INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.
Gas phase ion - molecule reactions studied by Fourier transform ion cyclotron resonance mass spectrometry

Ross, Charles William, III, Ph.D.

The Ohio State University, 1993
GAS PHASE ION - MOLECULE REACTIONS STUDIED BY FOURIER TRANSFORM ION CYCLOTRON RESONANCE MASS SPECTROMETRY

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in the Graduate School of the Ohio State University

By

Charles William Ross III, B. S.

*****

The Ohio State University

1993

Dissertation Committee:
Professor Alan G. Marshall
Professor Patrick K. Gallagher
Professor Terry L. Gustafson
Professor Eric R. Kreidler

Approved by

Advisor
Department of Chemistry
I was born not knowing and have only had a little time to change that here and there.

Richard P. Feynman
DEDICATION

I dedicate this work to my family: parents - Charles Jr. & Betty Ross; sisters - Rebecca Combs & Karen Davidson; grandparents - Charles Ross Sr. & Mary Cacciola; nieces - Ashley Combs & Amanda Davidson; nephews - Aaron Combs & Chad Davidson. Their encouragement and support have kept me going throughout my academic career. God bless all of you.
ACKNOWLEDGMENTS

I must first express my appreciation and gratitude to my research advisor, Dr. Alan Marshall, for his guidance, suggestions, and assistance during the past years. I am grateful to Dr. Tom Ricca for taking the extra time during our late evenings fixing the equipment to instruct me in the basics of electronics and troubleshooting. His patience was greatly appreciated. A warm thank you goes to the members of the Campus Chemical Instrument Center. David Chang, Minori Shoji, and Dr. Charles Cottrell gave me the chance to test my wings in sample analysis and group management. Kaye Craggs took on the monumental task of minimizing the bureaucratic red tape. I deeply thank her for helping me keep my sanity during my doctoral work. I wish to thank Dr. Terry Gustafson for his counsel and kindness. At times it was difficult to tell if I was part of his group or Dr. Marshall's.

I thank all of the members, past and present, of Dr. Marshall's research group for their friendship and help. In particular, Dr. Nick Hill, Dr. Zhenmin Liang, and Dr. George Alber for their efforts in educating me about the instrumentation. Dr. Peter Grosshans and I spent many hours in discussion and running a variety of computer simulations. My fellow classmates, Dr. Patrick Limbach and Dr. Winnie
Yin, afforded me the opportunity to test my knowledge through countless hours of mutual instruction. Troy Wood was invaluable in assisting me with routine and non-routine maintenance of the instrument when I became the senior member of the FTMS-2000. I am indebted to him for removing some of the burden during the past year. Dr. Lutz Schweikhard and Dr. Shenheng Guan were extremely helpful during the two-dimensional mass spectrometry work. Their insights helped me to overcome obstacles that I encountered.

My heartfelt thanks goes to David Baldwin, Troy Wood and Jarrod Marto for taking time from their busy schedules to proofread this dissertation, in particular chapter one. Any remaining errors are solely my own. A vote of gratitude to Dr. Bill Weaver for listening to my many problems and keeping me updated on developments in Raman spectroscopy.

This acknowledgment would not be complete if I did not thank my colleagues from The University of Akron. Especially Dr. James Hardy and Dr. David Jencen (now at Norwich-Eaton), who took the time to nurture and mold an eager young undergraduate in their laboratory and prepare him for graduate school.

Lastly, I wish to thank my family for putting up with me during my 23 years of formal education. From them I drew the power, strength and fortitude to complete this goal.
VITA

11 March 1965 ............................................... Born - Lakemore, Ohio

10 January 1988 ................................................. B. S., The University of Akron, Akron, Ohio

1988 - 1991 ..................................................... Graduate Teaching Associate, The Ohio State University, Columbus, Ohio

1992 - 1993 ..................................................... Graduate Research Associate, The Ohio State University, Columbus, Ohio

PUBLICATIONS


FIELD OF STUDY

Major Field: Chemistry
TABLE OF CONTENTS

DEDICATION.................................................................................................... ii

ACKNOWLEDGMENTS..................................................................................... iii

VITA................................................................................................................. v

LIST OF TABLES.............................................................................................. ix

LIST OF FIGURES............................................................................................. x

CHAPTER PAGE

I. DEVELOPMENT AND BASIC PRINCIPLES OF FOURIER TRANSFORM ION CYCLOTRON RESONANCE MASS SPECTROMETRY........................................ 1
   Introduction................................................................................................. 1
   Ion Cyclotron Resonance Spectrometry.................................................... 1
   Development of Fourier Transform Ion Cyclotron Resonance Mass Spectrometry.............................................................. 8
   Basic FT/ICR/MS Technique....................................................................... 9
   Ionization.................................................................................................... 13
   Trapped Ion Cells.................................................................................... 17
   Excitation.................................................................................................. 26
   Detection of The Ion Signal........................................................................ 36
      Nyquist Theorem................................................................................ 36
      Acquisition Time................................................................................. 37
   Benefits of Fourier Analysis..................................................................... 39
   Digital Filtering...................................................................................... 42
   Zero-filling.............................................................................................. 44

vi
## Applications and Other Improvements

- Mass Accuracy
- Ion Remeasurement
- Gas-Phase Chemistry
- Tandem Mass Spectrometry

### Summary

#### References

## II. DETERMINATION OF THE GAS PHASE BASICITY AND PROTON AFFINITY OF CARBENES BY FT/ICR/MS

### Introduction

#### Background

- Equilibrium Measurements
- Bracketing

### Experimental

#### Results and Discussion

- Dichlorocarbene
- Dimethoxy carbene and Phenylcarbene

### Conclusions

#### References

## III. TWO-DIMENSIONAL FOURIER TRANSFORM ION CYCLotron RESONANCE MASS SPECTROMETRY /MASS SPECTROMETRY WITH STORED-WAVEFORM ION RADIUS MODULATION

### Introduction

#### One-dimensional ICR MS/MS

- One-dimensional FT/ICR MS/MS
- Two-dimensional FT Spectroscopy
- 2D-FT/ICR MS/MS: parent ion cyclotron radius modulation

#### Parent ion cyclotron radius modulation by two excitation pulses separated by a variable delay period

#### Parent ion cyclotron radius direct modulation by stored-waveform excitation

- Comparison to prior Hadamard/FT 2D-ICR/MS

### Theory

- Parent ion cyclotron radius modulation by excite-(variable delay)-excite sequence
- Parent ion cyclotron radius modulation by a series of single-event SWIFT excitations

### Experimental

#### Results and Discussion

- Fundamental aspects of 2D-FT/ICR MS/MS
- Monomer-dimer interconversion: acetone

### References
# LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-1</td>
<td>66</td>
</tr>
<tr>
<td>2-2</td>
<td>76</td>
</tr>
<tr>
<td>2-3</td>
<td>77</td>
</tr>
<tr>
<td>2-4</td>
<td>80</td>
</tr>
</tbody>
</table>

- 2-1: Gas phase basicity bracketing of dichlorocarbene
- 2-2: Gas phase basicity bracketing of dimethoxycarbene
- 2-3: Gas phase basicity bracketing of phenylcarbene
- 2-4: Summary of Results
### LIST OF FIGURES

<table>
<thead>
<tr>
<th>FIGURE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1</td>
<td>4</td>
</tr>
<tr>
<td>1-2</td>
<td>5</td>
</tr>
<tr>
<td>1-3</td>
<td>11</td>
</tr>
<tr>
<td>1-4</td>
<td>18</td>
</tr>
<tr>
<td>1-5</td>
<td>20</td>
</tr>
</tbody>
</table>

**1-1** Representation of the relationship between an ion's velocity, \( v \), in a static magnetic field (vector into the plane of the paper) and the resultant Lorentz force, \( qvB \). Positive ions rotate counter-clockwise (top) and negative ions rotate clockwise (bottom).

**1-2** The relationship between cyclotron frequency and the mass-to-charge ratio of an ion at three magnetic field strengths in the absence of an electric field.

**1-3** Conversion of a frequency spectrum (a) into a mass spectrum (b). Each sinusoidal signal was observed for the same time with no damping. Notice that the peaks have the same frequency width but have different mass widths.

**1-4** A typical cubic static electromagnetic ion trap. Electron Ionization (EI) is shown. The magnetic field confines ions in the x-y plane and the electric field applied to the trap plates (T) confines the ions's z-motion. (Graphic provided by Winnie Yin)

**1-5** Magnetron motion. In (a) an ion with zero initial velocity, experiences only the force due to the electric field and moves upward. Once the ion has a velocity it will also experience the magnetic field force (directed to the left). The overall effect is that the ion drifts to the left at a velocity given by \( v=E/B \) around an equipotential line (dashed lines). In the ICR trapped ion cell (b), the equipotential lines are circles near the center of the cell in the x-y plane. The electric field is directed radially outward. Hence, the ion will drift around the cell to yield a low frequency magnetron motion.
1-6 Three motions are observed in the ICR ion trap. The quickly oscillating cyclotron motion (small circle) due to the magnetic field; the slower magnetron motion (large circle) due to the crossed electric and magnetic fields; and the trapping or axial motion due to the electric field. (Graphic provided by Jane Xiang)  

1-7 Typical cells used in FT/ICR/MS. (a) the cubic cell; (b) the open-ended cylindrical cell; (c) the hyperbolic cell; and (d) the screened elongated cell.  

1-8 Frequency-domain magnitude spectra of some standard FT/ICR time-domain excitation waveforms. (a) Rectangular pulse (encompassing a single frequency); (b) Frequency-sweep ("chirp"); (c) SWIFT for broad-band excitation; (d) SWIFT for MS/MS or ion-molecule reactions. (Figure provided by Alan Marshall from reference 69)  

1-9 Generation of a SWIFT excitation waveform. A frequency domain profile is specified (a) and an inverse Fourier transform (IFT) is performed to yield the time domain waveform (b). The large amplitude of the time domain spike can be reduced by scrambling the phase relationship of the frequencies before IFT to produce the lower amplitude time signal (c). The actual frequency profile is calculated via an FT after padding the time signal with an equal number of zeroes (d). Although the excitation amplitude is flat over most of the region, oscillations are observed at the boundaries.  

1-10 Prior to IFT, the requested excite spectrum is smoothed via a three-point moving average with 5 passes (a). The time domain signal (b) now tends smoothly to zero (compare to Figure 1-9c). The actual excite spectrum (c) does not have the 'ripples' observed in Figure 1-9d, and is the same as the requested excite spectrum (a).
2-1 Dual cell Fourier Transform Ion Cyclotron Resonance Mass Spectrometer. Carbene precursor molecules are constantly leaked into the Source region for ionization. Ions are transferred to the Analyzer cell, isolated and reacted with a reference base admitted via a pulse valve system.

2-2 Experimental event sequence. 1. All ions are removed from the cell by applying positive and negative voltages to the trap plates. 2. Variable delay to allow the analyzer region to return to base pressure. 3. Ionization of precursor molecule at low electron energy via El. 4. Transfer of ions to the Analyzer cell by dropping the conductance limit voltage. 5. All unwanted ions are ejected from the cell via SWIFT or linear sweep excitation. 6. Reference base is admitted to the chamber via a pulse valve system. 7. Variable reaction delay to monitor proton transfer. 8. Excitation and detection of ions.

2-3 Spectrum of deuterated dichlorocarbene ion isolated via SWIFT excitation. The SWIFT excitation frequency domain profile is also shown.

2-4 Upper bracket for dichlorocarbene. Phenol had the lowest gas phase basicity that showed the ability to remove the deuteron from the carbene. Self protonation of phenol was also observed.

2-5 High resolution spectrum of the reaction between phenol and the deuterated dichlorocarbene ion. The C-13 peak of (M+H)^+ of phenol is resolved from the (M+D)^+ peak due to deuteron transfer.

2-6 Lower bracket for dichlorocarbene. Benzonitrile had the largest gas phase basicity that was unable to remove the deuteron from dichlorocarbene.

2-7 Proton affinity ladder for dichlorocarbene. The results of Lias et. al are shown on the left and results from this study on the right. Previous results showed proton transfer for benzonitrile, but it was not observed in this study.

2-8 Proton affinity ladder for dimethoxycarbene and phenylcarbene.
3-1 Two alternative experimental event sequences for 2D-FT/ICR/MS. Ion formation (top row) is followed by an excitation which modulates the parent ion cyclotron radii according to their ion cyclotron frequencies, either by application of two identical excitation waveforms separated by a delay period whose duration is incremented linearly from one data acquisition to the next (second row), or by application of each of a series of stored-waveforms (third row). Following a reaction period during which product ions are formed with abundances determined by the parent ion cyclotron radii established in the previous event, conventional broad-band excitation and detection generate a time-domain response. Finally, ions are removed, and succeeding data sets are acquired, either for various delay period between the two-pulse excitation or for various SWIFT modulation waveforms, and the two-dimensional array is subjected to two-dimensional FT to generate a 2D-FT/ICR mass spectrum. (see text).

3-2 SWIFT magnitude-mode spectra (see Equation 3-3) of several parent-ion modulation waveforms, for j = 1, 2, and 10. Note that the excitation amplitude for ions of the highest cyclotron frequency, 1333.0 kHz, is modulated the fastest in proceeding from one waveform to the next, whereas the excitation amplitude for ions of the lowest cyclotron frequency, 100 kHz, is not modulated at all from one waveform to the next. The mass-to-charge ratio range corresponding to these ion cyclotron frequencies is 34.8 < m/z < 463. (B \approx 3.02 T)
3-3 A portion of the acetone FT/ICR magnitude-mode frequency-domain spectrum prior to Fourier transformation in the second (parent ion radius modulation) dimension. The rapid modulation of protonated acetone parent ion, MH⁺, carries over to the observed ICR signal magnitude of the product ion, M₂H⁺. (The slower modulation of protonated acetone dimer parent ion, M₂H⁺ produces a less obvious modulation in the ICR signal magnitude of its MH⁺ product ion.) These modulation transfers become apparent following a second FT of this data with respect to the modulation (here shown as "scan number") axis (see Figure 3-4).

3-4 Three dimensional stacked-plot display of a portion of the two-dimensional data obtained by padding the data of Figure 3 with an equal number (512) of zeroes in the modulation dimension, followed by Fourier transformation of the data with respect to that dimension. The diagonal peak at the cyclotron frequency of M₂H⁺ is rather broad in the modulation dimension, likely due to inadequate pressure control of acetone throughout the experiment. Some "T₁-noise" is also noticeable as rows of small peaks at the cyclotron frequencies of MH⁺ and M₂H⁺ (see text).

3-5 Two-dimensional iso-power contour (SWIM) FT/ICR mass spectrum for ions derived from acetone. A peak appears on the diagonal (dashed) line for parent ions of each m/z-value in the detected spectral bandwidth. Each off-diagonal peak results from a product ion (identified by vertical projection to the bottom horizontal axis) formed from a parent ion (identified by horizontal projection to the modulation frequency axis at the left of the figure). The small spot size for the various peaks results from the high mass spectral resolution under these experimental conditions (see text).
3-6 Stored-waveform ion modulation (SWIM) 2D-FT/ICR mass spectral iso-power contours, from which five ion-molecule proton-transfer reactions of pyrrolidine and 3-methylpyridine may be identified (see text) ............................................................... 113

3-7 Narrow-band SWIM 2D-FT/ICR mass spectral iso-power contours for the pyrrolidine molecular ion region. Experimental conditions are as in Figure 3-6, except that the SWIM modulation (and excitation/detection) frequency bandwidths were narrowed to provide higher analog and digital resolving power. ............................................................... 116

3-8 Time evolution of ions derived from pyrrolidine, based on one-dimensional FT/ICR mass spectra obtained at each of a series of reaction periods between ion formation by electron ionization and subsequent excitation/detection. Each data point represents an average of two peak area values. The protonated molecular ion, (M+H)+, is clearly a product of M+ and (M-H)+, whereas (M+H)+ simply grows with time and does not form additional product ions. These results strongly validate our interpretation of the two-dimensional data in Figures 3-6 and 3-7 ...................................................... 118

4-1 Representation of the possible information obtained from a single two-dimensional FT/ICR/MS experiment. Note that mass is plotted, not frequency as in the other 2D spectra of this dissertation ............................................................................. 130

4-2 SWIM 2D-FT/ICR/MS/MS iso-power contours of PFTBA ion reactions. Six reactions are identified. Reactions 1 - 4 are due to CID and reactions 5 and 6 are due to IIII (see text) .................................................................................. 134

4-3 Three dimensional stacked plot display of PFTBA reactions. See Figure 4-2 and text for an explanation of the reactions ............................................................. 135

4-4 Laser Desorption Ionization (LDI) SWIM 2D-FT/ICR mass spectral magnitude contours for ion-molecule reactions of uranium and a planar cyclotriyne (TBC). Five reactions can be identified in this single 2D spectrum .......................................................... 137
SWIM 2D-FT/ICR/MS iso-power contours for an eleven component mixture. Six molecular ions and seven fragment ions appear on the diagonal. Some CID peaks are observed, but the major pathways are due to the most abundant species, thiophene. Off-diagonal peaks to the left of thiophene, A, are charge transfer to form molecular ion. Peaks to the right are CID fragments of thiophene.

Representation of product ion signal for which the production is linear with respect to the reagent ion's kinetic energy. Energy regimes shown were used to produce the signals in Figure 5-2. The top two lines represent energy and radius modulation, respectively, across the linear energy region. The bottom line is radius modulation in which the modulation is conducted across the energy threshold for observation of product ion signal.

Theoretical spectra showing the effect on product ion signal (spectrum A) due to sinusoidal modulation of parent ion radius, for the case that the number of product ions varies linearly with energy (B).

Theoretical spectra showing the additional effect of a non-zero energy threshold for the formation of product ions. Spectrum A shows an energy threshold that is 4% of the maximum modulation energy. Spectrum B shows an energy threshold that is 25% of the maximum modulation energy. The thresholds produce clipped signals for product ion magnitude with the result of harmonics in the frequency domain.

Generation of SMOKE waveforms. At top is the normalized energy profile and at bottom the normalized radius profile for a value of j=8. See text for discussion.
3D displays of SMOKE waveforms. Each magnitude-mode frequency domain waveform is acquired by taking a slice at integer values of j (axis into the paper). Left is the surface for energy modulation of ions between 5 and 29 eV, and at right the corresponding radius modulation surface.

Comparison of SMOKE and SWIM 2D-FT/ICR/MS. Iso-power contours are the same level relative to the base peak, protonated diethyl ether, C. A second dimension harmonic line is visible in each spectrum, but is more pronounced in the SWIM spectrum (examine 2D projection of modulation). Reactions are discussed in the text.
Chapter I

Development and Basic Principles of Fourier Transform Ion Cyclotron Resonance Mass Spectrometry

Introduction

Fourier transform ion cyclotron resonance mass spectrometry (FT/ICR/MS) is the most versatile technique for identifying ion-molecule reaction pathways and quantifying ion-molecule reaction kinetics, equilibria, and energetics in the absence of solvent (i.e., the gas phase). As itemized in several recent reviews, FT/ICR/MS has many analytically important features: speed (~1 second per spectrum); ultrahigh mass resolving power and ultrahigh mass accuracy; low-volatility samples (10^{-9} torr); MS/MS/... with one spectrometer; wide mass range (1 \leq m \leq 32,000 u for singly-charged ions);\textsuperscript{19,20} positive and/or negative ion detection;\textsuperscript{21} multiple ion sources for analysis of involatile substances and mixtures; and simultaneous multiple-ion monitoring. In the past 19 years, the technique has undergone rapid growth in its development.

Ion Cyclotron Resonance Spectrometry

No known physical property can be measured more accurately than frequency.\textsuperscript{22,23} The basis of ion cyclotron resonance is quite
simple and follows from the basic principles of electromagnetism.\textsuperscript{24} The ion cyclotron principle was first used by Lawrence and Livingston in the early 1930's to accelerate particles such as protons and deuterons to high kinetic energy, which were then used as projectiles to bombard nuclei.\textsuperscript{25} They demonstrated that a charged particle in a static electromagnetic field undergoing circular motion will absorb energy from an oscillating electric field if the frequency of the electric field is equivalent to (in resonance with) the ion's angular frequency. The period of motion of the particle is independent of the ions velocity.

The Lorentz force, $\mathbf{F}_L$, exerted by a magnetic field, $\mathbf{B}$, on an ion of mass, $m$, and charge, $q$, moving with a velocity, $\mathbf{v}$, is given by (S.I. units)

$$\mathbf{F}_L = q\mathbf{v} \times \mathbf{B}_0$$  \hspace{1cm} (1-1)

The force is a vector pointing perpendicular to both the ion's velocity vector and the direction of the magnetic field. Due to the Lorentz force, the ions overall motion is circular. Equating the Lorentz force to Newton's second law, $\mathbf{F}=ma$, and substituting for the acceleration, $a$, the centripetal acceleration, $v^2/r$, in which $r$ is the radius of the ion's orbit, yields

$$\frac{mv^2}{r} = q\mathbf{v} \mathbf{B}_0$$, in which $\mathbf{v} \perp \mathbf{B}_0$  \hspace{1cm} (1-2)
Rearrangement of this equation produces the cyclotron equation of motion

\[ \omega = \frac{\gamma}{r} = \frac{qB_0}{m} \]  (1-3)

in which \( \omega \) is the angular frequency (radians/sec) of the ion (Figure 1-1). As is readily apparent from Equation 1-3, the cyclotron frequency of an ion is directly proportional to the magnetic field strength. Since a higher frequency signal can be measured more precisely than a lower frequency signal for a fixed detection period, it is useful to use as large a magnetic field as possible. Also, increasing the number of charges on an ion will increase the cyclotron frequency. Most importantly, an ion’s natural cyclotron frequency is independent of the ion’s velocity and radius, but depends on the ratio of the two parameters. Hence, the frequency is a constant determined by the magnetic field strength and inversely dependent on the mass-to-charge (m/q) ratio. Figure 1-2 shows the relationship between \( m/z \) (\( m \) in u, \( z \) in number of elementary charges) for an ion and its corresponding cyclotron frequency for three magnetic field strengths based upon Equation 1-3.

In 1949, Hipple, Sommer, and Thomas built the first mass spectrometer, the omegatron, based upon the cyclotron principle.\textsuperscript{26,27} Ions were confined to a region by a permanent magnet and a small quadrupolar electrostatic field parallel to the magnetic field. An alternating electric field caused the ions to increase the size of their
Figure 1-1. Representation of the relationship between an ion's velocity, \( v \), in a static magnetic field (vector into the plane of the paper) and the resultant Lorentz force, \( qvB \). Positive ions rotate counter-clockwise (top) and negative ions rotate clockwise (bottom).

\[
\omega = 2\pi v = \frac{v}{r} = \frac{qB}{m} \\
(S.I. \ units)
\]
Figure 1-2. The relationship between cyclotron frequency and the mass-to-charge ratio of an ion at three magnetic field strengths in the absence of an electric field.
orbit when the frequency of the field was in resonance with (equal to) the cyclotron frequency of the ion. The ion then collided with a detection plate and the current was measured with an electrometer. By scanning the frequency of the electric field, it was possible to acquire a mass spectrum by comparing the current versus the resonant frequency and converting the frequency to mass by means of Equation 1-3. The mass range of the omegatron was limited by the low field strength of the permanent magnet. The inhomogeneity of the magnet and the ion-neutral collisions limited the resolving power of the instrument. Nonetheless, the omegatron was used as a residual gas analyzer because of its small size.

In 1965, Wobschall developed an ICR spectrometer which improved the detection method by use of an rf-bridge circuit to measure ICR power absorption. The magnet was a low field solenoidal electromagnet, which again limited the mass range and resolution. The ion detection was also carried out while the ionizing electron beam was on which caused frequency shifts in the ions cyclotron motion and thereby reduced the accuracy of mass determination.

An ICR mass analyzer with three sections was introduced to avoid the problem of the continuous electron beam. In the source section, the ions are generated by an electron beam parallel to the magnetic field. A static voltage applied across the top and bottom plates causes the ions to drift in a direction perpendicular to both the magnetic and electric field into the analyzer section where a marginal oscillator is
used for detection. The last section is an ion collector. The high sensitivity of the marginal oscillator and the elimination of frequency shift due to the electron beam allowed the three section cell to be used for the study of ion-molecule reactions. An ion's reaction time is a function of its drift velocity and the overall distance between the source section and the detection section.

The ICR double resonance (ICDR) technique was also developed in the mid-1960's to help determine reaction pathways.\textsuperscript{30} Briefly, while one is detecting at the cyclotron frequency of the assumed product ion, the proposed reactant ion is excited to larger orbit. The kinetic energy of the ion is increased and the signal of any other species linked chemically to it will be affected. After the ICDR technique was implemented in ICR, many ion-molecule reaction mechanisms were established and the rate constants determined.

Although the ICR spectrometer was well established in the study of ion-molecule reactions, there were still problems to overcome. Detection and reaction of the ions were occurring at the same time. Since the ion populations change during the detection period, the relationship between ion signal and ion density is complicated. Also, the ions are detected by absorbing power from the marginal oscillator, which increases the kinetic energy of the ions above their thermal energy. This problem makes rate measurements difficult since it is preferred that rate constants be measured at thermal energies.

Mclver introduced a trapped ion cell in 1970.\textsuperscript{31} Instead of the ion creation, excitation, and detection events being separated in
space, now the events were separated in time. In other words, the ICR operations were no longer continuous but run in a pulsed mode. The development led to the ability to increase the time for ion-molecule reactions (a factor of nearly 1000 compared to sector instruments) and subsequently the pressure in the cell could be greatly reduced, thereby decreasing ion-neutral collisions, which increased the mass resolution of the technique. But, to acquire a mass spectrum with a sufficient signal-to-noise ratio (S/N) and resolving power required over 30 minutes.

**Development of Fourier Transform Ion Cyclotron Resonance Mass Spectrometry**

The ion trap was one of the significant developments necessary for the next major advancement of ICR mass spectrometry. The experiment could be performed in the pulsed mode and could use the discrete nature of the Fourier transform (FT) to analyze data. The Fourier transform had been known since the early 1900's, but it was not until 1965 that Cooley and Tukey developed the fast Fourier transform (FFT) algorithm that made it possible for the existing computers to process large data sets of up to 10,000 points in less than a minute. Quickly, the FFT was applied to infrared (FT/IR) and nuclear magnetic resonance (FT/NMR) spectroscopy. Comisarow and Marshall applied the FFT technique to ICR in 1974. Comisarow also developed a technique to detect the ion-induced image current produced on detector plates. The oscillating current is passed through an equivalent impedance, which produces a voltage that can
be amplified and digitized. Lastly, electronic analog-to-digital (ADC) converters were finally being produced that could handle the megahertz digitization rates necessary for collecting broadband ICR signals. The combination of all four of these improvements - trapped ion cell, FFT algorithm, image current detection, and fast ADC - made the FT/ICR/MS a viable technique.

**Basic FT/ICR/MS Technique**

Simply put, the FT/ICR experiment is a variable sequence of events under computer control; hence the technique is extremely versatile. Multiple MS/MS experiments and ion-molecule reaction pathways, energetics and rate constant measurements can be performed in the trapped ion cell without the need for extra devices as with sector instruments.

Ions are either formed directly in the cell (typical size of a cubic cell is 4.76 cm) or are transferred to the cell from an outside source. The cell consists of three pairs of opposed plates. The two plates perpendicular to the magnetic field axis have a small potential (± 1-3 volts) applied to keep ions from exiting the cell due to their velocity component parallel to the magnetic field. The magnetic field confines the ions in the other two directions. The other two pairs of plates are used for excitation of the cyclotron motion of the ions and for detection. An optional rf-pulse could now be applied to the cell as a preparation for subsequent ion-molecule reaction studies by either ejecting from the cell unwanted ions by means of an increase in their
orbital radii until they collide with one of the plates or 'heating' the ions as in ICDR experiments. A variable length delay time, which may be absent, allows ions to interact with the neutral background species. Then, the ions that are currently in the cell are excited to larger coherent (in-phase) orbits via a broadband frequency excitation event. Their combined cyclotron motions produce an image charge on the two detector plates which are connected by a resistor. The ion motions produce an alternating current through the resistor which is then converted to a voltage that is amplified and digitized via a fast ADC and stored in computer memory for subsequent signal processing. The image current has an amplitude that is proportional to both the radius or orbit (larger orbits bring the ions closer to the detector plates) and to the number of charges, but it is independent of the mass of the ions. As will be discussed later, it is imperative that all ions are excited to the same final radius to make quantitative measurements and comparisons of ion abundances. The voltage signal is a summation of signals of possibly many different frequencies dependent on the number of individual species in the cell. Finally, a quench pulse (trap plates are briefly set to the opposite polarity) is used to remove all ions from the cell before the sequence is repeated. The complex time domain transient signal is subjected to an FFT to produce the frequency spectrum and converted to a mass spectrum. Alternately, the signals from several successive pulse sequences can be co-added to produce a single time signal of higher S/N. Figure 1-3
Figure 1-3. Conversion of a frequency spectrum (a) into a mass spectrum (b). Each sinusoidal signal was observed for the same time with no damping. Notice that the peaks have the same frequency width but have different mass widths.
shows the conversion of frequency to mass. Note the broadening of high mass peaks due to the inverse relationship of frequency and \( m/z \).

The sequence described can easily be modified by addition of other pulse steps (i.e. excitation events, reaction delays, pulse valve operation, laser firing, etc.) for more elaborate experiments. Pressure in the cell is kept low (\( 10^{-8} \) to \( 10^{-9} \) torr or less) so that ion-molecule collisions do not damp the sinusoidal signal via loss of coherence or a reduction of the ion packets cyclotron radius. The time required to collect and process a standard mass spectrum consisting of ionization, excitation and detection, repeated 100 times to increase the signal-to-noise ratio, only takes a few seconds. Compared to the previous single-channel method of scanning and detecting each frequency separately, the Fourier transform multi-channel technique offers the Fellgett or multiplex advantage. In other words, an FT spectrum of \( N \) frequencies can be collected in a time of \( 1/N \) the time of a scanned spectrum with similar S/N. Or one can collect \( N \) individual time-domain transients to be co-added in the same time period for a single scan of each \( N \) frequencies separately. Signal averaging increases the signal by a factor of \( N \) and the noise only by a factor of \( \sqrt{N} \). Hence, the overall signal-to-noise ratio is increased by \( N/\sqrt{N} \), or \( \sqrt{N} \).

FT/ICR/MS overcame the serious detection limits of its predecessor. Also, the frequency based mass determination offers large improvement in resolution over other mass spectral techniques. Mass resolving power, \( m/\Delta m \) (where \( \Delta m \) is the peak width at half height) of 4,000 at mass 100 is routinely obtained in broadband
excitation-detection mode, and requires only minor adjustments, such as increasing the detection time, to obtain resolving powers over 50,000. Ultrahigh mass resolving power has been reported for N₃⁺ of 100,000,000,¹⁹ Ar⁺ of 200,000,000 and O⁺ of 300,000,000.³⁶

Lastly, the detection of ions in FT/ICR/MS is non-destructive. Hence, it has been shown that if one has a limited amount of sample, the quench pulse can be removed and the same ions can be detected numerous times.³⁷ The ions 'relax' back to the center of the cell via ion-molecule collisions. After some time, the ions can be re-excited and detected once again.

FT/ICR/MS has demonstrated tremendous potential as a mass analyzer and as a gas phase chemical synthesizer. Rapid advances in ionization, ion trapping, excitation methods and data transformation will keep the technique in the forefront of mass spectral analysis.

**Ionization**

Of course, before one can obtain mass spectral information it is necessary to produce representative ions of the species or unknowns. A number of different techniques have been used and only a few of those methods will be discussed.

Perhaps, the simplest and most common method for producing charged particles is electron ionization (EI). A beam of electrons is generated from a heated filament with a specified energy, usually in the range of a few electron-volts (eV) to 80 eV. Most often 70 eV electrons are used because a comparison of ion abundance versus
electron energy shows that the relative signal magnitude does not change by any significant amount above 60 - 70 eV. In the magnetic field, the electrons undergo high frequency cyclotron motion along the axis of the magnetic field and can pass through small apertures (≈ 2 mm) in the trap plates of the ICR cell. Typical electron current is in the range of 0.1 -100 μA for a duration of a few milliseconds. EI is a 'hard-ionization' method because of the extensive amount of fragmentation of the target neutrals by the large energy imparted by 70 eV electrons. Fragmentation of the species does help in structural analysis, however it is usually desirable to generate molecular ions for molecular weight determinations. The kinetic energy of the ionizing electron can be reduced to limit the amount of fragmentation with a trade-off in the number of ions produced. Also, even though the pressure used in FT/ICR/MS is below 10⁻⁸ torr and hence compounds with low vapor pressure can be ionized by EI, not all compounds are sufficiently volatile for EI. Solid samples can be heated on a probe placed near the cell, but modest to large molecules are not easy to ionize with electrons.

Chemical ionization (Cl) is a 'softer' technique which produces less fragmentation and more molecular ions. An excess pressure of reagent gas such as methane is added along with the volatilized sample. EI of this mixture produces predominantly reagent molecular ions. After a brief delay period, these ions can produce pseudomolecular ions of the sample via proton and hydride transfer. The extent of fragmentation is controlled via the thermochemistry of
the transfer. A more exoergic reaction will produce more fragment ions. Thus, by varying the reagent gas, it is possible to produce more or fewer molecular ions. Due to the large pressure of reagent gas needed, the resolution of the spectrum is degraded, but pulse-valve or dual trap cell systems can alleviate the problem. It is not always necessary to use a reagent gas. A typical substance will undergo self-Cl from its fragment ions if enough time is allowed for collisions to occur. Once again, Cl as for EI requires volatile samples.38

One of the more popular methods for producing ions of large mass species is laser desorption (LD). It is easily coupled to the vacuum chamber of the superconducting magnet and of course the photons are not affected by the magnetic field. The sample is placed on a probe which is then positioned near the ICR cell. A laser beam (IR or UV frequency) is directed onto the sample via mirrors or fiber optics. A plume of material consisting mostly of neutrals with some positive and negative ions, is expelled from the probe tip. Subsequent EI or Cl of the neutral material can enhance the ion signal. Also, the addition of a substance which is easily ionized can increase the number of molecular ions or more often pseudomolecular ions, such as sodiated, potassiated, and ammoniated molecular ions.39,40 Matrix assisted laser desorption ionization (MALDI) has proved to be extremely useful.41-43 The sample is mixed with a compound that strongly absorbs in, for example, the UV region. Photons in resonance with the absorption band of the matrix molecule are absorbed and the energy is gently transferred to the sample molecules. Most often MALDI produces
singly charged ions with little fragmentation. Initial attempts to merge MALDI with FT/ICR were limited in mass range and resolving power.\textsuperscript{44}

The most popular new ionization technique as of this writing is electrospray ionization (ESI).\textsuperscript{45} Electrospray is an extremely soft method. A solution of the sample is forced through a small needle at a relative potential of several kilovolts to produce small charged droplets. Electrodes transfer these droplets through a hot, high pressure drying gas where most of the solvent is evaporated leaving multiply charged analytes which separate due to the charge repulsion. The ions pass through skimmer cones and multiple stages of pumping to reduce the background pressure and are directed to the mass analyzer via lenses of some type. There are two major benefits of ESI. First, it produces ions of high-mass species. But, of most importance to FT/ICR/MS is the number of charges the species carry. Up to 100 charges have been observed, which is far more than any other technique can yield. As has been mentioned, signal precision is greatly enhanced at higher frequency. Therefore, as seen from Equation 1-3, the multiply charged ions have a much greater cyclotron frequency compared to their singly-charged counterparts, which can only improve the resolution and hence the mass accuracy determination.
**Trapped Ion Cells**

Once the ions are created, they must be contained for subsequent manipulations. As already stated, the magnetic field confines ions radially (x-y plane if the magnetic field is directed along the z-axis), however, the ions can freely drift parallel to the magnetic field. A small electric potential applied to two plates perpendicular to the field will keep the ions confined to a specified region. Positive voltages will trap positive ions and vice versa. Four other plates are present parallel to the magnetic field that can be used for excitation and detection. Together the six plates make up the basic cubic cell (see Figure 1-4) used in the majority of FT/ICR mass spectrometers. The electric field produces an approximately quadrupolar electrostatic potential near the center of the trap. The trapping voltage, $V_T$ causes the ions to oscillate between the two trapping plates, which is known as trapping motion. The trapping frequency is given by

$$v_T = \left(\frac{qaV_T}{\pi^2ma^2}\right)^{\frac{1}{2}}$$

(1-4)

in which $a$ is the distance between the trap plates, and $\alpha$ is a constant that depends on trap shape ( $\alpha=1.386$ for a cubic cell).

The trapping potential effectively 'squeezes' ions toward the z-axis center of the cell, but also produces an outward-directed radial electric force on the ion. The sum force effectively reduces the
Figure 1-4. A typical cubic static electromagnetic ion trap. Electron Ionization (El) is shown. The magnetic field confines ions in the x-y plane and the electric field applied to the trap plates (T) confines the ions's z-motion. (Graphic provided by Winnie Yin)
magnetic force on the ion, shifting the observed cyclotron frequency, \( \omega_+ \), to lower frequency as given by equation 1-5.

\[
\omega_+ = 0.5 \left\{ \omega_c + \omega_c \left( 1 - \frac{m}{m_{\text{crit}}} \right)^{1/2} \right\}
\]  

(1-5)

in which

\[
m_{\text{crit}} = \frac{qa^2 B_0^2}{8a V_T}
\]  

(1-6)

is the critical mass above which ions can not be trapped.

The outward directed electric force now puts the ion in a crossed electric-magnetic field. The crossed field produces a mass independent drift of the ion about an equipotential line. (The crossed field is used as a velocity filter [Wien filter] in other mass spectrometers.) In the cell the equipotential lines are actually approximately circles. Hence, the ions drift around the center of the cell at a fixed frequency, \( \omega_- \), the magnetron motion (Figure 1-5), given by

\[
\omega_- = 0.5 \left\{ \omega_c - \omega_c \left( 1 - \frac{m}{m_{\text{crit}}} \right)^{1/2} \right\}
\]  

(1-7)

The three motions are shown in Figure 1-6.

The trapping force not only causes additional frequencies but also limits the maximum ion mass that can be trapped in the ICR cell.
Figure 1-5. Magnetron motion. In (a) an ion with zero initial velocity, experiences only the force due to the electric field and moves upward. Once the ion has a velocity it will also experience the magnetic field force (directed to the left). The overall effect is that the ion drifts to the left at a velocity given by \(v = E/B\) around an equipotential line (dashed lines). In the ICR trapped ion cell (b), the equipotential lines are circles near the center of the cell in the x-y plane. The electric field is directed radially outward. Hence, the ion will drift around the cell to yield a low frequency magnetron motion.
Figure 1-6. Three motions are observed in the ICR ion trap. The quickly oscillating cyclotron motion (small circle) due to the magnetic field; the slower magnetron motion (large circle) due to the crossed electric and magnetic fields; and the trapping or axial motion due to the electric field. (Graphic provided by Jane Xiang)
Rearrangement of Equation 1-2 yields the magnetic-field-only ion cyclotron orbital radius

\[ r = \frac{mv}{qB_0} \]  

(1-8)

which for thermal, singly charged ions of mass less than 1100 u in a magnetic field of 3T is less than 0.25 mm. For a typical cell with a radius of 23 mm, an ion of mass 8.9 million u can be trapped in the x-y plane. The electric trapping force reduces the upper mass limit to about 21,000 u at 2V trapping. This is the ion's radius before excitation. The ions have yet to be excited to produce a coherent signal. Hence, the actual upper mass limit is smaller yet.

An important advantage of a perfect quadrupolar electrostatic potential is that the ICR orbital frequency, \( \omega_+ \), is independent of ICR orbital radius. Hence, there is no frequency spread for ions with different motional amplitude. The potential in a cubic cell is only approximately quadrupolar near the center of the cell. The hyperbolic trap provides a near-perfect quadrupolar potential.\(^{46,47}\) It has curved inner surfaces provided by a 'ring' electrode and two 'end caps'. A segmented ion trap was designed to allow easier access for ionization (Figure 1-7c).\(^{48}\) The hyperbolic cell improves mass accuracy and reduces spectral peak width.

The cubic cell and the hyperbolic cell suffer from a problem known as z-ejection. The rf excitation from the transmitter plates of the cells do not have field lines extending straight between the plates.
Figure 1-7. Typical cells used in FT/ICR/MS. (a) the cubic cell; (b) the open-ended cylindrical cell; (c) the hyperbolic cell; and (d) the screened elongated cell.
Instead, the lines are warped due to the other plates and the finite cell dimensions which produce a force in the z-direction of the cell. If the force is oscillating at twice the trapping frequency of an ion, then the ion will be ejected axially during excitation.\textsuperscript{49-52} The effect is greater at lower mass and is also radially dependent.\textsuperscript{50} Guard wires (for rf-shimming) were added to the cell to 'straighten' the field lines.\textsuperscript{53,54} Other traps designed to improve the excitation field include the 'infinity' cell\textsuperscript{55} and the linearized cell.\textsuperscript{56}

The outward force generated by the trapping potential, which shifts the observed frequency of the ion, can be greatly reduced by 'screening' the trap plates.\textsuperscript{57} In brief, a set of grounded screens is placed just inside the trap plates. Now, instead of a quadrupolar potential in the cell, the potential in the cell is reduced to near zero and is almost flat across most of the trap volume. It essentially eliminates the unwanted frequency shifts, improving mass accuracy, resolution, and excitation/ejection selectivity.

Other designs include the elongated cell (Figure 1-7d), and the standard cylindrical cell.\textsuperscript{58} A particularly useful cell for external injection of ions is the open-ended cylindrical cell (Figure 1-7b). The cylinder is segmented perpendicular to the magnetic field into three sections. The middle section is used as the ion 'trap', while the outer segments are used to trap the ions in the center section when a static potential is applied to them. The key advantage to the open-ended cell is that the ion beam need not be focused down to a small diameter
in order to get into the cell. In other words, the open-ended cell has a much greater acceptance angle to collect ions.

Lastly, a common cell system used in commercial instruments is the dual cell. Two cubic cells share a common trap plate that has a small hole (2 mm). This small hole acts as a conductance limit in the vacuum chamber which effectively isolates the cells from one another. Both sides can now be pumped separately and a pressure difference of about 100-500 can be maintained. The arrangement allows a large amount of sample to be ionized in one cell (commonly called the source cell) at high pressure and then the ions are transferred to the other cell (analyzer cell) by dropping the potential on the common trap plate. The lower pressure in the analyzer cell permits longer (less damping) detection of the ion signal than in the high pressure cell.

**Excitation**

After ionization (EI), the ions do not produce any measurable signal due to their small cyclotron radii and the random phase or distribution around a common center of the ions. The ions must be excited to larger orbits and brought into coherence in order to be detected.

A radio frequency (rf) signal is applied to two opposing plates of the cell. If the frequency of the rf signal matches one of the natural motions of the ion, then energy is absorbed and that motion is excited. For cyclotron motion, an increase in the cyclotron orbit is observed for
the entire ion packet which produces a coherent signal. The final radius of the ion packet is independent of the ion mass and charge. The radius in the cubic cell is proportional to the excitation amplitude, $E_0 T_{\text{excite}}/2B_0$, in which $T_{\text{excite}}$ is the excitation time and $E_0$ is the amplitude of the electric field. Hence, if the excitation is uniform in magnitude at each frequency, all ions will be at the same final radius.

There are three commonly used methods for ion excitation: single frequency, frequency sweep, and Stored Waveform Inverse Fourier Transform (SWIFT) excitation (Figure 1-8).

Single frequency excitation or single-pulse excitation was the method used to produce the first FT/ICR mass spectrum and is still the primary method of excitation for Fourier transform nuclear magnetic resonance spectrometry (FT/NMR). A single frequency pulse of duration, $T$, will produce in the frequency domain a sinc function centered at the frequency of excitation with a magnitude (absolute value) mode full width at half maximum (FWHM) value of $\approx 0.6/T$ Hz. To obtain a reasonably flat profile over a given frequency (mass/charge) range, requires an extremely short excitation period. For FT/NMR, where the spectral bandwidth is on the order of 10,000 Hz, a pulse of a few microseconds will produce sufficiently flat power across the frequency range of interest. But, in a fixed magnetic field of 3.0 T, the ion cyclotron frequencies vary from about 2.6 MHz to 46 kHz for ions of $18 - 1000$ m/z, respectively. For such a large frequency range, the pulse duration would need to be approximately
Figure 1-8. Frequency-domain magnitude spectra of some standard FT/ICR time-domain excitation waveforms. (a) Rectangular pulse (encompassing a single frequency); (b) Frequency-sweep ("chirp"); (c) SWIFT for broadband excitation; (d) SWIFT for MS/MS or ion-molecule reactions. (Figure provided by Alan Marshall from reference 69)
0.042 \mu s and the amplitude on the order of 60,000 V in order that the ions reach a significant radius (1.0 cm in a 4.7 cm cubic cell) for subsequent detection.\textsuperscript{60} However, this method is useful for excitation of a single m/z or over a limited frequency range.

To excite ions over such a broad frequency range, frequency sweep excitation was introduced.\textsuperscript{61} Frequency sweep or 'chirp' excitation is the most widely used excitation method in FT/ICR/MS. It eliminated the need to generate such short, strong pulses by means of single frequency excitation. The radio frequencies are scanned linearly in time over the frequency bandwidth of interest. Although this did improve excitation for broadband applications, it still has the problem of non-constant excitation amplitudes over the frequency range. Variations in amplitude of $\pm 25\%$ are observed in the frequency spectrum for linear sweep excitation, which makes quantification of ion intensities difficult. By slowing the frequency sweep, one can flatten the power spectrum and the frequency selectivity of excitation improved especially at the ends of the frequency range. But the signal from those ions excited initially will be lost before the detection event due to loss of coherence and a decrease in radius due to ion-molecule collisions.\textsuperscript{60} While frequency sweep is simple, it should be used with care, especially for quantitative work.

In the mid-1980's, Marshall, Wang and Ricca developed SWIFT excitation\textsuperscript{62,63} adapted from an earlier proposal by Tomlinson and Hill.\textsuperscript{64} It has become the excitation method of choice, when available, for FT/ICR/MS providing high selectivity, uniform excitation
magnitude profiles and the ability for windowed excitation/ejection. First, one specifies the desired frequency domain excitation profile (Figure 1-9a) and then a discrete inverse Fourier transform is performed to generate the needed time domain excitation profile (Figure 1-9b). The digitized waveform is clocked out by a digital-to-analog converter, amplified and applied to the transmitter plates of the ICR cell. In order to see the actual excitation frequency domain profile, one must pad the time domain signal with an equal number of zeroes before conducting the Fourier transform. Zero-filling effectively interpolates the frequencies between the initially specified frequencies. The resultant non-rectangular shape of the actual excitation spectrum (Figure 1-9d) is a result of the classical uncertainty principle. A time domain waveform of duration ,T, can not be known to a certainty greater than approximately ± 1/T Hz.

Even though we have now calculated a time domain signal that will yield a significantly flatter profile over the frequency range of interest, there are a few practical problems with the large dynamic range of the excitation. Essentially all of the excitation power is concentrated in a narrow burst due to the constant phase relationship of all of the specified frequencies (Figure 1-9b). The large vertical jump may exceed the linear response of the transmitter circuitry and the dynamic range may also exceed the digital dynamic range of the D/A converter or the computer in which the waveform is stored. The digital dynamic range can be reduced by removing the phase coherence of the frequencies either through a random sequence62,64
Figure 1-9. Generation of a SWIFT excitation waveform. A frequency domain profile is specified (a) and an inverse Fourier transform (IFT) is performed to yield the time domain waveform (b). The large amplitude of the time domain spike can be reduced by scrambling the phase relationship of the frequencies before IFT to produce the lower amplitude time signal (c). The actual frequency profile is calculated via an FT after padding the time signal with an equal number of zeroes (d). Although the excitation amplitude is flat over most of the region, oscillations are observed at the boundaries.
Figure 1-9.
or via quadratic phase modulation\textsuperscript{65} prior to inverse Fourier transformation (Figure 1-9c). Hence, the excitation spectrum is distributed between the real (in-phase) and imaginary (90°-out-of-phase) components rather than all of the signal residing in the real spectrum (pure cosine waves).

Secondly, the actual excitation spectrum reveals oscillations in magnitude at frequencies near the edges of the excitation bands (Figure 1-9d). Due to the complementary nature of the Fourier transform, a sharp variation in one domain requires a slow variation in the other domain, as in the case of single frequency excitation. The oscillations can be minimized by smoothing the transitions at the ends of the bands by applying a smoothing function to the requested frequency profile before inverse Fourier transformation\textsuperscript{66,67} (Figure 1-10) or apodizing the time domain waveform so that the ends tend smoothly to zero.\textsuperscript{68}

Although SWIFT has been shown to produce flat excitation so that quantification of the ion signals can be performed, perhaps its greatest advantage comes from the ability to specify unique excitation frequency profiles. One can tailor the waveform to excite only certain frequency ranges. To isolate ions of a single m/z, or multiple m/z's, requires multiple excitation pulses via chirp. The experimental time is extended and it is possible that unwanted reactions could occur during this time. Also, the frequency resolution (selectivity) of the chirp excitation events is greatly reduced when the time for each excitation event is subsequently reduced to eliminate the unwanted
Figure 1-10. Prior to IFT, the requested excite spectrum is smoothed via a three-point moving average with 5 passes (a). The time domain signal (b) now tends smoothly to zero (compare to Figure 1-9c). The actual excite spectrum (c) does not have the 'ripples' observed in Figure 1-9d, and is the same as the requested excite spectrum (a).
Figure 1-10.
reactions. By means of SWIFT, all of the individual frequency ranges are combined into one event, thereby eliminating the need to use multiple pulses. For \( n \) individual frequency sweep events, either one SWIFT event of the same total duration will produce a subsequent \( n \)-fold improvement in the frequency (mass) selectivity or a SWIFT event of a duration equivalent to one chirp event will produce the same selectivity but a reduction in time of \( 1/n \). One can also combine the ejection and excitation events into one SWIFT event by having different magnitudes at different frequency regions. By ejecting highly abundant ions, the FT/ICR dynamic range can be improved for the detection of less abundant ions.\(^{63}\)

**Detection of The Ion Signal**

As mentioned previously, the coherently moving ions produce an oscillating image current which is converted to an oscillating voltage by means of passage through an equivalent impedance. The continuous signal is sampled at equal intervals producing a discrete time-domain data set. The data set contains the sinusoidal signal for all ions excited in the cell. The Fourier transform converts the time-domain transient to the frequency-domain spectrum which can then yield the mass spectrum.

**Nyquist Theorem.** The speed at which one must sample is given by the Nyquist theorem which states that to identify a sinusoidally time-varying signal properly it is necessary to sample its amplitude
twice per period. In other words, the sampling frequency must be at least twice the highest frequency of interest, Equation 1-9.

\[ v_{\text{sampling}} = 2v_{\text{Nyquist}} \]  

(1-9)

Signals having frequencies smaller than the Nyquist frequency will appear correctly in the spectrum. Frequencies greater than \( v_{\text{Nyquist}} \) will be aliased or 'folded-over' into the bandwidth from 0 to \( v_{\text{Nyquist}} \), and will appear at

\[ v_{\text{apparent}} = \left| v_{\text{true}} - nv_{\text{sampling}} \right| \quad n = \frac{v_{\text{true}}}{v_{\text{Nyquist}}} \]  

(1-10)

\( n \) is rounded off to the next lowest integer. Examination of Equation 1-10 shows that when the true frequency is lower than the Nyquist frequency then \( v_{\text{apparent}} = v_{\text{true}} \). To determine if the peak is aliased, one need only to change the sampling rate and observe if the peak shifts. A true peak will not shift, unless of course the Nyquist frequency is less than the true frequency.

**Acquisition Time.** The observation period, \( T \), of the signal is given by

\[ T = N \Delta t \]  

(1-11)

in which \( N \) is the number of samplings (data points) and \( \Delta t \) is the delay time between each sampled point, also known as the dwell time. The dwell period is just the inverse of the sampling frequency, hence

\[ T = \frac{N}{v_{\text{sampling}}} = \frac{N}{2v_{\text{Nyquist}}} \]  

(1-12)
Frequency domain peak widths are inversely related to the acquisition period. Therefore, longer acquisition period produces narrower peak width and hence better resolution. To increase the time, $T$, it is necessary to either decrease the sampling frequency or increase the number of data points. In direct mode acquisition, the sampling frequency is specified by the highest frequency to be observed and the computer memory limits the total number of data points that can be acquired.

A simple question arises: How can one extend the time of acquisition, and hence improve the resolution, if the maximum number of data points is being collected and the sampling rate has been decreased to yield a Nyquist frequency just above the true frequency of the detected signal? A dispersive optical instrument allows one to acquire data between any frequency limits by adjusting the slit width so that a different frequency range can be monitored by the multichannel detector. However, in the case of FT/ICR/MS we can not 'raise' the lower frequency limit of detection. We are confined to collecting all frequency components less than $v_{\text{Nyquist}}$. Actually, there is a clever method which in effect does allow us to 'raise' the lower limit.

The time signal is passed through a mixer (non-linear device) with a reference frequency greater than the highest true frequency. The input to the mixture is a summation of all frequencies,

\[
\text{Input}(t) = A_0 \cos \omega_{\text{true}} t + B_0 \cos \omega_{\text{ref}} t
\]  

(1-14)
The non-linear output signal may be expressed as a non-linear power series. Examination of the first two terms yields

\[
\text{Output}(t) = c_1 A_0 \cos \omega_{\text{true}} t + c_1 B_0 \cos \omega_{\text{ref}} t + c_2 A_0^2 \cos^2 \omega_{\text{true}} t + c_2 B_0^2 \cos^2 \omega_{\text{ref}} t + 2c_2 A_0 B_0 \cos \omega_{\text{true}} t \cos \omega_{\text{ref}} t
\]  

(1-15)
in which \(c_x\) are constants. The original frequencies are present along with two squared terms which can be expressed as second harmonics of the original frequencies and the last term can be expressed as

\[
\cos \omega_{\text{true}} t \cos \omega_{\text{ref}} t = \frac{1}{2} \left[ \cos(\omega_{\text{true}} + \omega_{\text{ref}}) t + \cos(\omega_{\text{ref}} - \omega_{\text{true}}) t \right]
\]  

(1-16)
producing the sum and difference frequencies. The output signal goes through a low-pass filter, passing only the much lower difference frequency, which can be sampled at a lower rate \(v_{\text{sampling}} = 2(\omega_{\text{ref}} - \omega_{\text{true}})/2\pi\), increasing the acquisition time and therefore the resolution. The technique is called heterodyning.\(^{69}\)

**Benefits of Fourier Analysis.** A scanning instrument samples a given frequency for a fixed period of time and then moves on to the next frequency. The basic advantage of this method is that the measurement yields each amplitude directly without further calculations. But each frequency has only been detected once. Many more scans can be obtained and it will be observed that the signal amplitude will increase in proportion to the number of scans. The noise will also increase but much more slowly, proportional to the square root of the number of scans. Hence, the signal-to-noise ratio
(S/N) is proportional to \((N/\sqrt{N})\) or simply \(\sqrt{N}\), in which \(N\) is the number of scans.

It is reasonable to suggest that it would be better to examine all frequencies at once, which could be done with a multichannel detector. The spectrum could be acquired in less time \((1/N)\) for an \(N\) channel detector) with the same S/N, or improve S/N by a factor of \(\sqrt{N}\) in the same length of time it took to scan the frequency range. However, the cost to implement a multichannel detector for ICR would be very high.

As already noted, the excited ions produce a complex time domain signal that is ultimately converted to a voltage which is amplified and digitized to yield

\[
f(t) = \sum_{i=1}^{M} N_i e^{-t/\tau_i} \cos(\omega_i t + \phi_i) \quad (1-17)
\]

in which \(N_i\) is the number of ions, \(\tau_i\) the damping constant, \(\omega_i\) the ICR frequency, \(\phi_i\) is the initial phase of the \(M\) different mass/charge values. It is now obvious that all ion frequencies are detected simultaneously and we gain the Fellgett or multiplex advantage noted in the previous paragraph.\(^{70}\)

It is not easy to determine the amplitude and frequency of each ion by inspection of the transient signal. It is necessary to convert the transient to a frequency spectrum via the Fourier transform which
links the two domains. The complex Fourier transform of a continuous time-domain function, \( f(t) \), is

\[
F(v) = \int_{-\infty}^{+\infty} f(t) e^{-i2\pi vt} \, dt \tag{1-18}
\]

The formula for the discrete frequency-domain spectrum is

\[
F(n_m) = \sum_{n=0}^{N-1} F_{nm} f(t_n) \tag{1-19}
\]
in which \( t_n = nT/N \) are equally spaced sampling times and \( F_{nm} = \exp(-\omega_m t_n) = \exp(-i2\pi nm/N) \).

The frequency spectrum may be displayed in either absorption or dispersion mode. However, the spectral data is not pure absorption or pure dispersion but is a mixture of the two determined by the initial phases of the signals. Phase correcting the data for FT/ICR/MS is virtually impossible. The ions are not immediately detected after excitation to coherent orbits. The ions undergo many periods of rotation before detection begins. Also, all ions may be excited to the same final radius, but ions of different m/z ratios will not be in phase (i.e. at the same place on the circumference of the circle defined by the final radius). Therefore, frequency domain data is displayed in absolute value, more commonly known as magnitude, mode display given by

\[
M(\omega) = \sqrt{[A(\omega)]^2 + [D(\omega)]^2} \tag{1-20}
\]
in which the absorption and dispersion spectra are given respectively by

\[ A(\omega) = \frac{\tau}{1 + (\omega_0 - \omega)^2 \tau^2} \]  
(1-21a)

\[ D(\omega) = \frac{(\omega_0 - \omega)^2 \tau^2}{1 + (\omega_0 - \omega)^2 \tau^2} \]  
(1-21b)

in which \( \omega_0 \) is the true cyclotron frequency. The major disadvantage to magnitude-mode display is the decrease in resolution (widening of the peak shape) by a factor of \( \sqrt{3} \) (for a Lorentz lineshape).

**Digital Filtering.** The time-domain signal (henceforth transient) in ICR, as in NMR, is an exponentially damped signal. Relaxation or decay of the ion signal is caused by ion-neutral collisions, which removes energy from the ion. Thus ion speed and ion cyclotron radius will decrease to a point where no measurable signal is obtained. We have already discussed the results of truncating a sinusoidal signal in the excitation section. In review, the truncation produces unwanted 'wiggles' on the sides of the peak known as Gibbs oscillations. The oscillations arise from the sharp cut-off of the transient which introduces high frequencies. Conversely, acquiring signal for a time past that where the signal has decayed under the noise, will improve the digital resolution (i.e. more data points across the peak) but the width (resolution) of the peak will not decrease. Also, we will be acquiring more noise in our transient which will reduce S/N.
The purpose of digital filtering is to correct these problems. Filtering in Fourier spectroscopy is simply the point by point multiplication of the transient by a weighting function designed to either reduce the side lobes (apodization) or to narrow the spectral line widths (resolution enhancement).

Apodization, literally 'removing the feet', reduces the Gibbs oscillations by assuring that the transient decays smoothly to zero by the end of the acquisition time. A moment's reflection reveals that to smooth the data to zero will also reduce the total time period during which signal is actually observed. A number of apodization functions or windows are available, including Cosine, Hanning, Hamming and Kaiser windows. All can be boiled down to the amount of reduction in the ripple amplitude versus the inherent broadening of the spectral line width. The Kaiser and Hamming windows provide the best compromise.\textsuperscript{71}

Resolution enhancement is an attempt to narrow the spectral linewidths artificially. It is possible to design a weighting function that will effectively remove the damping profile of the true signal and replace it with a damping function specified by the operator. In general, it is desirable to increase the signal in the latter part of the transient so that the signal is in essence received for a longer time. However, this also inherently increases the noise in that section thereby reducing S/N. Therefore, the weighting functions are designed to increase smoothly past the middle of the transient and then decay to zero in order to minimize increase in noise in the
spectrum. Sine-bell and sine-bell-squared are two such windows used for resolution enhancement.\textsuperscript{71}

Two other methods used to improve the overall appearance of the frequency spectrum are linear prediction and maximum entropy. Linear prediction attempts to determine the N+1 unknown transient data point by the m previous data points. In other words it uses an m range of data points before the last one to determine the unknown next data point. The technique can be repeated to determine additional data points.\textsuperscript{72} Maximum entropy attempts to 'smooth' the spectrum by reconstructing the most likely spectrum by maximizing its entropy. Its major drawbacks are the long computing time and that an assumption must be made in the noise level that could ultimately cause the loss of information from small magnitude peaks. \textsuperscript{69}

**Zero-filling.** Fourier transformation of N equally spaced data points over a total time period of T seconds produces N/2 unique complex frequency-domain data points. At first it may seem that we have lost some data, but each complex frequency data point is a product of magnitude and phase or also defined as the sum of real and imaginary components. Therefore the complex data can be separated into an absorption and dispersion spectrum each of N/2 data points. One can then display either spectrum or compute the magnitude spectrum. By adding N zeroes to the end of the discrete transient data set will produce after Fourier transformation an N-point absorption and dispersion spectrum. What we have done is extend the data acquisition time, thereby spacing the frequency domain data at
intervals of 1/2T rather than 1/T Hz.\textsuperscript{73} It has been shown that the first zero-fill not only interpolates between the original frequency domain points but actually recovers the information in the other spectrum (i.e. recover dispersion information for an absorption plot).\textsuperscript{73,74}

**Applications and Other Improvements**

**Mass Accuracy.** Because frequency can be measured to such high precision, high mass resolving power and high mass accuracy result for the FT/ICR. Differentiation of Equation 1-3 and substitution produces

\[
\frac{m}{\Delta m} = -\frac{qB_0}{m2\pi\Delta v}
\]

which shows that the mass resolving power varies inversely with \(m/q\). Since in both the high pressure (large number of ion-neutral collisions) and low pressure regime the peak width does not vary significantly with \(m/q\).\textsuperscript{69}

Equation 1-3 could be used for mass calibration if there was not a trapping electric field. Instead, the calibration law used most often in the cubic cell ICR system is

\[
\frac{m}{q} = \frac{A}{v_{obs}} + \frac{B}{v_{obs}^2}
\]

in which \(A\) and \(B\) are constants that can be determined by two data points relating mass to frequency. The equation is sufficiently accurate to give errors in the part-per-million range under similar
experimental conditions (i.e. trapping voltage, magnetic field strength, excitation amplitude, pressure, etc.). Hence, elemental composition determinations can be made with just the molecular ion. Isobaric ions have been distinguished by FT/ICR. For ultrahigh mass accuracy determinations, other factors may need to be considered in the calibration equation, for instance relativistic frequency shifts for low mass ions and image charge shifts. FT/ICR/MS has recently demonstrated high mass accuracy measurements in the determination of the mass of deuterium by accurate mass measurements of H$_2$O$^+$ and OD$^+$. Perhaps the greatest demonstration of high mass accuracy has been recently demonstrated by Beu et al. with an electrospray ionization system in which mass accuracy of 1 ppm was obtained for multiply-charged protein ions.

**Ion Remeasurement.** As mentioned earlier, detection is non-destructive in FT/ICR so that it is possible to remeasure the frequency of the same ions repeatedly. Williams et al. showed that high mass ions are not significantly scattered during ion-molecule collisions so that the ion's kinetic energy is reduced which ultimately leads to the ions returning to near the center of the cell, where they may be re-excited and detected.

The remeasurement technique has recently been markedly improved due to the advent of quadrupolar excitation to axialize and cool the ions. As ions lose kinetic energy via collisions with neutrals the cyclotron radius decreases and the magnetron radius increases. This relaxation ultimately causes loss of ions due to the expansion in
the magnetron radius. If, however, quadrupolar excitation (both pairs of plates parallel to the magnetic field are used for excitation, with a 90° phase shift) is applied at the unperturbed cyclotron frequency, then magnetron motion is converted to the more quickly damped cyclotron motion with the overall result that the ions are thermally cool and axialized.81 Guan et al. applied the method to laser desorbed ions and showed an improvement in resolving power, sensitivity and selectivity.82 Also, Speir et al. showed that with the cooling system they could remeasure ions over 200 times with an efficiency of 99.5%. Ions were trapped for over an hour and low to high resolution experiments were conducted on these same ions.83

**Gas-Phase Chemistry.** Due to its ability to trap ions for a long period of time and isolate specific ions in the cell, FT/ICR is useful for determining ion reaction pathways, kinetics and thermodynamic quantities. Many proton transfer reactions (proton affinity) have been studied by ICR and now FT/ICR. Chapter two of this work will examine the measurement of the gas phase basicities of carbenes. Other ion and neutral properties can be examined such as electron affinity, hydride ion affinity, and anion proton affinity. FT/ICR is the method of choice for these determinations.

**Tandem Mass Spectrometry.** MS/MS has proven to be useful in structural identification of molecules.76,84,85 In general, ions are formed, ions of a single m/z are isolated and activated in some manner to promote fragmentation. FT/ICR again shows unique promise for such applications, mainly due to less sample consumption, rapid
collection of spectra and high resolution. Also, all stages of the MS/MS experiment takes place in the ICR cell and as such are separated in time rather than space. Ion transmission losses are greatly reduced and MS^n experiments can be conducted with the same equipment in contrast to other mass spectrometers which would require extra hardware. Many methods have been used to promote ion fragmentation including collision induced dissociation (CID)\textsuperscript{86}, surface-induced dissociation(SID)\textsuperscript{87,88}, and photodissociation.\textsuperscript{89,90} Chapters 4 and 5 will demonstrate an improvement in two-dimensional mass spectrometry for MS/MS.

**Summary**

Improvements over the past 17 years in ionization, trapping, excitation and detection have made Fourier transform ion cyclotron resonance mass spectrometry a versatile technique for mass analysis, thermochemical analysis and reaction pathway determinations. The objective of this work is to examine ion-molecule reactions and to develop an automated system for MS/MS experiments via two-dimensional analysis which eliminates the need to isolate each individual unknown. Cyclotron radius (ion speed) and kinetic energy modulation methods have been developed for the 2D experiments.
References


(76) Cody, R. B. Analysis 1988, 16, 30-36.


Chapter II

Determination of The Gas Phase Basicity and Proton Affinity of Carbenes by FT/ICR/MS

Introduction

For about 20 years, experimental techniques such as ion cyclotron double resonance (ICDR) have made it possible to quantitate the gas-phase thermochemistry of proton transfer reactions. By comparing the solution and gas-phase basicities, one can distinguish the intrinsic molecular basicity from solvation effects. Moreover, heats of formation and bond dissociation energies are in turn helpful in determining molecular stabilities and energetically favorable reaction pathways.

Carbenes, R–C–R′, are important short-lived intermediates in condensed-phase organic synthesis, photochemistry, and atmospheric chemistry. For example, cyclopropenylidene is the most abundant hydrocarbon in interstellar space, and other carbenes have been detected in interstellar and circumstellar space.\(^1\)\(^2\) Although proton affinity and gas phase basicity values have been determined for a wide variety of organic compounds.\(^3\) such data on carbenes have been limited to a few chloro- and fluorocarbenes.\(^4\)-\(^6\) In this chapter, the gas phase basicities of other carbenes are determined.
Background

The gas phase basicity (GB) and the proton affinity (PA) of a molecule, M, are defined as the negative of the free energy change and the enthalpy change, respectively, for the reaction:

\[ M + H^+ \rightarrow MH^+ \]

\[ \text{GB} = -\Delta G \]

\[ \text{PA} = -\Delta H \quad (2-1) \]

Equilibrium Measurements. A large number of organic substances have been determined by the equilibrium method. The unknown molecule, A, reacts with a compound of known GB, B, until equilibrium is established (Eq. 2-2c).

\[ A + H^+ \rightleftharpoons AH^+ \quad K_1 = \frac{[AH^+]}{[A][H^+]} \quad (2-2a) \]

\[ B + H^+ \rightleftharpoons BH^+ \quad K_2 = \frac{[BH^+]}{[B][H^+]} \quad (2-2b) \]

\[ AH^+ + B \rightleftharpoons A + BH^+ \quad K_3 = \frac{[A][BH^+]}{[B][AH^+]} \quad (2-2c) \]

The equilibrium constant, \( K_3 \), is determined by measuring the relative peak areas of the ions and the partial pressures of the neutrals. The equilibrium constant, \( K_1 \), for the unknown A is calculated from the ratio, \( K_2/K_3 \). Lastly, the gas phase basicity of unknown A is then

\[ \text{GB}(A) = -\Delta G = RT \ln(K_1) \quad (2-3) \]
If the entropy change of Reaction 2-2a can be determined or estimated then the enthalpy change and therefore the proton affinity of the unknown is obtained. In most cases, the entropy change for Reaction 2-2c is taken to be near zero and the proton affinity of A is calculated based on the known PA of the reference compound.³

**Bracketing.** If the compound of interest is low in abundance so that a stable neutral pressure is not obtainable, as in the case of carbenes, then the equilibrium method cannot be used. Instead, the protonated compound is produced and the proton transfer reaction is monitored for each of a series of reference bases. If reference base B₁ is observed to remove the proton and reference base B₂ does not remove the proton, then it can be inferred that the gas phase basicity of the unknown, A, is between that of B₁ and B₂ \([\text{GB}(B_2) < \text{GB}(A) < \text{GB}(B_1)]\). The technique is known as 'bracketing'.

Both techniques yield only relative information and not the absolute thermochemical data of the compound of interest. An absolute value is assigned by incorporating a standard into the gas phase thermochemical energy ladder. The proton affinity of the standard is calculated based upon heats of formation of the neutral and appearance energy measurements for the ions.³

Carbenes are highly reactive electrophilic intermediates. Protonated carbene ions can be generated by choosing a suitable precursor molecule that will easily fragment to the desired ion. Because the concentration of the neutral carbene is vanishingly small,
the bracketing technique is employed to measure the gas phase basicity.

**Experimental**

All experiments were performed on a dual-trap FTMS-2000 FT/ICR mass spectrometer (Extrel FTMS Millipore Inc., Madison, WI), operated at 3.0 tesla, equipped with Helix Technology CryoTorr-8 2000 L/s cryopumps (Waltham, MA) for both source and analyzer vacuum chambers, with two 4.76 cm cubic traps in a standard dual-trap configuration (Figure 2-1). The mass spectrometer was controlled by a Nicolet 1280 computer. Each gaseous sample was introduced through the batch inlet system: carbene precursor molecules via a gold-leak into the source region and the reference base via a pulse-valve system into the analyzer region.

The experimental sequence is as follows (see Figure 2-2). All ions are removed from the cells by briefly setting the trap plates to +9.75 V and then -9.75 V. A quench delay of from 1-30 seconds is used so that the analyzer region pressure returns to its base pressure after each pulse of the neutral reference base. The carbene precursor compound (source pressure of \(1 \times 10^{-7}\) torr) is ionized by low energy electrons (set just above the appearance potential for the protonated carbene) for 40 ms at a current of \(\sim 9 \, \mu A\). The conductance limit potential is dropped from 2V to 0 V to transfer the ions of interest to the analyzer cell. Either SWIFT or linear sweep excitation is used to eject all other ions. Next, the reference compound (reservoir pressure of 1 torr) is
Figure 2-1. Dual cell Fourier Transform Ion Cyclotron Resonance Mass Spectrometer. Carbene precursor molecules are constantly leaked into the Source region for ionization. Ions are transferred to the Analyzer cell, isolated and reacted with a reference base admitted via a pulse valve system.
Figure 2-1.

EXTREL FTMS-2000
Figure 2-2. Experimental event sequence. 1. All ions are removed from the cell by applying positive and negative voltages to the trap plates. 2. Variable delay to allow the analyzer region to return to base pressure. 3. Ionization of precursor molecule at low electron energy via EI. 4. Transfer of ions to the Analyzer cell by dropping the conductance limit voltage. 5. All unwanted ions are ejected from the cell via SWIFT or linear sweep excitation. 6. Reference base is admitted to the chamber via a pulse valve system. 7. Variable reaction delay to monitor proton transfer. 8. Excitation and detection of ions.
Figure 2-2.
pulsed into the analyzer region to a pressure of $9.0 \times 10^{-8}$ torr and allowed to react for a period of 10 ms to 3 s. Ions are then excited with either SWIFT or linear sweep excitation, detected and Fourier transformed. Detection of the ion signal was normally carried out in direct mode (Nyquist frequency = 2.666MHz) with either 16K or 32K data points.

**Results and Discussion**

Dichlorocarbene. Although the gas phase basicity of dichlorocarbene has already been determined, it is a reasonable starting point to determine if the experimental technique used in this study will provide the desired results. Deuterated-chloroform was used as the precursor molecule to the deuterated dichlorocarbene ion. Deuteration provides a convenient tag to monitor 'proton' transfer reactions because some compounds undergo self-protonation reactions which can provide false-positive data points if isotopic labeling is not used. Electron ionization with 10 eV electrons was used to produce the deuterated dichlorocarbene ion. The energy was just above that of the appearance energy for that ion. Figure 2-3 shows the isolation of CDCl$_2^+$ by use of a SWIFT excitation pulse prior to the admittance of the reference base.

Spectra of the reference bases were collected at 70 eV ionization and at 10 eV ionization. Reactions of the reference base ions (particularly the molecular ion) produced by 10 eV ionization were monitored at similar pressure and event timing as that later
Figure 2-3. Spectrum of deuterated dichlorocarbene ion isolated via SWIFT excitation. The SWIFT excitation frequency domain profile is also shown.
Figure 2-3.

\[
\text{CDCl}_3 \xrightarrow{\text{EI}} \text{CDCl}_2^+ \\
\text{Cl} \quad \text{Cl}
\]
used for the carbene reactions, which helped in later analysis of the data, in particular, in identifying compounds that underwent self-protonation and the formation of dimer ions.

The following table lists the reference bases used in the analysis of dichlorocarbene.

**Table 2-1. Gas phase basicity bracketing of dichlorocarbene**

<table>
<thead>
<tr>
<th>REFERENCE BASE</th>
<th>PA (kcal/mole)</th>
<th>GB (kcal/mole)</th>
<th>TRANSFER?</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyridine</td>
<td>220.8</td>
<td>213.1</td>
<td>YES</td>
</tr>
<tr>
<td>benzylamine</td>
<td>216.8</td>
<td>209.0</td>
<td>YES</td>
</tr>
<tr>
<td>2,5-dimethylfuran</td>
<td>209.0</td>
<td>201.3</td>
<td>NO</td>
</tr>
<tr>
<td>2-methylthiophene</td>
<td>205.4</td>
<td>197.9</td>
<td>NO</td>
</tr>
<tr>
<td>methyl benzoate</td>
<td>203.7</td>
<td>195.9</td>
<td>NO</td>
</tr>
<tr>
<td>mesitylene</td>
<td>200.7</td>
<td>193.6</td>
<td>NO</td>
</tr>
<tr>
<td>diethyl ether</td>
<td>200.2</td>
<td>192.4</td>
<td>YES</td>
</tr>
<tr>
<td>phenol</td>
<td>196.3</td>
<td>188.5</td>
<td>YES</td>
</tr>
<tr>
<td>m-xylene</td>
<td>195.9</td>
<td>188.1</td>
<td>NO</td>
</tr>
<tr>
<td>benzonitrile</td>
<td>195.9</td>
<td>188.1</td>
<td>NO</td>
</tr>
<tr>
<td>ethanol</td>
<td>188.3</td>
<td>180.2</td>
<td>NO</td>
</tr>
<tr>
<td>ethyl iodide</td>
<td>176 (br)</td>
<td>168 (br)</td>
<td>NO</td>
</tr>
</tbody>
</table>

Four compounds were not observed to remove the deuteron from the carbene even though their GB values are higher than that of diethyl ether and phenol. The anomaly is due to the very fast competing
reaction of charge exchange observed for each of these reference bases with the reagent ion producing the molecular ion of the reference base.

Figure 2-4 shows the upper bracket for dichlorocarbene. The compound with the lowest gas phase basicity that was observed to undergo deuteron transfer was phenol (M). The peak two nominal mass units higher than M+ has a magnitude greater than that due to the C-13 peak of (M+H)+. A high resolution spectrum was obtained and is shown in Figure 2-5, where the C-13 peak of (M+H)+ is clearly resolved from the (M+D)+ signal.

The lower bracket for dichlorocarbene was determined as benzonitrile. As seen in Figure 2-6, no deuteron transfer peak was observed over a reaction period of 3 seconds. Further corroboration of this result is given by m-xylene, which has the same GB as benzonitrile and also showed no deuteron transfer peak.

A comparison of these experiments with the results of Lias et al. is shown as a 'proton affinity ladder' in Figure 2-7. Notice that our result is 3 kcal/mole higher than that of Lias's work. Also, they observed proton transfer for benzonitrile whereas we did not. Discussions with Lias led to the conclusion of excess energy in their reagent ion which allowed the endothermic proton transfer reaction to be observed. The excess energy most likely came from using high energy electron ionization.
Figure 2-4. Upper bracket for dichlorocarbene. Phenol had the lowest gas phase basicity that showed the ability to remove the deuteron from the carbene. Self protonation of phenol was also observed.
C₆H₅OH + CDCl₂⁺ → CCl₂ + [C₆H₅OH]D⁺

Figure 2-4.
Figure 2-5. High resolution FT/ICR mass spectrum of the reaction between phenol and the deuterated dichlorocarbene ion. The C-13 peak of (M+H)$^+$ of phenol is resolved from the (M+D)$^+$ peak due to deuteron transfer.
Figure 2-5.
Figure 2-6. Lower bracket for dichlorocarbene. Benzonitrile had the largest gas phase basicity that was unable to remove the deuteron from dichlorocarbene.
C₆H₅CN + CDCl₂⁺ → CCl₂ + [C₆H₅CN]D⁺

105 amu

Figure 2-6.
Figure 2-7. Proton affinity ladder for dichlorocarbene. The results of Lias et al. are shown on the left and results from this study on the right. Previous results showed proton transfer for benzonitrile, but it was not observed in this study.
Dichlorocarbene


Figure 2-7.
**Dimethoxycarbene and Phenylcarbene.** The precursor molecules to the protonated carbenes of dimethoxycarbene and phenylcarbene were trimethyl orthoformate, (OCH$_3$)$_3$CH, and benzylbromide, respectively. 10 eV electron ionization was used to produce the needed reagent ions.

Deuterated compounds were not available for the precursor molecules; therefore reference compounds were chosen that did not show self-protonation from their respective molecular ions. Tables 2-2 and 2-3 list the reference bases used and whether or not proton transfer was observed for dimethoxy- and phenylcarbene, respectively. Figure 2-8 shows the 'proton affinity' ladder for the two molecules.

### Table 2-2. Gas phase basicity bracketing of dimethoxycarbene

<table>
<thead>
<tr>
<th>REFERENCE BASE</th>
<th>PA (kcal/mole)</th>
<th>GB (kcal/mole)</th>
<th>TRANSFER?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,5-dimethylfuran</td>
<td>209.0</td>
<td>201.3</td>
<td>YES</td>
</tr>
<tr>
<td>2-methylthiophene</td>
<td>205.4</td>
<td>197.9</td>
<td>YES</td>
</tr>
<tr>
<td>m-xylene</td>
<td>195.9</td>
<td>188.1</td>
<td>YES</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>182.4</td>
<td>174.6</td>
<td>YES</td>
</tr>
<tr>
<td>benzene</td>
<td>181.3</td>
<td>174.6</td>
<td>YES</td>
</tr>
<tr>
<td>trichloroacetonitrile</td>
<td>175.9</td>
<td>168.0</td>
<td>NO</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>169 (br)</td>
<td>161 (br)</td>
<td>NO</td>
</tr>
<tr>
<td>fluoroform</td>
<td>147.0</td>
<td>139.0</td>
<td>NO</td>
</tr>
</tbody>
</table>
Table 2-3. Gas phase basicity bracketing of phenylcarbene

<table>
<thead>
<tr>
<th>REFERENCE BASE</th>
<th>PA (kcal/mole)</th>
<th>GB (kcal/mole)</th>
<th>TRANSFER?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,5-dimethylfuran</td>
<td>209.0</td>
<td>201.3</td>
<td>YES</td>
</tr>
<tr>
<td>m-xylene</td>
<td>195.9</td>
<td>188.1</td>
<td>YES</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>182.4</td>
<td>174.6</td>
<td>NO</td>
</tr>
<tr>
<td>benzene</td>
<td>181.3</td>
<td>174.6</td>
<td>YES</td>
</tr>
<tr>
<td>hexafluorobenzene</td>
<td>177.7</td>
<td>171.3</td>
<td>NO</td>
</tr>
<tr>
<td>trichloroacetonitrile</td>
<td>175.9</td>
<td>168.0</td>
<td>NO</td>
</tr>
<tr>
<td>fluoroform</td>
<td>147.0</td>
<td>139.0</td>
<td>NO</td>
</tr>
</tbody>
</table>
Figure 2-8. Proton affinity ladder for dimethoxycarbene and phenylcarbene.
Dimethoxy- and Phenyl-carbene

2,5-dimethylfuran 209.0
2-methylthiophene 205.4
m-xylene 195.9
bromobenzene 182.4
benzene 181.3
hexafluorobenzene 177.7
trichloroacetonitrile 175.9
cyclohexane 169(br)
fluoroform 147.0

Proton Affinity (kcal/mole)

$\text{C}_6\text{H}_5-\text{C-H}$
$179.5 \pm 1.8$

$\text{H}_3\text{CO-C-OCH}_3$
$178.6 \pm 2.7$

Figure 2-8.
Conclusions

The gas phase basicities of two carbenes have been determined by use of FT/ICR/MS. Table 2-4 summarizes the results. It is apparent that isotopic labeling is extremely useful in determining whether or not a true 'proton' transfer reaction has occurred. The dual cell helps to eliminate the possibility of the reagent ion of interest reacting with its neutral precursor.

### Table 2-4. Summary of Results

<table>
<thead>
<tr>
<th>Carbene</th>
<th>PA (kcal/mole)</th>
<th>GB (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dichlorocarbene</td>
<td>196.1 ± 0.2</td>
<td>188.3 ± 0.2</td>
</tr>
<tr>
<td>Dimethoxycarbene</td>
<td>178.6 ± 2.7</td>
<td>171.3 ± 3.3</td>
</tr>
<tr>
<td>Phenylcarbene</td>
<td>179.5 ± 1.8</td>
<td>173.0 ± 1.7</td>
</tr>
</tbody>
</table>
References


Chapter III

Two-Dimensional Fourier Transform Ion Cyclotron Resonance Mass Spectrometry/Mass Spectrometry with Stored-Waveform Ion Radius Modulation

Introduction

One-dimensional ICR MS/MS. Of particularly high interest to chemists is the high-resolution FT/ICR mass spectrometric detection of ions trapped for extended periods (up to $10^6$ collisions), during which ion-molecule reaction chemistry may be observed and quantitated. From the cyclotron equation (S.I. units),

$$\omega_c = \frac{qB}{m}$$  \hspace{1cm} (3-1)

in which $\omega_c$ is the cyclotron frequency of ions of mass, $m$, and charge, $q$, moving in a magnetic field, $B$, it is clear that the mass-to-charge ratio of a given ion may be accessed according to its cyclotron frequency. Thus, just as populations of nuclear spin energy levels may be perturbed by selective irradiation at the appropriate transition frequency in so-called "double-resonance" nuclear magnetic resonance (NMR) experiments,\(^1\) ion populations may be altered by selective "double-resonance" irradiation at $\omega_c$ to "heat" ions of the
corresponding mass-to-charge ratio, \( m/z \) (\( m \) in u, \( z \) in number of elementary charges per ion) to higher translational energy, thereby changing the relative abundance of those ions and any others connected to the irradiated ions by ion-molecule reactions.\(^2\) The "double-resonance" ICR experiment is a form of what has later been denoted as "tandem mass spectrometry",\(^3\) or MS/MS. However, in both types of one-dimensional experiments, only one spin-spin (or parent ion-product ion) connection may be established at a time.

**One-dimensional FT/ICR MS/MS.** The introduction of broadband excitation and detection, followed by Fourier transform data reduction revolutionized infrared, NMR, and ICR mass spectrometry, by making it possible to acquire a full-range spectrum in the time previously required to scan through a single peak.\(^4\) In all three cases, roughly comparable advantages in speed (factor of \( 10^4 \)) or signal-to-noise ratio (factor of \( 10^2 \)) were demonstrated. Fourier transform ion cyclotron resonance mass spectrometry (FT/ICR/MS) provided the unique additional advantage of higher spectral resolution and (especially) higher mass accuracy (factor of up to \( 10^7 \)).\(^5\) Following the advent of Fourier transform techniques in NMR\(^6\) and ICR,\(^7,8\) the "double-resonance" experiment was immediately improved by simultaneous detection of all spins (or "product" ions) connected to a given irradiated spin (or "parent" ion\(^9\)), due to the multiplex advantage of FT data reduction.\(^4\) In ICR, the MS/MS method is further improved by prior selective radial ejection of ions of all but the "parent" ion \( m/z \) of interest, optimally by use of "SWIFT" (stored-waveform excitation
based on inverse Fourier transform of the desired frequency-domain excitation spectrum).\textsuperscript{10,11}

**Two-dimensional FT spectroscopy.** In one-dimensional FT/ICR MS/MS, a given ion fragmentation or reaction pathway is established by: (a) isolating the parent ions of interest (by ejecting ions of all other \( m/z \) values); (b) (optionally) resonantly cyclotron-exciting those parent ions to a larger cyclotron orbital radius and thus higher kinetic energy; (c) waiting for a fixed period to allow for collision-induced dissociation and/or ion-molecule reactions; and finally (d) detecting and Fourier transforming the time-domain response to a broadband excitation of ions throughout the \( m/z \) range of interest. Although such a scheme achieves multiplex detection of all product ions deriving from parent ions of a given \( m/z \), only one parent \( m/z \) is interrogated at a time, and the experiment must be repeated for each parent \( m/z \) of interest. Thus, the approach is feasible for sparse spectra of ions of relatively few \( m/z \) values, but is inefficient for complex mixtures such as crude oil distillates which may contain thousands of comparably abundant components.

One is therefore led to seek a two-dimensional MS/MS experiment with multiplexing with respect to both parent and product ions. Again, we look to NMR, where a second revolution followed the introduction of various two-dimensional FT/FT experiments,\textsuperscript{12} principally COSY\textsuperscript{13} and NOESY.\textsuperscript{14} The appeal of 2D-FT/NMR is obvious: it is possible to establish the "couplings" (e.g., "scalar" or "dipolar") between two spins, even in a highly overlapped
spectrum, from a two-dimensional contour plot in which the spectrum itself is either dispersed along the diagonal (NOESY) or visualized by projection (COSY), and the couplings are manifested as off-diagonal peaks whose horizontal and vertical projections to the diagonal identify the chemical shifts of the two coupled spins. The COSY 2D-FT/NMR idea has since been extended to microwave pure rotational and electron paramagnetic resonance spectroscopy.

The fundamental requirements of a 2D-FT experiment are the generation of some sort of "coherence" (i.e., all spins or ions moving together) and a means for "modulating" that coherence sinusoidally to generate a second FT dimension. If the coupling between two spins is inherently coherent (as in "scalar", or J-coupling, which is the same for all molecules in the sample), then a 90° pulse generates an observable signal whose amplitude is modulated by the J-coupling during a subsequent "evolution period", leading to the COSY-type 2D-FT/NMR experiment. Alternatively, even though spin populations are coupled by inherently incoherent dipole-dipole or chemical-exchange interactions, it is possible to modulate the spin populations with a coherent excitation (which is the same for all molecules in the sample), leading to a NOESY-type 2D-FT/NMR experiment. Because ion-molecule reactions represent an inherently incoherent coupling (i.e., different for different ions in the sample), there is no ICR analog of COSY 2D-FT/NMR experiments. However, following the demonstration of the ICR analog of a coherent 180° NMR pulse, Pfändler et al. were led to develop an ICR analog to NOESY 2D-
FT/NMR, as discussed below. The ICR analog of NMR spin-"coupling" is ion-neutral reaction or collisional dissociation.

**2D-FT/ICR MS/MS: parent ion cyclotron radius modulation.** The key concept for 2D FT/ICR is that if, in proceeding through a series of otherwise identical experiments, one can somehow sinusoidally modulate the ICR orbital radius (and hence the speed) of parent ions of one m/z value, then the yield of product ions of different m/z ratio(s) formed by ion-neutral collisions or reactions of that parent ion will be modulated at that same frequency [because, in the hard-sphere collision limit (see below) faster-moving parent ions will collide with more neutrals during a given time period].21 If it can then be arranged that parent ions of different m/z can be modulated at different frequencies from one experiment to the next, then the parent-product connections can be established by determining which product ion abundances are modulated at the frequencies of which parent ions, by taking a (second) FT of the frequency-modulated series of spectra. In this way, one achieves multiplexing with respect to the parent ions as well as the product ions, in a single automated experiment. Given the strong dependence of ion-molecule reaction rates on kinetic energy, especially for endothermic (CID) reactions, it is in principle preferable to modulate ion kinetic energy rather than ion radius (velocity) (see Results and Discussion).

**Parent ion cyclotron radius modulation by two excitation pulses separated by a variable delay period.** The key concept for 2D in the
Bodenhausen-Gäumann 2D-FT/ICR experiment\textsuperscript{18-20} is that the parent ion cyclotron orbital radius is modulated from one event sequence to the next by linearly incrementing the delay period, $t_1$, between two identical rf single-frequency (or frequency-sweep) excitation events (see Fig. 3-1). The first excitation is designed to drive ions radially outward from the center of the ion trap part-way to one of the sides. Then, if $t_1$ is exactly an odd integer multiple of one-half period of the ICR frequency of a given parent ion, that parent ion will be de-excited by the second pulse back to near-zero ICR radius before the ion-molecule reaction period. However, if $t_1$ is exactly an integer multiple of one period of the parent ICR frequency, then the second pulse will excite those parent ions out to twice the ICR radius reached at the end of the first pulse. (A one-dimensional version of the Bodenhausen-Gäumann experiment was later used by Russell for mass-selective axialization of previously broadband-excited ions in coherent cyclotron orbits,\textsuperscript{22} and a more general axialization method based on quadrupolar excitation has since been demonstrated for FT/ICR/MS\textsuperscript{23,24}). Since the accumulated phase during the delay period, $t_1$, is simply $\omega_p t_1$, where $\omega_p$ is the ICR frequency of the parent ion, it is clear that the radius of parent ions in successive event sequences will be modulated at frequency, $\omega_p$, as a function of $t_1$, as $t_1$ is incremented from one event sequence to the next. The number of product ions produced after a fixed ion-neutral reaction period, $t_{\text{rx}}$, from those parent ions
Figure 3-1. Two alternative experimental event sequences for 2D-FT/ICR/MS. Ion formation (top row) is followed by an excitation which modulates the parent ion cyclotron radii according to their ion cyclotron frequencies, either by application of two identical excitation waveforms separated by a delay period whose duration is incremented linearly from one data acquisition to the next (second row), or by application of each of a series of stored-waveforms (third row). Following a reaction period during which products are formed with abundances determined by the parent ion cyclotron radii established in the previous event, conventional broad-band excitation and detection generate a time-domain response. Finally, ions are removed, and succeeding data sets are acquired, either for various delay period between the two-pulse excitation or for various SWIFT modulation waveforms, and the two-dimensional array is subjected to two-dimensional FT to generate a 2D-FT/ICR mass spectrum. (see text).
Figure 3-1.
will therefore also be modulated at frequency, \( \omega_p \). Thus, the parent ion speed modulation is converted to a product ion population modulation by means of ion-molecule reactions. Next, conventional broad-band excitation and detection followed by Fourier transformation yields an FT/ICR mass spectrum for each delay period, \( t_1 \). Finally, a second Fourier transform with respect to the \( t_1 \)-axis then yields the full two-dimensional display. (These stages will be illustrated below for the presently proposed modulation method.)

**Parent ion cyclotron radius direct modulation by stored-waveform excitation.** Here we demonstrate experimentally for the first time a second means for parent ion radius modulation, based on use of a single excitation time-domain waveform whose magnitude varies sinusoidally (rather than is constant) with frequency, as shown in Figure 3-2 ("SWIM" is our acronym for "stored waveform ion modulation"). (Each time-domain excitation waveform is produced by inverse FT\(^{10,11,25-29}\) of the corresponding frequency-domain magnitude spectrum in Figure 3-2.) In proceeding from one experiment to the next (see Theory), we vary the frequency of sinusoidal excitation magnitude across the spectrum (Scan 1, 2, ...10 in Figure 3-2). The net result is the same as that of the Bodenhausen-Gäumann modulation, with the advantage that we can more easily vary the modulation from one scan to the next because the excitation period is fixed and does not need to be varied in inconveniently short increments (as is the case for the Bodenhausen-Gäumann experiment for large spectral bandwidth). Although the presently proposed
Figure 3-2. SWIFT magnitude-mode spectra (see Equation 3-3) of several parent-ion modulation waveforms, for $j = 1, 2, \text{ and } 10$. Note that the excitation amplitude for ions of the highest cyclotron frequency, 1333.0 kHz, is modulated the fastest in proceeding from one waveform to the next, whereas the excitation amplitude for ions of the lowest cyclotron frequency, 100 kHz, is not modulated at all from one waveform to the next. The mass-to-charge ratio range corresponding to these ion cyclotron frequencies is $34.8 < \text{m/z} < 463$. ($B = 3.02 \text{ T}$)
2D-FT/ICR SWIFT Excitation
Magnitude Spectra

Scan 1

Scan 2

Scan 10

Frequency (kHz)

Figure 3-2.
method was conceived independently (and previously) by Williams and McLafferty,\textsuperscript{30} we are the first to reduce it to practice. In this chapter, we proceed to develop the (simple) theory of the SWIM experiment, and then go on to demonstrate its value experimentally on two simple chemical systems.

**Comparison to prior Hadamard/FT 2D-ICR/MS.** Before proceeding to the present experiments, we digress briefly to compare the presently proposed FT/ICR MS/MS method to the prior Hadamard transform 2D ICR experiment (henceforth denoted as HT/FT/ICR MS/MS). As originally devised and demonstrated by Williams & McLafferty,\textsuperscript{31,32} HT/FT/ICR MS/MS replaces the present stored-waveform ion modulation (SWIM) of Figure 3-2 with a "comb" excitation spectrum whose "teeth" are positioned to excite equally a particular combination of about half of the possible parent ions of interest. In proceeding from one experiment to the next, one chooses an appropriately different (and linearly independent) combination of parent ions. The "Hadamard" aspect simply prescribes the elements of the "code" which determines which parent ions are excited in which experiment. After N experiments (corresponding to N different linear combinations of the original N parent ions), a Hadamard (rather than Fourier) "decoding" produces a 2D-display consisting of N spectra, each of which is the spectrum of product ions resulting from excitation of just one parent ion. The HT/FT approach requires a smaller minimum number of scans than the FT/FT approach, because the Hadamard experiment requires interrogation
only at the ICR frequencies of the parent ions, rather than interrogation at all of the discrete frequencies in the spectrum.

However, it is fair to note that although HT/FT methods have been available in NMR for more than a decade,\textsuperscript{33} FT/FT data reduction\textsuperscript{12} is overwhelmingly preferred. We believe that the same will be true for 2D-FT/ICR MS/MS. First, Hadamard (or FT) techniques are most efficient when the number of data points, \( n \), is \( 2^n - 1 \) (or \( 2^n \) for FT), \( n \) = an integer). Although it is relatively easy to choose the number of time-domain data points to be \( 2^n \), it is not in general true that the number of parent ions in the spectrum will match the \( 2^n - 1 \) value. Of course, in the Hadamard method, \( n \) is the number of parent ions, which is in general much less than the number of spectral data points (\( n \) in the FT case). However, 2DFT closes the gap as the spectrum becomes denser (as for complex mixtures of many components), particularly at high mass (where the exact masses do not necessarily cluster near the nominal mass). Moreover, the 2DFT peak heights more accurately reflect the relative ion-molecule reaction rate constants (because the 2DFT data are sampled from a range of ion translational energies) than the HT (which, for optimal SNR, would be conducted at very high translational energy where CID is nearly collision-limited for all species). Also, the Hadamard technique requires that each parent ion be excited to its optimal radius (because the kinetic energy-dependence of different ion-molecule reactions is different) to produce product ions (information generally not known in advance of the experiment). The FT/FT approach, on the other
hand, inherently depends on modulation of the parent ion energy over a range of kinetic energy, and thus should be more generally applicable. It is important to note that the Hadamard technique requires prior knowledge of which parent ion m/z-values are to be examined, whereas the FT method requires no such prior knowledge. Finally, in the FT/FT experiment, all parent ions (rather than approximately half) are interrogated in each scan. Comparison of signal-to-noise ratio for HT/FT and FT/FT experiments is thus a complex issue which is currently under investigation.

**Theory**

**Parent ion cyclotron radius modulation by excite-(variable delay)-excite sequence.** The prior cyclotron radius modulation method employed by Pfändler et al. uses two identical single-frequency or frequency-sweep events separated by a time period, t₁, which is incremented to generate successive rows of a two-dimensional signal, s(t₁,t₂), as shown in Figure 3-1. The final (parent) ion cyclotron radius following the excite-delay-excite sequence therefore varies sinusoidally as a function of t₁. If the two excitation waveforms are identical, then the sinusoidal radius modulation frequency for parent ions of a given m/z is simply the cyclotron frequency corresponding to that m/z value. In practice, Pfändler et al. changed the phase of their second excitation with respect to the first in order to achieve effectively heterodyne detection in the t₁-domain, so that their parent ion cyclotron radius was modulated at the difference in frequency between their rf carrier (for single-frequency excitation) or
highest sweep frequency (for frequency-sweep excitation) and the parent ion cyclotron frequency.

**Parent ion cyclotron radius modulation by a series of single-event SWIFT excitations.** Once one recognizes that the end result of the excite-delay-excite sequence is to produce a sinusoidal excitation vs. frequency spectrum of the type shown in a given row of Figure 3-2, then it is clear that, because the ICR system is highly linear the same result could be obtained simply by irradiation with a time-domain waveform obtained by inverse Fourier transformation of the desired sinusoidal excitation spectrum of the appropriate frequency. One then simply increments the sinusoid frequency in proceeding from one event sequence to the next. Because the parent ion radius is modulated by stored waveform excitation, we propose the acronym, SWIM (stored-waveform ion modulation) for this technique.

To satisfy the Nyquist criterion with the minimum number of experiments in the \( t_1 \)-dimension, we choose a frequency-domain representation for the \( j \)-th SWIM excitation waveform magnitude, \( M_j(v) \), given simply by

\[
M_j(v) = \frac{1 + \sin \left( \frac{2 \pi v_{\text{modulation}} j \Delta t - \pi}{2} \right)}{2} ; \quad j = 1, 2, \cdots, N \tag{3-2a}
\]

in which

\[
v_{\text{modulation}} = v_{\text{high}} \left( \frac{v - v_{\text{low}}}{v_{\text{high}} - v_{\text{low}}} \right) ; \quad 0 < v_{\text{modulation}} < v_{\text{high}} \tag{3-2b}
\]
and $\Delta t = \frac{1}{2v_{\text{high}}}$ is the sampling interval in the $t_1$-dimension. Thus, $v_{\text{high}}$ represents the Nyquist (modulation) frequency in the $t_1$-dimension, so that the sampling frequency is $2v_{\text{high}}$ in the $t_1$-dimension. Clearly, $0 \leq M_j(v) \leq 1$. Substitution of Equation 3-2b and $\Delta t = \frac{1}{2v_{\text{high}}}$ into Equation 3-2a yields Equation 3-3, which was used to generate the SWIFT ion modulation waveforms.

$$M_j(v) = \frac{1 + \sin \left( j \pi \left( \frac{v - v_{\text{low}}}{v_{\text{high}} - v_{\text{low}}} - \frac{\pi}{2} \right) \right)}{2} \quad (3-3)$$

For example, for $j = 1$, the SWIFT excitation waveform varies sinusoidally by one-half period over the excitation frequency range (Fig. 3-2, scan 1). For $j=2$, there is one full period over that range (Fig. 3-2, scan 2). For $j=3$, there are one and a half periods over the range and so on. The parent ion modulation frequencies therefore range from 0 for ions of lowest cyclotron frequency, $v_{\text{low}}$, to $v_{\text{high}}$ for ions of highest cyclotron frequency, $v_{\text{high}}$, across the SWIFT-excited frequency range.

Specifically, $M(v)$ varies most rapidly (1, 0, 1, 0, 1, 0, from one row to the next) as a function of $j$ at the high-frequency limit of the range ($v_{\text{high}}$), whereas $M(v)$ is constant (0, 0, 0, 0, ..., from one row to the next) at the low-frequency limit of the range ($v_{\text{low}}$). At the the midpoint frequency in the range, the excitation values vary as (1/2, 1, 1/2, 0, 1/2, 1, etc.). Thus, the cyclotron radius for ions of any given $m/z$ ratio is modulated at a unique modulation frequency. The modulation of Equation 3-3 is such that ions of higher cyclotron
frequency will have a higher modulation frequency. If the sine function in Equation 3-3 were replaced by a cosine, then ions of higher cyclotron frequency would have a lower modulation frequency.

**Experimental**

Analytical reagent grade acetone was obtained from Mallinckrodt Specialty Chemicals Co. (Paris, Kentucky). Pyrrolidine and 3-methylpyrididine were obtained from Aldrich Chemical Co. Inc. (Milwaukee, WI). All chemicals were used as supplied except for multiple freeze-pump-thaw cycles to de-gas the sample.

The stored-waveform ion-modulation (SWIM) 2D/FT/FT/ICR/MS experiments were implemented on a dual-trap FTMS-2000 FT/ICR mass spectrometer (Extrel FTMS Millipore Inc., Madison, WI), operated at 3.0 tesla, equipped with Helix Technology CryoTorr-8 2000 L/s cryopumps (Waltham, MA) for both source and analyzer vacuum chambers, with two 4.76 cm cubic traps in a standard dual-trap configuration. The mass spectrometer was controlled by a Nicolet 1280 computer. Each gaseous sample was introduced through a leak valve (Model 951-5100, Varian, Palo Alto, CA) connected to the batch inlet system of the instrument. All experiments were conducted in the "source" compartment of the dual-trap.

A 1280 computer Fortran program was written to produce the modulation waveform data (see appendix). A series of 512 magnitude-mode excitation spectra was generated from Equation 3-3, with quadratically modulated phase,\textsuperscript{25,26} and inverse Fourier transformed to produce 512 SWIFT modulation waveforms of 4K data points each.
Those waveforms were stored in the 1280 data system for subsequent one-at-a-time loading into the buffer memory of a homebuilt SWIFT module. Figure 3-2 shows three representative frequency-domain magnitude-mode excitation profiles used to synthesize (by inverse FT) three corresponding SWIM time-domain excitation waveforms. For subsequent excitation and detection, a single flat-amplitude SWIFT excitation waveform of flat frequency-domain magnitude over the ICR frequency range of interest was generated with the same bandwidth and frequency range as the SWIM data sets.

For acetone ion-molecule chemistry, the experimental event sequence (Fig. 3-1) begins with electron ionization (70 eV for 10 ms at emission current of 4.1 µA measured just behind the filament) of acetone (10⁻⁶ Torr). Following a short (0.5 s) equilibration period, SWIM excitation (frequency bandwidth = 1.000 MHz; \(v_{\text{low}} = 75\) kHz; \(v_{\text{high}} = 999.75\) kHz) is applied for 2.048 ms at a maximum of 27.6 V(\text{p-p}) which excites ions to a maximum radius of approximately 2.8 mm, and the variably-excited ions are allowed to collide and/or react with neutrals for a fixed reaction period of 1.0 s, followed by SWIFT broadband direct-mode excitation for 8.192 ms at 19.6 V(\text{p-p}) to excite ions to a cyclotron radius of 4.0 mm. A single transient ICR signal was direct-mode acquired (1.333 MHz Nyquist frequency for 1.54 ms to yield 4096 data points). The signal-to-noise ratio was sufficiently high that signal-averaging was not required for this experiment. All ions were then removed from the ICR ion trap by successive application of +10 V to both trap electrodes and then −10 V
to both trap electrodes. The time-domain digitized transient signal from this experiment constitutes one row of a two-dimensional time-time data array. The same experimental event sequence was then repeated for each of the 512 SWIM excitations to produce a two-dimensional time-time data array, \( D(i,t_2) \), in which \( 1 \leq i \leq 512 \).

The 2-D time-time data array was transferred from the 1280 computer to a PC AT-compatible computer (AT&T model # 6300+) via a homebuilt parallel data transfer channel which provided an 8-fold increase in the data transfer rate compared to a standard serial port connection. The data were converted to a FELIX (a commercial NMR data processing program from Hare Research, Inc., Seattle, WA) file format. The converted data were transferred to an IBM RISC-6000 workstation through a local network. A data processing protocol written in the FELIX microformat was used for 2D-FT data reduction (512 x 2048 data points) and display.

Each of the 512 rows of the two-dimensional time-domain data \( s(t_1,t_2) \) consisting of 4096 data points was Fourier transformed with respect to the acquisition period, \( t_2 \), without apodization or zero-filling to generate a series of 512 magnitude-mode spectra \( S(t_1,\omega_2) \) and the phase portion of the spectra was discarded.\(^{21}\) Each of the resultant 2048 columns of \( S(t_1,\omega_2) \) consisting of 512 data points were then padded with 512 zeroes and Fourier transformed with respect to the "j" index and the resulting two-dimensional spectral array, \( S(\omega_1,\omega_2) \), recorded on an HP line plotter in magnitude-mode, either as
a stack plot or as two-dimensional contours of constant magnitude (1D) or power (2D).

For the pyrrolidine/3-methylpyridine experiments, the conditions were: electron ionization (9 eV for 10 ms at a measured current of 12.7 μA), at equal partial pressure (2 x 10^-7 Torr). A preparation delay of 20 ms and a reaction period of 150 ms were used before and after SWIM excitation, respectively. The SWIM modulation waveform parameters were: frequency bandwidth = 2.666 MHz; \( v_{\text{low}} = 100.0 \) kHz; \( v_{\text{high}} = 2.600 \) MHz; \( 17.85 < m/z < 463.4, B \approx 3.02 \) T; 4096 time-domain data to give a 0.768 ms excitation event; time-domain amplitude, 98 V\(_{\text{p-p}}\) (see Equation 3-3). The same excitation conditions were used for the final excitation except that the frequency-domain SWIFT magnitude spectrum was constant (rather than sinusoidal) over the excited frequency range. Ten co-added digitized (Nyquist bandwidth, 1.600 MHz) time-domain transients of 4096 data points each were acquired to increase the signal-to-noise ratio, to compensate for the reduced number of ions resulting from much lower electron beam energy (9 eV vs. 70 eV) for pyrrolidine/3-methylpyridine compared to acetone.

For the pyrrolidine data shown in Fig. 3-7, conditions were identical to those listed above except that the SWIFT excitation bandwidth was narrowed from 2.6666 MHz to 1.0 MHz for both excitations, to yield higher digital spectral resolution. 4096 SWIFT data yielded a modulation-excitation event of 2.048 ms, at 34.5 V\(_{\text{p-p}}\) time-domain excitation amplitude. Ten 4K time-domain transients
were coadded at a Nyquist bandwidth of 1 MHz for each SWIFT modulation waveform excitation.

Finally, peak areas for the one-dimensional double-resonance experiments were calculated from a simple program written in resident Extrel software. Each peak area represents the product of the peak maximum magnitude value and the full peak width at half-maximum peak height. 36,37

**Results and Discussion**

**Fundamental aspects of 2D-FT/ICR MS/MS.** For low-energy ion-molecule reactions, the ion-molecule reaction rate is well-described by a Langevin ion-induced dipole collision model, 38-42 for which the ion-molecule collision frequency is independent of ion speed. However, above a critical suprathermal ion speed, the reaction is better described by a hard-sphere model, for which the ion-molecule collision frequency (and thus the ion-molecule reaction rate) is directly related to ion speed. 43 For example, for N₂⁺, the crossover from Langevin to hard-sphere collision mechanism occurs at an ion cyclotron orbital radius of only a few mm at a magnetic field of 4.7 tesla. 43 Since ion cyclotron orbital speed is proportional to ion cyclotron orbital radius, 4 the present SWIM technique can thus be expected to produce a sinusoidal modulation of product ion yield from sinusoidally modulated parent ion cyclotron radius, provided that the ion cyclotron radius is modulated over a range which exceeds a few mm. 44

Another underlying assumption of the present scheme is that the
response amplitude (i.e., ion cyclotron orbital radius) is linearly proportional to the on-resonance excitation amplitude. Unlike NMR, for which the detected signal varies approximately as the sine of the excitation amplitude, the ICR response to dipolar radial excitation has been shown to be quite linear out to an ion cyclotron radius more than 90% of the radius of the trap, particularly if the rf excitation field is "shimmed" to spatial homogeneity. Thus, SWIFT excitation (which is based on the linear proportionality between time-domain and frequency-domain representations of an excitation waveform) is eminently suitable for use in 2D-FT/ICR MS/MS.

**Monomer-dimer interconversion: acetone.** As our first experimental test of the SWIM 2D-FT/ICR MS/MS method, we chose the simple ion-molecule reaction system derived from electron-ionized acetone. Electron ionization generates molecular ions, \( M^+ \), which react rapidly on the ICR time scale to form protonated acetone, \( MH^+ \). \( MH^+ \) ions (\( m/z \) 59) trapped for tens of collisions with acetone neutrals (e.g., \( \sim 0.5 \) s at \( 10^{-6} \) Torr) react further to form abundant proton-bound dimer ions, \( M_2H^+ \) (\( m/z \) 117), by the exoergic reaction

\[
MH^+ + M \rightarrow M_2H^+ \tag{3-4}
\]

An increase in kinetic energy of the parent \( MH^+ \) ions may actually decrease the yield of \( M_2H^+ \) ions. Conversely, the rate of collision-induced fragmentation of \( M_2H^+ \) with a neutral, \( N \),

\[
M_2H^+ + N \rightarrow MH^+ + M + N \tag{3-5}
\]
to form MH⁺ increases with increased M₂H⁺ ion cyclotron radius (and thus ion speed). Therefore, modulation of the cyclotron radius of either MH⁺ or M₂H⁺ parent ions produces a modulation in the number of product M₂H⁺ or MH⁺ ions, respectively.

Figure 3-3 shows a stack plot of some of the 512 spectra, S(t₁, ω₂), following the first FT (with respect to t₂) in each row of a two-dimensional array of FT/ICR time-domain data, s(t₁,t₂) for electron-ionized acetone. Two principal ionic species, protonated acetone, MH⁺, and protonated acetone dimer, M₂H⁺, are present in each spectrum, but the relative magnitude of each peak is modulated as one proceeds from one spectrum to the next.

The frequencies of that modulation are revealed by subjecting the data to a second FT with respect to the scan number as the second "time" axis (padded with 512 zeroes before FT), to yield the 2D-FT/ICR mass spectrum, S(ω₁,ω₂), shown in Figure 3-4. The "autocorrelated" peaks rising along the diagonal from lower left to upper right of Figure 3-4 constitute the conventional one-dimensional FT/ICR parent-ion mass spectrum, because the ICR orbital radius of a given parent ion just after the SWIM excitation period determines the subsequent ICR signal for that same parent ion observed after the second excitation. The off-diagonal peaks arise from ion-molecule reactions.

For example, we observe an off-diagonal peak (see lower right of Figure 3-4) if the modulated frequency is that of M₂H⁺ and the detected ICR frequency is that of MH⁺; in other words, modulation of
Figure 3-3. A portion of the acetone FT/ICR magnitude-mode frequency-domain spectrum prior to Fourier transformation in the second (parent ion radius modulation) dimension. The rapid modulation of protonated acetone parent ion, MH⁺, carries over to the observed ICR signal magnitude of the product ion, M₂H⁺. (The slower modulation of protonated acetone dimer parent ion, M₂H⁺ produces a less obvious modulation in the ICR signal magnitude of its MH⁺ product ion.) These modulation transfers become apparent following a second FT of this data with respect to the modulation (here shown as "scan number") axis (see Figure 3-4).
FT/ICR magnitude-mode spectra of acetone (M) after 1st FT

\[ M_2H^+ + M \rightarrow MH^+ + 2M \]

\[ MH^+ + M \rightarrow M_2H^+ \]

Figure 3-3.
Figure 3-4. Three dimensional stacked-plot display of a portion of the two-dimensional data obtained by padding the data of Figure 3-3 with an equal number (512) of zeroes in the modulation dimension, followed by Fourier transformation of the data with respect to that dimension. The diagonal peak at the cyclotron frequency of $M_2H^+$ is rather broad in the modulation dimension, likely due to inadequate pressure control of acetone throughout the experiment. Some "$T_1$-noise" is also noticeable as rows of small peaks at the cyclotron frequencies of $MH^+$ and $M_2H^+$ (see text).
2D FT/ICR/MS

\[ \text{MH}^+ + M \rightarrow \text{M}_2\text{H}^+ \]

\[ \text{M}_2\text{H}^+ + M \rightarrow \text{MH}^+ + 2M \]

Ion Cyclotron Frequency

M = Acetone

Figure 3-4.
the speed of $M_2H^+$ produces a modulation of the $MH^+$ abundance, establishing the "coupling" reaction $M_2H^+ \rightarrow MH^+$ (presumably collision-induced dissociation, as shown in Fig. 3-4). Similarly, the off-diagonal peak at upper left of Figure 3-4 establishes the presence of the "coupling" reaction, $MH^+ \rightarrow M_2H^+$. The mirror-image off-diagonal peaks in Fig. 3-4 are of unequal magnitude, because ion-molecule forward and reverse reactions are generally of unequal rate, and may (as in this example) not even correspond to the same process.

The ion-molecule reaction pathways are visualized more directly if the data of Fig. 3-4 are replotted as an iso-power rectilinear 2D-contour plot (Figure 3-5), from which it is easier to see that modulation at the ICR frequency of $M_2H^+$ leads to an observed signal at the ICR frequency of $MH^+$, and vice versa. The diagonal along which the parent ion mass spectrum lies does not pass through the corners of the display, because of the unequal frequency ranges in the modulation ($v_1$) and observed ($v_2$) frequency dimensions. $v_1$ has a frequency range of 924.75 kHz (i.e., not extending to 0 Hz) whereas $v_2$ has a frequency range of 1.3333 MHz (which does extend to 0 Hz). The frequency range in the modulation dimension is determined by the range of excitation ($v_{\text{high}} - v_{\text{low}}$). Hence, diagonal peaks are observed at a position where $v_1 = v_2$.

The spurious peaks observed in the 3D stacked plot in the modulation frequency direction at the observed cyclotron frequencies of protonated acetone and its proton-bound dimer are due to variation in the number of ions from one event sequence to the next. Such
Figure 3-5. Two-dimensional iso-power contour (SWIM) FT/ICR mass spectrum for ions derived from acetone. A peak appears on the diagonal (dashed) line for parent ions of each $m/z$-value in the detected spectral bandwidth. Each off-diagonal peak results from a product ion (identified by vertical projection to the bottom horizontal axis) formed from a parent ion (identified by horizontal projection to the modulation frequency axis at the left of the figure). The small spot size for the various peaks results from the high mass spectral resolution under these experimental conditions (see text).
Figure 3-5.

- Constant-power contours from 2D-FT/ICR mass spectrum of acetone
- Protonated acetone product ion modulated at the same frequency as protonated dimer parent ion
- Modulation Frequency
- Ion Cyclotron Frequency
- $M = \text{acetone}$
variations arise from fluctuation in neutral pressure of acetone in the vacuum chamber, as well as fluctuation in electron beam current during the ionization event. This effect is analogous to "T$_1$-noise" observed in 2D-FT/NMR, arising from variation in spin populations from scan to scan.

Finally, in our experiments, the SWIM event excites ions to a radius of only about 17% of the trap radius. Thus, no ions are ejected, and the excitation is highly linear, as evidenced by the absence of harmonics along the modulation frequency axis.

Proton-transfer reactions: pyrrolidine and 3-methylpyridine. Our second experimental example (see 2D-SWIM FT/ICR MS/MS contour plot in Fig. 3-6) begins to show the power of the two-dimensional approach. Here we examine an electron-ionized mixture of two heterocyclic nitrogen-containing bases, pyrrolidine (M) and 3-methylpyridine (N). Ionization with low energy electrons produces almost exclusively molecular ions, which are SWIM-modulated and then allowed to react for 150 ms at equal partial pressures (10$^{-7}$ Torr total pressure) before broadband excitation/detection. At least five distinct ion-molecule reactions are readily identified from the corresponding off-diagonal peaks in the 2D mass spectrum. It is important to note that all five ion-molecule reactions can be inferred without any prior knowledge of the system. The contour level shown was intentionally set low so that all peaks could be seen in a single display. Thus, the peaks in the vicinity of the cyclotron frequency of
Figure 3-6. Stored-waveform ion modulation (SWIM) 2D-FT/ICR mass spectral iso-power contours, from which five ion-molecule proton-transfer reactions of pyrrolidine and 3-methylpyridine may be identified (see text).
Modulation Frequency

\[ \frac{1}{\tau} \approx \frac{\pi}{\Gamma} \]

Ion Cyclotron Frequency

Reactions identified from off-diagonal peaks in this 2-D FT/ICR mass spectrum

1) \( M^+ + N \rightarrow (M - H) + NH^+ \)
2) \( NH^+ + M \rightarrow N + MH^+ \)
3) \( M^+ + M \rightarrow (M - H) + MH^+ \)
4) \( (M - H)^+ + M \rightarrow (M - 2H) + MH^+ \)
5) \( N^+ + N \rightarrow (N - H) + NH^+ \)

Figure 3-6.
the protonated pyrrolidine ion appear unresolved but would in fact be resolved if the contour level were set higher.

Figure 3-7 shows the increased digital resolution resulting from repetition of the experiment for pyrrolidine alone (i.e., no 3-methylpyridine present), conducted over a narrower spectral bandwidth (corresponding to the area bounded by the dashed rectangle in Figure 3-6), from which the processes, \((\text{M-H})^+ \rightarrow \text{MH}^+\) and \(\text{M}^+ \rightarrow \text{MH}^+\) are clearly resolved. As for one-dimensional FT/ICR/MS, one would usually perform a low-resolution experiment first, to determine the \(m/z\)-range(s) for which higher resolution is needed. Then, if necessary, one could "zoom" in on that range (i.e., narrower bandwidth and/or more data points/bandwidth to achieve the needed mass resolving power.

**One-dimensional double resonance confirmation of 2D-SWIM FT/ICR MS/MS results.** To confirm the reaction connectivities inferred from the SWIM 2D-FT/ICR MS/MS data shown in Figures 3-6 and 3-7 for ions derived from pyrrolidine, we carried out a series of conventional one-dimensional double-resonance experiments. Each of the pyrrolidine-derived ions, \((\text{M-H})^+, \text{M}^+, \text{and} (\text{M+H})^+\), was isolated in turn, and its reaction with neutral pyrrolidine monitored from 0 - 400 ms in 40 ms increments. The data in Figure 3-8 (top) show that \((\text{M-H})^+ (m/z 70)\) disappears at the same rate as the protonated pyrrolidine ion, \((\text{M+H})^+ (m/z 72)\), is produced. Similarly, Figure 3-8 (middle) shows that the pyrrolidine molecular ion, \(\text{M}^+ (m/z 71)\), produces \((\text{M+H})^+ (m/z 72)\), and Figure 3-8 (bottom) shows that
Figure 3-7. Narrow-band SWIM 2D-FT/ICR mass spectral iso-power contours for the pyrrolidine molecular ion region. Experimental conditions are as in Figure 3-6, except that the SWIM modulation (and excitation/detection) frequency bandwidths were narrowed to provide higher analog and digital resolving power.
High-Resolution 2D-FT/ICR/MS Contour Plot

Modulation Frequency

Ion Cyclotron Frequency

(M-H)$^+$

$M^+$

$MH^+$

$\text{H}_2\text{C}\text{CH}_2$

$\text{H}_2\text{C}\text{N}\text{CH}_2$

$M = \text{Pyrrolidine}$

Figure 3-7.
Figure 3-8. Time evolution of ions derived from pyrrolidine, based on one-dimensional FT/ICR mass spectra obtained at each of a series of reaction periods between ion formation by electron ionization and subsequent excitation/detection. Each data point represents an average of two peak area values. The protonated molecular ion, (M+H)$^+$, is clearly a product of M$^+$ and (M−H)$^+$, whereas (M+H)$^+$ simply grows with time and does not form additional product ions. These results strongly validate our interpretation of the two-dimensional data in Figures 3-6 and 3-7.
Figure 3-8.
neither $M^+$ or $(M-H)^+$ are produced from $(M+H)^+$. Thus, the one-
dimensional double-resonance results fully corroborate the ion-
molecule reactions identified from the 2D mass spectra of Figures 3-6
and 3-7.

**Fragmentation vs. ion-molecule reactions.** A little reflection
reveals that collision-induced fragmentation of parent ions will yield
SWIM 2D-FT/ICR MS/MS peaks on only one side of the diagonal of the
display. Some ion-molecule reactions, on the other hand, are
reversible, and can produce peaks on both sides of the diagonal. A
particularly interesting application for this experiment might be
MS/MS of multiply-charged ions generated by electrospray ionization,
because both the mass and charge of such ions can change during
fragmentation; hence, fragment ions do not necessarily have lower
$m/z$ than their parent ions.

**Radius modulation vs. energy modulation.** In some endoergic
reactions, e.g., collision-induced dissociation, a minimum energy
threshold must be overcome for a reaction to occur. Thus, a simple
sinusoidal modulation of parent ion cyclotron radius from zero to (say)
50% of the trap radius will result in a "clipped" (i.e., distorted)
sinusoidal modulation of the product ion abundance, resulting in non-
linear response, and introduction of signals at harmonic and
combination frequencies. However, the problem is readily avoided by
modulating the parent ion cyclotron radius from a minimum value (by
adding a constant to Equation 3-3) chosen to correspond to a kinetic
energy above the reaction energy threshold.
Moreover, ion-molecule reaction rates may vary directly with ion kinetic energy rather than with ion cyclotron radius.\textsuperscript{44} Since ion kinetic energy varies as the square of ion cyclotron radius, a sinusoidal modulation of ion cyclotron radius will \textit{not} produce a sinusoidal modulation of parent ion kinetic energy (or product ion abundance) in such a case. However, with stored-waveform ion modulation, it is possible to tailor the excitation profile so as to produce a sinusoidal modulation of ion kinetic energy as a function of cyclotron frequency, so that SWIM 2D-FT/ICR MS/MS could remain linear even in that situation. We denote the energy-modulation 2D experiment as SMOKE (stored-waveform modulation of kinetic energy).

\textbf{Generality of the SWIM method for 2D-FT/ICR MS/MS.} Stored-waveform excitation includes all other excitation waveforms as subsets. Thus, for example, Hadamard FT/ICR MS/MS experiments\textsuperscript{32} could be conducted as shown here, simply by tailoring a series of square-wave modulated (rather than sine-wave modulated) SWIM excitation spectra. Alternatively, one could tailor waveforms so as to eject undesired high-abundance ions throughout an experiment, by introducing a high-magnitude spike at the cyclotron frequency corresponding to each undesired $m/z$ in the series of excitation spectra shown in Figure 3-2.

\textbf{SWIM vs. excite-delay-excite for 2D-FT/ICR MS/MS.} The present stored-waveform method offers several advantages over the original excite-delay-excite method.\textsuperscript{18-20} First, broadband excitation requires inconveniently small time increments in the variable-delay event of
the excite-delay-excite sequence, but is not a problem with SWIM. Second, with SWIM, we can more easily modulate the parent ion radius between two finite values. Third, sinusoidal modulation of ion kinetic energy (rather than ion cyclotron radius) requires SWIM. Fourth, the duration of the excitation event is fixed in SWIM but necessarily varies in excite-delay-excite; therefore, SWIM should provide a more accurate measure of ion-neutral collision and reaction products. Finally, SWIM excitation makes possible the introduction of mass "windows" for simultaneous ion modulation, ejection, and non-excitation, for systems in which one wants to observe low-abundance ions in the presence of (less interesting) high-abundance ions.48

**Equilibrium constants from SWIM 2D-FT/ICR MS/MS.** The reader will by now recognize that, for bi-molecular processes, the relative magnitudes of the off-diagonal peaks in a SWIM 2D-FT/ICR MS/MS display are directly related to the respective ion-molecule reaction rate constants. Thus, just as it is possible to determine an ion-molecule reaction equilibrium constant as the ratio of the forward to reverse rate constants,

\[
K_{eq} = \frac{k_{forward}}{k_{reverse}}
\]  

(3-6)

in the so-called "kinetic" method49 for determining \(K_{eq}\), we propose that the equilibrium constant for a reversible reaction could (with the same limitations as the one-dimensional kinetic method) be determined from the ratio of the areas37 of the mirror-image peaks on either side of the diagonal of a SWIM 2D-FT/ICR MS/MS plot.
Phasing and display of 2D-FT/ICR MS/MS data. In the present work, we have performed a magnitude calculation after the first FT stage. As a result, overlapped peaks in the spectrum can be expected to exhibit some distortion which could be manifested as peaks at harmonic or combination frequencies following the second FT. However, in practice we do not typically see such spurious peaks, and magnitude-mode calculation is much simpler than phasing after the first FT.

The 2D mass spectral representations in Figures 3-5 through 3-7 are displayed as contours of constant power rather than contours of constant magnitude. As in 2D-FT/NMR, it is convenient to use power spectral display, because the peaks are narrower than in magnitude-mode display. One should of course be aware that the relative peak heights in such a display are not linearly related to relative ion abundances (e.g., a peak of twice the magnitude will have four times larger power). However, for quantitative work, the relevant off-diagonal peak magnitudes can readily be extracted from the data.

In principle, phase-sensitive 2D FT/ICR MS/MS could make it possible to distinguish between ion-molecule reactions whose rates increase or decrease with increasing ion energy. We are investigating this possibility.

SWIM 2D-NOESY NMR. In the limit of very small "tip" angle, \( \sin \theta \approx \theta \), NMR response amplitude becomes linearly proportional to excitation amplitude. Certain NMR pulse sequences are designed to take advantage of this linear limit. Therefore, the method proposed
here could be used to produce NOESY-type 2D/FT/NMR spectra, provided that the excitation modulation range was limited to small tip angles.

**Conclusion**

In summary, we have devised and demonstrated a fundamentally new scheme, based on the high linearity of the ICR experiment, for obtaining MS/MS data, multiplexed with respect to both parent and product ions. The method provides a simple graphical means for identifying all ion-molecule pathways simultaneously from a single automated experiment. Such capability should prove especially useful in analysis of complex mixtures containing a large number of overlapped peaks, as well as better-controlled measurements of multiple equilibria (such as proton-transfer equilibria between an unknown and a series of reference bases) in a single experiment. With suitable precautions, it should prove possible to determine relative ion-molecule reaction rate constants and equilibrium constants from relative peak areas and peak area ratios for a whole family of interconnected reactions at once. Finally, the present method, although devised expressly for FT/ICR/MS, can be extended to 2D-NOESY NMR in the limit of small tip angle.
References


Chapter IV

Further Experiments with SWIM 2D-FT/ICR/MS

Introduction

Stored waveform ion modulation two-dimensional Fourier transform ion cyclotron resonance mass spectrometry, SWIM 2D-FT/ICR/MS, offers the advantage of simultaneously identifying all ion-molecule reactions in a single automated experiment. The FT multiplex advantage for product ions realized with the advent of FT/ICR/MS,\textsuperscript{1,2} is now available for the parent ions. Connections between reagent ions and their product ions are easily identified by vertical and horizontal projections to the two-dimensional axis. Figure 4-1 shows the various possible experiments that can be conducted and information readily obtained from a single 2D spectrum. They include: collision-induced dissociation; fixed product ion scan; neutral loss scan; adducts; and forward & reverse reaction mechanisms. Other mass spectrometers can acquire only one of these experiments at a time.

The development of SWIM 2D-FT/ICR/MS was discussed in chapter three. In this chapter, other chemical systems are examined by use of the SWIM technique.
Figure 4-1. Representation of the possible information obtained from a single two-dimensional FT/ICR/MS experiment. Note that mass is plotted, not frequency as in the other 2D spectra of this dissertation.
**Experimental**

All experiments were conducted on a dual-trap FTMS-2000 FT/ICR mass spectrometer (Extrel FTMS Millipore Inc., Madison, WI). Further information concerning the instrument is available in chapter three. All experiments were performed in the 'source' compartment of the dual cell.

**Perfluorotributylamine.** PFTBA was obtained from Scientific Instrument Services, Ringoes N.J., and was leaked into the source region by use of a leak valve (Model 951-5100, Varian, Palo Alto, CA) to a pressure of $3.5 \times 10^{-7}$ torr. Ionization was performed with 70 eV electrons for 5 ms at a measured current of 4.9 μA. After a 20 ms delay, a SWIM excitation pulse (Nyquist frequency of 2.6666 MHz, 4096 data points, frequency range of 100 kHz to 2.6000 MHz) was applied for 0.787 ms at a time-domain amplitude of 98 V(p-p). A reaction delay period of 150 ms allowed ions to undergo possible CID collisions. The final excitation was identical to the SWIM waveforms except that the frequency profile was flat. Four 4K data time-domain transients (Nyquist frequency of 2.666 MHz) were co-added and stored for subsequent processing.

**Uranium-cyclotriyne reaction.** U-238 metal sample was provided by Professor Antonio Pires de Matos and Dr. Winnie Yin. Tribenzocyclotriyne (TBC) was graciously provided by Professor Wiley J. Youngs of The University of Akron, Akron, OH. TBC was dissolved in methylene chloride and applied to one half of the direct-insertion probe. U-238 was placed on the other half of the probe. The probe
was inserted to within a few millimeters of the trap electrode of the 'source cell'. The probe was heated to a temperature of 150 K to increase the vapor pressure of TBC. Uranium ions were generated by laser desorption ionization. Details of the mechanical and electronic interface between the mass spectrometer and a Continuum (Santa Clara, CA) Model YG-660A Nd:YAG laser operating at mixed wavelengths of 1064 and 532 nm with an output power of ~ 300 mJ per pulse are described elsewhere.³

After the laser pulse, a preparation delay of 0.6 ms was followed by SWIM excitation (Nyquist frequency of 500 kHz, excitation frequency range of 18.8 kHz to 487 kHz, 34.8 V\textsubscript{(p-p)} for 4.096 ms). After allowing the ions to react for 0.6 seconds, a final excitation pulse was applied with the same conditions as the SWIM excitation pulse except the frequency profile was flat. Five 4K time-domain transients were co-added with a Nyquist frequency of 222.2 kHz

**11-component mixture.** The following chemicals were obtained from Aldrich Chemical Co. Inc. (Milwaukee, WI): thiophene; cyclohexanone; 1,2-dimethylbenzene; 3-methylanisole; 2-methoxyphenol; n-butylbenzene; 1-fluoro-4-nitrobenzene; 2-fluorobenzotri fluoride; 1-bromo-4-fluorobenzene; 1,2,4-trichlorobenzene; 4-bromoanisole. An equal volume mixture was prepared and admitted via a leak valve to a pressure of 4 x 10^{-8} torr. Argon collision gas was introduced through a gold leak to a total pressure of 2 x 10^{-7} torr (uncorrected ion gauge reading). Approximately halfway through the experiment the total pressure had
dropped to about $8 \times 10^{-8}$ torr, and argon was added to bring the total pressure back to $2 \times 10^{-7}$ torr. Electron ionization conditions were 12 eV electrons for 40 ms at a measured current of 10.8 µA.

A 0.1 s preparation delay was used before the SWIM excitation pulse (Nyquist frequency of 1.0 MHz, 62 $V_{(p-p)}$ for 2.05 ms over a frequency range of 37.5 kHz to 975 kHz) and a reaction delay of 1.5 s. The final excitation was performed by use of a 4K flat frequency profile SWIFT waveform with a frequency range of 100 kHz to 2.6000 MHz for 0.769 ms with a time-domain amplitude of 98 $V_{(p-p)}$. Four 4K time-domain transients were coadded at a Nyquist bandwidth of 1.3333 MHz for each SWIFT modulation waveform excitation.

All data sets were padded with an equal number of zeroes in both dimensions before Fourier transformation.

**Results and Discussion**

**Perfluorotributylamine.** Figure 4-2 shows the SWIM 2D-FT/ICR/MS iso-power contour plot for PFTBA. Axial projections are also shown. Figure 4-3 is the three-dimensional stack plot of the 2D data set. The following six reactions are identified from the off-diagonal peaks of the 2D display:

\[
C_3F_5^+ + M \rightarrow CF_3^+ + C_2F_2 + M \tag{4-1}
\]
\[
C_4F_9^+ + M \rightarrow CF_3^+ + C_3F_6 + M \tag{4-2}
\]
\[
C_8F_{16}N^+ + M \rightarrow CF_3^+ + C_7F_{13}N + M \tag{4-3}
\]
Figure 4-2. SWIM 2D-FT/ICR/MS/MS iso-power contours of PFTBA ion reactions. Six reactions are identified. Reactions 1 - 4 are due to CID and reactions 5 and 6 are due to IIII (see text).
Figure 4-3. Three dimensional stacked plot display of PFTBA reactions. See Figure 4-2 and text for an explanation of the reactions.
\[
\text{C}_8\text{F}_{16}\text{N}^+ + \text{M} \rightarrow \text{C}_3\text{F}_5^+ + \text{C}_5\text{F}_{11}\text{N} + \text{M} \quad (4-4)
\]
\[
\text{CF}_3^+ + \text{C}_{12}\text{F}_{27}\text{N} \rightarrow \text{C}_3\text{F}_5^+ + \text{C}_9\text{F}_{22}\text{N} + \text{CF}_3^+ \quad (4-5)
\]
\[
\text{CF}_3^+ + \text{C}_{12}\text{F}_{27}\text{N} \rightarrow \text{C}_8\text{F}_{16}\text{N}^+ + \text{C}_4\text{F}_{11}\text{N} + \text{CF}_3^+ \quad (4-6)
\]
in which M refers to the neutral molecule PFTBA used as a collision gas.

Reactions 4-1 through 4-4 are 'normal' CID reactions in which the initial ion is fragmented after collision with a neutral molecule. Reactions 4-5 and 4-6 are not charge exchange reactions nor neutral addition reactions since the corresponding neutral concentrations required to form the product ions are vanishingly small, if present at all. Therefore, it is surmised that these reactions are evidence of internal ion impact ionization (I\(^4\)).\(^4\) CF\(_3^+\) is used as a projectile ion which fragments the neutral molecule, PFTBA, producing the two ions given in 4-5 & 4-6. Wood and Marshall have used this technique for its high collision energy in the center-of-mass frame.\(^4\)

**Uranium-cyclotriyne reaction.** Tribenzocyclotriyne (TBC) is a highly conjugated planar molecule that has a cavity large enough to fit certain transition metals (see Figure 4-4). Other cyclotriyne compounds have been made and reacted with a wide variety of metals.\(^5,6\) It is helpful if predictions can be made as to whether the metal will fit into the cavity or a sandwich complex will form. A collaborative effort has been undertaken to determine which metal atoms will react with certain cyclotriyne molecules and the kinetics of these reactions.
Figure 4-4. Laser Desorption Ionization (LDI) SWIM 2D-FT/ICR mass spectral magnitude contours for ion-molecule reactions of uranium and a planar cyclotriyne (TBC). Five reactions can be identified in this single 2D spectrum.

1) $\text{U}^+ + \text{O}_2 \rightarrow \text{UO}^+ + \text{O}$
2) $\text{UO}^+ + \text{O}_2 \rightarrow \text{UO}_2^+ + \text{O}$
3) $\text{U}^+ + \text{L} \rightarrow \text{UL}^+$
4) $\text{UO}^+ + \text{L} \rightarrow \text{UOL}^+$
5) $\text{UO}_2^+ + \text{L} \rightarrow \text{UO}_2\text{L}^+$

$L =$

\[ \begin{array}{c}
\text{TBC}
\end{array} \]
Uranium-238 was reacted with TBC as specified in the experimental section. However, side reactions of U-238 with oxygen were dominant so that the magnitude of the complex ion of interest was small. Multiple product ions were observed over a 3 s reaction period culminating in the production of mostly UO\(^+\) and UO\(_2\)\(^+\). The background pressure of air was approximately 5 x 10\(^{-8}\) torr, which was leaking into the vacuum chamber via the direct-insertion probe. Laser desorption SWIM 2D-FT/ICR/MS data was collected in order to unravel the possible reaction pathways.

Figure 4-4 shows the 2D iso-power contour plot for this system. The first two reactions (U\(^+\) and O\(_2\)) shown are very intense and fast and have been observed experimentally prior to this work.\(^7\),\(^8\) Also observed are the reactions between U\(^+\), UO\(^+\), and UO\(_2\)\(^+\) with TBC to produce U(TBC)\(^+\), UO(TBC)\(^+\), and UO\(_2\)(TBC)\(^+\), respectively. No significant off-diagonal peak was observed suggesting that UO\(_2\)\(^+\) will produce the desired ion of U(TBC)\(^+\) by loss of the small neutral O\(_2\). Hence, it has been experimentally observed that uranium-238 does react with TBC.

Previous methods for determining reaction pathways by isolating the reagent ion, uranium, and reacting it with the neutral, proved unsatisfactory since the reaction with oxygen was dominant. Under these experimental conditions, only the SWIM 2D experiment proved useful in determining whether the desired reaction was or was not occurring.
**11-component mixture.** Williams et al. showed in 1990 that the second Fourier transform of the 2D-FT/ICR/MS experiments could be replaced with Hadamard transform in which the SWIM sinusoidal modulation is replaced with 'comb' function excitation frequency profiles. They demonstrated the technique on an 11-component mixture consisting of: thiophene; cyclohexanone; 1,2-dimethylbenzene; 3-methylanisole; 2-methoxyphenol; n-butylbenzene; 1-fluoro-4-nitrobenzene; 2-fluorobenzotri fluoride; 1-bromo-4-fluorobenzene; 1,2,4-trichlorobenzene; 4-bromoanisole. As mentioned in chapter three, the HT/FT technique requires prior knowledge of the system under study in order to create by use of SWIFT the 'comb' frequency profiles, whereas SWIM does not require prior knowledge and should prove to be more useful overall. We attempted to analyze the same mixture by use of SWIM 2D/FT/ICR/MS for a comparison of the two methods.

An equal volume mixture of the 11 compounds was introduced to the ICR cell. Low energy electron ionization was used in order to produce molecular ions only. Argon was used as the collision gas for collision-induced dissociation (CID) of the molecular ions. The ionizing electron energy was lower than that required to ionize argon.

Figure 4-5 shows the iso-power contour plot for this mixture. Only six molecular ions, A - F, are observed on the primary ion line (fundamental diagonal) in the 2D display representing those compounds with the highest vapor pressure. Other peaks on the diagonal are fragment ions initially observed from these six molecules.
A = thiophene
B = o-xylene
C = 3-methylanisole
D = n-butylbenzene
E = 2-fluorobenzotrifluoride
F = 1-bromo-4-fluorobenzene

Figure 4-5. SWIM 2D-FT/ICR/MS iso-power contours for an eleven component mixture. Six molecular ions and seven fragment ions appear on the diagonal. Some CID peaks are observed, but the major pathways are due to the most abundant species, thiophene. Off-diagonal peaks to the left of thiophene, A, are charge transfer to form molecular ion. Peaks to the right are CID fragments of thiophene.
Products of the molecular ion of thiophene, A, dominate the data (dashed box). Three fragment ions of thiophene (m/z = 84) are observed at a frequency corresponding to a mass-to-charge ratio of m/z = 58, 45, and 39. Peaks to the left of the diagonal peak of thiophene are due to charge transfer to the other five molecules.

Also observed in the display is 'T₁-noise' due to fluctuations in the number of initial ions formed during ionization and a second dimension harmonic line (to be discussed in the next chapter). The CID data of the other species are not observed due to the domination of thiophene. Although thiophene could be removed from the mixture (i.e. not added initially) it will prove more useful in the future for mixtures in which a dominating component can not be easily removed prior to analysis to modify the SWIM waveforms to eject the dominant molecular ion. The modified experiment will be examined in the near future.

**Conclusions**

The MS/MS technique of SWIM 2D-FT/ICR/MS has been shown useful in the identification of reaction pathways. Ion connectivities are easily determined by use of the 2D display.

Future work will be concerned with better pressure control to eliminate 'T₁-noise' and a reduction in the experimental time. Currently, about one hour of the experimental time is used just in loading SWIFT waveforms and storing the detected time-domain
transients. The time can be reduced by use of a faster more powerful computer data station which is currently under development.
References


Chapter V

Ion Energy-Modulated Stored Waveform Ion Modulation (SWIM) Two-Dimensional FT/ICR MS/MS

Introduction

With the implementation of Stored Waveform Ion Modulation (SWIM) 2D-FT/ICR/MS\textsuperscript{1} it is now possible to identify simultaneously all ion-neutral reactions in a single automated experiment. The familiar one-dimensional mass spectrum appears as peaks along the diagonal of a two-dimensional display. Off-diagonal peaks result from forward and reverse ion-neutral reactions. The parent ion cyclotron orbital radii (and thus parent ion speeds, and hence the relative abundances of product ions formed by ion-neutral reactions of those parent ions), may be modulated by applying a series of sinusoidal single-pulse excitation magnitude-mode stored inverse Fourier transform waveforms of increasing frequency over a given bandwidth.

However, in some endoergic reactions there is a minimum energy threshold that must be overcome for a reaction to occur. Hence, a simple sinusoidal modulation of parent ion cyclotron radius leads to a clipped sinusoidal signal of the product ion abundance in the second dimension, which upon Fourier transformation produces signals with harmonic and combination ion cyclotron resonance frequencies.
Moreover, ion-molecule reaction rates may vary directly with ion kinetic energy rather than with ion cyclotron radius. Since ion kinetic energy varies as the square of ion cyclotron radius and is proportional to the cyclotron frequency, a sinusoidal modulation of ion cyclotron radius will not produce a sinusoidal modulation of parent ion kinetic energy in such a case. However, with SWIM, it is possible to tailor the excitation profile so as to produce a sinusoidal modulation of ion kinetic energy as a function of cyclotron frequency, so that SWIM 2D-FT/ICR MS/MS could remain linear even in that situation. We denote the energy-modulation SWIM 2D experiment as SMOKE (stored-waveform modulation of kinetic energy).

Figure 5-1 shows a plot of product ion abundance vs. kinetic energy of the reactant ion in which a minimum kinetic energy must be overcome for a reaction to occur. The plot is based on data given by Hop et al. in their 1990 paper discussing bond dissociation energies determined through collision-induced dissociation experiments. Three modulation regimes are shown, one modulating kinetic energy of a linear part of the energy range (SMOKE) and two modulating radius (SWIM) one over the linear energy range and the other over the threshold. The theoretical threshold energy is given in this example to correspond to a value that is 25% of the maximum energy value to which ions are modulated.

Figures 5-2 and 5-3 show the effect on the second dimension product ion signal for the energy regimes shown in Figure 5-1. A linear modulation function of product ions will produce only a signal at
Figure 5-1. Representation of product ion signal for which the production is linear with respect to the reagent ion's kinetic energy. Energy regimes shown were used to produce the signals in Figures 5-2 and 5-3. The top two lines represent energy and radius modulation, respectively, across the linear energy region. The bottom line is radius modulation in which the modulation is conducted across the energy threshold for observation of product ion signal.
Figure 5-2. Theoretical spectra showing the effect on product ion signal (spectrum A) due to sinusoidal modulation of parent ion radius, for the case that the number of product ions varies linearly with energy (B).
Figure 5-3. Theoretical spectra showing the additional effect of a non-zero energy threshold for the formation of product ions. Spectrum A shows an energy threshold that is 4% of the maximum modulation energy. Spectrum B shows an energy threshold that is 25% of the maximum modulation energy. The thresholds produce clipped signals for product ion magnitude with the result of harmonics in the frequency domain.
the modulation frequency (cyclotron frequency) of the parent ion (Fig. 5-2 A). However, if radius modulation was used in the linear energy regime of Figure 5-1, signals would be observed at the 2nd and 3rd harmonic of the true frequency (Fig. 5-2 B). The time domain signal is no longer a pure sinusoid but is now the square root of a pure sinusoid. Also, if the radius modulation were to extend below the energy threshold for the creation of product ions, then a clipped sinusoidal signal would be obtained. The relative magnitudes of the harmonic signals will depend upon how far below the energy threshold modulation is extended (Fig. 5-3 A & B).

**Theory**

In order to modulate the kinetic energy of the ions as a function of their cyclotron frequencies requires determining the appropriate frequency domain profile as a function of ion radius since the response amplitude (i.e., ion cyclotron orbital radius) is linearly proportional to the on-resonance excitation amplitude.\(^3\)\(^4\) We start with an equation that varies energy as a function of frequency

\[
E_j(v) = \frac{\sin \left( j \pi \left( \frac{v - v_{\text{low}}}{v_{\text{high}} - v_{\text{low}}} \right) \right) + 1}{2}
\]  

(5-1)

in which \(v_{\text{low}}\) and \(v_{\text{high}}\) are the frequency limits for energy modulation and \(E(v)\) is a value ranging from 0 to 1 at a frequency of \(v\) in hertz and \(j\) is the index for the waveform. The reader will note that the equation
is the same as that used for radius modulation (SWIM) given in chapter three, Equation 3-3. We do not want the modulation extending to a zero value, but to an energy value just above the threshold energy for reaction, hence

\[
E_j(v) = \sin \left( j \pi \left( \frac{v - v_{\text{low}}}{v_{\text{high}} - v_{\text{low}}} - \frac{\pi}{2} \right) \right) + 1 \quad \left[ 1 - f \right] + f \quad (5-2a)
\]

in which

\[
f = \frac{E_{\text{min}}}{E_{\text{max}}} \quad (5-2b)
\]

is the fractional amount of the maximum energy for minimum energy modulation. Equation 5-2a is plotted in the top of Figure 5-4. To obtain the equation for kinetic energy in units of joules requires multiplying Equation 5-2a by the maximum kinetic energy to yield

\[
E_j(v) = \left\{ \sin \left( j \pi \left( \frac{v - v_{\text{low}}}{v_{\text{high}} - v_{\text{low}}} - \frac{\pi}{2} \right) \right) + 1 \right\} \left[ 1 - f \right] + f E_{\text{max}} q \quad (5-3)
\]

in which \( E_{\text{max}} \) is given in electron-Volts (eV) and \( q = 1.602 \times 10^{-19} \) C.

Equation 5-3 yields energy modulation as a function of frequency over the frequency range and energy range of interest. However, we
Figure 5-4. Generation of SMOKE waveforms. At top is the normalized energy profile and at bottom the normalized radius profile for a value of \( j=8 \). See text for discussion.
must still convert the equation to radius in order to generate the SWIFT waveforms.

Given that kinetic energy is $\frac{1}{2}mv^2$ and making the substitutions of

$$v = 2\pi vr$$

(5-4)

and

$$m = \frac{qB}{2\pi v}$$

(5-5)

upon rearrangement we obtain

$$r = \sqrt{\frac{KE}{qB\pi v}}$$

(5-6)

Finally, substitution of Equation 5-3 for $KE$, kinetic energy, in Equation 5-6 yields

$$r_j(v) = \sqrt{\left[\sin \left(j \pi \frac{v - v_{low}}{v_{high} - v_{low}} - \frac{\pi}{2}\right) + 1\right] \left(1 - f\right) + f} \frac{E_{max}}{B\pi v}$$

(5-7)

Figure 5-4 bottom shows the normalized radius of Equation 5-7 obtained by division of the maximum radius to which the SWIFT waveform could excite ions. The maximum radius, $r_{max}$, is calculated from equations given by Guan et al.
in which \( t \) is the total excitation period of the SWIFT pulse, \( \Delta v \) is \( V_{\text{high}} - V_{\text{low}} \), \( d \) is the distance between the excitation plates, and \( \beta \) is a trap geometry constant (\( \beta = 0.72167 \) for a cubic trap). The maximum kinetic energy can then be calculated by use of equation 5-9.

\[
KE = qB\pi vr^2
\]  
(5-9)

Examination of this equation shows that the maximum kinetic energy to which ions can be modulated is limited by the lowest frequency, \( v_{\text{low}} \), that one wishes to modulate. Hence, SMOKE waveforms once created are not as easily manipulated to modulate over other frequency ranges with the same energy range initially specified as are SWIM waveforms which modulate ion radius. Figure 5-5 shows SMOKE waveform surfaces in units of energy and radius. SMOKE waveforms are acquired by taking slices at integer values of \( j \), axis into the paper.
Figure 5-5. 3D displays of SMOKE waveforms. Each magnitude-mode frequency domain waveform is acquired by taking a slice at integer values of j (axis into the paper). Left is the surface for energy modulation of ions between 5 and 29 eV, and at right the corresponding radius modulation surface. (j=1-10)
Experimental

The stored-waveform modulation of kinetic energy (SMOKE) 2D/FT/FT/ICR/MS experiments were implemented on a dual-trap FTMS-2000 FT/ICR mass spectrometer (Extrel FTMS Millipore Inc., Madison, WI), operated at 3.0 tesla, equipped with Helix Technology CryoTorr-8 2000 L/s cryopumps (Waltham, MA) for both source and analyzer vacuum chambers, with two 4.76 cm cubic traps in a standard dual-trap configuration. The mass spectrometer was controlled by a Nicolet 1280 computer. Each gaseous sample was introduced through a leak valve (Model 951-5100, Varian, Palo Alto, CA) connected to the batch inlet system of the instrument. All experiments were conducted in the "source" compartment of the dual-trap.

SMOKE waveforms were created by use of equations 5-7 through 5-9 (see appendix). Equation 5-7 was normalized based upon the maximum radius given by Equation 5-8 to produce the SWIFT frequency domain profiles.

An equal volume mixture of absolute ethanol and methanol was prepared and leaked into the chamber to a total pressure of $5.2 \times 10^{-8}$ torr. Ionization was performed with 11 eV electrons for 5 ms at a measured current of 14.8 μA. After a delay of 600 ms, the molecular ions of the two alcohols produced the protonated ions of the following molecules by ion-molecule reactions: dimethyl ether; ethylmethyl ether; diethyl ether; and diethyl ether with an associated water molecule. The SMOKE modulation waveform parameters were: frequency bandwidth = 2.000 MHz; $v_{\text{low}} = 100.0$ kHz; $v_{\text{high}} = 2.000$
MHz; 4096 time-domain data to give a 1.024 ms excitation event; time-domain amplitude, 110 V(p-p); kinetic energy range of 5 - 29 eV. After another 600 ms time delay for the excited ions to react and or dissociate, a flat frequency domain profile SWIFT waveform with the same parameters as the SMOKE waveforms, except the amplitude was 73.5 V(p-p), was used to excite all ions to coherent motion. Nine 4K time-domain transients were co-added and stored for subsequent processing. The signal was acquired in direct mode with a Nyquist frequency of 2.000 MHz. The same experimental event sequence was then repeated for each of the 512 SMOKE excitations to produce a two-dimensional time-time data array, D(j,t), in which 1 ≤ j ≤ 512.

The experiment was repeated with replacement of SMOKE waveforms by similar SWIM waveforms (frequency bandwidth = 2.000 MHz; νlow = 75.0 kHz; νhigh = 1.950 MHz; 4096 time-domain data to give a 1.024 ms excitation event; time-domain amplitude, 110 V(p-p)).

**Results and Discussion**

Figure 5-6 shows a comparison of 2D-FT/ICR/MS spectra obtained by use of SWIM (left) and SMOKE (right) modulation waveforms. The contour levels shown are the same percentage of the base peak, protonated diethyl ether. Both spectra have the same diagonal peaks but differ in the magnitudes of the off-diagonal peaks. Peaks to the right of the diagonal are the result of CID. Two reactions show the same neutral loss, CH₂.
Figure 5-6. Comparison of SMOKE and SWIM 2D-FT/ICR/MS. Iso-power contours are the same level relative to the base peak, protonated diethyl ether, C. A second dimension harmonic line is visible in each spectrum, but is more pronounced in the SWIM spectrum (examine 2D projection of modulation). Reactions are discussed in the text.
shown as reaction 1 and 4 respectively in the figure.

A second dimension harmonic line is also observed in the spectra. The magnitudes of the harmonics in the SMOKE spectrum are smaller than those in the SWIM spectrum (examine the modulation dimension projection shown at the left of each spectrum). It is more easily observed in a 3D stacked plot, not shown.

Lastly, note that the higher frequency signals show greater magnitudes in the SMOKE compared to the SWIM spectrum. This difference is possibly a result of decreasing the excitation radius for higher frequency ions in energy modulation.

A harmonic line is still observed in the SMOKE spectrum since it is possible that the energy limits specified contained the energy thresholds for CID of these ethers. The energy range chosen was based upon results obtained by Hop et al. on the proton bound dimer ion of diethyl ether. Fragmentation was observed to start at a kinetic energy of 5 eV (1 eV center-of-mass frame). Fragmentation of the protonated ethers would most likely occur at higher energy. The harmonic line should be eliminated by increasing the minimum energy of modulation.
Conclusions

Preliminary experiments for energy modulation show promise for the technique. Better comparisons between SWIM and SMOKE are continuing to be produced by: acquiring SWIM and SMOKE data alternately so that the two methods experience similar pressure fluctuations; and generating both sets of waveforms with the same excitation parameters (i.e. frequency range, data points, clocking speed, etc.). To verify that the energy range is as specified, SMOKE waveforms will be attenuated so that the energy range lies above, below, and across the energy barrier for fragmentation.
References


APPENDIX

PROGRAM SFG
C AUTHOR: CHARLES W. ROSS III
C ALL RIGHTS RESERVED
C
********************************************************************
C COMBINE SFG.ASC WITH SUB'S FROM TLR SWIFT4.  3/4/92
C
C SWIFT SINE WAVE FUNCTION GENERATOR. IT WILL MAKE N
C TIME DOMAIN SWIFT WAVEFORMS WITH A SINE FUNCTION
C MAGNITUDE MODE EXCITATION WAVEFORM.
C
********************************************************************
C VARIABLE DEFINITIONS
C
C ANSWER - LOGICAL VARIABLE FOR QUESTIONS
C PI - TRIGONOMETRIC CONSTANT
C NTP - NUMBER OF POINTS AFTER FFT
C NDP - NUMBER OF TIME DOMAIN POINTS.
C HZPPT - FREQUENCY POINT SPACING
C ZFILL - MULTIPLIER FOR FINAL NUMBER OF DATA POINTS
C AFTER ZERO FILLING, (NDPFINAL=NDP*ZFL)
C BWIDTH - SPECTRAL FREQUENCY RANGE
C KSPEC - NUMBER SPECIFYING DATA TYPE (TIME, PHASE,)
C D - SET EXTENSION REGISTER TO ONE
C SPACE - CALCULATED FREQUENCY POINT SPACING
C STNAME - FILENAME TO STORE SWIFT WAVEFORMS
C COMTAG - THREE LETTER NICOLET COMMAND
C K - NUMBER OF DATA POINTS IN K UNITS (1024)
C LO - LOWEST FREQUENCY REQUIRED TO MODULATE
C HI - HIGHEST FREQUENCY REQUIRED TO MODULATE
C X - REAL VARIABLE. DATA POINT CORRESPONDING TO
C HI FREQUENCY
C X1 - INTEGER VARIABLE. SAME AS X
C Y - REAL VARIABLE. DATA POINT CORRESPONDING TO
C LO FREQUENCY
C N - NUMBER OF WAVEFORMS TO CREATE
C I - INDEX FOR DO LOOP

161
C INDEX - INDEX FOR DO LOOP
C SDATA - ARRAY HOLDING POINT INFORMATION
C

LOGICAL ANSWER
REAL PI
  INTEGER SDATA(65535),ZFILL
COMMON /ZFILL/ZFILL
COMMON /SDATA/SDATA
COMMON /NTP/NTP
REAL X,Y,SPACE,HI,LO
COMMON /BWIDTH/BWIDTH
  INTEGER NDP,K,N,I
COMMON /HZPPT/HZPPT
COMMON /DEFSIZ/NDP
  INTEGER KSPECT, X1, Y1, D, Z
  CHARACTER STNAME*8, COMTAG*3
COMMON /KSPECT/KSPECT
PI=3.1415927

C GET BASIC INFORMATION FROM USER
  PRINT *,'****************************************'
  PRINT *, 'SWIFT SINE WAVE FUNCTION GENERATOR'
  PRINT *,'****************************************'
  PRINT *, 'ENTER THE NDP VALUE IN K UNITS.'
READ (1,*)K
NDP=K*1024
ZFILL=1
NTP=NDP/2
PRINT *, 'HOW MANY WAVEFORMS DO YOU NEED?'
READ (1,*)N
PRINT *, 'ENTER THE LOFREQ VALUE.'
READ (1,*)LO
PRINT *, 'ENTER THE HIFREQ VALUE.'
READ (1,*)HI
KSPECT=1
CALL RSETUP(200)
PRINT *, 'WHAT FILENAME TO STORE WAVEFORMS AS?'
PRINT *, '7 LETTERS MAXIMUM FOLLOWED BY A "\".'
C BACKSLASH REQUIRED AS A TERMINATOR IN FCOMSTR
C SUBROUTINE CALLED TO PUT NAME INTO FNS.
110 FORMAT (A)
  READ (1,110)STNAME
  COMTAG='FNS'
  CALL FCOMSTR(COMTAG,STNAME,1000)
D=1
  COMTAG='FXS'
  CALL FCOMINT(COMTAG,D,1000)
C CALCULATE FREQUENCY DOMAIN POINT SPACING
    SPACE=BWIDTH/NTP
    PRINT *, 'SPACE =', SPACE
    PRINT *, 'HZPPT=', HZPPT
    PRINT *, 'SET HZPPT=SPACE?'
    CALL YESNO(ANSWER)
    IF(. NOT. ANSWER) GOTO 45
    HZPPT=SPACE

C  ************************************************************
C CALCULATE THE LAST DATA POINT THAT NEEDS TO BE ZEROED
C IN THE FIRST SECTION, X1. CORRESPONDS TO HI FREQ.
45  X=(BWIDTH-HI)/SPACE
    X1=INT(X)-1
C
C CALCULATE THE FIRST DATA POINT THAT NEEDS TO BE ZEROED
C IN THE SECOND SECTION, Y1.
    Y=(BWIDTH-LO)/SPACE
    Y1=INT(Y)+1
C
C  *******************************************************
C LOOP 60 FOR NUMBER OF WAVEFORMS REQUESTED.
    DO 60 I=1,N
    KSPECT=1
C LOOP 65 ZEROES ALL OF SDATA.
    DO 65 Z=1,NDP
    SDATA(Z)=0
    65 CONTINUE
C LOOP 70 CALCULATES THE AMPLITUDE OF THE SDATA POINT IN
C THE FREQUENCY RANGE OF INTEREST (LO TO HI).
    DO 70 INDEX=X1+1,Y1-1
    FREQ=BWIDTH-INDEX*SPACE
    ARG=I*(PI*(FREQ-LO)/(HI-LO)-(PI/2)
    SDATA(INDEX)=500000*(1+SIN(ARG))/2
    70 CONTINUE
C INSERTIONS OF SWIFT CALLS HERE (TOM L. RICCA PRGS.):
CALL FCOMNO('NMX',1000)
C
CALL QPMSUB
    CALL FCOMNO('INV',1000)
CALL SH1SUB
CALL NNNSUB
C STORE SWIFT WAVEFORM AND INCREASE EXTENSION NUMBER.
   COMTAG='AST'
   CALL FCOMM(COMTAG,1000)
   COMTAG='IXS'
   CALL RDEFINE(200)
   CALL FCOMM(COMTAG,1000)

60 CONTINUE
   PRINT *, 'SPACE = ', SPACE
   PRINT *, 'HZPPT = ', HZPPT
   PRINT *, 'DONE.'
   GOTO 300

200 PRINT *, 'ERROR IN SUBROUTINE RSETUP OR RDEFINE.'
1000 PRINT *, 'ERROR. PROGRAM ABORTED.'
300 CALL EXIT

STOP
END
PROGRAM TD1
C *************************************************************
C AUTHOR: CHARLES W. ROSS III
C ALL RIGHTS RESERVED
C *************************************************************
C NOW HAS TOM L. RICCA'S ADDITIONS. 3/5/92.
C TD1 - TWO DIMENSIONAL ONE PULSE.
C 2D-FTICR PROGRAM, THE PROGRAM WILL LOAD SWIFT
C WAVEFORMS AND STORE COLLECTED SPECTRA
C SEQUENTIALLY.

INTEGER SDATA,RPT,AMPLTD,ZFILL,HAMP
REAL LMASS,LMASST,VOLT,QNT
INTEGER N,I,D,B
REAL ATN,RXN,E,XBWI
LOGICAL ANSWER
CHARACTER LONAME*8,ANS*1,STNAME*8,COMTAG*3
CHARACTER EXPER*8
COMMON /SDATA/SDATA(4096)
COMMON /DEFSIZ/NDP
COMMON /BWIDTH/BWIDTH
COMMON /HIFREQ/HIFREQ
COMMON /REFFRQ/REFFRQ
COMMON /HNDP/HNDP
COMMON /NTP/NTP
COMMON /ZFILL/ZFILL
COMMON /KSPECT/KSPECT
COMMON /NCW/NCW
COMMON /CWA/CWA
COMMON /CW/CW(96)
COMMON /IZDB2/IZDB2(31)
COMMON /SADDR/SADDR(31)
COMMON /NDPL/NDPL(31)
COMMON /ATN/ATN
COMMON /NSWEEP/NSWEEP
COMMON /BMVOLT/BMVOLT

PRINT *, ' » » 2D FTICR ACQUISITION « « '
PRINT *, ' >>>
C*************************************************************
C GET THE SWIFT FILE INFORMATION. INCLUDING EXPERIMENTAL
C PARAMETERS
C*************************************************************
100 PRINT *, 'WHAT IS THE NAME OF THE SWIFT FILES?'
PRINT *, '7 LETTERS MAX FOLLOWED BY A "\".'
C BACKSLASH REQUIRED AS A TERMINATOR IN FCOMSTR
C SUBROUTINE CALLED TO PUT NAME INTO FN.
PRINT *,''
READ(1,110)LONAME
110 FORMAT(A)
PRINT *,''
PRINT *,'HOW MANY WAVEFORMS ARE THERE?'
PRINT *,'NOTE:THIS IS ALSO THE # OF SPECTRA TO ACQUIRE.'
PRINT *,''
READ(1,*)N
PRINT *,'WHAT ATTENUATION WILL BE NEEDED?'
PRINT *,''

READ(1,*)ATN
IZDB2(1)=NINT(2.0*ATN)
PRINT *,'TIME DELAY BEFORE THE MODULATION WAVEFORM?'
PRINT *,''
READ(1,*)E
PRINT *,'WHAT REACTION TIME (THIS IS FOR DLE)?'
PRINT *,''
READ(1,*)RXN
PRINT *,''
PRINT *,'HOW MANY SWEEPS PER EXPERIMENT(NSW)?'
PRINT *,''
READ (1,*)B
PRINT *,'WHAT ELECTRON BEAM VOLTAGE IS REQUIRED?'
READ (1,*)BM
PRINT *,'DURATION OF ELECTRON BEAM?'
READ (1,*)BE
PRINT *,''
PRINT *,'WHAT DETECTION BANDWIDTH TO USE?'
READ (1,*)BDW
COMTAG=' BWI'
CALL FCOMREAL(COMTAG,BDW, 1000)
BDW=BWIDTH
PRINT *,'WHAT EXCITATION BANDWIDTH TO USE FOR MOD.?'
PRINT *,'RECALL SWIFT BOX IS LIMITED TO CERTAIN VAL.'
READ (1,*)XBWI
PRINT *,'
PRINT *,'NAME OF EXPERIMENTAL SEQUENCE (INCLUDE \\)?'
READ (1,110)EXPER

C ASK USER IF INFO IS CORRECT.
PRINT *,''
PRINT *,''
PRINT *,'
PRINT *, 'IS THE FOLLOWING CORRECT?'
PRINT *, 'SWIFT FILENAME = ', LONAME
PRINT *, '# OF WAVEFORMS = ', N
PRINT *, 'ATTENUATION = ', ATN
PRINT *, 'DELAY TIME = ', E
PRINT *, 'REACTION TIME = ', RXN
PRINT *, 'SWEEPS = ', B
PRINT *, 'VBM = ', BM
PRINT *, 'BEM = ', BE
PRINT *, 'BANDWIDTH (DET) = ', BDW
PRINT *, 'BANDWIDTH (EXC) = ', XBW1
PRINT *, 'EXPERIMENT = ', EXPER
CALL YESNO(ANSWER)
IF(.NOT. ANSWER) GOTO 100
COMTAG = 'FNL'
CALL FCOMSTR(COMTAG, LONAME, 1000)
PRINT *, 'LOADING INFORMATION RECEIVED.'

C ************************************************************
C INPUT STORING INFORMATION
C ************************************************************
120   PRINT *
PRINT *
PRINT *
   PRINT *, 'STORE INFORMATION.'
PRINT *
PRINT *
PRINT *, 'WHAT FILENAME TO SAVE SPECTRA AS?'
C PRINT *, '7 LETTERS MAX FOLLOWED BY A "\".'
PRINT *
READ(1,110) STNAME
PRINT *
PRINT *
PRINT *
PRINT *
   PRINT *, 'IS THE FILENAME', STNAME, 'CORRECT?'
CALL YESNO(ANSWER)
IF(.NOT. ANSWER) GOTO 120
PRINT *, 'STORING INFORMATION RECEIVED.'
C DATA SAVING REQUESTED BY S. GUAN
   OPEN(9, FILE = STNAME)
   D = 1
C SET LOADING FILE EXTENSION TO 1.
   COMTAG = 'FXL'
   CALL FCOMINT(COMTAG, D, 1000)
PRINT *
PRINT *
PRINT *,'*****************************************
PRINT ',:THANK YOU.'
PRINT ','TWO DIMENSIONAL FTICR PROGRAM INITIATED.'
PRINT *,:'*****************************************
PRINT '','
PRINT '','

C**********************************************************
C DO LOOP TO COLLECT SPECTRUM, STORE IT, AND INCREMENT
C EXTENSION.
   DO 20 I=1,N
      COMTAG='ALO'
      CALL FCOMM(COMTAG,1000)
   C**********************************************************
C INSERT HERE THE ABILITY TO RUN LSI AND LCV (SWIFT
C FUNCTIONS) TO LOAD THE SWIFT WAVEFORM INTO THE SWIFT
C BOX THE KEY IS TO INPUT THE REQUESTED
C INFORMATION (NUMBER OF EVENTS, TYPE OF
C WAVEFORM, STARTING ADDRESS, ETC.) THIS IS ACCOMPLISHED
C BY MAKING THE SWIFT COMMANDS AS SUBROUTINES.
C**********************************************************

C SET EXCITATION BANDWIDTH.
   COMTAG='BWI'
   CALL FCOMREAL(COMTAG,XBWI,1000)

C DOWNLOAD SWIFT FILE TO SWIFT BOX.
   PRINT *,:'INTO LSISUB'
   CALL LSISUB
   PRINT *,:'INTO LCVSUB'
   CALL LCVSUB

C**********************************************************
C SET OTHER PARAMETERS VIA EXTREL CALLS.
   QNT=0.040
   COMTAG='QNC'
   CALL FCOMREAL(COMTAG,QNT,1000)
   COMTAG='EXP'
   CALL FCOMSTR(COMTAG,EXPER,1000)
   COMTAG='BEM'
   CALL FCOMREAL(COMTAG,BE,1000)
   COMTAG='VBM'
   CALL FCOMREAL(COMTAG,BM,1000)
   COMTAG='NSW'

C**********************************************************
CALL FCOMINT(COMTAG,B,1000)
COMTAG='DLE'
CALL FCOMREAL(COMTAG,RXN,1000)
COMTAG='BWI'
CALL FCOMREAL(COMTAG,BDW,1000)
COMTAG='DLr'
CALL FCOMREAL(COMTAG,E,1000)
COMTAG='ZER'
CALL FCOMM(COMTAG,1000)
COMTAG='RUN'
CALL FCOMM(COMTAG,1000)
COMTAG='WAI'
CALL FCOMM(COMTAG,1000)

C WRITE TRANSIENT DATA TO FILE.
WRITE(9) NDP
WRITE(9) SDATA

C INCREMENT LOADING EXTENSION.
COMTAG='IXL'
CALL FCOMM(COMTAG,1000)
PRINT *,
PRINT *,'COMPLETION OF WAVEFORM','I
PRINT *','
20 CONTINUE
CLOSE (9)
PRINT *','
PRINT *','
PRINT *,DATA HAS BEEN COLLECTED,'
PRINT *','
PRINT *','

C *************************************************
C INQUIRE IF PROGRAM SHOULD BE RERUN.
PRINT *,ACQUIRE WITH SAME SWIFT WAVEFORMS?
CALL YESNO(ANSWER)
IF(ANSWER)GOTO120
PRINT *','
PRINT *,RERUN WITH NEW SWIFT WAVEFORMS?
CALL YESNO(ANSWER)
IF(ANSWER)GOTO100
PRINT *','
PRINT *','
PRINT *,2DFTICR ACQUISITION COMPLETE. THANK YOU.'
GOTO 1050
1000 PRINT *,ERROR. PROGRAM ABORTED.'
1050 CALL EXIT
C PROGRAM FOR 2D DATA TRANSFER.
C FROM 1280 COMPUTER TO A PC VIA PRINTER PORT.
C DATA TRANSFER IN 4K BLOCKS
C 1/20/1992. BY SHENHENG GUAN.

INTEGER SDATA,HNDP,NP
CHARACTER*80 FILENAME
COMMON /SDATA/ SDATA(4096)
COMMON /DEFSIZ/ NDP

C
C A .ABSADD PNTF 645037
A .ABSADD RISH8 716010
A .ABSADD OUTP 621033

CONTINUE

C THIS CONTINUE HAS TO BE THERE FOR PROG. TO WORK.

PRINT *, 'INPUT NO. OF BLOCKS (4K) TO BE
TRANSFERED'
READ *, NP
PRINT *, 'INPUT 1280 2D DATA FILE NAME'
READ(*,30) FILENAME
30 FORMAT(A80)
OPEN(11,FILE=FILENAME,STATUS='OLD')
NDP=4096

C LOOP TO GET DATA AND SHOOT TO PRINTER.
DO 40 I=1,NP
READ(11) SDATA
PRINT *, I
PRINT *, 'BLOCK TO BE TRANSFERED'
C
CONTINUE

C GET ADDRESS AND SET COUNTERS.
A MEMA &SDATA /GET ADDRESS OF SDATA ARRAY
A ACCM TEMP /PUT IT IN TEMP
A MEMA NDP /GET NDP
A ACCM ICTR /PUT IT IN COUNTER ICTR
A JMS SUBP /SEND NP TO THE PRINTER
A RISH8
A JM S SUBP
A RISH8
A JM S SUBP
C
C LOOP TO OUTPUT DATA THROUGH PRINTER PORT.

A LOOP, MEMA @ TEMP /GET YOUR DATA.
A JMS SUBP /PUT 8 LOWEST BITS OUT
C /TO PRINTER PORT
A RISH8 /RIGHT SHIFT 8 TIMES
A JMS SUBP /"PRINT" AGAIN
A RISH8 /RIGHT SHIFT 8 TIMES
A JMS SUBP /"PRINT" AGAIN
A MPOM TEMP /INCREASE TEMP BY ONE,
C /BUMP TO NEXT WORD
A MMOMZ ICTR /DECREASE ICTR BY ONE,
C /SKIP IF ZERO
A JMP LOOP /DO SOME MORE
A JMP DONE /FINISHED BLOCK TRANSFER,
C /GET OUT NOW.
C

A ICTR, 0
A TEMP, 101
A ICTC, 0
A EIGHT, 10
C
C SUBPROGRAM TO SHOOT DATA TO PRINTER.
A SUBP, 0
A OUTP /SHOOT IT TO PRINTER, DONOT WAIT.

C SUBPROGRAM CHECK FOR PRINTER OKAY.
A SUB1, PNTF /SKIP IF PRINTER ACKNOWLEDGED ALREADY.
A JMP SUB1 /GO BACK TO CHECK AGAIN
A JMP @ SUBP /RETURN FROM SUBROUTINE SUBP
C
A DONE, MEMA ICTR /FAKE COMMAND, USE FOR DESTINATION
C
CONTINUE
40 CONTINUE
C
CLOSE(11)
END
PROGRAM SWG
C
******************************************************************************
C AUTHOR: CHARLES W. ROSS III
C ALL RIGHTS RESERVED
C******************************************************************************
C SWG IS A MODIFICATION TO THE SFG(SWIFT FUNCTION
C GENERATOR) PROGRAM. SWG(SMOKE-{STORED WAVEFORM
C MODULATION OF KINETIC ENERGY} WAVEFORM GENERATOR)
C GENERATES SWIFT WAVEFORMS THAT MODULATE THE IONS
C KINETIC ENERGY.
C
C******************************************************************************

LOGICAL ANSWER
  CHARACTER STNAME*8,COMTAG*3
  REAL PI,BETA,EKMAX,EKMIN,RMAX,RMIN,RFRAC
  REAL ARG,ARG1,ARG2
  INTEGER KSPECT,X1,Y1,D,Z,Z1,INDEX1
  INTEGER NDP,K,N,I,MAX,MIN,TEMPD(4096)
  REAL LOFREQ,X,Y,SPACE,HI,LO,T,Q,B,VPP,DIAM,DELTA,EFRAC
  INTEGER SDATA(65535),ZFILL
  COMMON /ZFILL/ZFILL
  COMMON /SDATA/SDATA
  COMMON /NTP/NTP
  COMMON /LOFREQ/LOFREQ
  COMMON /HIFREQ/HIFREQ
  COMMON /BWIDTH/BWIDTH
  COMMON /HZPPT/HZPPT
  COMMON /DEFSIZ/NDP
  COMMON /KSPECT/KSPECT
  PI=3.1415927
  BETA=0.72167
  Q=1.602E-19
  B=3.00000
  VPP=110
  DIAM=0.047625
  MAX=0
  MIN=0
C******************************************************************************
C VARIABLE NAME TABLE
C
C ANSWER - LOGICAL VARIABLE FOR QUESTIONS
C BETA - CUBIC CELL PARAMETER
C EKMAX - KINETIC ENERGY MAXIMUM BASED ON LO FREQ.
C VALUE
C EKMIN - KINETIC ENERGY MINIMUM USER INPUT
C RMAX - MAXIMUM RADIUS FOR LO FREQ. TO GET EKMAX
C RMIN - MINIMUM RADIUS FOR LO FREQ. TO GET EKMIN
C EFRAC - RATIO OF EKMIN:EKMAX
C RFRA# - SQUARE ROOT OF EFRAC
C ARG# - SEPARATE SECTIONS OF THE SMOKE EQUATION
C LO - LO FREQ. TO BE MODULATED
C HI - HI FREQ. TO BE MODULATED
C B - MAGNETIC FIELD STRENGTH
C Q - ELECTROSTATIC CHARGE CONSTANT
C T - TIME OF SWIFT EXCITATION PULSE
C VPP - MAXIMUM PEAK TO PEAK VOLTAGE OUTPUT OF INSTRUMENT
C DIAM - TRAP DIMENSION. LENGTH OF A SIDE.
C DELTA - FREQ DIFFERENCE OF HI AND LO
C PI - MATHEMATICAL CONSTANT
C MAX - MAXIMUM VALUE OF TIME DOMAIN WAVEFORM USED LATER IN THE NORMALIZATION PROGRAM NN1
C MIN - MINIMUM VALUE OF TIME DOMAIN WAVEFORM
C SPACE - FREQUENCY DOMAIN POINT SPACING CALC BY PROG.
C HZPPT - HERTZ PER POINT SPACING CALC. BY FTMS.
C SDATA - ARRAY WHERE FUNCTION IS KEPT
C TEMPD - TEMP ARRAY TO DISPLAY FUNCTION WITHOUT NORM.
C

C GET BASIC INFORMATION FROM USER
PRINT *. '**************************************************'
PRINT *, 'SWIFT SMOKE(KINETIC ENERGY)WAVEFORM GENERATOR'
PRINT *. '**************************************************'
PRINT *, 'HOW MANY WAVEFORMS DO YOU NEED?'
READ (1,*) N
20 PRINT *, '
PRINT *, 'ENTER THE NDP VALUE IN K UNITS FOR SWIFT.'
READ (1,*) K
NDP=K*1024
ZFILL=1
NTP=NDP/2
PRINT *, '
PRINT *, 'ENTER THE SWIFT FREQUENCY BANDWIDTH (HZ).'</PRINT *, '(NOTE: VALUES OF 2.666, 2.000, 1.000 MHZ ETC.)'
READ (1,*) BWIDTH
PRINT *, '
PRINT *, 'ENTER THE LOFREQ VALUE.'
READ (1,*) LO
PRINT *, '
PRINT *, 'ENTER THE HIFREQ VALUE.'
C CALCULATE MAXIMUM RADIUS AND MAXIMUM KINETIC ENERGY FOR GIVEN VALUES.
DELTA=HI-LO
T=NDP/(2*BWIDTH)
RMAX=((BETA*VPP)/(2*B*DIAM))*((0.75*T/DELTA)**0.5)
EKMAX=0.5*B*LO*[2*PI]*(RMAX**2)
PRINT *, 'THE MAXIMUM RADIUS IS', RMAX
PRINT *, 'AND THE MAX. KINETIC ENERGY IS', EKMAX
PRINT *, 'THE RADIUS CAN BE INCREASED BY INC. NDP OR'
PRINT *, 'DECREASING THE BANDWIDTH, AND THE KINETIC'
PRINT *, 'ENERGY CAN BE INCREASED BY INCREASING THE'
PRINT *, 'LOFREQ VALUE.'
PRINT *, 'DO YOU WISH TO CONTINUE? Y/N'
CALL YESNO(ANSWER)
IF(.NOT.ANSWER)GOTO20
PRINT *, ''
PRINT *, 'WHAT KIN. ENERGY (EV) MINIMUM WOULD YOU LIKE?'
READ (1,*) EKMIN
EFRAC=EKMIN/EKMAX
RFRAC=(EFRAC)**0.5
PRINT *, 'ENERGY FRACTION IS', EFRAC
PRINT *, 'RADIUS FRACTION FOR LO FREQ IS', RFRAC
KSPECT=1
CALL RSETUP(200)
PRINT *, 'WHAT FILENAME TO STORE WAVEFORMS AS?'
PRINT *, '7 LETTERS MAXIMUM FOLLOWED BY "".'
C BACKSLASH REQUIRED AS A TERMINATOR IN FCOMSTR
C SUBROUTINE CALLED TO PUT NAME INTO FNS.
110 FORMAT (A)
READ (1,110)STNAME
COMTAG='FNS'
CALL FCOMSTR(COMTAG,STNAME,1000)
D=1
COMTAG='FXS'
CALL FCOMINT(COMTAG,D,1000)
OPEN(9,FILE='NUMBER')

C CALCULATE FREQUENCY DOMAIN POINT SPACING
SPACE=BWIDTH/NTP
PRINT *, 'SPACE =', SPACE
PRINT *, 'HZPPT =', HZPPT
PRINT *, 'SET HZPPT=SPACE?'
CALL YESNO(ANSWER)
IF(.NOT.ANSWER)GOTO45  
HZPPT=SPACE

C CALCULATE THE LAST DATA POINT THAT NEEDS TO BE ZEROED  
C IN THE FIRST SECTION, X1.  
45   X=(BWIDTH-HI)/SPACE  
     X1=INT(X)-1
C CALCULATE THE FIRST DATA POINT THAT NEEDS TO BE ZEROED  
C IN THE SECOND SECTION, Y1.  
     Y=(BWIDTH-LO)/SPACE  
     Y1=INT(Y)+1

C LOOP 60 FOR NUMBER OF WAVEFORMS REQUESTED.  
    DO 60 I=1,N  
    KSPECT=1  

C LOOP 65 ZEROES ALL OF SDATA.  
    DO 65 Z=1,NDP  
        SDATA(Z)=0  
        TEMPD(Z)=0  
    65 CONTINUE

C LOOP 70 CALCULATES THE AMPLITUDE OF THE SDATA POINT IN  
C THE FREQUENCY RANGE OF INTEREST.  
    DO 70 INDEX=X1+1,Y1-1  
    FREQ=BWIDTH-INDEX*SPACE  
        ARG=I*(PI*(FREQ-LO)/(HI-LO))-(PI/2)  
        ARG1=((SIN(ARG)+1)/2)*(1-EFRAC)+EFRAC  
        ARG2=(ARG1*EKMAX)/(B*PI*FREQ*RMAX)  
        SDATA(INDEX)=ARG2*500000  
        TEMPD(INDEX)=SDATA(INDEX)  
    70 CONTINUE

C CALL FCOMNO('NMX',1000)  
    DO 80 INDEX1=1,NDP,1  
        SDATA(INDEX1)=TEMPD(INDEX1)  
    80 CONTINUE

C INSERTIONS OF SWIFT CALLS HERE:  
    CALL QPMSUB  
    CALL FCOMNO('INV',1000)  
    CALL SH1SUB
C LOOP 90 GETS MAX AND MIN VALUE FOR ALL WAVEFORMS FOR
C USE LATER IN NORMALIZATION PROGRAM NN1.
   DO 90 INDEX1=1,NDP
      IF (SDATA(INDEX1).GT.MAX) THEN
         MAX=SDATA(INDEX1)
      ENDIF
      IF (SDATA(INDEX1).LT.MIN) THEN
         MIN=SDATA(INDEX1)
      ENDIF
   90 CONTINUE
C STORE WAVEFORM AND WRITE OUT VALUES FOR MIN AND MAX.
   COMTAG='AST'
   CALL FCOMM(COMTAG,1000)
   COMTAG='IXS'
   CALL RDEFINE(200)
   CALL FCOMM(COMTAG,1000)
   PRINT *, 'COMPLETION OF WAVEFORM',I
   PRINT *, 'MIN =',MIN
   PRINT *, 'MAX =',MAX
   WRITE (9) I,MAX,MIN
   60 CONTINUE
   CLOSE (9)
   PRINT *, 'SPACE =',SPACE
   PRINT *, 'HZPPT= ',HZPPT
   PRINT *, 'DONE.'
   GOTO 300
200 PRINT *, 'ERROR IN SUBROUTINE RSETUP OR RDEFINE.'
1000 PRINT *, 'ERROR. PROGRAM ABORTED.'
300 CALL EXIT
STOP
END
LIST OF REFERENCES


Williams, E. R.; McLafferty, F. W., Unpublished results.


