [57] and the mini-series of three volumes edited by March and Todd [58]. The theoretical discussions are followed by a description of the instrumental hardware and the experimental procedures that made it possible to measure the spectra presented throughout this thesis. The FTICR-MS technique is considered in Section 2.2. The ITMS technique will be considered in Section 2.3.

2.2 Fourier transform Ion Cyclotron Resonance Mass Spectrometry

A schematic diagram of the analyzer cell in the FTICR-MS instrument used within the framework of this thesis is shown in Figure 2.1. The analyzer cell is positioned inside the bore of a 7T superconducting magnet, to produce a homogeneous magnetic field in the $z$-direction inside the cell. The magnetic force that acts on ions with non-zero kinetic energy induces these ions to move in stable cyclotron orbits in the $xy$-plane, and therefore confines them in this plane. The ions are prevented from escaping in the $z$-direction from the
cell by the application of an electrostatic potential well between the two opposed trapping electrodes. The use of a homogeneous magnetic field and an electrostatic potential to confine charged particles in space dates from the 1930s and is known as a Penning trap [59]. The natural ion motions induced by such a combination of fields are discussed in Section 2.2.1. From this discussion it will also follow that a determination of the frequency of the ion cyclotron motion is synonymous to a measurement of the mass-to-charge ratio of the ions. In section 2.2.2 it will be shown how an oscillating radiofrequency electric field applied to the excitation electrodes produces a coherent cyclotron motion. This motion can be detected by measurement of the image current that is induced by the coherently orbiting ions in the set of detection electrodes. The resulting time domain signal contains a manifold of frequency components that correspond to the different masses inside the cell. The Fourier analysis method transforms this complex waveform into a frequency domain index that describes the individual frequencies and their magnitudes. This information is used to determine the masses and abundances, and thus describes the ion population. The layout of the instrument used for the FTICR-MS measurement and the experimental procedures are described in detail in section 2.2.3.
2.2.1 Natural Motions inside the ICR Cell

The motion of ions in circular orbits originates from the magnetic force that acts on the ions. The understanding of this cyclotron motion starts with the Lorentz force equation

\[
\vec{F}_L = m \frac{d\vec{v}}{dt} = q\vec{E} + q\vec{v} \times \vec{B}
\]  

(2.1)

which gives the force that acts on a point charge \( q \) with velocity \( \vec{v} \) and mass \( m \) in the presence of electric and magnetic fields \( \vec{E} \) and \( \vec{B} \). Consider the case of an ion that moves in the \( xy \)-plane with velocity \( v_\perp \) in a uniform magnetic field along the \( z \) axis and in the absence of electric fields, as is depicted in Figure 2.2. It is seen from eqn. 2.1 that this ion experiences a Lorentz force in the direction parallel to the \( xy \)-plane and perpendicular to its velocity. The Lorentz force will therefore act as a centripetal force, which changes only the direction of the ion velocity and not its magnitude. Consequently, the magnitude of the Lorentz force will remain constant as well, and the ion will move in a stable circular orbit with radius \( r \). The frequency of this ion cyclotron motion is found by equation of the Lorentz force to the centripetal acceleration in a circular motion, \( v_\perp^2 / r \), multiplied by the ion mass:

\[
qv_\perp B = \frac{mv_\perp^2}{r}
\]  

(2.2)

This immediately gives the radius of the cyclotron motion:

\[
r_c = \frac{mv_\perp}{qB}
\]  

(2.3)
Because angular velocity is defined by $\omega = v_\perp / r$, the frequency of the cyclotron motion in the absence of electric fields is given by:

$$\omega_c = \frac{qB}{m} \quad (2.4)$$

These expressions reveal several important aspects of the ICR technique. Firstly, it is seen from eqn. 2.4 that all ions of a given mass-to-charge ratio, $m/q$, have the same cyclotron frequency, independent of their initial velocity. Measuring the cyclotron frequency of an ion is therefore synonymous to measuring its $m/q$ ratio. Secondly, differentiation of eqn. 2.4 with respect to $m$ leads to:

$$\frac{\omega_c}{\omega_c} = - \frac{m}{dm} \quad (2.5)$$

In other words, frequency resolution equals mass resolution in ICR mass spectrometry (except for a minus sign). Finally, insertion of the average $v_\perp$ of a thermal ion at room temperature ($m < v_\perp^2 > = 2kT$ where $k$ is the Boltzmann constant) into eqn. 2.3 yields that at a magnetic field strength of for example 7 T even relatively heavy ions are confined to small ($< 1$ mm) orbits. Conversely, computation of the translational energy of an ion at a larger orbital radius with eqn. 2.3 shows that ions can be “heated” to high translational energy in the relatively small ICR cell. This feature can be used to advantage to fragment ions by collisions with neutral gas molecules. The magnitude of the ion’s translational energy is plotted as a function of the mass-to-charge ratio for different cyclotron radii at a 7 T magnetic field strength in Figure 2.3.

The natural motion of ions in the presence of a magnetic field along the $z$-direction effectively confines these ions in the $xy$-plane. Let us now consider the confinement in the $z$-direction by the application of an electrostatic potential $V_T$ to each of the two trapping electrodes, with the remaining electrodes electrically grounded. This produces an approximately quadrupolar electric potential near the center of the trap, which can be written in the form

$$V = V_T \left( \alpha + \frac{z^2 - r^2/2}{2d^2} \right) \quad (2.6)$$

Here, $\alpha$ is a coefficient that depends on the trap dimensions as well as the configuration and shape of the trap electrodes, and $d$ is the internal diameter of the trap. Note the presence of the radial coordinate $r$ in the potential. This can be understood by Gauss’s law of electrostatics, which states that electric field lines that enter a closed electrically neutral region must also leave that region. The static voltage applied to the trap electrodes generates an electric field pointing inward along the $z$-axis to the center of the cell, and will therefore necessarily result into an electric field pointing radially outward.

The electric field in the axial direction is obtained from the negative $z$-derivative of the electrostatic potential:

$$E(z) = -\frac{dV}{dz} = -\frac{V_T}{d^2} \quad (2.7)$$
Figure 2.3: Translational energy of ions in an ICR cell at a 7 T magnetic field strength as a function of the ion’s mass-to-charge ratio for different cyclotron radii.

Insertion of this electric field strength into the Lorentz force equation (eqn. 2.1) gives the equation of motion of the ion in the z direction:

$$ F(z) = m \frac{dv_z}{dt} = -\frac{qV_T}{2} z $$

(2.8)

Eqn. 2.8 is immediately seen to describe an harmonic oscillator in a quadratic potential well. Accordingly, the ions oscillate along the z-direction at a natural trapping frequency

$$ \omega_T = \sqrt{\frac{qV_T}{md^2}} $$

(2.9)

With the addition of the electrostatic potential, the radial motion of the ions is no longer described by eqn. 2.2. The radial component of the potential of eqn. 2.6 introduces a radially repulsive electric field strength given by:

$$ E_r = \frac{V_T}{2d^2} r $$

(2.10)

The total radial force on the ion is obtained from the radial component of the Lorentz force equation (eqn. 2.1):

$$ m \frac{dr}{dt} = qv_r B - \frac{qV_T}{2d^2} r $$

(2.11)

The repulsive radial potential has two consequences for the ions natural radial motion. First, the frequency of the cyclotron rotation is reduced because the centrifugal force on
the ion (i.e., the radial Lorentz force) is reduced. Second, a drift of the center of the cyclotron orbit is superimposed in the direction perpendicular to the radial electric field. This drift is called magnetron motion. The reason for the magnetron motion becomes obvious from the physical picture drawn in Figure 2.4. There, it is seen that the ion is accelerated by the radial electric field when it moves radially outward due to its cyclotron motion. This increase in $v_z$ induces necessarily an increase in $r_c$. In the second half-cycle, when the direction of the cyclotron motion is radially inward, the ion is decelerated and decreases in $r_c$. The difference in $r_c$ on the exterior and interior sides of the cyclotron orbit relative to the center of the analyzer cell causes a drift of the guiding center.

To investigate the nature of the magnetron motion in more detail, it is realized that the cyclotron motion is unimpeded according to an observer moving with the guiding center. This means that with respect to the guiding center the electric force in the Lorentz force equation (eqn. 2.1) is canceled by the magnetic force:

$$\vec{E} + \vec{v}_{gc} \times \vec{B} = 0$$  \hspace{1cm} (2.12)

Here, $v_{gc}$ is the drift velocity. The vector product with $\vec{B}$ gives:

$$\vec{E} \times \vec{B} = \vec{B} \times (\vec{v}_{gc} \times \vec{B})$$

$$= \vec{v}_{gc} B^2 - \vec{B} (\vec{v}_{gc} \cdot \vec{B})$$  \hspace{1cm} (2.13)

The transverse components of this equation are

$$\vec{v}_{z,gc} = \vec{E} \times \vec{B} / B^2$$  \hspace{1cm} (2.14)
Elimination of the radial electric field with eqn. 2.10 shows that the motion of the guiding center is a circular motion with the same direction of rotation as the cyclotron orbit along a path of constant radial electric potential. The angular frequency of this motion, which is independent of \( m \) and \( q \), is given by:

\[
\omega_{\perp,ge} = \frac{V_T}{2\beta} = \frac{\omega^2}{2\omega_c}
\]  

(2.15)

The frequencies of the natural ion motions in the \( xy \)-plane are again obtained by balancing the Lorentz force to the centripetal acceleration multiplied by the ion mass:

\[
qv \frac{v}{c} B - q \frac{V_T}{2\beta} = m\frac{v^2}{r}
\]  

(2.16)

Rewriting with the angular velocity \( \omega = \omega_{\perp}/r \) and the unimpeded cyclotron and trapping frequencies yields:

\[
\omega_c \omega_T - \frac{1}{2}\omega_T^2 r = \omega^2 r
\]  

(2.17)

Eqn. 2.17 has to two solutions for the natural frequency of ion motion in the \( xy \)-plane

\[
\omega^+ = \frac{1}{2} \left( \omega_c + \sqrt{\omega_c^2 - 2\omega_T^2} \right)
\]  

(2.18)

\[
\omega^- = \frac{1}{2} \left( \omega_c - \sqrt{\omega_c^2 - 2\omega_T^2} \right)
\]  

(2.19)

Here, \( \omega^+ \) represents the reduced cyclotron frequency and \( \omega^- \) the frequency of the magnetron motion.

The frequencies of the natural ion motions have been calculated with eqns. 2.9, 2.18 and 2.19 for ions trapped in a cylindrical cell (\( d = 0.06 \) m) at a magnetic field strength of 7 T. The potential applied to the trapping electrodes was assumed to be 1 V. The results are plotted as a function of the ion mass in Figure 2.5. The plot shows that the trapping frequency is typically much smaller than the cyclotron frequency, and that the magnetron motion is again much smaller than the trapping frequency.

### 2.2.2 Excitation and Detection of ICR signals

In the previous section it was shown that the mass of an ion can be measured by detection of its cyclotron frequency. However, it is obvious that no measurable signals can be obtained when a large number of ions is orbiting with random phase and thermal energies. It is therefore necessary to move ions with equal mass spatially coherent off-center. This can be realized by application of an oscillating field to a pair of opposed excitation electrodes, which is resonant with the cyclotron frequency of the ions of interest, as is illustrated in Figure 2.6. Because the excitation plates are positioned parallel to the \( xz \)-plane, this will
Figure 2.5: The natural frequencies of motion as a function of the mass-to-charge ratio for ions in a 6 cm diameter cylindrical cell at a magnetic field strength of 7 T and a trapping potential of 1 V.

Figure 2.6: Excitation of the ion cyclotron orbital motion. Application of a dipole field oscillating at the ICR frequency of the ions to the excitation plates converts incoherent cyclotron motion (left) to coherent motion (right).
generate an electric excitation field inside the cell of the form

\[ \vec{E}_{\text{exc}}(t) = E_0 \sin \omega_c t \hat{j} \]  

(2.20)

Here, \( \hat{j} \) is the unit vector in the \( y \)-direction. Ions in resonance with this field will absorb power according to

\[ A(t) = q \vec{E}_{\text{exc}}(t) \cdot \vec{v} \]  

(2.21)

to increase their cyclotron radius in time. The inner product in eqn. 2.21 is readily calculated if the excitation field is resolved into two counter-rotating components:

\[ \vec{E}_{\text{exc}}(t) = \vec{E}_1(t) + \vec{E}_2(t) \]

\[ \vec{E}_1(t) = \frac{1}{2} E_0 (\sin \omega_c t + \cos \omega_c t) \]

\[ \vec{E}_2(t) = \frac{1}{2} E_0 (\sin \omega_c t - \cos \omega_c t) \]  

(2.22)

Here, only the field that rotates in the same sense as the ions of interest is of importance for the absorption of energy because the time average of the energy absorption of the other field component is zero. Insertion of eqns. 2.22 into 2.1, solving for \( v_\perp \), and finally inserting \( v_\perp \) into eqn. 2.21 yields for the instantaneous rate of power absorption (in the absence of dampening mechanisms during the excitation):

\[ A(t) = \frac{E_0^2 q^2 t}{4m} \]  

(2.23)

The cyclotron radius of an excited ion is calculated by integration of eqn. 2.23 over the total excitation time, \( T_{\text{excite}} \). If it is assumed that this total absorbed energy is entirely converted into kinetic energy, the ions are excited to a cyclotron radius of:

\[ r = \frac{E_0 T_{\text{excite}}}{2B_0} \]  

(2.24)

It is immediately seen from eqn. 2.24 that the cyclotron radius is independent of the ionic mass. Consequently, if the frequency spectrum (or magnitude spectrum) of the applied excitation electric field is constant over a certain frequency range, then all ions within the corresponding \( m/q \) range are excited to the same cyclotron radius.

There are four methods commonly employed in FTICR-MS for the production of excitation signals with a reasonably flat magnitude spectrum over a desired \( m/q \) range. The first and simplest excitation waveform is the rectangular pulse (or “impulse”) excitation and is shown in the top panel of Figure 2.7. It is seen that its magnitude spectrum significantly varies with frequency. The central peak in the spectrum corresponds to the frequency interval that is effectively excited and its width is inversely proportional to the excitation time.

The second method is generally used in high-resolution experiments. It is the single-frequency excitation, which is shown in the second panel of Figure 2.7. The excitation
Figure 2.7: The three different excitation waveforms and their frequency-domain magnitude spectra, which are frequently employed in FTICR-MS: for narrow band excitation the rectangular pulse excitation and for broad band excitation the frequency sweep and the SWIFT waveform.
waveform is a sinusoid with fixed amplitude and frequency. The corresponding magnitude spectrum shows that this method is only suitable for excitation of ions within a very small mass range.

The cyclotron motion of ions can be excited over a wide $m/q$ range by application of a frequency sweep (“chirp”) excitation. This waveform consists of a sinusoid with constant amplitude, whose frequency changes linearly in time. An example of a frequency sweep excitation waveform and its magnitude spectrum are shown in the third panel of Figure 2.7. The figure indicates that the magnitude spectrum is relatively uniform over the scanned frequency range. The amplitude of the oscillations in the frequency spectrum is determined by the rate of frequency change in the excitation waveform. A slower sweep rate will lead to a more uniform excitation magnitude spectrum. The sweep excitation method is generally applied in broad band experiments.

The most sophisticated excitation method is the so-called Stored Waveform Inverse Fourier Transform (SWIFT) method [60]. According to this method, first the desired magnitude spectrum is specified. Subsequently, an inverse Fourier transformation is performed to generate the corresponding (discrete) time-domain excitation waveform. This waveform is stored in the memory of an arbitrary waveform generator and passed through a digital-to-analog converter to yield an analog signal, which can be used for excitation. The advantage of this method is that it is able to produce excitation waveforms with optimal flat magnitude spectra, as is illustrated in the bottom panel of Figure 2.7. In addition, it allows excitation magnitude spectra of nearly arbitrary shape. The SWIFT method will be described in more detail in Chapter 5, where the development of a novel arbitrary wave generator is discussed.

The necessity for an excitation waveform with a constant magnitude spectrum was already emphasized in the discussion of the different methods for the excitation of the ion cyclotron motion. This becomes more clear from the method that is applied to detect ionic masses from their excited cyclotron motion. In FTICR-MS, the cyclotron motions of all ions are first excited to an orbital radius that is a little smaller than the separation between the two opposed detector plates. Subsequently the excitation power is switched off and the image current on the detector plates resulting from the alternating charge induced by the coherently orbiting ions is measured. It is evident that the induced image current is proportional to the distance between the cyclotron orbit of the ions and the detector plates. Consequently, the relative intensities in the mass spectrum will be distorted if ions of different mass are excited to different cyclotron radii.

The mass resolution in FTICR-MS is proportional to the time domain acquisition period (assuming that no signal dampening is present) and inversely proportional to the mass-to-charge ratio of the ions [57]. The fundamental limitation for the mass resolution is the duration of a detectable image current signal (which is determined by loss of phase-coherence due to collisions or significant variations in the individual average cyclotron frequencies [57]). On the other hand, the resolution might be unnecessarily limited if the image current signal is sampled directly (the so-called “broad band” or “direct” mode). This occurs if the memory size of the digitizer is not sufficient to store the entire ion signal
for a given digitizer speed (the latter is determined by the lowest $m/z$ value of interest). In that case, the acquisition period can be elongated by application of an alternative detection mode: the "high-resolution" or "heterodyne" mode. In this mode, the ion signal is mixed with the signal of a reference oscillator, whose frequency is centered at the cyclotron frequency range of interest. The result is that all cyclotron frequency components present in the original ion signal are lowered to their difference with the reference frequency. In this way, it is possible to sample data at a much lower speed and thus for much longer acquisition times. The width of the frequency range that can be measured in the heterodyne mode is determined by the speed of the digitizer.

### 2.2.3 Instrumental Layout and Experimental Procedures for FTICR-MS measurements

The FTICR-MS experiments were performed on a heavily modified Bruker-Spectrospin (Fällanden, Switzerland) APEX 7.0e FTICR-MS with an external ion source [61, 62]. A schematic of its vacuum system, which was in-house designed and build, is depicted in Figure 2.8. It consists of three regions, which are separated by pumping restrictions.

The ICR analyzer cell, a so-called Infinity Cell [63], is installed in the UHV region, which is centered inside the bore of the 7 T superconducting magnet. The external ion source is mounted inside the source region at the other side of the vacuum system. In
between is a region for intermediate pumping. The UHV region is pumped by a hybrid
titanium sublimation and turbodrag pump, backed by an oil-free membrane pump. The
other regions are pumped by a combination of a turbomolecular pump and a turbodrag
pump, backed by an oil-free membrane pump. In this way, it is possible to maintain a
pressure difference of 5 orders of magnitude between the ICR cell region (typically at a
base pressure of $\sim 1 \cdot 10^{-10}$ mbar) and the ion source (typically at a base pressure of
$\sim 1 \cdot 10^{-6}$ mbar). The advantages of this pumping scheme include a high compression
rate for helium, optimal cleanliness inside the vacuum system, and ease of operation. The
UHV region can be heated to 175°C while inserted in the bore of the superconducting
magnet that is kept at room temperature. Bake out of the system for 2 days allows UHV
pressures of $< 5 \cdot 10^{-11}$ mbar in the ICR cell region. Two pulsed valves are mounted
on the UHV stage, which allow controlled introduction of collision gases for collisionally
activated dissociation or quadrupolar axialization experiments [64].

At the beginning of an FTICR-MS experiment, the analyzer cell is emptied by applica-
tion of a quench pulse to the trap electrodes. Subsequently, ions produced in the
external ion source and extracted from the source region are injected into the cell. These
ions are first accelerated to 3 keV through Bruker’s electrostatic ion optics for penetra-
tion of the inhomogeneous strayfield of the magnet and finally decelerated to typically -1.9
eV at the entrance of the analyzer cell. In the configuration of the Infinity Cell, injection
is realized by lowering the voltage on the source-side trapping electrode and a deflection
electrode (positioned in front of this trapping electrode) to a negative entrance potential.
This creates a channel for the ions through the trapping field. If ions are created by means
of a pulsed ionization technique, this cell gating is accompanied by a TTL trigger pulse
for the ionization event. The rear trapping electrode remains at typically 3.5 V to prevent
ions from escaping the cell at the rear end. After a trapping delay, these electrodes are
reset to a source-side trapping voltage of typically 2.5 V. In this way, ions are efficiently
trapped inside the analyzer cell and further injection of ions is blocked as the ion beam
is no longer directed to the cell entrance. The duration of the trapping delay is typically
10 – 100 ms for ionization techniques producing a continuous ion beam. In the case of
pulsed ionization techniques, this time delay is determined by the time required by the
ions in the mass range of interest to travel from the source to the cell (see Chapter 3.4.1).
After a delay of typically 50 ms to permit the trapped ions to equilibrate inside the cell,
the trapped ions are coherently excited to a radius close to the cell radius by means of a
frequency sweep excitation from a frequency synthesizer. This excitation waveform con-
sists of a number of single-frequency pulse excitations, which are shifted over the desired
excitation frequency range. For example, ions in the mass range $m/z$ 280-6000 are effi-
ciently excited in the present instrument if the frequency range 385.0-17.9 kHz is covered
in 70 steps of 12 µs duration with an increment of 5240 Hz. The coherent cyclotron mo-
tion is detected by digitizing the image current induced on the detection electrodes using a
12-bit, 20 MHz analog-to-digital converter. The resulting time domain signal is stored in
a 128 kbyte fast memory. Finally, discrete Fourier transformation and magnitude calcu-
lation of the time domain signal produces the frequency spectrum, which is transformed to
a mass spectrum.

Control of the measurements on the FTICR-MS and data acquisition and processing are performed by the Bruker software XMASS running on an SGI Indigo R4000 (Silicon Graphics, Mountain View, CA) UNIX-based workstation.

### 2.3 Ion Trap Mass Spectrometry

The quadrupole ion trap is the three-dimensional analogue of the two-dimensional quadrupole mass filter. It consists of an arrangement of three electrodes that allows the confinement of gaseous ions by application of electric fields only. One of these electrodes is a cylinder symmetrical ring electrode that is positioned between the remaining two end cap electrodes, as is illustrated by the exploded schematic in Figure 2.9. In the case of

**Figure 2.9:** Schematic of the ion trap. The trap consists of three electrodes: two end caps and a cylinder-symmetric ring electrode.

the ideal quadrupole ion trap, the internal surfaces of the electrodes are shaped such that a pure quadrupole electric potential inside the trap is produced by application of a potential difference to the ring electrode, whereas the two end caps remain at ground potential. This requires that the internal surfaces correspond to hyperbolic equipotential surfaces of the desired potential.

The confinement of ions within the ion trap is illustrated by the quadrupole potential that is plotted in Figure 2.10 for a plane that intersects the trap’s symmetry axis. The gradient of this potential is equal to the force that acts on ions. Because the potential is purely quadrupolar, this force varies linearly with the ion’s position inside the trap. It can readily be seen from the plot that ions in the central region of the trap are confined in the
Figure 2.10: Parabolic potential well that acts within an ideal ion trap if a potential difference is applied to the ring electrode whereas the end caps remain at ground potential. The z-axis is chosen along the trap’s symmetry axis and the x-axis perpendicular to this axis.

axial z-direction. However, in the radial direction, ions are accelerated towards the end caps and are not confined. Confinement in all directions can be obtained if the direction of the field is changed every time that the ions approach one of the trap electrodes. In other words, radial deceleration and axial acceleration constantly change to radial acceleration and axial deceleration and visa versa. This is realized by application of a radio frequent (rf) signal in the MHz range to the ring electrode. The result is that ions with a mass-to-charge ratio falling within appropriate limits will undergo stable oscillations.

2.3.1 Theory of the Ion Motion in a Quadrupole Ion Trap

In this discussion it is assumed that both end cap electrodes are grounded and that an electric potential of [58]

$$\Phi = U + V \cos \Omega t$$  \hspace{1cm} (2.25)

is applied to the ring electrode, where $U$ and $V$ are the direct and the alternating components of the potential and $\Omega$ is the angular frequency of the alternating component. In the ideal ion trap, this establishes the pure quadrupole potential that is in cylindrical polar coordinates.
coordinates \((r, z)\) given by
\[
\Phi(r, z) = (U + V \cos \Omega t) \frac{r^2 - 2z^2 + 2z_0^2}{r_0^2 + 2z_0^2}
\] (2.26)

Here, \(r_0\) and \(z_0\) are the inner radius of the ring electrode and the closest distance from the center of the trap to the end-cap electrode, respectively. The differential equations of motion are readily obtained from the gradient of this potential:
\[
\frac{d^2 r}{d t^2} = -\frac{2e}{m(r_0^2 + 2z_0^2)} (U + V \cos \Omega t) r
\] (2.27)
\[
\frac{d^2 z}{d t^2} = \frac{2e}{m(r_0^2 + 2z_0^2)} (U + V \cos \Omega t) z
\] (2.28)

It is seen that the axial component of motion is out-of-phase by half a cycle with respect to the radial component (hence the difference in sign), and the factor of two arises because of the asymmetry of the ion trap brought about by the need to obey the Laplace condition \(\nabla^2 \Phi = 0\) when applied to eqn. 2.26. These equations can be cast in the canonical form of the Mathieu equation, which has the generalized form
\[
\frac{d^2 u}{d \xi^2} + (a_u - 2q_u \cos 2\xi) u = 0
\] (2.29)

where \(u = r, z, \xi = \Omega t/2\), and the Mathieu parameters \(a_u\) and \(q_u\) are given by
\[
a_u = -2a_r = \frac{-16eU}{m(r_0^2 + 2z_0^2)\Omega^2}
\] (2.30)
\[
q_u = -2q_r = \frac{8eV}{m(r_0^2 + 2z_0^2)\Omega^2}
\] (2.31)

The Mathieu parameters are fundamental to the operation of the ion trap since they determine whether the solutions of the Mathieu equation are bounded and the ion motion is stable. Solutions of eqn 2.29 have been studied in detail by McLachlan [65]. Stable solutions are known to have the general form
\[
u(\xi) = A_u u_c(\xi) + B_u u_s(\xi)
\] (2.32)

where \(A_u\) and \(B_u\) are arbitrary constants and
\[
u_c(\xi) = \sum_{n=-\infty}^{+\infty} C_{2n, u} \cos(2n + \beta_u)\xi
\] (2.33)
and
\[
u_s(\xi) = \sum_{n=-\infty}^{+\infty} C_{2n, u} \sin(2n + \beta_u)\xi
\] (2.34)
The coefficients $C_{2n,u}$ give the amplitudes of the allowed modes in the spectral analysis of $u$. The spectrum of frequencies corresponding to the parameter pair $(a_u, q_u)$ is determined by $\beta_u$. Recalling that $\xi = \frac{1}{2} \Omega t$ it is seen that these frequencies $\omega_{u,n}$ are equal to

$$\omega_{u,n} = n + \frac{1}{2} \beta_u \Omega, \quad -\infty < n < \infty$$

(2.35)

It is beyond the scope of this discussion to solve the Mathieu equation to obtain expression for the various parameters in eqn. 2.32. Instead, only the resulting continued fraction expression for $\beta_u$ in terms of the Mathieu parameters as was deduced by McLachlan [65] is stated here for completeness:

$$\beta_u^2 = a_u + \frac{q_u^2}{(\beta_u^2 + 2) - a_u - \frac{q_u^2}{(\beta_u^2 + 4) - a_u - \frac{q_u^2}{(\beta_u^2 + 6) - a_u - \frac{q_u^2}{\ldots}}}}$$

$$+ \frac{q_u^2}{(\beta_u^2 - 2) - a_u - \frac{q_u^2}{(\beta_u^2 - 4) - a_u - \frac{q_u^2}{(\beta_u^2 - 6) - a_u - \frac{q_u^2}{\ldots}}}}$$

(2.36)

This relationship has been used to produce the Mathieu stability diagrams that are shown in the subsequent discussion on stable ion motion.

### 2.3.2 Stable Ion Motions in the Quadrupole Ion Trap

The primary concerns in the operation of the ion trap are the experimental conditions that determine whether an ion is confined within the trap or is ejected, and either detected or lost to the environment. Evaluation of the solutions of the Mathieu equation [65] pointed out that these are stable for those values of $a_u$ and $q_u$ for which $2n < \beta_u < 2n + 1$. For other values, the solutions may be periodic but are unbounded. The stable solutions can be plotted in a diagram with $a_u$ and $q_u$ as coordinate axes. Such graphical representations of stable solutions are called stability diagrams. The stability diagrams for the axial and radial component of the Mathieu equation are depicted in Figure 2.11 A and 2.11 B, respectively. Note that only the positive values are shown along the $q_u$-axis. This is because symmetry exists about the $a_u$-axis. For the same reason, it is allowed to ignore the sign difference between $q_r$ and $q_z$ in the further discussion on stability diagrams. The regions that represent the $(a_z, q_z)$ values for which the Mathieu equation leads to stable solutions are shaded in Figure 2.11 A. The regions which correspond to solutions that are stable in the radial direction, are indicated in Figure 2.11 B, and are twice the size of the axial direction regions rotated about the $q_z$-axis.

Ions are confined in the ion trap if they are stable in both directions simultaneously. This condition is investigated by the superimposition of the stability diagrams in Figure 2.11 C. It should be noted that the scales of the axes in Figure 2.11 C are in units of $a_z$ and $q_z$, although the axes are labeled $a_u$ and $q_u$. The region closest to the origin in which
Figure 2.11: Graphical representation of stable solutions of the Mathieu equation by stability diagrams. Shown are the stability diagram in the axial direction (A), in the radial direction (B), and for simultaneous stability in both directions (C). In C, the axes are labeled $a_u$ and $q_u$, but the scales are in units of $a_z$ and $q_z$.

the condition of simultaneous stability is met, is shaded and indicated as region A. This region is of the greatest importance and is plotted in greater detail in Figure 2.12. Finally, it is important to mention that ions of different $m/z$ can simultaneously have a position within the stability region. The motion of these ions is however characterized by different $a_z$ and $q_z$ values for fixed $U$ and $V$. This dispersion according to mass is the basis of the mass separation with an ion trap, which is discussed in the next section.

2.3.3 Mass Separation with the Quadrupole Ion Trap

There have been three essentially different methods to separate ions according to their mass when they were stored in the quadrupole ion trap. Initially, “mass-selective detection” was applied. According to this method, the motion of the ions was sensed by means of tuned circuits [66]. Subsequently, the method of “mass-selective storage” was introduced, in which the ions were trapped according to their $m/z$ ratios and then were ejected into an external detector [67, 68]. The current separation method relies on “mass-selective ejection” of ions [54, 69].

The operation of the ion trap in the mass-selective ejection mode is explained in Figure
Figure 2.12: Stability diagram in \((a_z, q_z)\) space for the region of simultaneous stability in both axial and radial directions. The iso-\(\beta_r\) and iso-\(\beta_z\) are shown in the diagram. The \(\beta_z = 1\) boundary and the \(q_z\)-axis intersect at \(q_z = 0.908\).

Figure 2.13: Position of ions in the stability diagram for different \(m/z\) ratios and \(rf\) amplitudes.
2.13. In this figure, the position of different \( m/z \) ions is depicted in the stability diagram for different rf amplitudes. It shows that an ion with a high \( m/z \) becomes unstable at a higher rf amplitude than those with a lower \( m/z \) ratio. In a mass-selective ejection scan, the rf voltage is linearly raised in time to increase the \( q_z \) of all ions. If the \( q_z \) value for a specific \( m/z \) reaches the boundary of the stability region (where \( q_z = 0.908 \) if no direct voltage is applied and thus \( a_z = 0 \)), the corresponding ions will become unstable in the axial direction and be ejected from the trap through one of the end caps. In this way, ions of increasing \( m/z \) are ejected in sequence and can be detected as a function of the applied rf voltage (i.e., time). The voltage scale is easily converted into a mass scale by rewriting the expression for \( q_z \) (eqn. 2.31):

\[
\frac{m}{e} = \frac{4V}{r_0^2 \Omega^2 q_{z\text{eject}}} \tag{2.37}
\]

Here, \( q_{z\text{eject}} \) is the value of \( q_z \) at which instability occurs.

Eqn. 2.37 reveals also that the mass range in which ions can be analyzed is limited for given frequency and maximum amplitude of the rf voltage. For example, in the Finnigan MAT ion trap, which is the first commercial instrument that applied the mass-selective ejection scan, masses up to approximately \( m/z 650 \) can be analyzed (rf frequency 1.1 MHz; maximum rf voltage 7500 V, \( \text{rad} \); radius \( r_0 = 0.01 \) m). There are obviously four ways to extend the mass range of the ion trap to higher masses:

1. Operation of the trap at lower angular frequencies (\( \Omega \)).
2. Operation of the trap at higher values of rf voltages (\( V \)).
3. Reduction of the trap dimensions (\( r_0 \))
4. Ejection of ions at a lower value of \( q_z \).

The first two options have already been implemented in recent instruments. For example, the commercial Bruker ion trap that is used for the experiments described in this thesis (Chapter 7 and 8) employs an rf frequency of 781 kHz, and a maximum voltage of 10,000 V, \( \text{rad} \). This extends theoretically the mass range to \( m/z 1600 \). A further decrease of \( \Omega \) and increase of \( V \) is instrumentally demanding and therefore not attractive. The same applies to a reduction of the trap dimensions.

The simplest way to extend the mass range is to cause the trapped ions to become unstable at a value of \( q_z \) lower that 0.908. This is achieved by modulation of the ion motion at a chosen frequency with a dipole electric field applied across the end caps. Ions that have a secular frequency in the axial direction equal to the applied dipole frequency increasingly gain amounts of translational energy and are ejected from the trap. This means that the value of \( q_{z\text{eject}} \) can be arbitrarily set by adjustment of the dipole frequency. This process is known as resonant ejection.

Conceptually, the supplementary dipole field creates a line of resonant ejection in the stability diagram for which \( q_{z\text{eject}} \) corresponds to the frequency applied to the end caps. This
Figure 2.14: The effect of resonant ejection on the stability of ions. The dashed line indicates where instability is introduced by the dipole field. Intersection of this iso-$\beta$ line and the scan line corresponds to $q_{\text{eject}}^{z}$. 

is visualized in Figure 2.14 by the dashed line. The intersection of this iso-$\beta$ line with the mass-selective instability scan line, which is the $q_{z}$-axis if the instrument is operated without a direct voltage on the ring electrode, creates a hole in the stability diagram that corresponds to $q_{\text{eject}}^{z}$.

The potential of the resonant ejection mode to extend the mass range is nicely illustrated by high mass experiments carried out by Kaiser et al. [70]. They used a reduced rf frequency of 920 kHz and a resonance dipole frequency of 4600 Hz ($\beta_{\text{eject}} = 0.01$, $q_{\text{eject}}^{z} = 0.02$). The result was an expected mass range extension to 72,000 u, which allowed the measurement of positive singly-charged (CsI)$_n$Cs$^+$ cluster ions up to $n = 171$ ($m/z$ 44,560).

2.3.4 Experimental Procedures for ITMS Measurements

The ITMS experiments described in this thesis were performed with an in-house constructed instrument. The ion trap in this instrument was obtained from Bruker-Franzen Analytik GmbH (Bremen, Germany), and is identical to the one in the commercial Bruker Esquire instrument. The operation of the trap is discussed in this section. Details on the complete instrument will be given in the instrumental sections of Chapter 7 and 8, because
its construction was an important aspect of the work described in these chapters. A schematic diagram of the Bruker-Franzen ion trap is shown in Figure 2.15. It is a so-

called “multipole-superimposed” ion trap. This means that the mainly quadrupolar field has contributions from hexapolar and octopolar fields. These contributions are created by a slight change in the angle of the asymptotes associated with the hyperbolic shape of the end caps and ring electrode. The effect of higher order poles in the design has been discussed by Franzen et al. [71]. The practical importance is that additional resonances are introduced in the stability diagram. The resonance at $\Omega/3$ is in particular of interest, because this is also the secular frequency at which ions are resonantly ejected from the trap in the standard measuring mode.

The frequency of the rf voltage that is applied to the ring electrode is 781 kHz and its maximum amplitude is 10 kV$_{0-p}$. The exit end cap that faces the ion detector is connected to the auxiliary rf voltage for resonant excitation, whereas the entrance end cap is kept at ground potential (Figure 2.15). The primary and the dipole field are phase locked, which provides reproducible ion excitation and preferential ejection of ions through the exit end cap. The amplitude of both rf voltages are ramped during the non-linear resonance ejection scan. The ramp rate of the primary rf voltage and the frequency of the dipole field depend on the mode of analysis. These are listed in Table 2.1. The externally produced ions are injected into the active trapping field of the ion trap. Helium background gas is introduced into the ion trap at an estimated pressure of $10^{-3}$ mbar to aid in the ion trapping by collisional dampening of the ion kinetic energies. The amplitude of the rf voltage during injection is determined by the so-called cut-off mass $M_{\text{cut-off}}$. The value of $M_{\text{cut-off}}$ corresponds to the $m/z$ ratio that is in resonance with the dipole field at that
Table 2.1: The four modes of measuring and the corresponding operation parameters that are available in the Bruker software. * The upper mass limit for the high mass mode was restricted to 3400 u due to software limitations during the measurements presented in this paper. ** Maximum scan width for which it is possible to store the complete multiplier signal as function of time.

<table>
<thead>
<tr>
<th>Mode of analysis</th>
<th>Mass range</th>
<th>Scan rate</th>
<th>Maximum dipole analysis scan width**</th>
<th>dipole frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>50-2000</td>
<td>~2000 u/s</td>
<td>800</td>
<td>Ω/3</td>
</tr>
<tr>
<td>High res.</td>
<td>50-2000</td>
<td>~500 u/s</td>
<td>400</td>
<td>Ω/3</td>
</tr>
<tr>
<td>Extended</td>
<td>50-3400</td>
<td>~1700 u/s</td>
<td>1200</td>
<td>Ω/6</td>
</tr>
<tr>
<td>High</td>
<td>100-6000*</td>
<td>~8000 u/s</td>
<td>1200</td>
<td>Ω/11</td>
</tr>
</tbody>
</table>

amplitude. The relation between the amplitude during injection and the cut-off mass is in the standard mode given by:

\[ V_{rf} = \frac{0.2}{e} \Omega^2 r_0^2 M_{\text{cut-off}} \]  

(2.38)

This relation is obtained by insertion \(q_{\text{eject}} = 0.8\) into eqn 2.37. As can be deduced from the stability diagram in Figure 2.12, \(q_{\text{eject}} = 0.8\) corresponds to \(\beta_z = 0.67\), which in turn corresponds to a secular frequency that is equal to that of the dipole field.

In case tandem mass spectrometry experiments are performed, a (software imposed) maximum of six stages of precursor ion isolation and subsequent excitation can be included in the experiment (prior to the mass-selective ejection scan). Precursor ions are isolated by application of a dipole field with an associated broad band frequency spectrum that contains all resonance frequencies covered by the analyzed mass range except for the resonance frequency of the precursor ion. The time required for the isolation step is typically 60 ms. This is followed by resonant excitation to induce decomposition by collisions with the background gas. The excitation waveform comprises a small frequency band around the precursor ion’s resonance frequency.

Ions that are ejected from the trap are detected by the combination of a conversion dynode and an electron channeltron detector. In this configuration, the ions are accelerated over 7 kV towards the dynode to induce a secondary electron signal. This signal is detected by the channeltron (model 7596mh3, K and M Electronics, Westspringfield, MA) that is operated at typically -1.2 kV (maximum operation voltage 3000 V). The multiplier signal is digitized at a rate of 10 u^-1 for the standard and the high resolution measuring mode and at a rate of 6 u^-1 in the other modes. This is however only possible if the maximum width of the mass range that is listed in Table 2.1 is not exceeded. The multiplier signal is converted in a bar graph that represents intensities for integer masses only if larger mass ranges are examined.