A PERSONAL SCIENTIFIC HISTORY

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Received 1 April 2019; revised 24 September 2020; accepted 30 September 2020

Published online 23 October 2020 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/mas.21666

I. INTRODUCTION

This issue of *Mass Spectrometry Reviews* is a celebration of Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS). I begin by thanking the guest editor, Dr. Shenheng Guan. Because I have reviewed the technical aspects of FT-ICR MS extensively elsewhere (Marshall, 1978, 1982, 1985; Marshall & Grosshans, 1991; Marshall & Schweikhard, 1992; Schweikhard & Marshall, 1993; Guan et al., 1994; Guan & Marshall, 1995, 1996; Bowers, Marshall, & McLafferty, 1996; Marshall & Guan 1996; Marshall, Hendrickson, & Jackson, 1998; Marshall & Hendrickson, 2002; Marshall, Hendrickson, & Shi, 2002; Marshall & Rodgers, 2004; Cooper, Håkansson, & Marshall, 2005; Rodgers, Schaub, & Marshall, 2005; Rodgers & Marshall, 2006; Marshall & Hendrickson, 2008; Marshall & Rodgers, 2008; Marshall & Hendrickson, 2008; Xian, Hendrickson, & Marshall, 2012) this brief article focuses on my personal scientific history leading up to the coinvention and continuing development of FT-ICR MS techniques and applications. As for many scientific developments, many of the elements were conceived by analogy to prior ideas from other fields, notably Fourier transform nuclear magnetic resonance (FT-NMR) spectroscopy. The main message, therefore, is that it is important to continuously broaden one's scientific range, because one never knows where the next idea will originate.

II. PREHISTORY

From my earliest memories, I was always interested in science. At age 7, my Grandma Minnie used to send me out into her yard with a small horseshoe magnet, which I would drag through the dirt and collect the adherent iron filings (to intensify the blue color of her hydrangeas). I loved puzzles of all kinds, and took my first science course in eighth grade, right about the time that Russia launched the first Sputnik satellite. That event triggered an explosion in interest and federal funding for science: for example, there were more new Ph.D.'s in Chemistry in 1969 (the year I completed my own Ph.D.) than for the next 30 years.

III. NORTHWESTERN UNIVERSITY (1961–1965)

In high school, I took biology, chemistry, and physics, and math up through first-year calculus. I applied for, and was admitted to Northwestern University's inaugural 6-year medical program class, which was to consist of 2 years undergraduate, followed by 4 years of medical school, and end up with M.D. and Ph.D. degrees in 8–9 years. I completed the two undergraduate years and the first year of medical school. However, although I liked (and continue to like) medical science, I hated medical school, because it was too much memorization. One day in histology lab, I couldn't tell the difference between tissue sections of thymus and pancreas. I asked the T.A., and he said, "Thymus is more purple." I said, "Maybe they used more dye that day," and he repeated, "Thymus is more purple." That day I decided not to continue in medical school, and that meant that the only B.A. degree I could complete in the remaining fourth year was Chemistry, so that's how I became a chemist. The year 1965 was doubly meaningful, because I graduated from college, and was married the next day to Marilyn, my wife of 53 years.

IV. STANFORD UNIVERSITY (1965–1969)

Moving on to graduate school at Stanford University, I joined the research group of John Baldeschwieler, who had just moved there

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from Harvard. He proposed Ph.D. projects in both NMR and with the first commercial ICR instrument. Wobschall at Cornell had introduced an ICR-based "omegatron" in the early 1960's for study of gas-phase ion-molecule reaction pathways. Ions of a given mass-to-charge ratio (*m/z*) were resonantly excited with a linearly-polarized electric field, by applying a radiofrequency (rf) electric field between two opposed plates. The linearly-polarized field can be thought of as the sum of two counter-rotating fields, one of which rotates in the same sense as the ions and the other has no effect—the first of several parallels to NMR. The ions then spiraled outward until they struck a detector electrode. Shortly thereafter, Varian introduced power absorption-based detection with a marginal oscillator—another parallel to NMR. And, as in early NMR experiments, ions of different *m/z* were detected sequentially at fixed detection frequency by scanning the applied magnetic field of an electromagnet.

For my first 3 years at Stanford, I pursued an NMR project that turned out to be less than exciting. Therefore, I looked for other related projects, and was able to transfer my NMR knowledge to related relaxation problems in depolarized light scattering and perturbed angular correlations of gamma rays (like fluorescence depolarization except that both photons come from the sample rather than one from outside). I also learned about dielectric relaxation, notably a 1941 paper by Cole and Cole (the most highly cited in its field), in which they introduced a plot of in-phase versus 90° out-of-phase dielectric constant. For a system with a single dielectric constant, the plot yielded a semicircle, whereas if there was a distribution in dielectric constants, the data points fell inside that semicircle. I realized that the same idea should hold for spectroscopy, by plotting dispersion versus absorption (see below), to yield a complete "DISPA" circle. In that case, a distribution in resonant frequencies displaced the data points outside the circle, whereas mis-phasing by φ radians simply rotated the circle by φ radians. Later on, we used the DISPA plot as the first general way to phase FT-ICR spectra. In my fourth and final year, I switched to ICR, beginning with theory to extract ion-molecule reaction rate constants from ICR spectra. During that year, Melvin Comisarow joined Baldeschwieler's group as a postdoc in ICR. We each built a Heathkit color TV (when they were about half the cost of a fully assembled set), and discussed ICR spectral peak shape, but didn't formally collaborate.

V. UNIVERSITY OF BRITISH COLUMBIA (1969–1980)

In 1969, I accepted an Instructor II position in Chemistry at the University of British Columbia (U.B.C.) for two reasons: (a) it was my only faculty offer (mainly due to not having postdoc'd first); (b) it was relatively easy to obtain initial research funding. (The Canadian National Research Council (N.R.C.) awarded about the same total dollars per capita as the USA's National Science Foundation, but distributed the money to five times as many investigators per capita); and (c) my initial research was mostly theoretical, so I didn't need much funding. U.B.C. gave me $3 K as first-year start-up support, and my first N.R.C. grant the next year was $4.5 K/year. For the next 4 years, I pursued NMR relaxation theory and experimental projects. NMR relaxation rates derive from the spectrum of random noise. The noise has a time-average value of zero, so one needs to obtain the frequency spectrum of the *square* of the noise, which is obtained from the Fourier transform of the time-domain "correlation function." By this time, U.B.C. had obtained its first Fourier transform NMR spectrometer (Richard Ernst at Varian had introduced FT-NMR in 1966), so it was easy to adapt what I had learned about FT of noise to FT of a time-domain signal.

Meanwhile, Mel Comisarow joined me on the U.B.C. faculty in 1971, and by 1973 had built a conventional magnetic field-sweep scanning ICR spectrometer. In mid-1973, during one of our daily after-lunch strolls around the campus, I asked him why no one had applied FT data reduction to ICR. Eventually, I was able to convince him to reconfigure his instrument into fixed-field operation, with pulsed single-frequency excitation followed by digitization of the resulting time-domain signal, and then FT to yield a frequency-domain spectrum that could be converted to an *m/z* spectrum. The result would be to obtain a mass spectrum in ~1 sec rather than ~30 min with the field-scanning instrument, because all of the ICR frequencies could be obtained simultaneously rather than one at a time. The immediate problem was that we didn't have enough funds to acquire the requisite digitizer. Fortunately, we were able to borrow a 1024-point digitizer from our U.B.C. colleague, Chris Brion. However, it reported the data in conventional base-10 format, so Mel would read out the data points one at a time; I recorded them, and then manually converted each one to base-8, because that was the only format that the Departmental FT-NMR computer would accept. I then entered the 1024 base-8 numbers onto paper tape, fed it into the NMR computer, and finally obtained our first FT-ICR spectrum on 17 December, 1973.

We submitted our first result to the *International Journal of Mass Spectrometry and Ion Physics*, and it was promptly rejected, mainly because the spectrum showed only one peak (for CH_4^+). However, the mass resolving power was already ~100× higher than for a scanning instrument, because, as we soon realized, the scanning instrument measures power absorption as the ion spirals outward, whereas with FT operation, the ions are excited and detected afterward (at constant ICR orbital radius), so the inherent cyclotron rotation effectively averages away inhomogeneities in the applied magnetic field (analogous to physically spinning the sample in NMR). In any case, we prevailed upon the U.B.C. Chemistry Department Head, Charles McDowell, who was then a member of the Editorial Board of *Chemical Physics Letters*, to oversee our subsequently successful submission to that journal.

An immediate experimental problem was that although ^{1}H NMR frequency at the time was ~100 MHz, the spectral range was only ~1000 Hz, which could be spanned by single-frequency excitation for a few microseconds. Although ICR frequencies are much lower in frequency (kHz to MHz), one has to cover that entire spectral range, which was not feasible by single-frequency pulsed excitation. My next idea was "correlation spectroscopy," in which one scanned the excitation frequency while simultaneously detecting (analogous to NMR crossed-coil excitation/detection). That method was later pursued briefly by another Baldeschwieler graduate, Robert McIver, at U. California Irvine. In the end, we decided to employ the same temporally separated excitation and detection as in our original single-frequency pulsed excitation, but with a short frequency-sweep excitation pulse.

From the outset, I knew that Fourier transformation of a time-domain signal produces two spectra, which (after appropriate phase correction) become "absorption" and "dispersion" spectra, $A(\omega)$ and $D(\omega)$. In the absence of phase correction, only the "magnitude" spectrum, $M(\omega) = [(A(\omega))^2 + (D(\omega)))^2)^{1/2}$ is available. Although mass resolving power is up to twice as high for $A(\omega)$ as for $M(\omega)$, it took about another 35 years for my group to successfully phase-correct a broadband FT-ICR spectrum.

From 1973 to 1980, Comisarow and I coauthored eight publications introducing FT-ICR MS to the mass spectrometry community. I solved for the FT-ICR mass spectral peak shape, first for an undamped time-domain signal and then for partially and fully damped signal. Meantime, I continued with biochemical applications of NMR, and also spent a year writing a monograph, *Biophysical Chemistry* (Marshall, 1978).

VI. THE OHIO STATE UNIVERSITY (1980–1993)

By 1980, my Canadian research funding had peaked (at $25 K/year). Moreover, although I hadn't moved to Canada to escape the Vietnam draft, many U.B.C. graduate students from the United States had done so. As a result, when the Vietnam war ended, those graduate students disappeared, and, as a nominally "physical" chemist, I could anticipate one new graduate student every 17 years. Therefore, in 1980, I moved to Ohio State University, as professor and inaugural director of their first campus-wide NMR and MS Facility. My research was now listed as "analytical" rather than "physical," so my research group rapidly grew to about a dozen Ph.D. students. However, I had to start over from zero for federal research funding. My first grant (from NIH) was to continue our use of NMR to map the base-stacking patterns in ribosomal RNAs. My first NSF grant for ICR in 1983 enabled me to purchase a commercial 3 T FT-ICR instrument. Over the next several years, we extended FT-ICR theory and instrumentation. For example, I learned from Wolfgang Paul that the optimal "trapping" electric potential should be quadrupolar (most directly generated by use of hyperbolic-shaped electrodes). Fortunately, Peter Grosshans in my group showed that the potential near the center of an orthorhombic or cylindrical trap approaches the ideal qauadrupolar limit—that's why our early FT-ICR experiments with a simple cubic trap worked so well. Similarly, it turned out that the excitation potential for flat or cylindrical electrodes approaches the ideal dipolar potential near the center of the trap. Next, by analogy to a prior NMR development, I introduced stored waveform inverse Fourier transform (SWIFT) excitation (my second most-cited paper, after the original FT-ICR paper). One simply specifies a desired *m/z* domain (and thus frequency-domain) excitation spectrum, for which inverse FT produces the corresponding time-domain waveform to yield that spectrum. SWIFT provides theoretically optimal linearity and selectivity for FT-ICR MS, and has been extended to other types of mass analyzers as well.

At this stage, it is important to note that ICR MS (and early FT-ICR MS) was uniquely suited for determination of ion-molecule reaction pathways, kinetics, equilibria, and energetics of ions formed *inside* the ICR detection "cell," and was therefore limited to volatile analytes. We therefore applied pulsed laser desorption of a solid sample placed just outside the ICR cell, so that ions could be trapped, excited, and detected in the cell. The experiment attracted the first of many external collaborators with applications to carbohydrates, drugs, polymers, etc. In the late 1980's, I abandoned FT-NMR, in order to focus exclusively on FT-ICR MS.

VII. NATIONAL HIGH MAGNETIC FIELD LABORATORY/FLORIDA STATE UNIVERSITY (1993-PRESENT)

A. Instrumentation

When I learned that the National High Magnetic Field Laboratory (NHMFL) had moved from M.I.T. to Tallahassee in 1990, I contacted John Eyler at U. Florida, and we approached the new MagLab Director, Jack Crow, to explore the possibility of high-field magnets for FT-ICR MS. As detailed in Eyler's article in this issue, we held a workshop to define major thrust areas for high-field FT-ICR MS applications, and approached several federal agencies for support without success, mainly because there was no category to fit such a facility. Then, in 1993, Argonne National Laboratory approached NSF to fund a new synchrotron beam line (~$1 M/year). NSF responded by creating a new "Chemical Instrumentation Facility" category (up to $1 M/year), and that's when I decided to move to Florida State University and apply for NSF support for an FT-ICR MS User Facility. The premise was that, unlike traditional user facilities, which were funded for new instrumentation only in the first year of a grant, we proposed continuing instrumentation development, so that our Facility would maintain world-leading capability continuously. In the end, Argonne asked for $3 M/year, and was eliminated after the first round of review, and the other finalists were M.I.T., U. California Berkeley, and Yale U. (each of whom sought to acquire 750 MHz ^{1}H NMR capability at a time when the highest-field commercial NMR was at 600 MHz). In contrast, we proposed to advance from then-available 7 T to a 9.4 T magnetic field for FT-ICR MS. We were initially funded for $1 M/year for 5 years, and have been renewed continuously since then. A primary theme of the NHMFL ICR Program has been to develop new instrumentation and apply it to chemical and biological projects with external users of the Facility.

Because our FT-ICR spectrometers are custom-built, we can quickly repair any component failures. Moreover, when any new technique appears, whether originated in our laboratory or elsewhere, we can implement it immediately, whereas others must wait, typically a couple of years or more, until the technique is available commercially. As a result, in 2019, we served more than 300 external users from 80 research groups, nationally and internationally. Shenheng Guan, who joined my group at Ohio State in 1991, agreed to join me at NHMFL as ICR Associate Director and Director of ICR Instrumentation. He oversaw the construction of our first FT-ICR instrument, for which the State of Florida contributed $500 K to purchase an Oxford 9.4 T superconducting magnet. Our first NHMFL postdoc Ljiljana Paša-Tolić, a theoretician from Croatia, was tasked with mastering AutoCad programming for the mechanical schematics of the instrument, and interfacing a matrix-assisted laser desorption/ionization (MALDI) ion source. This first magnet was passively shielded in a 12-ton iron housing—with the added benefit of very good magnetic field homogeneity, because the field lines had to pass through the shield, which was flat. Guan designed our first (octopole) ion guide for external ion injection. Postdoc Michael Senko developed our first computerized data acquisition system and introduced

external ion accumulation, thereby enabling continuous accumulation of ions followed by pulsed injection into the ICR cell. Postdoc Chris Hendrickson joined Senko and Pasa-Tolic to implement external MALDI and electrospray ionization (ESI) sources. Postdoc Mark Emmett brought microelectrospray capability and became our first Biological Applications Director. Chris Hendrickson replaced Guan following Guan's departure to Symyx Technologies, Santa Clara, California in 1996, and has remained with the Program ever since. In 2014, Chris assumed the position of Director of the ICR Program, while I remain as Chief Scientist.

One of our most successful collaborations was a joint effort with John Eyler to interface an FT-ICR mass analyzer with a free electron laser in The Netherlands. Since 2005, that instrument has generated more than 250 journal publications, including our achievement of the first mid-infrared spectrum of a gas-phase protein (cytochrome *c*). We observed multiple long-lived conformations and confirmed the presence of the amide II vibrational mode that is characteristic of protein solution-phase secondary structure. We also interfaced other ionization sources, notably atmospheric pressure photoionization and atmospheric pressure chemical ionization. The former proved especially valuable for accessing polycyclic aromatic hydrocarbons (which are not observable by ESI) in petroleum and its products. In another direction, we showed that the cyclotron rotation of trapped gas-phase electrons in a magnetic field self-cools the electrons in about 1 sec at 7 T, enabling their attachment to fullerenes to form gas-phase anions.

A mainstay of the NHMFL ICR Program has been MS/MS, with external collision-induced dissociation (CID), electron capture dissociation (ECD) and electron transfer dissociation (ETD), and internal infrared multiphoton dissociation (IRMPD) and ultraviolet (UV) photodissociation (UVPD). Of these ETD has proved particularly useful in achieving extensive amino acid sequence coverage for electrosprayed proteins up to 80 kDa in molecular weight. We collaborated with a consortium in the first paper defining the "proteoform" (i.e., a particular combination of mutations and posttranslational modifications) (Smith et al., 2013) Our most recent proteomics applications have been clinical collaborations: identifying mutations in human hemoglobin variants (He et al., 2019a) and identifying proteoforms in plasma cell disorders (e.g., multiple myeloma) (He et al., 2019b).

For the past two decades, our consultant, Steven Beu, has employed SIMION to simulate ion trajectories during external injection as well as subsequent ICR excitation and detection. Those results have been invaluable in guiding our developments of ion optics, ICR cell design, and signal analysis.

The crowning achievement of the NHMFL ICR Program is the current 21 T (highest magnetic field in world for ICR) FT-ICR mass spectrometer, which incorporates all of our prior instrumentation developments (Hendrickson et al., 2015). Chris Hendrickson was the lead designer for the project, and continues to oversee maintenance and installation of new capabilities.

VIII. NATIONAL HIGH MAGNETIC FIELD LABORATORY/FLORIDA STATE UNIVERSITY (1993-PRESENT)

A. Applications

At first, we published a number of MALDI and ESI applications to individual peptides and carbohydrates, but soon turned to complex mixtures, starting with humic acids and petroleum crude oil. This research area was pioneered by Ryan Rodgers, first as an FSU Ph.D. student and subsequently as an NHMFL research faculty member. Although we chose the mixtures mainly because they were compositionally complex, with thousands of different molecular elemental formulas, we soon found that we could identify the chemical nature of deposits in oil production and refining *before* the deposits formed, thereby enabling oil companies to inject the appropriate detergent to prevent deposit formation. Later on, we analyzed oil spills and their chemical evolution due to photo- and bio-degradation. We coined the term, "petroleomics," as the determination of petroleum properties and behavior, based on FT-ICR MS determination of their detailed molecular composition. Ultimately, we resolved and identified more than 125,000 molecular elemental compositions in a single 9.4 T FT-ICR mass spectrum (Krajewski, Rodgers, & Marshall, 2017). Crude oil refining consists of separating species according to boiling point: for example, naphtha, gasoline, kerosene, jet fuel, lube oil, etc. We were able to explain why crude oil components of the *same* molecular weight can exhibit *different* boiling points, thereby greatly improving understanding of the distillation process. Recently, we have applied what we learned about petroleum to dissolved organic matter in the environment, laying a rational basis for the carbon cycling as well as the fate of various pollutants in the "built" environment (e.g., water-soluble species produced by photooxidation of asphalt from highways).

FT-ICR MS is uniquely advantageous for mapping contact surfaces in protein complexes by H/D exchange monitored by MS, because it can access protein complexes too large for FT_NMR and/or uncrystallizable for X-ray diffraction. The experiment starts by diluting solutions of free and bound protein in excess D_2O, after which the backbone amide hydrogens begin to be replaced by deuteriums. The exchange is then quenched by lowering the pH to ~2.5, followed by rapid de-salting by liquid chromatography (LC), and weighing the various proteolytic fragments by MS. Because there is insufficient time to separate the fragments by LC (due to back-exchange of D to H), it is necessary to simultaneously resolve and identify dozens or hundreds of fragments, requiring ultrahigh mass resolving power. Protein segments at the binding interface can be recognized by reduced solvent access (and thus less deuterium uptake). As examples, we applied the method to (a) elucidate the structure of the HIV protein "capsid" that envelopes and protects the viral RNA, (b) reveal the mechanism of binding of double-stranded RNA to a bacteriophage, and (c) determine the inter-subunit structure in the largest protein complex analyzed by H/D exchange to date (CopII, 7.7 MDa).

^{13}C and ^{15}N NMR of proteins is difficult, due to the low natural abundance of ^{13}C (~1%) and ^{15}N (~0.4%). Therefore, for prokaryotic protein NMR, it is advantageous to grow bacteria in a medium containing glucose *enriched* in ^{13}C and ammonium sulfate *enriched* in ^{15}N. Conversely, mass analysis of gas-phase proteins is rendered difficult by the wide distribution of isotopologues, containing different number of ^{13}C and ^{15}N. It therefore occurred to me that prokaryotic protein MS could be simplified by growing bacteria in a medium containing glucose *depleted* in ^{13}C and ammonium sulfate *depleted* in ^{15}N. We demonstrated the effect in 1997, and are currently following up with bacterial and eukaryotic cell lysates in collaboration with Roman Zubarev.

About 10 years after I moved to FSU, Harold Kroto (Nobelist for the discovery of C_{60} (Buckminster fullerene, or

"buckyball") joined the FSU Chemistry faculty, where he spent the last 10 years of his career. As soon as C_{60} was discovered, one immediate question was, what is the smallest possible fullerene? It turns out that every fullerene must contain 12 pentagons, so the smallest possible fullerene should be C_{28}. However, it has never been observed, because it has 4 unstable carbons. Therefore, Harry theorized that C_{28} could be stabilized if one could insert a tetravalent metal ion inside it. By laser ablation of graphite coated with the appropriate metal salt we were able to observe "endohedral" $Ti@C_{28}$, $Hf@C_{28}$, and $Zr@C_{28}$. Ultrahigh mass resolution was critical, because Ti has a nominal mass of 48 Da, but so does $^{12}C_4$.

Finally, FT-ICR MS can generate 8 Mwords of data in ~3 sec. Ergo, automated data reduction is essential. For complex mixture analysis, we introduced the use of Kendrick mass (i.e., IUPAC mass of CH_2, 14.01565 Da, becomes Kendrick mass of 14.00000 Da), to make it easy to identify homologous series of molecules with the same heteroatom class, $O_oN_nS_s$, but differing degree of alkylation $(CH_2)_n$, enabling rapid automated mass calibration. That idea has since been adapted to characterizing polymers and other mixtures. We also demonstrated ~3-fold improvement in mass accuracy for directly infused samples, by selectively removing any time-domain transients that deviated by (say) 10% from the average total integrated mass spectral peak magnitudes. Furthermore, "walking" mass calibration (i.e., separate calibration for small segments of a mass spectrum) yielded another factor of ~2 in mass accuracy.

ACKNOWLEDGMENTS

My career has been built largely on collaboration: I have benefited enormously from mentoring 14 M.S., 72 Ph.D., and 79 postdocs, and have coauthored refereed journal articles with 208 other independent principal investigators. For the past 26 years, another linchpin has been continuous support for the NHMFL ICR Program from National Science Foundation Division of Chemistry (currently NSF/DMR-1644779) and the State of Florida. I need to thank the current NHMFL ICR Program permanent staff, whose invaluable ideas and efforts have built the world's leading FT-ICR MS laboratory. Research Faculty: Christopher L. Hendrickson, Director; Ryan P. Rodgers, Associate Director; Greg T. Blakney; Amy M. McKenna; Chad R Weisbrod; Lissa C. Anderson; Donald F. Smith; Martha L. Chacón-Patiño; Huan Chen; Technician: John P. Quinn; and Machinist: Daniel G. McIntosh. Finally, I acknowledge my wife, Marilyn, whose unflinching life support has enabled me to devote full time to my career.

REFERENCES

Bowers MT, Marshall AG, McLafferty FW. 1996. Mass spectrometry: Recent advances and future directions. J Phys Chem 100:12897–12910.

Cooper HJ, Håkansson K, Marshall AG. 2005. The role of electron capture dissociation in biomolecular analysis. Mass Spectrom Rev 24:201–222.

Guan S, Marshall AG. 1995. Ion traps for Fourier transform ion cyclotron resonance mass spectrometry: Principles and design of geometric and electric configurations. Int J Mass Spectrom Ion Proc 146:261–296.

Guan S, Marshall AG. 1996. Stored waveform inverse Fourier transform (SWIFT) ion excitation in trapped-ion mass spectrometry: Theory and applications. Int J Mass Spectrom Ion Proc 158:5–37.

Guan S, Kim HS, Marshall AG, Wahl MC, Wood TD, Xiang X. 1994. Shrink-wrapping an ion cloud for high performance Fourier transform ion cyclotron resonance mass spectrometry. Chem Rev 94:2161–2182.

He L, Rockwood AL, Agarwal AM, Anderson LC, Weisbrod CR, Hendrickson CL, Marshall AG. 2019a. Diagnosis of hemoglobinopathy and Thalassemia by 21 tesla Fourier transform ion cyclotron resonance mass spectrometry and tandem mass spectrometry of hemoglobin from blood. Clin Chem 65:986–994.

He L, Anderson LC, Barnidge DR, Murray DL, Dasari S, Dispenzieri A, Hendrickson CL, Marshall AG. 2019b. Classification of plasma cell disorders by 21 tesla Fourier transform ion cyclotron resonance top-down and middle-down MS/MS analysis of monoclonal immunoglobulins in human serum. Anal Chem 91:3263–3269.

Hendrickson CL, Quinn JP, Kaiser NK, Smith DF, Blakney GT, Chen T, Marshall AG, Weisbrod CR, Beu SC. 2015. 21 tesla Fourier transform ion cyclotron resonance mass spectrometer: A national resource for ultrahigh resolution mass analysis. J Am Soc Mass Spectrom 26:1626–1632.

Krajewski LC, Rodgers RP, Marshall AG. 2017. 126,264 assigned chemical formulas from an atmospheric photoionization 9.4 tesla Fourier transform positive ion cyclotron resonance mass spectrum. Anal Chem 89:11,318–11,324.

Marshall AG. 1978. Biophysical chemistry: Principles, techniques, and applications. New York: Wiley & Sons. p. 832.

Marshall AG. 1982. In: Marshall AG, editor. Advantages of transform methods in chemistry, in Fourier, Hadamard, and Hilbert transforms in chemistry. New York: Plenum. pp. 1–43.

Marshall AG. 1985. Fourier transform ion cyclotron mass spectrometry. Acc Chem Res 18:316–322.

Marshall AG, Guan S. 1996. Advantages of high magnetic field for Fourier transform ion cyclotron resonance mass spectrometry. Rapid Commun Mass Spectrom 10:1819–1823.

Marshall AG, Grosshans PB. 1991. Fourier transform ion cyclotron resonance mass spectrometry: The teenage years. Anal Chem 63:215A–229A.

Marshall AG, Hendrickson CL. 2002. Fourier transform ion cyclotron resonance detection: Principles and experimental configurations. Int J Mass Spectrom 215:59–75.

Marshall AG, Hendrickson Cl. 2008. High-resolution mass spectrometers. Ann Rev Anal Chem 1:575–599.

Marshall AG, Hendrickson CL, Jackson GS. 1998. Fourier transform ion cyclotron resonance mass spectrometry: A primer. Mass Spectrom Rev 17:1–35.

Marshall AG, Hendrickson CL, Shi DH. 2002. Scaling MS plateaus with high-resolution FTICR MS. Anal Chem 74:253A–259A.

Marshall AG, Rodgers RP. 2004. Petroleomics: The next grand challenge for chemical analysis. Acc Chem Res 37:53–59.

Marshall AG, Rodgers RP. 2008. Petroleomics: Chemistry of the underworld. Proc Natl Acad Sci U S A 105:18090–18095.

Marshall AG, Schweikhard L. 1992. Fourier transform ion cyclotron resonance mass spectrometry: Technique developments. Int J Mass Spectrom Ion Proc 18:37–70.

Rodgers RP, Marshall AG. 2006. Petroleomics: Advanced characterization of petroleum-derived materials by fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS). In: Mullins OC, Sheu EY, Hammami A, Marshall AG, editors. Asphaltenes, heavy oils, and petroleomics. New York, NY: Springer. pp. 63–93.

Rodgers RP, Schaub TM, Marshall AG. 2005. Petroleomics: Mass spectrometry returns to its roots. Anal Chem 77:20A–27A.

Schweikhard L, Marshall AG. 1993. Excitation modes for Fourier transform ion cyclotron resonance mass spectrometry. J Am Soc Mass Spectrom 4:433–452.

Smith LM, Kelleher NL, Consortium for Top Down Proteomics. 2013. Proteoform: A single term describing protein complexity. Nat Methods 12:186–187.

Xian F, Hendrickson CL, Marshall AG. 2012. High resolution mass spectrometry. Anal Chem 84:708–719.