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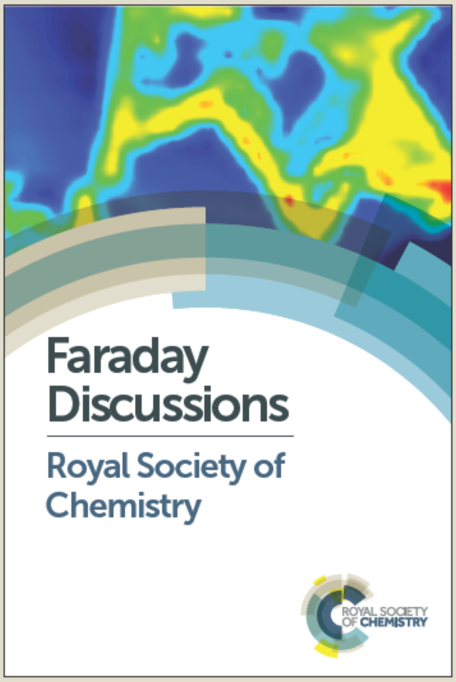

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Introductory Lecture:

Advances in Ion Spectroscopy: From Astrophysics to Biology

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Abstract

This introduction provides a historical context for the development of ion spectroscopy over the past half century by following the evolution of experimental methods to the present state-of-the-art. Rather than attempt a comprehensive review, we focus on how early work on small ions, carried out with fluorescence, direct absorption, and photoelectron spectroscopy, evolved into powerful technologies that can now address complex chemical problems ranging from catalysis to biophysics. One of these developments is the incorporation of cooling and temperature control to enable the general application of "messenger tagging" vibrational spectroscopy, first carried out using ionized supersonic jets and then with buffer gas cooling in radiofrequency ion traps. Some key advances in the application of time-resolved, pump-probe techniques to follow ultrafast dynamics are also discussed, as are significant benchmarks in the refinement of ion mobility to allow spectroscopic investigation of large biopolymers with well-defined shapes. We close with a few remarks on challenges and opportunities to explore molecular level mechanics that drive macroscopic behavior.

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I. Introduction

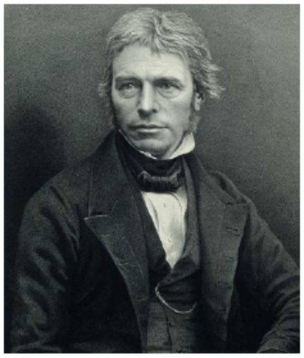

Fig. 1 Portrait of Michael Faraday. Permission to reuse from Ref. 1 obtained under CC by 4.0 license.

Fig. 2 **(A)** Photograph of a Commodore PET 2001 computer by Rama, Wikimedia Commons. Permission to reuse obtained under CC-by-sa-2.0-fr license. **(B)** Image of a smart watch by Andrej Radisic.

We meet here in York to discuss the present state of "ion spectroscopy" in the tradition established by Michael Faraday (Fig. 1),[1] the scientific giant who laid the foundation for our current understanding of electricity and magnetism, and thereby the fundamental principles at the core of contemporary personal electronics and communication. The exquisite control we presently command over chemical and biological processes that is enabled by ion spectroscopy methods is an amazing achievement. For those among us arriving in this on-going enterprise in the 1970s, the explosive growth in the sophistication and chemical scope of ion spectroscopy rivals that of the revolution in personal electronics over the same period of time. In those days, few experiments were computer-controlled, and if so, this was accomplished with toy computers like the Commodore Personal Electronic Transactor (PET, Fig. 2A). And this control came at the cost of months spent learning how to make primitive processors communicate with the outside world using binary "machine language". A smart device (Fig. 2B) can now provide personal communication across the globe and execute computations that were unimaginable in the limited architecture of the PET. Carrying out our discussion at the standard set by Faraday is a daunting challenge. He wrote about lectures: "A flame should be lighted at the commencement and kept alive with unremitting splendor to the end."[2] Of all the achievements made by the great electrochemist Humphry Davy, such as the discovery of the elements sodium and chlorine and the curious phenomenon of solvated electrons, Davy is supposed to have claimed Faraday as his greatest discovery.[3] The ions that we dissect this week with spectroscopy are, in fact, the molecular species at the heart of the electrochemical principles uncovered in the Davy-Faraday era.

Over the next few days, we will learn about all manner of clever manipulations that reveal how electric charge is accommodated by atoms, molecules, and supramolecular assemblies with increasingly complex compositions. We will elucidate their properties by studying the optical (electric dipole) spectra of systems isolated at low temperature and then warmed to systematically explore the topology of their phase space. These isolated systems will then be reunited with layers of solvent to recreate replicas of macroscopic systems from the "bottom up". Critical to this endeavor is the ability to capture ions in the "gas phase" to eliminate perturbations from the chaotic environment at play in condensed media. Once isolated, the shapes of these assemblies can be gauged using ion mobility separation methods followed by determination of their exact compositions with the aid of high resolution mass spectrometry and other techniques.

The explosive growth of recent activity in ion spectroscopy is evident in its application to fields ranging from astrochemistry to biology, and it is therefore fitting that this discussion aims to canvas this scope, and benchmark where we are in 2019. But the breadth of activity also makes it impossible in this introductory lecture to cast a sufficiently wide net to capture all of the exciting directions currently under exploration. Rather, in this presentation we will discuss representative exciting recent activities in the context of the overall trajectory of our field. We hope to accomplish this by pointing out how primitive apparati, often built for extremely focused applications, have been adiabatically transformed

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into powerful tools for general chemical analysis. A wonderful challenge in setting the tone for our discussion is the rampant, often scandalous cross-fertilization of ideas among nominally distinct sub fields in our discipline.

We caution that the selection of these topics in this lecture is necessarily subjective and thus incomplete. Our remarks are therefore NOT intended to provide a comprehensive review of ion spectroscopy, and omissions only reflect our limited perspective. In particular, we emphasize experimental aspects of the discipline, and recognize that there is a parallel story to be told in the evolution of theoretical methods over the past fifty years. Indeed, dramatic advances in the sophistication and accuracy in the theoretical analysis of complex systems are critical to the impact that we now enjoy, as ion spectroscopy has emerged as a powerful way to understand macroscopic phenomena at the molecular level.

II. Ions and the chemistry of interstellar clouds

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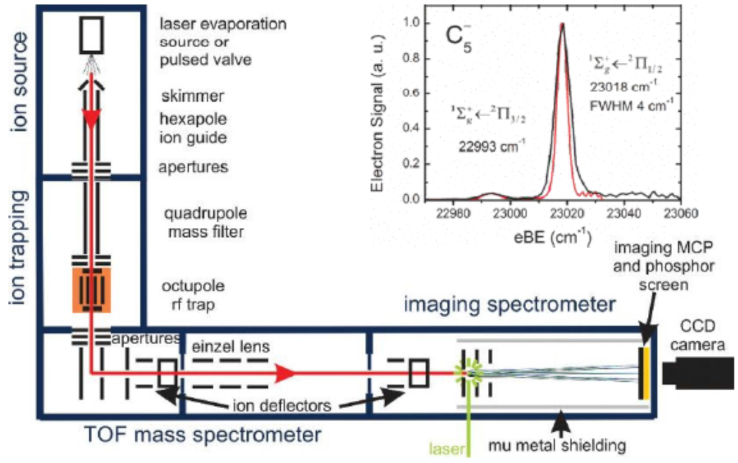

Fig. 4 Schematic of the cryo-SEVI experimental apparatus from Neumark's group with an inset showing a spectrum of C_5^- as an example. Reprinted from Ref. 21, with the permission of AIP Publishing.

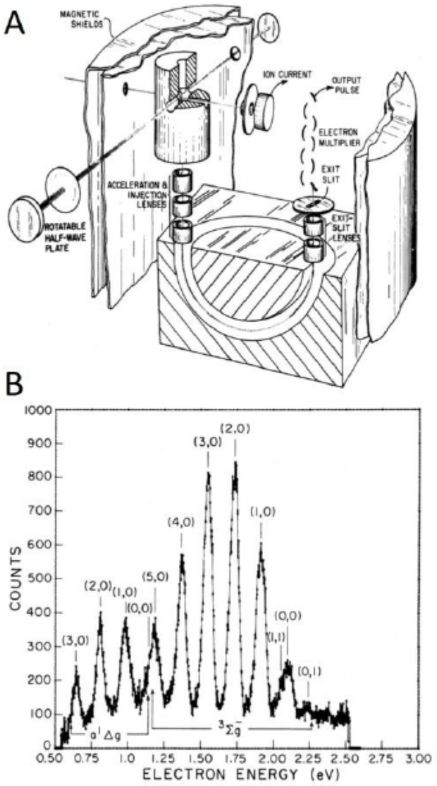

Fig. 3 **(A)** Diagram of the interaction chamber including the hemispherical electron monochromator from Hall's negative ion photoelectron spectrometer. Reprinted (Fig. 4) with permission from Ref. 12. Copyright (1972) by the American Physical Society. **(B)** O_2^- photoelectron spectrum. Reprinted (Fig. 2) with permission from Ref. 13. Copyright (1972) by the American Physical Society.

Gerhard Herzberg was one of the early voices calling for the study of ion spectra in his 1971 Nobel lecture,[4, 5] in which he described experimental schemes to accomplish this task. His motivation was to use these spectra to establish the roles that ions play in the formation of molecules in interstellar clouds.[6] Douglas and Herzberg had already identified CH^+ in a cloud from its optical emission spectrum in 1941,[7] but such resolved spectra were scarce. The emphasis on ions was driven by the fact that the Langevin rates of ion-molecule reactions[8] enable efficient kinetics at low temperatures (10-20 K) and low pressures ($<10^6$ molecules/cm^3),[6] indicating that ions were surely at the heart of complex molecule formation. Interestingly, negative ions were also invoked early on. Specifically, continuum absorption by H^- photodetachment was suggested as the cause of distortions in the shape of the solar emission spectrum.[9] In 1955, Lewis Branscomb heroically determined the absolute electron photodetachment cross section by photoexcitation of H^- anions in an ion beam with filtered light from a 1 kW projection lamp.[10] That successful effort was associated with the formation of the Joint Institute for Laboratory Astrophysics (JILA) at the University of Colorado in 1962. New JILA arrival Carl Lineberger quickly integrated these techniques with tunable lasers, and used resonant two-photon photodetachment to obtain the vibrationally resolved spectrum of the C_2^- anion.[11] That achievement was, in fact, featured prominently in Herzberg's 1971 Nobel lecture.[4] Boulder led the way through the 1960s and 1970s in negative ion spectroscopy with 2008 Physics Nobelist John Hall leading the team that coupled (home built!) fixed frequency ion lasers to a negative ion beam, and then measured anion photoelectron spectra with an electrostatic kinetic energy analyzer (Fig. 3A).[12] That effort resulted in the first accurate measurements of the electron binding energies of atoms and small molecules (especially NO^- and O_2^-, Fig. 3B) that were of great importance in the race to understand the plasma chemistry at play in high velocity vehicles returning to Earth from orbit.[12, 13] Lineberger quickly adapted this technique for general use in the characterization of unusual neutral molecules, radicals and anions.[14] The generalization of negative ion photoelectron spectroscopy to much higher photon energies was then introduced at Yale

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using pulsed excitation of bunched ions.[15] A decade later the efficiency of this method was dramatically improved by Andrei Sanov using velocity map imaging,[16-18] which also yielded the photoelectron angular distributions. In the past ten years, integration with cryogenic ion cooling brings us to the state-of-the-art "SEVI" (Slow Electron Velocity map Imaging) high resolution instruments in use today (Fig. 4).[19-21] Lai-Sheng Wang's current SEVI instrument, for example, routinely yields a resolution on the order of a wavenumber,[22, 23] about a factor of ~1000 improvement over that obtained with Hall's sector instrument, forty years and many innovations later!

Another important development in photoelectron spectroscopy brought about by ion and electron imaging is the extension of coincidence methods (like photoelectron-photoion coincidence (PEPICO))[24] to include fully spatially resolved images of the angular distributions of the photoelectrons and the photofragments with schemes such as COLTRIMS (COLd Target Recoil Ion Momentum Spectroscopy).[25] Exploiting these technologies, one now has an exquisite appreciation for both photodissociation and photoelectron kinematics that are fully resolved in the molecular frame.[26, 27]

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Astrochemistry also provided the initial motivation for laboratory measurements of the microwave (rotational) spectra of ions. In the 1960s, for example, a particularly strong line at 2.975 cm^{-1} (89.189 GHz) observed in interstellar clouds was assigned to “X-ogen” pending the identification of the carrier. Bill Klemperer famously suggested its assignment to HCO$^+$ by estimating bond lengths in 1970,[28] but the proof required laboratory measurements.[29] This breakthrough was carried out (interestingly by Lineberger’s Georgia Tech classmate) Claude Woods at Madison. He reported the first observations of the CO$^+$ and HCO$^+$ ions using direct millimeter (mm) wave absorption in liquid nitrogen cooled plasma tubes in 1975.[30, 31] Looking back on this era, it is easy to forget the challenges faced by these pioneers. For example, the free electron density in an electrically neutral plasma is very high, creating a large background that complicates the detection of very small fractional absorptions available at the low ion densities typical in that environment. Wood’s CO$^+$ absorption dip obtained after averaging over 1000 scans is displayed in Fig. 5, which interestingly does not have an abscissa! Another early benchmark for microwave measurements was Oka’s laboratory observation of H_3^+, a key species in the formation of covalent bonds of molecules in interstellar clouds.[32] This was followed by his first observation of the complex band system displayed by the “Cheshire cat” ion CH_5^+,[33, 34] a pentavalent hydrocarbon that has fascinated physical organic chemists for decades.[35] This long standing spectroscopic puzzle was finally solved in 2015 through analysis of the cold ion spectra by Stephen Schlemmer

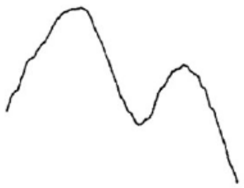

FIG. 1. The $J=\frac{1}{2}\rightarrow\frac{3}{2}$ transition of CO$^+$ after an average of 200 scans at a time constant of 100 msec. Each scan contained 1000 individual points and required about 15 sec. The width of the region shown is approximately 5 MHz. The discharge current was 395 mA in 32 mTorr of 90% He–10% CO with liquid-nitrogen cooling. The absorption line is the central depression which lies near a maximum in the baseline curve. The baseline pattern (but not the absorption line) may be completely changed by slight movement of the microwave horns.

Fig. 5 The $J = 1/2 \rightarrow 3/2$ transition of CO$^+$ in a 90% He-10% CO discharge. Reprinted (Fig. 1) with permission from Ref. 31. Copyright (1975) by the American Physical Society.

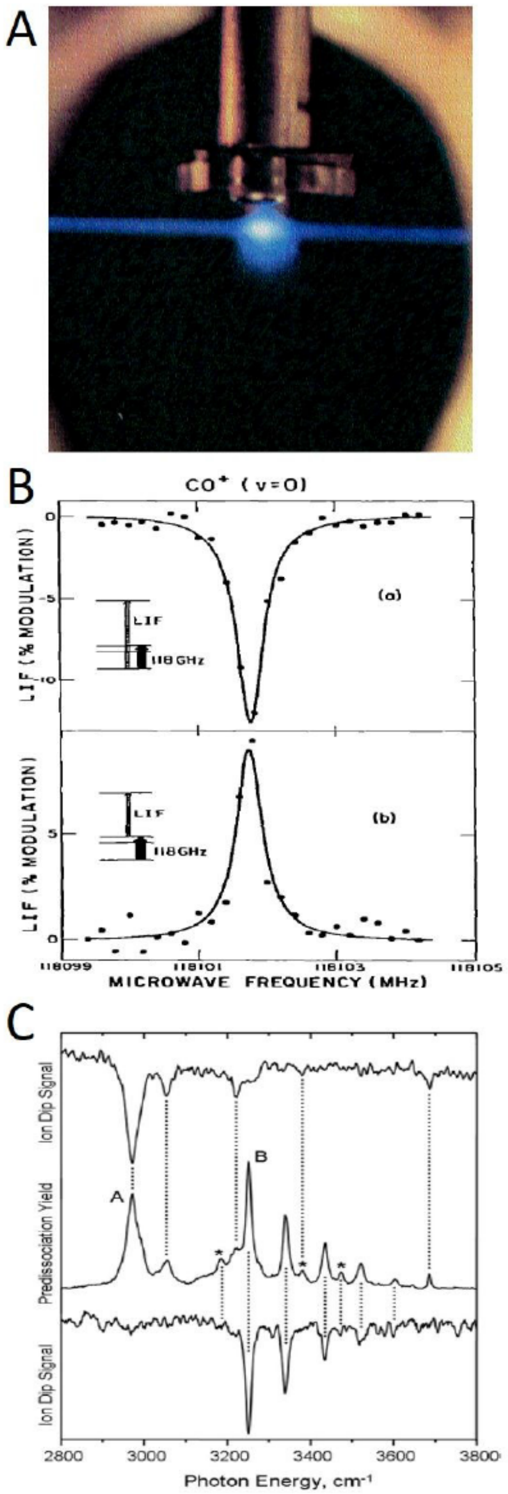

Fig. 6 (A) Photograph of an N_2/Ar supersonic jet excited by a 1 keV electron beam. **(B)** MODR spectrum of CO$^+$ $N = 1 \leftarrow 0$, |0,1,3/2>-|0,0,1/2> spin-rotation component. Reprinted from Ref. 57, with permission from Elsevier. **(C)** OH stretching region of the $NO_2^-\cdot H_2O\cdot Ar$ predissociation spectrum (center) and the isomer specific double resonance dip spectra (top and bottom) obtained by fixing the probe laser on A and B, respectively. Reprinted from Ref. 59, with the permission of AIP Publishing.

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and co-workers.[36]

A major advance in the observation of ion absorptions in a plasma was contributed in the early 1980s with Rich Saykally's introduction of the velocity modulation approach to isolate features arising from ions and at the same time reveal their charge states. Application of this method led to the first structural characterizations of the most important molecular ions in electrolyte chemistry, H_3O^+ and OH^-.[37, 38] Meanwhile, Marilyn Jacox was busy isolating ions in rare gas matrices, and identified various molecular ions (e.g. CO_2^+ and CO_2^-, O_4^+ and O_4^-) through their IR vibrational signatures.[39, 40] And then John Maier succeeded in embedding size-selected ions in matrices to facilitate the assignments of the carriers.[41]

III. Cool ions: Supersonic jets, population labeling and laser-induced fluorescence (LIF)

Early efforts to obtain the spectra of low temperature ions were driven by the fact that the interstellar clouds are rather cold (~50 K).[42, 43] An obvious choice in the 1970s was to leverage the fantastic cooling properties of the seeded supersonic expansion, first popularized by John Fenn at Princeton[44] and quickly exploited to obtain velocity-selected molecular beams for reactive scattering by Herschbach and Lee.[45, 46] The first application to electronic spectroscopy was carried out by Smalley and Levy, who reported the ~3 K spectral simplification of the astonishingly complex spectra displayed by NO_2 at 300 K.[47] A very early adaptation of this approach to molecular ions was reported around 1980 by Carrington and Tuckett[48] in Southampton and Maier's lab in Basel.[49, 50] Their scheme integrated electron-beam induced fluorescence to disperse the electronic emission spectra of 20 K N_2^+ and CO_2^+. The emission from jet cooled N_2^+ is displayed in Fig. 6A, taken at Yale in 1987. The CO_2^+ band system was under intensive study at that time in the context of the UV glow from Halley's comet.[51, 52] The theoretical work was spearheaded by Herzberg's recent postdoc Joëlle Rostas, working in Sydney Leach's Laboratoire de Photophysique Moléculaire (PPM) in Orsay. Maier's jet cooling breakthrough was immediately capitalized on by Dick Zare's lab at Stanford the following year to include their signature laser-induced fluorescence (LIF) method. Working together, the Stanford/PPM team were able to unravel the various perturbed states complicating the CO_2^+ electronic band systems using "population labeling" optical-optical double resonance (OODR),[53] a spectral simplification technique that had been recently introduced by a group led by the (subsequently) dual Nobelists Art Schawlow and Ted Hänsch at Stanford.[54-56]

The extension of population manipulation methods to the mm wave region with microwave-optical double resonance (MODR) was developed at JILA in 1983 and used to detect the CO^+ resonances of the isolated ions, which were reported earlier by Woods in a plasma environment. The MODR signals were obtained using a ~5 K supersonic plasma.[57] That method relied on monitoring the population changes in rotational levels using LIF, which are large when the ions are cooled such that $k_BT < B$, the rotational constant. The MODR spectra of CO^+ are displayed in Fig. 6B. An important, and largely accidental breakthrough in this period was the discovery that the ionized free jets were outstanding sources of delicate molecular negative ions. This was traced to the fact that the high density of low energy secondary electrons arising from direct electron impact ionization of Ar were efficiently cooled in the expanding plasma.[58]

We reflect back on this early population labeling work here because it is the direct progenitor of a scheme introduced 25 years later that provided a general way to obtain isomer-selective vibrational spectra of "tagged" ions. The only difference is that infrared predissociation is now used to follow population changes in a two-color, IR-IR double resonance mode. The application of population labeling to isolate the spectra of two isomers adopted by the Ar-tagged $NO_2^-\cdot H_2O$ ion is shown in Fig. 6C.[59] Very recently, this general approach has been extended further by Etienne Garand at Wisconsin who

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demonstrated a variation where pump laser excitation occurs directly in a cryogenic ion trap, enabling the deconvolution of over 10 different conformers of a hydrated peptide ion.[60]

Although LIF is a very sensitive technique, and in many ways the ultimate "messenger tag" for action spectroscopy, it is rather limited in that it requires available excited states with high fluorescence quantum yields. As such, photofragmentation presents an attractive alternative, but requires working outside the plasma environment that is in play for the ionized free jets, where density is *much* lower (by ~10^6). The coupling of laser sources with mass spectrometers was, of course, not new, and indeed John Brauman carried out many pioneering spectroscopic studies of ions with filtered arc lamps in the 1970s.[61] And Jack Beauchamp at Caltech demonstrated IR multiple photon dissociation (IRMPD) of protonated diethyl ether in 1978 using cw CO_2 laser excitation in an ICR.[62, 63] That general scheme was advanced to an almost industrial scale of productivity starting in the early 2000s with the addition of mass spectrometers to the powerful IR free electron lasers in Paris (CLIO) and Rijnhuizen (FELIX), spearheaded by Philippe Maître,[64] Gerard Meijer and Jos Oomens.[65]

But in the 1980s, the available wavelength range of cw lasers, which were naturally most compatible with the duty cycle and operation of commercial mass spectrometers (e.g. magnetic sectors and quadrupole mass filters), severely limited access to the UV region where most molecules absorb. Pulsed lasers, on the other hand, could easily extend the range down to the vacuum ultraviolet through harmonic generation and mixing.[66] To meet this challenge, Johnson and Lineberger built the first "ion bunching" tandem time-of-flight photofragmentation spectrometer at JILA in 1984.[15] That instrument exploited the magical properties of the "reflectron" mass analyzer introduced by Mamyrin ten years earlier,[67] and demonstrated in early ion photodissociation experiments by Ulrich Boesl and Ed Schlag as well as by Will Castleman's group.[68, 69] The first application by the JILA team was to measure the dissociative electronic spectra of molecular "polarons". These are species formed upon the ionization of molecular clusters, and they focused on the $(CO_2)_n^+$ and Ar_n^+ cations, mostly because they were already in the ionized plasma in the free jets used to study the CO_2^+ spectrum earlier. The spectra of the covalently bound $(C_2O_4)^+$ and Ar_3^+ "core ions" at the heart of the these clusters were obtained by monitoring the subsequent photoevaporation of the weakly bound solvent neutrals (CO_2 and Ar), providing a harbinger of the tagging revolution that was waiting just around the corner.[15, 70]

By the mid-1980s, the goal of observing more complex organic structures in interstellar clouds coincided with Smalley's adaptation of the ionized free jet ion sources that incorporated a laser-driven plasma.[71] This resulted in the discovery of C_{60} through the observation of the size distributions of the cation and anion clusters.[72] Skipping ahead a few decades, perhaps in the spirit of the PET/iPhone analogy (Fig. 2), we are now enjoying the fruits from decades of effort to improve both theory and experimental techniques. A major dividend of that effort is the recent report from Maier's lab[73] that the electronic spectrum of ~3 K C_{60}^+ provides a compelling assignment for two of the many diffuse interstellar bands that have puzzled astrochemists for decades.[74, 75]

IV. Universal vibrational (and electronic!) spectra of cold ions: Messenger tagging

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The general application of mass-selective active methods for vibrational spectroscopy, a breakthrough for the field, was reported in 1985 by Mitchio Okumura and (another Nobelist!) Y.T. Lee.[76] Their approach exploited the molecular ion spectrometer based on a linear RF octopole trap[77, 78] introduced to the Lee group in 1978 during a very influential visit by Dieter Gerlich.[79] Okumura proceeded to measure landmark spectra in the high frequency OH stretching range of protonated water clusters with H_2 tagging. This work essentially verified the earlier spectrum of $H_9O_4^+$, the "Eigen ion," observed heroically by Schwarz using very primitive equipment.[80] The Lee group then exploited a combination of non-dissociative IR excitation and selective IRMPD to obtain what is—to this day—the only high resolution spectrum of the "Zundel" ion, $H_5O_2^+$ (Fig. 7A).[81] Those spectra were obtained using difference-frequency generated IR from a pulsed dye laser and the Nd:YAG fundamental in a Li:NbO$_4$ crystal. Okumura then adopted the TOF based techniques and obtained the first spectrum[82] of the $I^-{\cdot}H_2O$ anionic complex at Caltech to usher in the modern era.

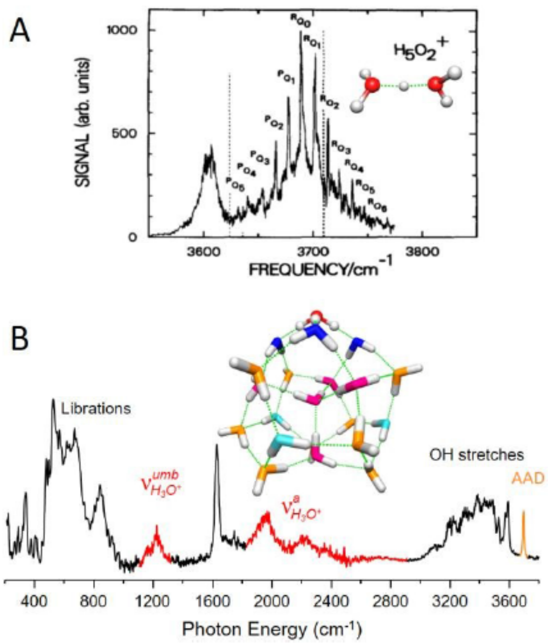

Fig. 7 (A) IR spectrum of $H_5O_2^+$ obtained using two color IRMPD technique. Reprinted from Ref. 81, with the permission of AIP Publishing. **(B)** Vibrational predissociation spectrum of $H^+(H_2O)_{21}$ obtained using D_2 messenger tagging technique. Reprinted from Ref. 94. Copyright (2014) National Academy of Sciences.

The year 1995 brought a major breakthrough in IR laser design with the Laser Vision cascading OPO/OPA scheme based on KTP and KTA non-linear crystals. The now ubiquitous scheme using four KTA crystals in the OPA stage was, in fact, specifically designed by Dean Guyer to meet the demand of tagging in the free jet based, double focusing tandem TOF instruments just constructed at Yale. In an interesting turn of events, the first experiments that utilized this configuration measured the vibrational spectra of the hydrated electron clusters reported by Haberland[83] and studied by Kit Bowen in the 1980s with photoelectron spectroscopy.[84] These anions were the microscopic analogues of the solvated electrons identified two hundred years earlier by Davy! By carrying out reactions with the highly reactive hydrated electron clusters, which were easily formed with many (~20) Ar atoms in a free jet,[85] the Yale team could generally convert them into any number of molecular anions using the "evaporative electron attachment" process[86]:

$$(H_2O)_n^-{\cdot}Ar_m + RM \rightarrow M^-{\cdot}(H_2O)_n{\cdot}Ar_p + R + (m\text{-}p)Ar.$$

The hydrated $M^-{\cdot}(H_2O)_n$ product ions were cooled by Ar evaporation under single collision conditions, leaving the hydrated target already "tagged" for characterization with vibrational spectroscopy. Caroline Dessent at Yale used a clever variation of the approach to systematically generate the delicate "dipole bound" CH_3CN monomer and dimer anions by near threshold photodetachment of $I^-{\cdot}(CH_3CN)_n$, and identified the electronic spectroscopy precursors of the famous charge-transfer-to-solvent (CTTS) bands displayed by halide ions in water.[87] Another particularly interesting variation of that technique allowed the capture of entrance channel complexes in the bimolecular S_N2 reaction:

$$Cl^-{\cdot}Ar_n + CH_3Br \rightarrow Cl^-{\cdot}(CH_3Br){\cdot}Ar_m + (n\text{-}m)Ar$$

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and activate it to form Br^- products over the Walden inversion barrier through excitation of the CH stretching vibrational modes.[88] It is now easy to anticipate a new wave of experiments that capitalize on the unique properties of ions captured in He droplets[89] that will dramatically expand on this theme. Time-ordering of neutral uptake onto embedded ions, for example, will very likely generate highly unstable assemblies that access the properties of systems far from equilibrium. Photoexcitation of these assemblies can then probe barriers to rearrangement and pathways of chemical transformations.

The last element needed to complete a generally useful implementation of vibrational spectroscopy required extension of the table-top methods to cover the "fingerprint" region from 600-2000 cm^{-1}. This was accomplished by parametric conversion in $AgGaSe_2$, an innovation demonstrated early by Markus Gerhards[90] and adapted for use in the Laser Vision platform by Tim Zwier's group at Purdue.[91] Using these methods to understand the "excess proton" in water remains a very active area of research. Recent advances include finally tracking down the spectral signature of the charge defect in the famous $H^+(H_2O)_{21}$ "magic number" cluster[92] discovered by John Fenn in the very early studies of cluster ions prepared in ionized jets.[93] This contemporary effort involved the exploitation of cryogenic ion traps in conjunction with the wide frequency range available using both $AgGaSe_2$ and the IR free electron laser at the Fritz Haber Institute. The current spectrum of the cold $H^+(H_2O)_{21}$ (Fig. 7B)[94] is compared with the pioneering work by Lee on the Zundel ion in Fig. 7A,[81] and reveals the tell-tale bands associated with the positive charge defect colored in red. Interpreting the complex band patterns displayed by these floppy systems has proved to be a substantial theoretical challenge. Fortunately, an array of new methods have been developed to specifically address these anharmonic effects, ranging from reduced dimensionality vibrational quantum mechanics[95] to autocorrelation approaches on accurate potential surfaces[96-98] to full dimensional, many body treatments of the vibrational Hamiltonian.[99, 100]

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V. Time-resolved photophysics and photochemistry

Time-resolved experiments were introduced in the late 1980s with the Lineberger group again taking a pioneering role. They succeeded in observing the intracluster kinetics of the "cage recombination" of diatomic ions photodissociated within size-selected cluster ions, specifically $IBr^{-} \cdot CO_2$. These pump-probe experiments monitored the recovery of ground state absorption as the atoms settle back to their ground vibrational levels with evaporation of the solvent. This approach was quickly supplemented by the more powerful scheme in which the dynamics of the excited state prepared by photoexcitation were followed by time-resolved photoelectron spectroscopy. Neumark carried out an elegant series of experiments around 2000[101] on the $I_2^{-} \cdot Ar_n$ system in the spirit of the earlier Lineberger approach. He did so with exquisite control of the dynamics using pump-probe stimulated emission to drive ground state vibrational wavepackets whose subsequent quenching could be followed using femtosecond time-resolved photoelectron spectroscopy (FPES). Theory has played an important role in the conceptual design of the experimental approach, with the early work on the semiclassical of spectroscopy through time-dependent wavepacket dynamics by Rick Heller[102] in 1981. More recently, Todd Martinez[103] has introduced powerful new methods to address the wavepacket evolution and curve-crossings that are embedded in the time-resolved shapes of the photoelectron envelopes.[104, 105]

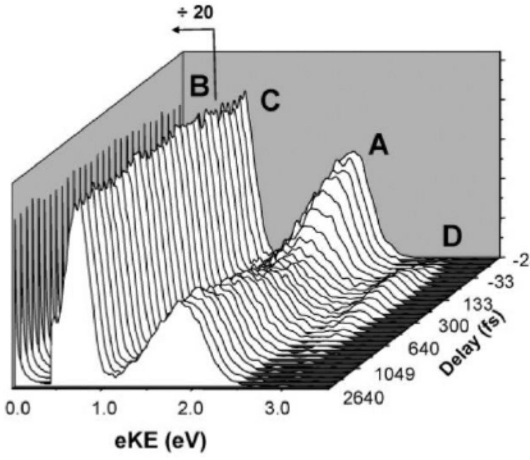

Fig. 8 Spectral waterfall plots of representative relaxation dynamics for one of the isomers of $(D_2O)_{25}^{-}$, whereby λ_{pump} = 1250 nm and λ_{probe} = 395 nm. Pump–probe delays are indicated. Reprinted (adapted) with permission from Ref. 106. Copyright (2005) American Chemical Society.

A particularly important discovery made using this methodology concerns the chemical nature and photophysics of the hydrated electron. Using FPES methods, the Neumark group followed the relaxation photophysics displayed in Fig. 8, which convincingly demonstrated that the first electronically excited state decays remarkably fast by internal conversion to the ground state.[106] These results settle a long standing controversy on the kinetics displayed by bulk water.[107] Another elegant scheme demonstrated in the 1990s involved a charge-reversal method in which a neutral wavepacket was launched by fs photodetachment of a size-selected negative ion (Ag_3^{-}) followed by photoionization (hence denoted NeNePo for negative-neutral-positive) so that the vibrational coherences could be monitored by resolving the cation yield as a function of time.[108] The extension of coherent spectroscopies like 2D-IR to ions is now at hand, where again we

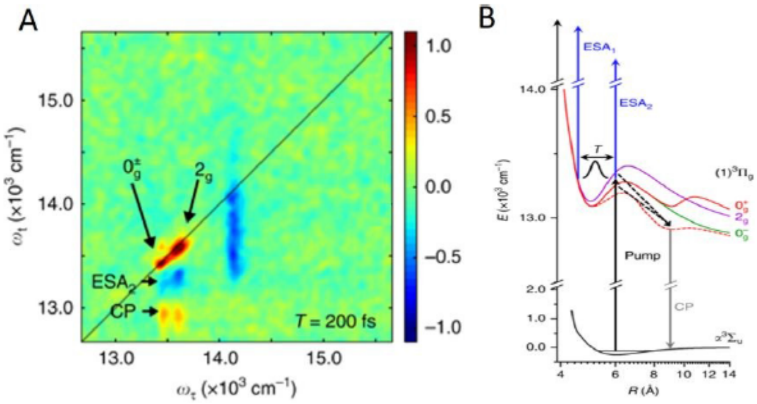

Fig. 9 (A) Rb_2 and Rb_3 2D-ES results. Photoelectron-2D correlation spectra of isolated Rb_2 molecule with selective enhancement of Rb_2 features using a wavelength-optimized fifth pulse combined with photoion detection. **(B)** Rb_2 PECs and concluded photodynamics. Both are reprinted from Ref. 109, under Open Access.

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envision reading out the signal in an action mode that is compatible with the low ion densities available after mass selection. A very exciting development in this regard is the photoion action detected in 2D electronic spectra (Fig. 9) reported by Stienkemeier in 2017.[109] An outstanding target for this methodology would be its extension to the IR in order to capture the excited state "excess" proton dynamics in water clusters, which would directly challenge current interpretations of signals generated in ambient water.[110, 111]

VI. Cryogenic ion traps and the electrospray interface: Meeting the challenges of biological macromolecules

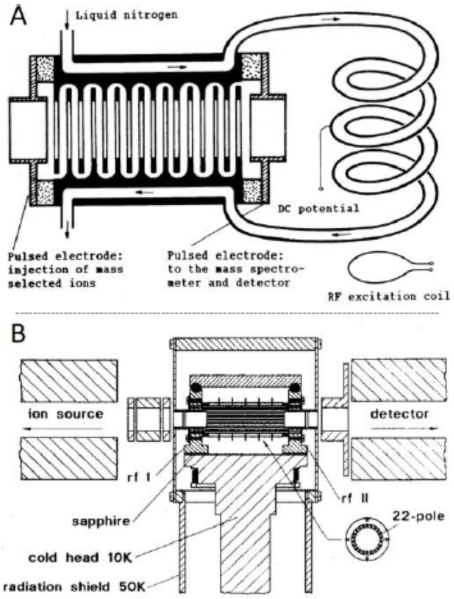

Fig. 10 **(A)** The first cold RF ion trap cooled by liquid nitrogen apparatus applied to physical chemistry experiments in 1988. Reproduced from Ref. 114 by permission of AAS. **(B)** A further developed, cold 22-pole RF ion trap cooled by a closed cycle He cryostat from 1995. Reprinted from Ref. 115, with permission from Elsevier.

Our discussions of the trajectories carved over the years in the optimization of both anion photoelectron and vibrational predissociation tagging spectroscopies necessarily included the relatively recent addition of cryogenic RF ion traps. These are crucial because they provide a rational way to control both temperature and formation of weakly bound complexes. Here we pause to consider the evolution of these trapping techniques in a historical context. The development of cryogenic traps was significantly influenced once again by JILA, when in 1984, Gordon Dunn reported ion-molecule reaction rates in a ~10 K hyperbolic Penning trap.[112, 113] This led to a growing interest in observing the radiative association of collision complexes at low temperature. But the central figure in the integration of cryogenic ion traps for spectroscopy is Dieter Gerlich, who introduced the first (we think!) cooled RF ion trap in 1988 in the configuration illustrated in Fig. 10A.[114] This powerful combination of robust ion trapping and buffer gas cooling has slowly but surely overtaken the entire worldwide effort to control the temperature of complex ions. Gerlich's early efforts were directed at understanding the chemistry of simple ions like H_3^+ under conditions relevant to the interstellar medium, and indeed thermalization of such a light mass at low temperature is a profound challenge due to the forces at play in the RF trapping conditions. Overcoming this challenge resulted in the "22-pole" trap, which minimized these forces to create a near field-free "box" in which to process ions, which is illustrated schematically in Fig. 10B.[115] Many groups followed this lead, including the instrument designed by Asmis in 2002[116] and later by Maier[20] and Dopfer.[117] As the chemical complexity of the target systems evolved towards larger systems, however, the special features of the 22-pole that enabled control of light masses were less important. Instead, the large mass difference between the He buffer and the larger ions allowed the effective use of simpler n-poles, which provided more

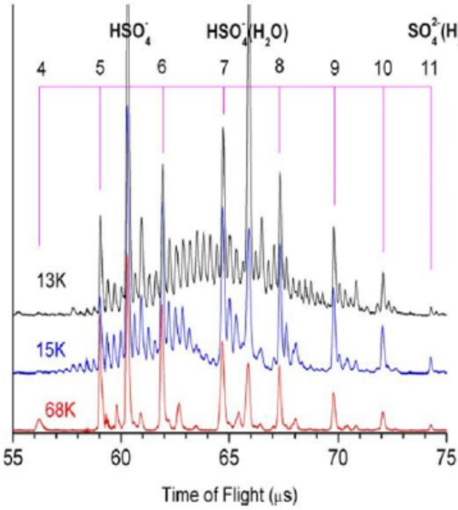

Fig. 11 Mass spectra displaying hydrated sulfate clusters with H_2 messenger tags. Reprinted from Ref. 119, with the permission of AIP Publishing.

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localized ion clouds that could be efficiently excited with lasers. The “wire quadrupole” is an especially inspired solution, which minimizes collisions with the buffer gas while allowing tight compression of the ions at the center of the trap.[118] Xuebin Wang and Lai-Sheng Wang at PNNL were among the first to capitalize on this situation in 2008 as a scheme to efficiently generate H_2 molecular tags to ions stored in a cryogenic 3-D quadrupole Paul trap.[119] The mass spectrum demonstrating this accomplishment is displayed in Fig. 11. With this generalization of tagging (beyond the restricted regime of supersonic jets), the door was opened to application of vibrational tagging spectroscopy to ions generated using versatile ambient ionization sources like electrospray (ESI). ESI exploded on the scene in 1984 from the creative efforts of John Fenn at Yale,[120] fresh off his recent revolutionary contributions with seeded free jets as discussed above. Early efforts by Lynmarie Posey at Vanderbilt[121] and Peter Chen at ETH[122] coupled ESI sources with RF traps, and the configuration developed by Asmis in combination with the FELIX facility was an important benchmark.[123] Then the Yale team, in collaboration with PNNL, combined H_2 tagging with ESI generated peptides and isomer-selectivity in 2010 to demonstrate a powerful general platform for structural characterization of biologically relevant ions.[124-126] Recent applications to uncover the molecular-level mechanisms of homogeneous catalysis by Jana Roithová’s group in Nijmegen[127] as well as parallel efforts by Knut Asmis and Joachim Sauer in Berlin[128, 129] indicate that this will become an increasingly impactful direction for “real world” applications of ion spectroscopy.

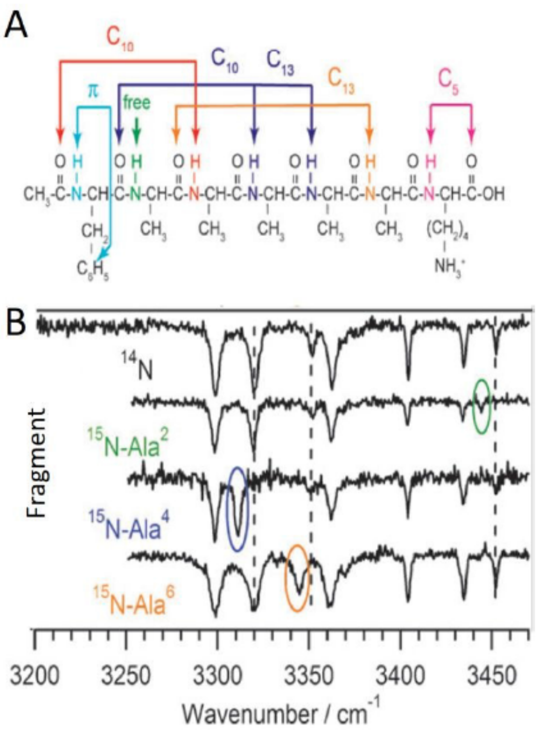

Fig. 12 (A) Scheme showing different N positions that can be isotopically labeled with ^{15}N in a peptide chain. **(B)** Double resonance spectra of the peptide chain shown in **A**, isotopically labeled at various different positions which allows the assignment of specific NH stretches. Both are reproduced from Ref. 130 with permission from the PCCP Owner Societies.

A particularly influential study in the structural characterization of biological ions was that carried out by Rizzo in 2008,[130] which addressed the important issue that vibrational band patterns alone provide limited evidence for *structure*. The EPFL team demonstrated that in the cold ion regime, site specific isotopic labeling brings a powerful way to assign particular bonds to specific transitions. This is illustrated in Fig. 12, where bands associated with particular ^{15}N-H stretches (indicated by ovals) are isolated in the helical structure of a pentapeptide. This is a gas phase analogue of venerable “isotope edited” spectroscopy long used to analyze the spectra of peptides in solution, and the key point is that the intrinsically narrow linewidths of the features in cold, isolated ions yield a much richer definition of conformer structures.

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VII. The rise of ion mobility

With larger systems in play, the questions evolve from the detailed quantum mechanics of molecules and molecular assemblies to those related to how shapes of macromolecules drive their function. That is best addressed using the gas phase analogue of widely used gel electrophoresis, known as Ion Mobility Spectrometry (IMS). This is an old story, initially developed by none other than Carl Lineberger's PhD thesis advisor E. W. McDaniel at Georgia Tech. He used a ~1 m drift tube (See Fig. 13A) with an electric field applied down its axis with a series of ring electrodes to study ion-molecule reactions of hydrogen in the 1950s and 1960s.[131] An important advance occurred in the 1990s when Mike Bowers introduced the double-focusing, reverse geometry mass spectrometer with a new drift cell (4.0 cm x 1.52 cm) with a uniform field using eight guard rings operating over a temperature range from 100-500 K.[132] The ions were decelerated and focused before entering the reaction cell and re-accelerated upon leaving the cell for subsequent mass analysis. He used this instrument to measure the reactivity of Co^+ ions in ground and metastable excited electronic states which were separated by their different arrival times. This was followed by its application to cationic systems to reveal the formation mechanisms and shapes of cationic carbon clusters by Radi and von Helden.[133-135] The next innovation came in 1995 when David Clemmer demonstrated that protein (cytochrome *c*) conformers could be resolved using ion mobility,[136] and since then IMS has emerged as a

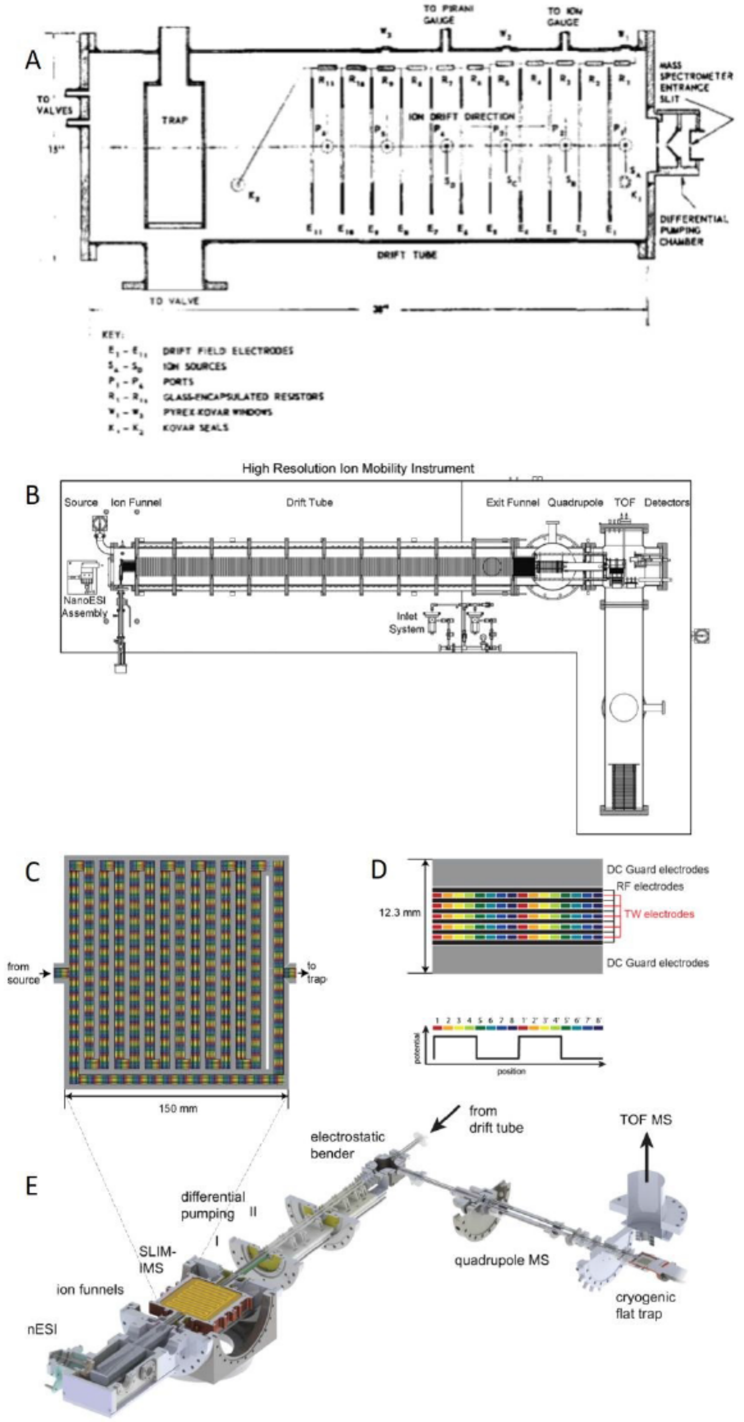

Fig. 13 **(A)** Diagram of McDaniel's drift tube and differential pumping section. Reprinted from Ref. 131, with the permission of AIP Publishing. **(B)** Diagram of the 2 m long drift tube by Bowers. Reprinted from Ref. 138, with permission from Elsevier. **(C)** Expanded view of the 15 cm SLIM board, with an overall single pass drift length of 1.8 m. **(D)** Schematic of the electrode positions and shape of the square travelling potential wave. **(E)** Rizzo's SLIM-IMS cryo-IR setup. Reprinted (adapted) with permission from Ref. 140. Copyright (2019) American Chemical Society.

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workhorse technique for the analysis of biomolecules and clusters.[137]

The application to increasingly complex, biologically relevant systems led to the need to differentiate between isomers and oligomers (singly charged monomer, doubly charged dimer, etc.) of similar m/z. This challenge was met by the development of the ~2 m long drift tube in 2009[138] (see Fig. 13B) capable of resolving ions with cross sections differing by less than 1%. Ion funnels were then added to both ends of the tube to reduce ion loss and increase sensitivity. The evolution of IMS also follows the paradigm of personal electronics, where miniaturization has been accomplished with vastly enhanced performance. Thus, Dick Smith at PNNL introduced a new IMS platform in 2016 which replaces the long drift tube with a pair of mirror-image printed circuit boards (PCBs), bringing the physical dimension of the apparatus down to about 30 cm.[139] These "Structures for Lossless Manipulations" or SLIM boards (Fig. 13C) feature coordinated RF, DC, and travelling wave (TW) voltages on the electrodes (Fig. 13D), allowing ions to travel through a long serpentine path (13 m). This method can now resolve isomers that differ in collisional cross section by as little as 0.2%. And completing the transition from shape to spectroscopy, Rizzo's lab has integrated SLIM analysis (15 cm board) into a cryogenic ion trap-based vibrational spectroscopy instrument (Fig. 13E).[140] This brings us to the present moment, where it is now routine to acquire the vibrational (and electronic) spectra of very large, multiply-charged ions with shape-selectivity.

VIII. Challenges and Opportunities

Whilst being fully aware of the folly inherent in making predictions, we nonetheless close this introduction by highlighting areas where we see opportunities for available technologies and offer a few aspirational goals for what might come next.

1. Very high resolution spectroscopy of key systems

Perhaps in a look "back to the future," we see a need to bring rigorous spectroscopy back into the fold to solve the molecular physics of small but complex systems. In the 1970s, for example, we saw a flurry of activities in the application of fast ion beam methods to obtain very high resolution spectroscopy of atomic and molecular ions. This method relies on the simple kinematic Doppler compression available in the coaxial excitation geometry, and when combined with very high resolution cw lasers, yields sub MHz linewidths.[141] There is a strong need at present to bring this method to bear on important small ions such as $H_5O_2^+$ (a personal favorite), the interesting, quantum-delocalized $H^-\cdot H_2O$ anion[142] as well as the metastable S_N2 reaction intermediate $Cl^-\cdot CH_3Br$.[88] Another important aspect of current research that would benefit from high resolution is an investigation of the explicit IVR rates and associated linewidths at play in the canonical tagging experiments. Outstanding examples include the photodetachment spectrum of H^- near relativistic speeds, the fine structure near the OH^- and OD^- photodetachment thresholds[143] and the electric predissociation spectrum of N_2O^+.[144] Another technology that appears always on the verge of making a transformative change in ion spectroscopy is the coupling to chirped pulse microwave methods[145] to obtain the rigorous quantum structures and associated tunneling splittings in clusters. Yet another breakthrough would be the implementation of tag-detected stimulated Raman spectroscopy to access symmetry forbidden levels in the IR as well as low frequency modes presently out of range with table-top laser systems.

2. Extension to very large assemblies to recover macroscopic behavior with precise control of composition

At perhaps the opposite extreme of point #1, we also see an opportunity to expand the system complexity to develop composition and temperature controlled "micro test tubes" in which to isolate and study chemical processes. This is already under way in many laboratories at the upper limit, where

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RF[146, 147] and electrostatic[148] traps are being used to study mesoscopic particles. This regime offers an excellent way to monitor reactions in these "droplets" as well as surface reactions and the speciation of ions at the air-water interface. Working with smaller particles, however, will allow exact control of compositions when working at the upper limit of high resolution mass spectrometers. One area that would be clearly benefit from this type of approach would be clarifying the molecular-level photochemical pathways taking place on atmospheric aerosols, where large clusters yield sufficient complexity that they faithfully display bulk properties.[149] An important unsolved problem, for example, is to clarify the origin of the reaction rate enhancements that are suggested to occur at the surfaces of micron-sized liquid droplets. Is it local electric field? Or concentration of ions? pH? This looks to be ready to a full frontal assault with the arsenal of tools we have created based on "ion spectroscopy". We also see an opportunity here to monitor reaction kinetics in this regime using action spectroscopy in a modern adaptation of the classic "T-jump" experiments that Manfred Eigen mastered in the 1950s. An attractive target for such experiments is the identification of the microscopic motions that underlie spectral diffusion in liquids.

3. Development of accurate, general theoretical methods for handling highly anharmonic vibrational mechanics and simulations of complex systems

We began this introduction by stating that we did not include the important benchmarks for theoretical advances over the past 50 years. But we recognize that theoretical support has marched hand-in-hand with experimental efforts, sometimes guiding experimental strategies while at other times providing new conceptual paradigms to accommodate observations that fall far outside the bounds of canonical treatments. Examples of the latter include Hans-Dieter Meyer's 15-dimensional treatment of the vibrational structure displayed by the $H_5O_2^+$ "Zundel" ion[100] and the heroics needed to understand the symmetries and angular momentum couplings that are encoded in the surprisingly complex CH_5^+ spectrum. With recent advances in the ability to map out high dimensionality potential energy surfaces using tools such as machine learning,[150] we anticipate that accurate treatments of highly anharmonic vibrational structures will become more widely available. This is crucial because it will allow us to move beyond comparisons with harmonic predictions for the identification of ion structures from vibrational band patterns. Perhaps the next challenge will be to extend these methods to predict how local media affect the photochemical pathways and ultrafast kinetics of chromophores embedded in complex matrices such as cluster mimics of sea spray aerosols. The current pace of discovery ensures that however our field evolves, another Faraday Discussion will be mandatory, and in short order. Such a venue will both allow next generation researchers to muse at these misguided predictions as well as mark the role that disruptive technologies will likely play to set the course for future work that rests on the solid foundation set by this generation in the application of spectroscopy to ions.

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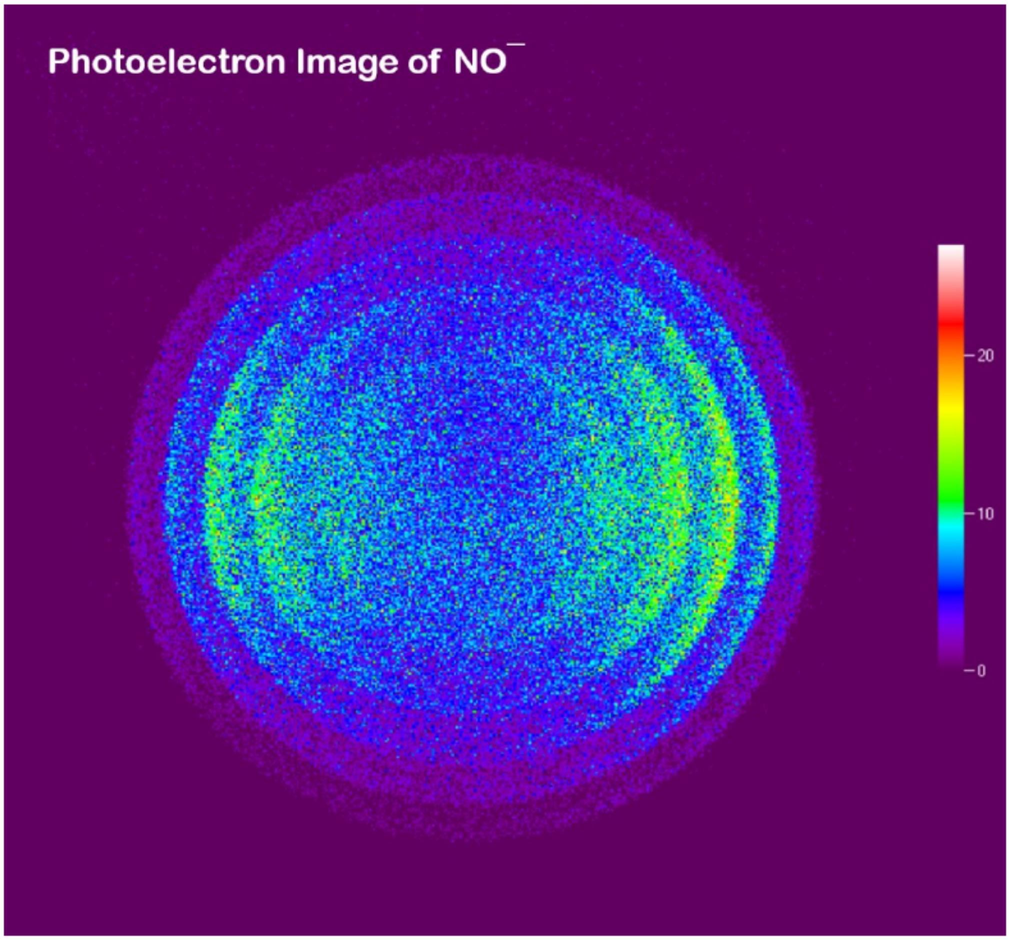

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