

REVIEW ARTICLE

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The emerging interface of mass spectrometry with materials

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Abstract

Mass spectrometry (MS), a hundred-year-old subject, has been a technique of profound importance to molecular science. Its impact in solid-state materials science has not been evident, although many materials of modern science, such as fullerenes, have their origins in MS. Of late, mass spectrometric interface with materials is increasingly strengthened with advances in atomically precise clusters of noble metals. Advances in instrumentation along with recent developments in synthetic approaches have expanded the chemistry of clusters, and new insights into matter at the nanoscale are emerging. High-resolution MS coupled with soft ionization techniques enable efficient characterization of atomically precise clusters. Apart from that, techniques such as ion mobility, tandem MS, etc. reveal structural details of these systems. Growth, nucleation, and reactivity of clusters are also probed by MS. Some of the recent advancements in this field include the development of new hyphenated techniques. Finer structural details may be obtained by coupling MS with spectroscopic tools, such as photoelectron spectroscopy, vacuum ultraviolet spectroscopy, etc. With such advancements in instrumentation, MS can evolve into a universal tool for the characterization of materials. The present review captures highlights of this area.

Introduction

Mass spectrometry (MS), a century-old discipline concerning the investigation of matter using ions, is undergoing revolutionary changes. While the systems being examined went through systematic changes from atomic and molecular species to proteins and macromolecules in the course of evolution of MS, the perception of matter itself underwent a drastic transformation in this period. Materials science is becoming increasingly molecular today, and constituents of molecular matter are acquiring new properties leading to novel applications. Investigations require newer tools, and MS has evidently met the needs in this area. This has happened due to efficient methods of ionization of large molecular systems^{1,2}.

The first use of MS dates back to a century ago when Sir J.J. Thomson measured the m/z values of gaseous ionized molecules^{3,4}. He also found the first evidence of isotopes

of an element⁵. Later in 1922, Aston received a Nobel Prize in Chemistry for his discovery of isotopes in several nonradioactive elements⁵. Initially, MS gained importance in the analysis of organic molecules, and ionization techniques like electric discharge and electron impact (EI) were used in such studies. Slowly, scientists started using MS for the analysis of sugars, alkaloids, and peptides⁶. The development of hyphenated techniques like gas chromatography–mass spectrometry (GC–MS)^{7,8} further strengthened the use of MS as an analytical tool. The use of tandem MS (MS/MS) techniques, where mass spectrum of a mass-selected species is analyzed, became a popular tool for understanding the structures of molecules. For extending MS/MS studies to larger molecules like proteins and peptides, Todd, McGilvery, and Baldwin constructed a high-resolution double-focussing mass spectrometer⁹. But still, MS/MS studies for large molecules were possible only with harsh ionization techniques like fast atom bombardment. For the study of large molecules like proteins, there was a need for the development of softer ionization techniques. Such needs led to

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the development of electrospray ionization (ESI)¹, and for this breakthrough development, a Nobel Prize was awarded to John Fenn in 2002. Koichi Tanaka was also awarded a Nobel Prize in the same year for his development of soft laser desorption (SLD) and its applications for ionization of macromolecules¹⁰. Moreover, for the analysis of complex mixtures, high-resolving power ($m/\Delta m$) is desired¹¹. The use of time-of-flight (TOF) mass analyzers came into use in the year 1948¹². By using dual-stage reflectrons, the flight path of the ions could be extended by multiple reflections, and at present TOF analyzers can reach a resolving power of about 50,000 or more at m/z 20–16,000. In 1974, fourier-transform ion cyclotron resonance (FTICR) analyzers were introduced¹³, which exhibited higher-resolving power compared with the TOF analyzers¹⁴. The orbitrap was invented in 1999¹⁴, and at present, they can reach a resolution of 6,00,000 at m/z 195¹⁵. The gas-phase ions generated inside the mass spectrometer can also be confined for a significant amount of time in “ion traps”, and properties of the trapped ions have been studied in the literature¹⁶. Though MS is mainly used for proteomics these days, it also became popular for studying materials. In this review, we have captured how MS has enriched the field of materials science.

Extended solids have been the materials of recent past. They had unique tools for structural characterization, principally revolving around diffraction techniques of various forms¹⁷. The molecular systems on the other extreme had MS as their integral or most essential tool for compositional (to a lesser degree structural as well) analysis. As extended solids became molecular in their building blocks, as evident from the recent advances in nanoscale matter, analytical requirements to understand composition reached newer scales. Molecular materials of the past were composed of smaller constituents weighing a few hundred mass units. Many of them were stable under the harsh conditions of electron impact MS, and therefore were investigated extensively using sector-based instruments. Coupled with methods of ion activation, fragmentation gave a wealth of information on molecular structure¹⁸. These studies were complemented by nuclear magnetic resonance (NMR) spectroscopy, and structural details of molecules with NMR active nuclei could be understood with precision^{19,20}. This was expanded to even solution-state structure determination of macromolecules. The other extreme of structural insight came from electron diffraction, which was instrumental in understanding structures of simple molecules at the early part of the last century²¹. Soon, structural details of small molecules in the gas phase were understood mostly by spectroscopy, particularly for those molecules in the

atmosphere as well as in interstellar space. Electron diffraction of another kind became a prominent analytical tool with the advent of electron microscopy (EM). With cryo-EM in low-dose diffraction, structures were being solved at Angstrom (\AA) resolution in conjunction with high-quality modeling. In addition to single-crystal diffraction, NMR, electron diffraction, and spectroscopy, there are a number of scattering and analytical tools involving X-rays, electrons, positrons, neutrons, photons, and ions to unravel the structure and properties of materials. While this review does not intend to cover comprehensively any of these techniques, we wish to note that the evolution of materials demands new kinds of techniques for compositional and structural analysis. This has happened because constituent units in advanced materials became more and more discrete while increasing in complexity. Along with this change, constituents of matter expanded from diatomics to polyatomics to macromolecules to nanoparticles. While the need to study all of them in isolation became intense, experimental methods of MS in ionization and ion analysis also got evolved.

The importance of MS as a tool for characterization of materials^{22–24} has got strengthened with the advancement in the science of atomically precise nanoclusters (NCs)^{25,26}, which are materials with atomic precision. Such clusters exhibit unique electronic and optical properties, and have precision in its compositional structure in the metal core and the protecting ligand layers. Till date, single-crystal X-ray crystallography has been used to resolve the structures of several clusters like $\text{Au}_{25}\text{L}_{18}$ ²⁷, $\text{Au}_{28}\text{L}_{20}$ ²⁸, $\text{Au}_{38}\text{L}_{24}$ ²⁹, $\text{Au}_{40}\text{L}_{24}$ ³⁰, $\text{Au}_{52}\text{L}_{32}$ ³¹, $\text{Au}_{92}\text{L}_{44}$ ³², $\text{Au}_{102}\text{L}_{44}$ ³³, $\text{Au}_{133}\text{L}_{52}$ ³⁴, $\text{Ag}_{44}\text{L}_{30}$ ³⁵, $\text{Ag}_{25}\text{L}_{18}$ ³⁶, $\text{Ag}_{29}\text{L}_{12}$ ³⁷, etc., where L corresponds to different types of ligands. However, due to their extremely small size, size determination by other techniques like transmission electron microscopy (TEM) or powder XRD has been less reliable. In contrast, MS can accurately identify precision in their compositions. Techniques such as ion mobility–MS (IM–MS) and tandem MS (MS/MS) are becoming increasingly important for understanding the size, shape, and dynamics of cluster systems. Moreover, advancement in instrumentation has enabled the determination of inherent properties of clusters like electron affinity (EA), ionization energy (IE), electronic transitions, etc., through the development of new hyphenated techniques. In this review, we will discuss the recent advances in those emerging directions, and elucidate how MS is evolving into a promising tool for materials characterization.

This has become possible due to advancements in various areas of ionization, mass analysis, detection, sensitivity, resolution, etc. The landmark developments in these aspects are captured in Table 1.

Table 1 Landmark events in the history of mass spectrometry and their importance in enabling the characterization of materials

Progress in instrumentation		Systems studied by MS	Resolution ^{6,134*}	Mass range (m/z) ^{134,5}	
1912	Measurement of m/z values by Thomson ³	Isotopes of elements Atomic weights using MS ⁶	100	100	
1918	Electron ionization ¹³⁵		Aston (130) ⁵	Aston (~100) ⁵	
1936-37	Secondary ion MS ¹³⁶				1,000
1946	Time of flight ¹³⁹	1940s Organic mass spectrometry, Mixture of organic analytes could be separated by GC-MS ⁶	TOF (4000-5000 at m/z ~100) ¹³⁷	Magnetic sector (~2000) ¹³⁸	
1952	Double-focussing instruments ¹⁴⁰		10,000	10,000	
1955	Advanced TOF ¹⁴¹		W geometry ortho-TOF (70,000 at m/z 316) ¹⁴⁷	FTICR (~29,000) ¹⁴⁸	
1956	GC-MS, ^{7,8} high-resolution MS ¹⁴²				1,00,000
1953-58	Quadrupole analyzers ¹⁴³		MS in proteomics and living cells	Orbitrap (6,00,000 at m/z 195) ¹⁵	MALDI TOF (~2,00,000) ¹⁵⁸
1962	Ion mobility ¹⁴⁴			10,00,000	10,00,000
1966	Chemical ionization ¹⁴⁵	1980s high molecular-weight polymers, peptides, proteins, nucleic acids, ESI for macromolecules ⁶ 1996 Analysis of intact live viruses ¹⁵⁶ 1985 Discovery of fullerenes by laser-induced vaporization ³⁸ 1996 LDI for characterization of thiol-protected clusters ⁴⁷ 2008 MS of intact Au ₂₅ (PET) ₁₈ clusters ⁵² 2018 MS of Au-2000 NPs ¹²⁴	FTICR (20,00,000 at m/z 66,000) ¹⁵⁷	Cryo MALDI TOF (~20,00,000) ¹⁵⁹	
1967	Tandem MS ¹⁴⁶		100,000	100,000	
1968	Electrospray ionization (ESI) ¹⁴⁹		Analysis of materials with MS	100,000	100,000
1974	Fourier transform (FT) Ion cyclotron resonance ¹³ , Atmospheric pressure chemical ionization ¹⁵⁰				
1975	Surface-induced dissociation ¹⁵¹				
1978	Triple quadruple ¹⁵²				
1981	Fast atom bombardment MS ¹⁵³				
1987	MALDI ^{10,154}				
1999	Orbitrap ¹⁴				
2004	Desorption electrospray ionization ¹⁵⁵				

*Does not strictly correspond to the time evolution presented in the left column

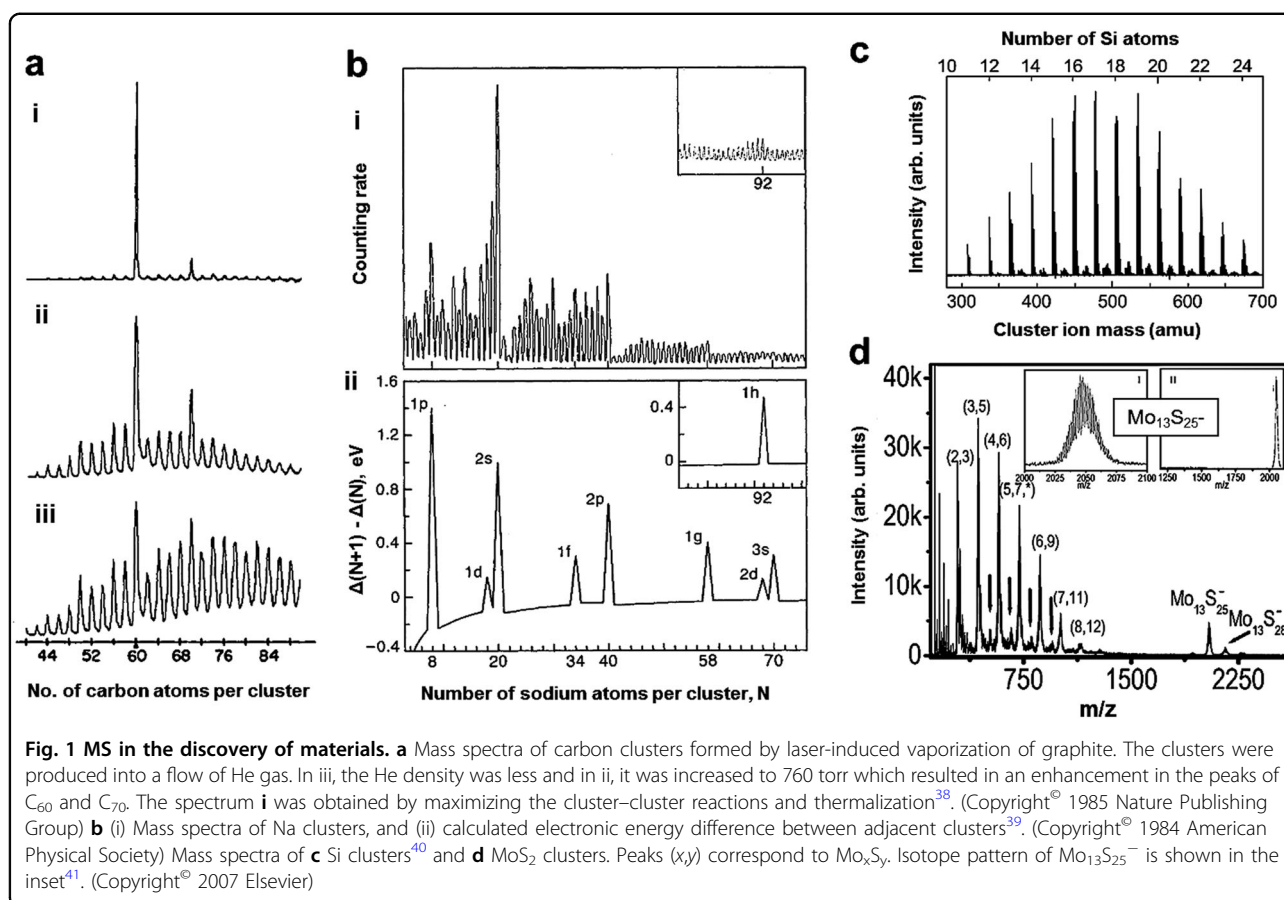
Role of MS in the discovery and characterization of materials

One of the most popular classes of materials of modern science, fullerenes, was discovered using a mass spectrometer³⁸. When a pulsed laser evaporated a solid disk of graphite, cooling of the resulting carbon species by a high-density helium flow resulted in the formation of carbon clusters, which were then detected by a TOF MS (Fig. 1a)³⁸. In low density of He gas, even numbered clusters, C_n ($n = 38-120$) were formed (Fig. 1(iii)), with increase in the He pressure to ~760 torr, the abundances of the peaks due to C₆₀ and C₇₀ were increased (Fig. 1(ii)) and the peak for C₆₀ became predominant upon maximizing the cluster-cluster reactions and thermalization (Fig. 1(i)). Apart from fullerenes, MS was immensely used for the characterization of gas-phase metal clusters of Na, namely Na_n ($n = 4-100$)³⁹. The discontinuous intensities for the clusters of $n = 8, 20, 40, 58,$ and 92 observed in MS (Fig. 1b)

were attributed to the stability of closed shell electronic configurations. Apart from that, there has been extensive research in the field of gas-phase semiconductor clusters like Si clusters ($n = 8-24$) (Fig. 1c)⁴⁰ and molecular clusters like MoS₂ clusters (Fig. 1d)⁴¹.

Early stages of characterization of noble metal clusters by MS

Gas-phase clusters of noble metals like Au_n or Ag_n were also investigated by MS⁴². Furche et al. assigned the structures of Au_n ($n < 13$) clusters by a combination of mass spectrometric and theoretical studies⁴³. Lechtken et al. determined the structures of Au₁₄⁻ - Au₁₉⁻ clusters by trapped ion electron diffraction⁴⁴. Later, in 2003, Li et al. observed that Au₂₀ cluster which possesses a tetrahedral structure, shows similar atomic packing but largely different properties compared with bulk gold⁴⁵. By photoelectron spectroscopy (PES), the authors



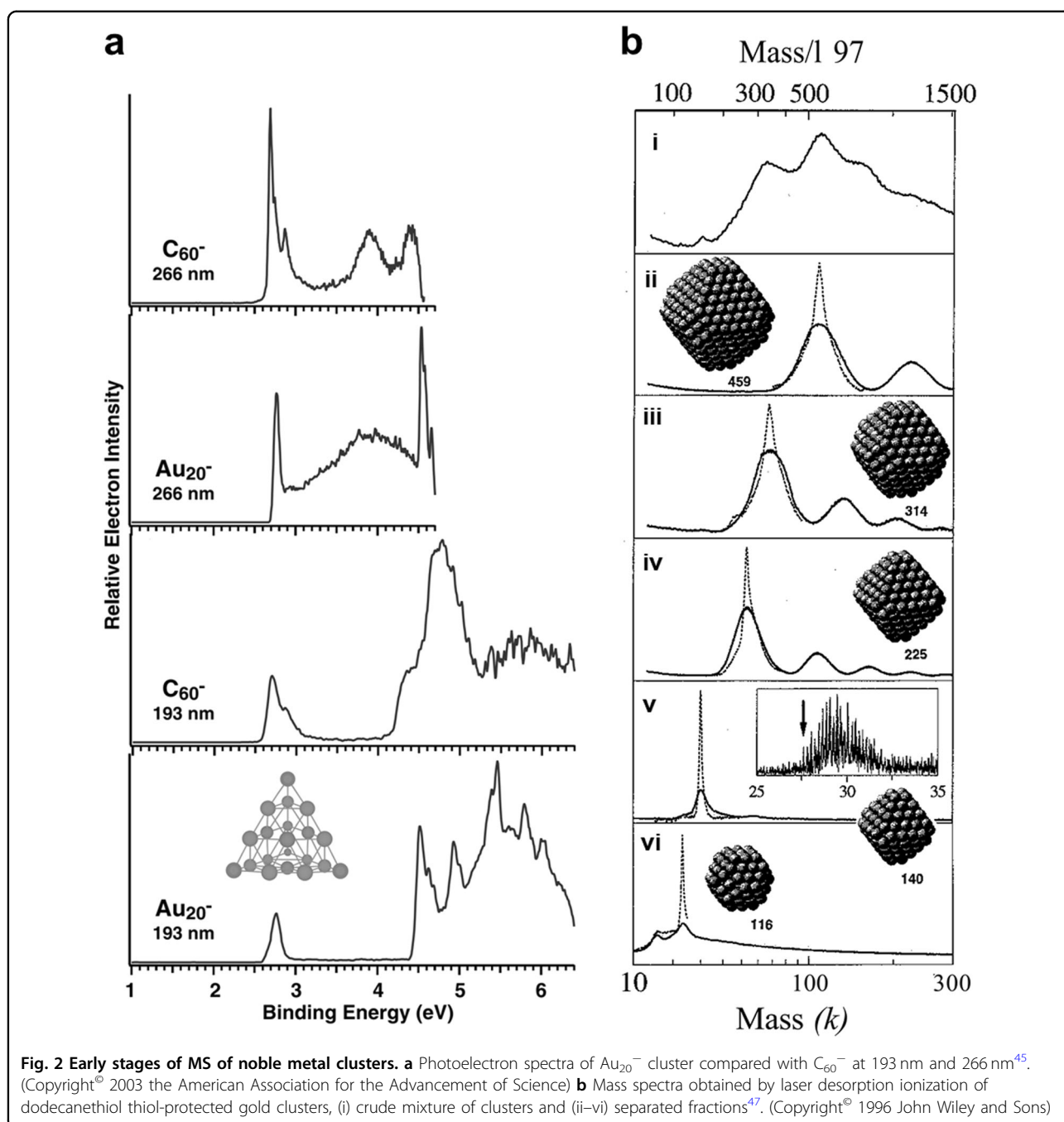
demonstrated that the EA of Au₂₀ cluster was comparable with that of C₆₀, as shown in Fig. 2a. Along with such studies on gas-phase bare metal clusters, MS slowly evolved into a powerful tool for the characterization of ligand-protected noble metal NCs also.

After Brust reported a new method of synthesis of thiol-protected gold NPs in 1994⁴⁶, scientists started the synthesis of monodisperse NPs with molecule-like optical absorption features. In 1996, Whetten et al. used laser desorption ionization (LDI) for the characterization of dodecanethiol protected gold NCs having mass in the range of 27–93 kDa (Fig. 2b)⁴⁷. The LDI measurements suggested that the gold cores consisted of 140–459 atoms, which was also consistent with their TEM measurements.

Advances in the study of noble metal clusters

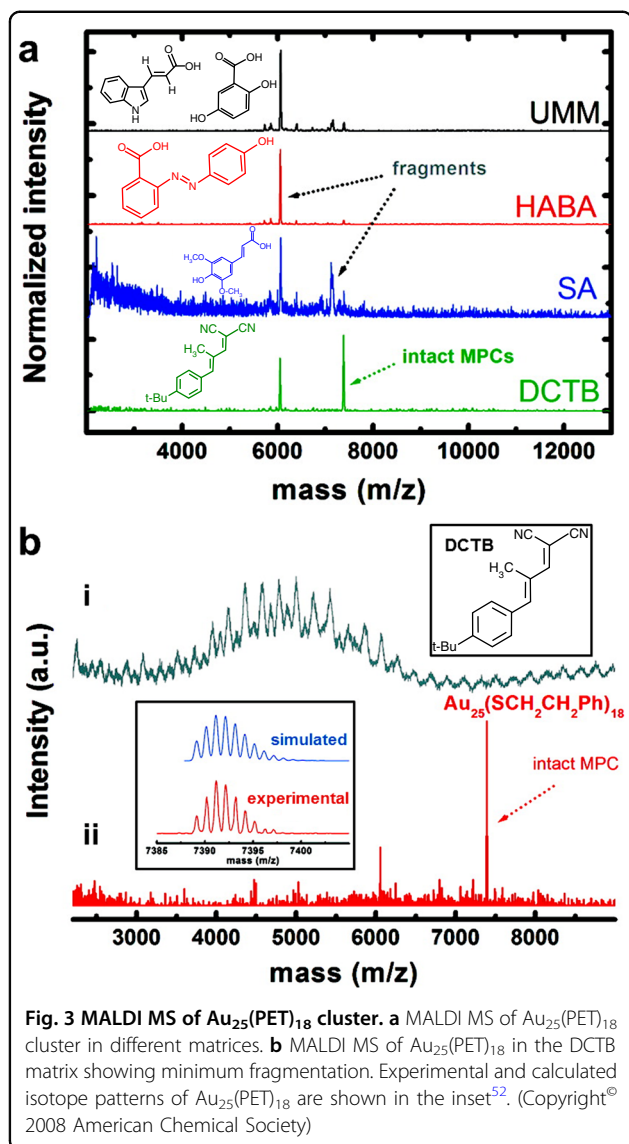
Though LDI was used as the primary characterization tool in the 1990s, softer techniques like matrix-assisted laser desorption ionization (MALDI) and ESI became more popular for the ionization of intact ligand-protected clusters. In 1998, Schaff et al. reported a 10.4 kDa Au-GSH (GSH = glutathione) cluster, Au₂₈(SG)₁₆⁴⁸. The composition was proposed from both MALDI MS and ESI MS. Following this, several other reports came on the

same cluster until in 2005, it was reassigned as Au₂₅(SG)₁₈ by Negishi et al.⁴⁹. With advancement in instrumentation, resolution of the mass spectral measurements improved, which enabled successful characterization of the cluster. MS has largely been used in the characterization of gold clusters, particularly due to their high stability under ambient conditions. Though ESI efficiently ionized water-soluble gold clusters, organic-soluble clusters often showed poor ionization efficiency in this technique. In order to overcome this, scientists implemented new approaches like ligand exchange with ionizable ligands⁵⁰, using Ce(SO₄)₂⁵¹, or CsOAc to enhance the ionization^{52,53}. In most cases, with the choice of appropriate matrices like sinapinic acid, cinnamic acid, etc., MALDI worked better for the ionization of NCs. In 2008, Dass et al. introduced the use of trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene] malonitrile (DCTB) matrix which proved to be more effective⁵², and MALDI MS of intact Au₂₅(PET)₁₈ clusters was successfully measured (Fig. 3b). Comparison of MALDI MS of Au₂₅(PET)₁₈ clusters in different matrices showed the superiority of using DCTB (Fig. 3a). Larger NCs like Au₁₀₂(pMBA)₄₄⁵⁴ were also characterized using a combination of ESI and MALDI MS. However, due to lesser



stability, mass spectral characterization of silver clusters has always been challenging. As Ag has two isotopes (107 and 109), silver clusters show broader isotope patterns. At the initial stages of research in the field of Ag clusters, mercaptosuccinic acid (H_2MSA) protected Ag_7 , Ag_8 ^{55,56}, glutathione protected $Ag_{11}(SG)_7$ ⁵⁷, $Ag_{15}(SG)_{11}$ ⁵⁸, $Ag_{31}(SG)_{19}$ ⁵⁸, and $Ag_{32}(SG)_{19}$ ⁵⁹, etc., clusters were characterized by MS. In 2012, Harkness et al. reported the $Ag_{44}(SR)_{30}$ NCs⁶⁰, which was later crystallized in 2013 by Desiredy et al.³⁵ and Yang et al.⁶¹. Recently, in 2015,

Bakr et al. reported $Ag_{25}(SR)_{18}$ NCs which exhibits identical structure as that of $Au_{25}(SR)_{18}$ ³⁶. A luminescent Ag NC, $[Ag_{29}(BDT)_{12}(TPP)_4]$ ³⁷, and a box-shaped $[Ag_{67}(SPhMe_2)_{32}(PPh_3)_8]$ ⁶² were also reported from the same group. High-resolution ESI MS gave the accurate molecular formulae of these clusters, which matched exactly with their composition found in crystal structures. This highlights the importance of using MS as a versatile tool for the characterization of the NCs. Most recently it has been possible to characterize new types of silver



clusters, $[\text{Ag}_{18}\text{H}_{16}(\text{TPP})_{10}]^{2+}$, $[\text{Ag}_{25}\text{H}_{22}(\text{DPPE})_8]^{3+}$, and $[\text{Ag}_{26}\text{H}_{22}(\text{TFPP})_{13}]^{2+}$, which are protected by hydrides and phosphines⁶³. Hydride-doped gold cluster $[\text{Au}_9\text{H}(\text{PPh}_3)_8]^{2+64}$ and bimetallic $[\text{HPdAu}_9(\text{PPh}_3)_8]^{2+}$ clusters⁶⁵ were also characterized by ESI MS. The crystal structures of many such clusters are not yet available.

Apart from research in the field of Au and Ag NCs, the applicability of MS has also been extended to the field of clusters of other noble metals, eg., Pt NCs^{66,67}, Pd NCs^{68–70}. MS has also been proved to be useful in case of non-noble metals; eg. Cu NCs like $[\text{Cu}_{20}\text{H}_{11}(\text{S}_2\text{P}(\text{OiPr})_2)_9]^{71}$, Fe NCs like $[\text{Fe}_6\text{H}_{10}(\text{PMe}_3)_8]^{+72}$, Ir NCs like $\text{Ir}_9(\text{PET})_6^{73}$, etc.

High-resolution mass spectrometry (HRMS)

Over the years, there has been a tremendous improvement in instrumentation, which has enabled to obtain HR mass spectra of clusters with minimum fragmentation. A

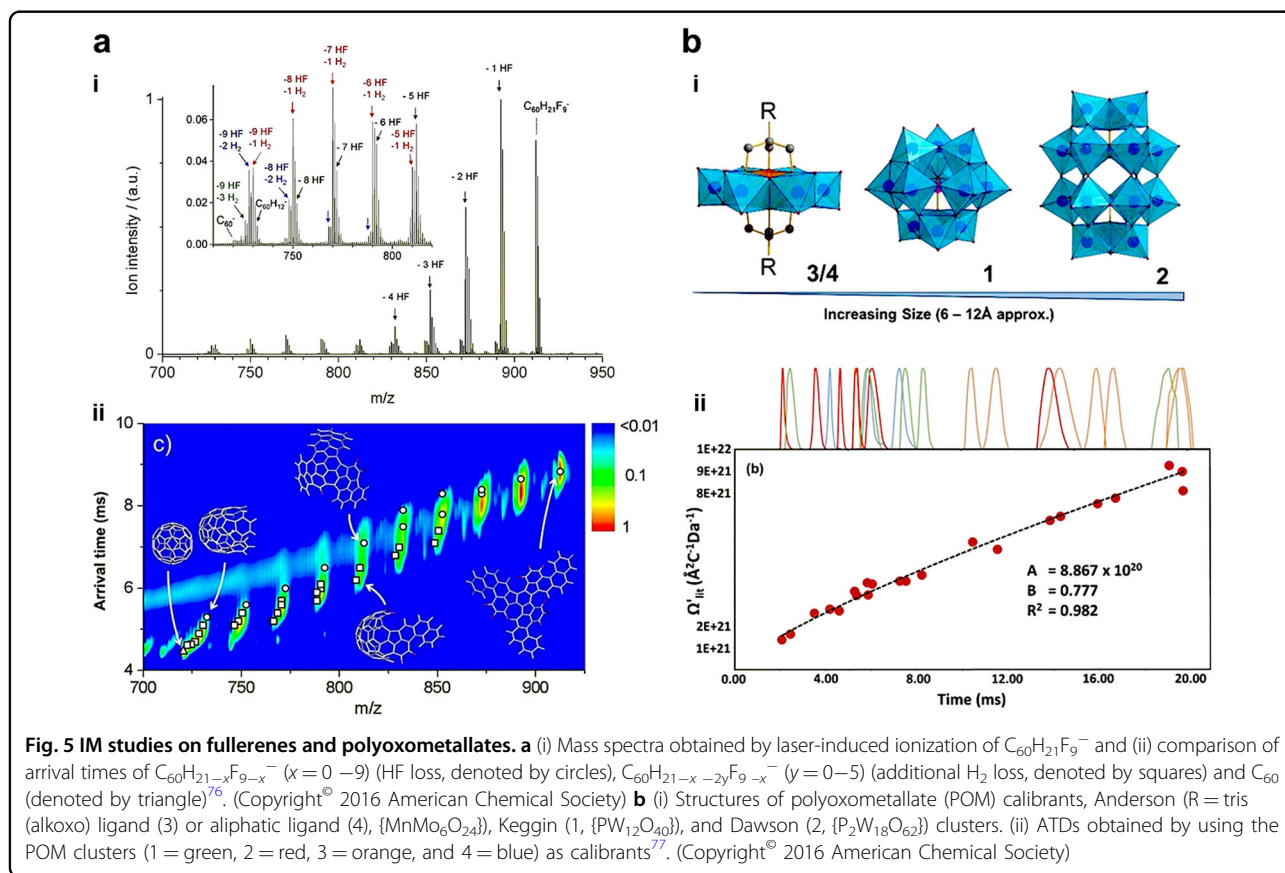
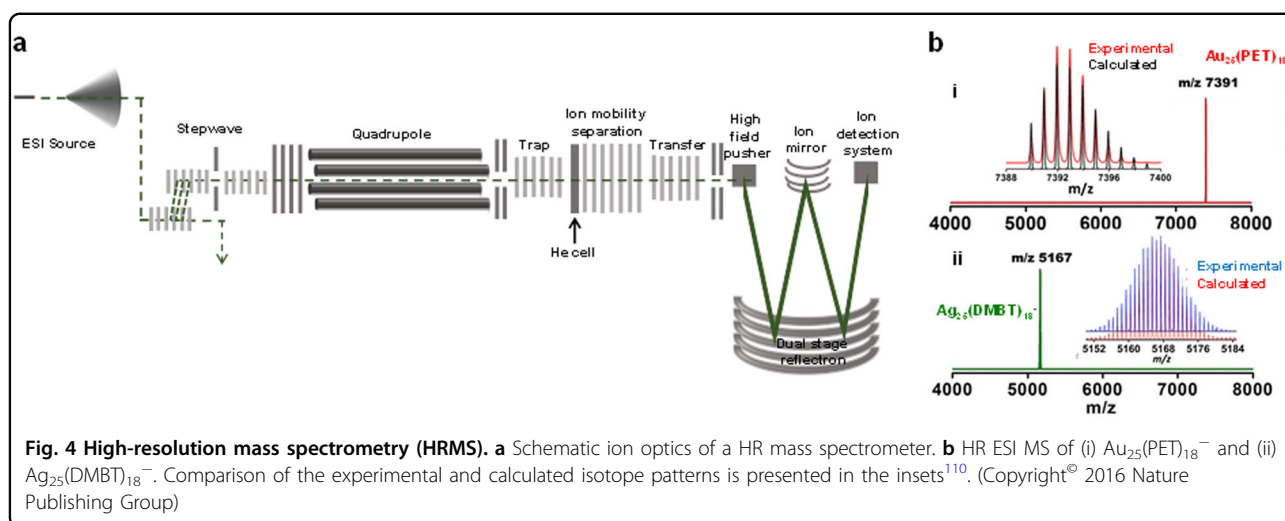
schematic of a HRMS instrument is shown in Fig. 4a. In the TOF analyzer, the trajectory of the ions can be controlled in a shorter “V” or a longer “W” path. With the increase in the path of the ions, the resolution ($m/\Delta m$) increases from $\sim 20,000$ – $35,000$ to $\sim 35,000$ – $50,000$ in the m/z range of 20–16000. Additional parts like “stepwaves” are used to remove all contaminants before the ions enter the quadrupole of the mass spectrometer. This also increases the sensitivity of the measurement. Precise composition of the core and the ligands and charge states of the cluster can be determined accurately by using HRMS. The compositions are further confirmed from the isotope patterns of the metals (Au, Ag, Pt, Pd, etc.) and that of C, H, and S present in the ligands. HR ESI MS of $\text{Au}_{25}(\text{PET})_{18}^-$ (PET is phenyl ethane thiol) and $\text{Ag}_{25}(\text{DMBT})_{18}^-$ (DMBT is 2,4-dimethyl benzene thiol) are presented in Fig. 4b.

Apart from the conventional ESI MS analysis, HR mass spectrometers of the present day are also equipped with several other advanced features that enable further studies on the gas-phase cluster ions. Some such recent studies are summarized below.

Ion mobility–mass spectrometry (IM-MS)

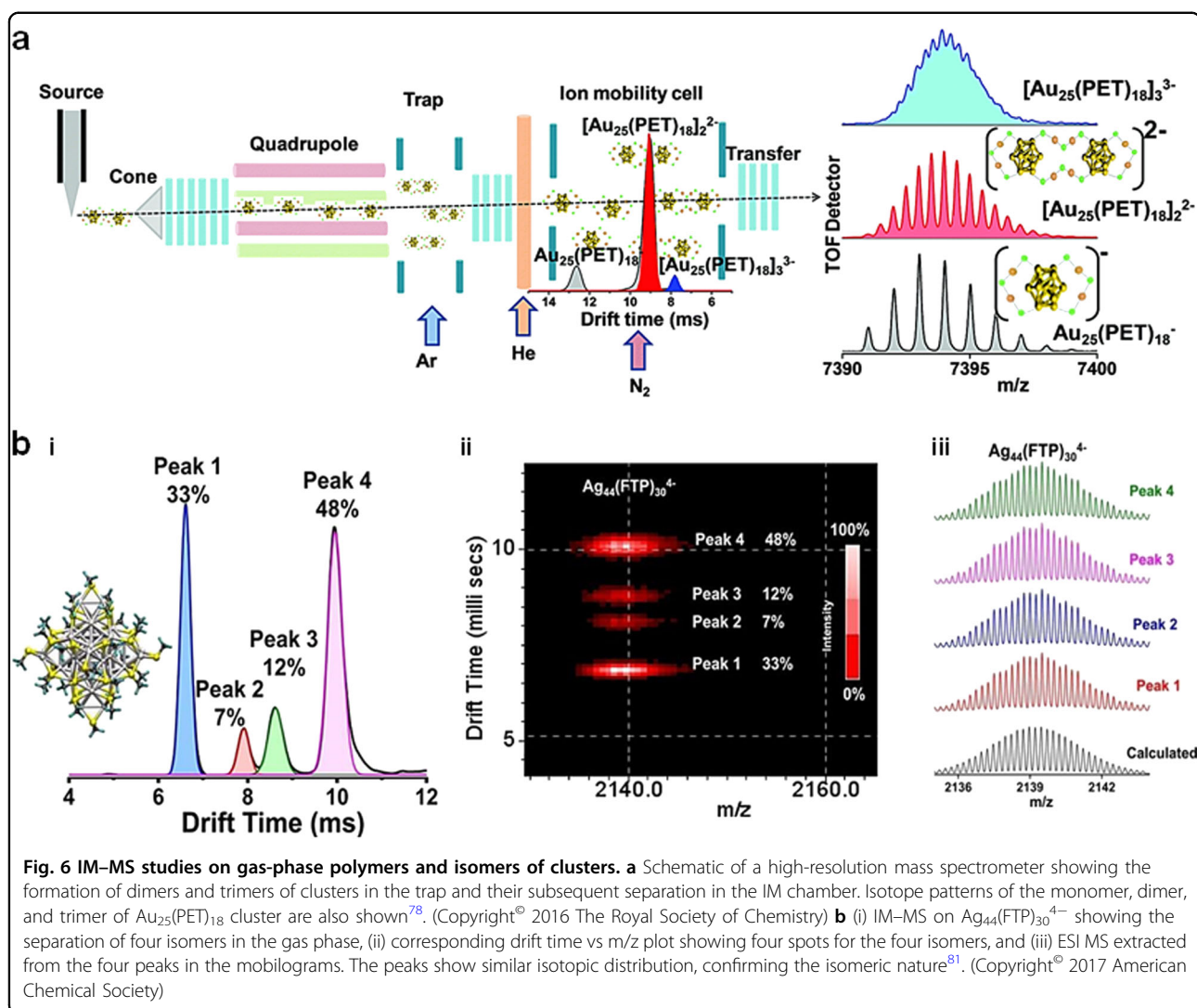
MS coupled with IM has proved to be an important tool for structural characterization, and has enhanced research in many areas of biochemical and biophysical studies⁷⁴. In the IM cell, the ions are passed through buffer gases like He, N_2 , etc. As a result, species having the same mass but different size and shape exhibit different collision cross-section (CCS), hence show different drift times and get separated. IM–MS is capable of studying the conformational dynamics present in a system, and has largely been used to understand the folding and unfolding mechanism in proteins⁷⁵. In materials science, IM–MS has been used to study the mechanism of formation of fullerenes from polycyclic aromatic hydrocarbons (PAH). Laser desorption of PAHs like $\text{C}_{60}\text{H}_{21}\text{F}_9^-$ causes stepwise loss of HF and H_2 (Fig. 5ai), which results in increasing curvature of the remaining PAH fragments and finally closed-cage fullerenes are formed⁷⁶. To understand the mechanism, the extent of curvature in the structure of the products at each step was modeled by comparing the CCS of the computed structures with the experimental CCS observed in IM–MS (Fig. 5aii). IM–MS has also been largely used for understanding the structures of polyoxometallates. Surman et al. showed that Keggin or Dawson type POM clusters (structures are shown in Fig. 5bi) can be used as IM calibrants for high mass negatively charged ions, and using the calibration curves (Fig. 5bii), structures of other POM clusters can be determined⁷⁷.

Recently, IM–MS has also gained importance in the field of protected noble metal NCs. Baksi et al. separated dimers and trimers of $[\text{Au}_{25}(\text{SR})_{18}]^-$ using IM–MS⁷⁸. A



schematic of the instrumental setup showing the formation of aggregates of the cluster under increased pressure conditions in the trap, and its subsequent separation in the IM chamber is presented in Fig. 6a. Chakraborty et al. have also shown that alkali metal ions can induce dimerization of $[\text{Ag}_{29}(\text{BDT})_{12}]^{3-}$ NCs in a similar manner⁷⁹. Baksi et al. identified isomerism in $[\text{Ag}_{11}(\text{SG})_7]^-$

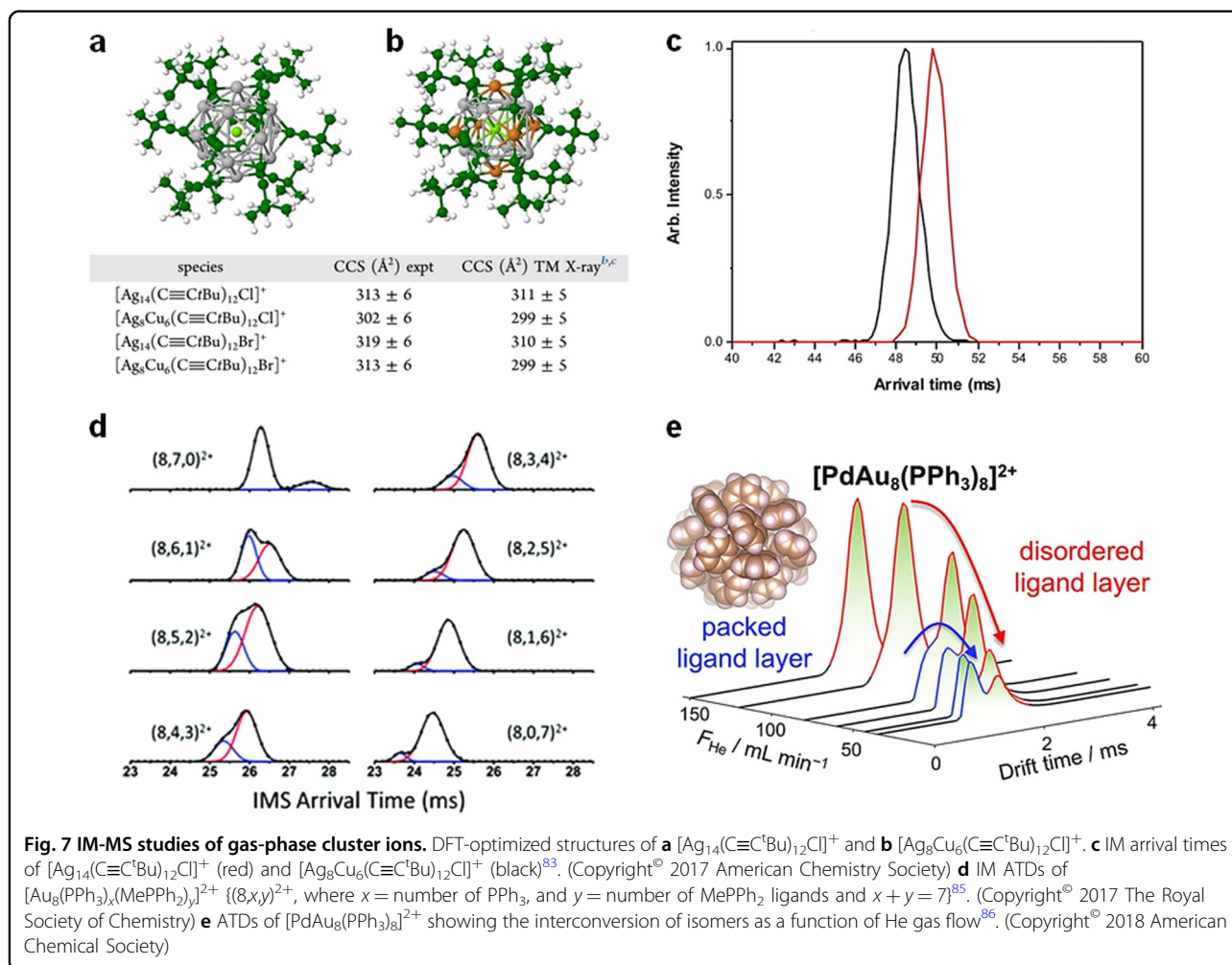
cluster in the gas phase⁸⁰. However, as the crystal structure of $[\text{Ag}_{11}(\text{SG})_7]^-$ is not known, the correlation with the condensed-phase structures could not be established. In another report, the authors showed that $[\text{Ag}_{44}(\text{SR})_{30}]^{4-}$ and $[\text{Ag}_{29}(\text{BDT})_{12}]^{3-}$ clusters also show isomerism in the gas phase⁸¹, which do not show any isomers in their crystal structure. Four distinct isomeric peaks were



observed in IM-MS of [Ag₄₄(FTP)₃₀]⁴⁻ (Fig. 6b). However, two isomers were separated for [Ag₄₄(FTP)₃₀]³⁻, which indicated that isomerism is charge-state dependent. The influence of the ligand shell in isomerism was studied by using [Ag₄₄(SR)₃₀] clusters protected by different ligands, which showed different number of isomers. Also, Au₂₅(SR)₁₈ and Ag₂₅(SR)₁₈ clusters showed a single peak in IM, suggesting that isomerism is highly selective to the structure and the symmetry of the cluster.

Kappes et al. performed IM studies on Au cluster cations Au_n⁺. Comparison of experimental CCS with that of theoretical CCS from DFT-optimized structures revealed that Au_n⁺ have planar structures for *n* = 3–7, while for *n* = 8–10, they show three-dimensional structures⁸². In a recent study, Daly et al. characterized homometallic cluster ions, [Ag₁₄(C≡C^tBu)₁₂Cl]⁺, [Ag₁₄(C≡C^tBu)₁₂Br]⁺ and heterometallic clusters ions, [Ag₈Cu₆(C≡C^tBu)₁₂Cl]⁺, [Ag₈Cu₆(C≡C^tBu)₁₂Br]⁺ by

IM-MS⁸³. These cluster ions showed a single peak in IM, and comparison of the CCS values derived from IM with the CCS values modeled from its X-ray crystal structure suggested that the gas-phase structures of the clusters resembled their condensed-phase structures (Fig. 7a, b). The shorter arrival time of the heterometallic cluster ions in comparison with that of the homometallic cluster ions was consistent with the observation from their crystal structures and DFT calculations (Fig. 7c). Thus, IM proved to be an effective tool not only for the separation of gas-phase entities but also for structural characterization of the clusters. In another study by Soleilhac et al., the size of GSH-protected clusters were compared in the solid, liquid, and gas phase by using X-ray powder diffraction (XRPD), time-resolved fluorescence anisotropy (TRFA), and IM-MS, respectively⁸⁴. From the CCS values obtained from IM, the radii of the clusters were calculated as 1.22, 1.31, and 1.47 nm for Au₁₅(SG)₁₃, Au₁₈(SG)₁₄, and



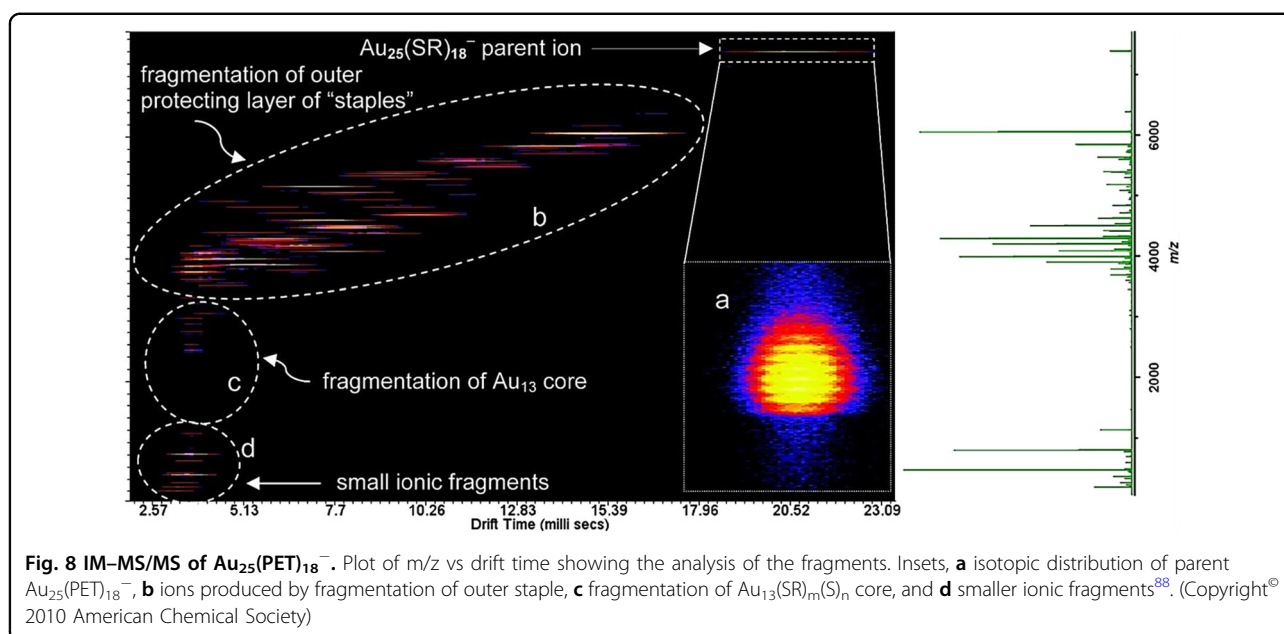
Au₂₅(SG)₁₈, respectively. Though the absolute values differed, the trends in the size of the above NCs were similar in all the three phases. In comparison with techniques like XRPD and TRFA, IM-MS is expected to become a more convenient technique for determining the size of the clusters due to the ease of sample preparation and lower limit of error (~2%) compared with other techniques.

Ligare et al. used ESI IM-MS to study the structural changes upon systematic ligand exchange of [Au₈(PPh₃)₇]²⁺ and [Au₁₁(PPh₃)₉H]²⁺ with methyl-diphenylphosphine (MePPh₂)⁸⁵. Studies revealed that [Au₈(PPh₃)₇]²⁺ cluster showed two isomers, and on increasing ligand exchange with MePPh₂, these isomers underwent a change in relative population from a more compact structure showing lower arrival time to a more extended structure showing larger arrival time, as shown in Fig. 7d. In contrast, [Au₁₁(PPh₃)₉H]²⁺ cluster showed only one isomer. Recently, Hirata et al. showed that phosphine-protected gold clusters like [Au₉(PPh₃)₈]³⁺ and [PdAu₈(PPh₃)₈]²⁺ undergo conversion to more

compact isomers upon collisional excitation (Fig. 7e)⁸⁶. Such studies help to understand the fluxionality in the structures of the NCs.

Gas-phase dissociation studies of noble metal nanoclusters

While IM-MS reveals enormous information regarding the shape, size, and conformations of the cluster ions, more information regarding their structure and bonding can be obtained from dissociation studies. In collision-induced dissociation (CID), mass-selected ions are subjected to dissociation by collision with gases like Ar, N₂, He, etc. Fields-Zinna et al. reported CID studies on ligand-protected Au₂₅ NCs and showed that the dissociation involved the Au₂L₃ semirings, which are the staples motifs present in its crystal structure⁸⁷. The authors used Au₂₅(SC₂H₄Ph)₁₈ cluster, and ligand-exchanged it with -S(CH₂CH₂O)₅CH₃ (-SPEG) to facilitate ionization and studied CID on these mixed ligand-protected Na_xAu₂₅(SC₂H₄Ph)_{18-y}(S(CH₂H₄O)₅CH₃)_y clusters using ESI TOF and ESI FTICR MS. CID produced

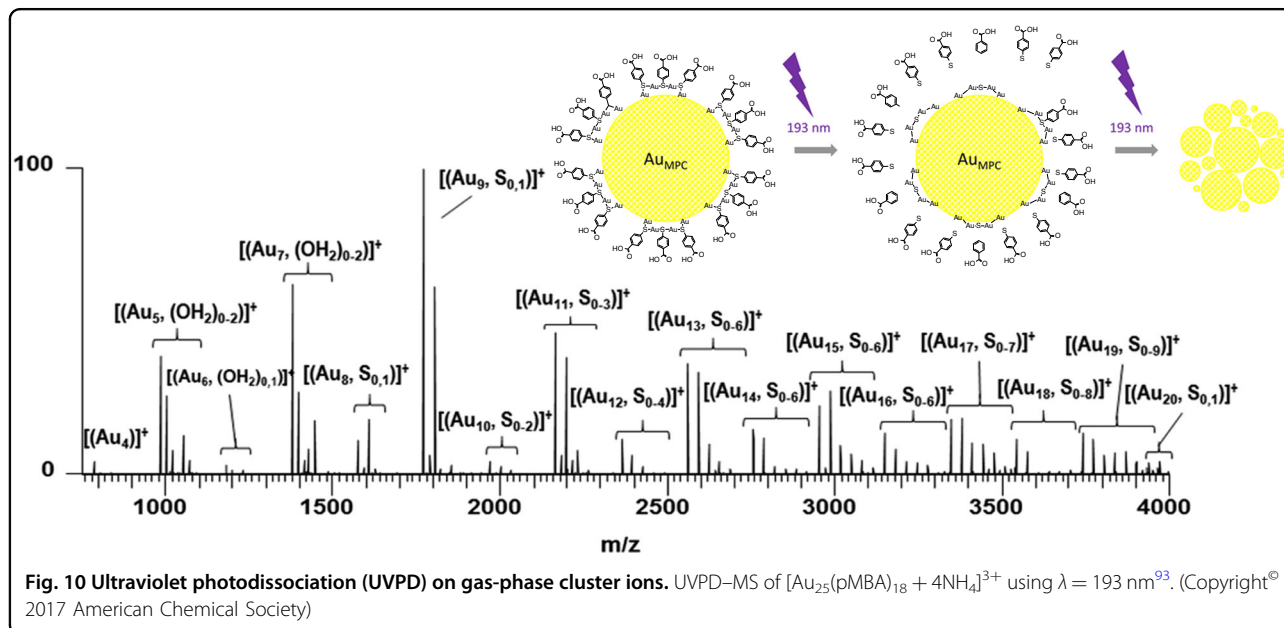
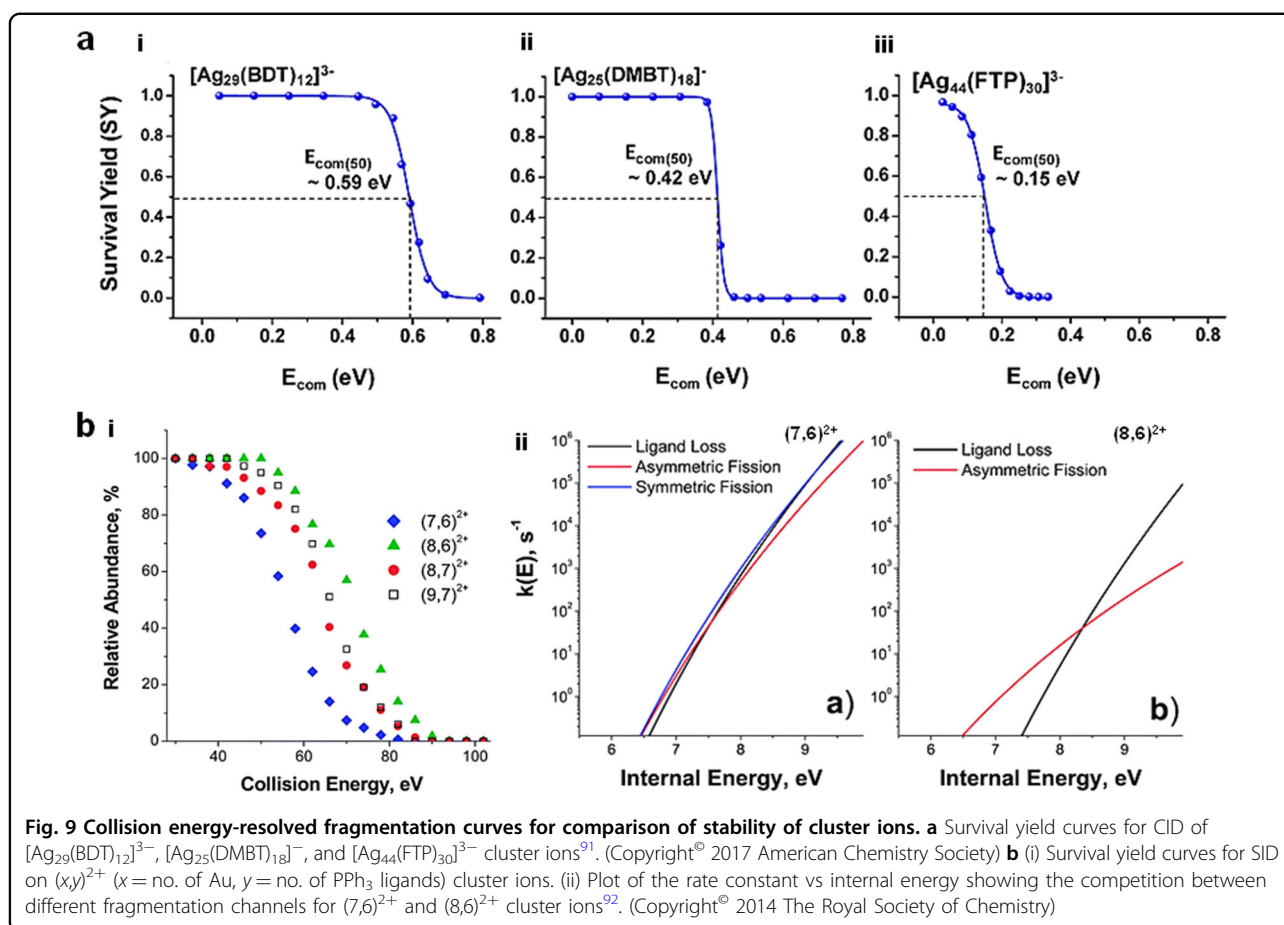


fragments such as $[\text{Na}_2\text{Au}_2\text{L}_3]^{1+}$ representing the loss of a single semiring and fragments such as $[\text{NaAu}_3\text{L}_3]^{1+}$ and $[\text{NaAu}_4\text{L}_4]^{1+}$ representing the loss of multiple semirings⁸⁷. Later, Angel et al. studied the fragmentation of $\text{Au}_{25}\text{L}_{18}^-$ NCs using HR ESI MS⁸⁸. The predominant fragmentation pathway involved the loss of Au_4L_4 leading to the formation of fragment ions, such as $\text{Au}_{21}\text{L}_{14}^-$ and $\text{Au}_{17}\text{L}_{10}^-$. They also introduced the use of IM-MS/MS, a technique where IM is coupled to CID, which could differentiate between fragmentation from the outer staples, fragmentation from the icosahedral core and the smaller ionic fragments, by separating them into distinct bands (Fig. 8). Black et al. carried out CID on larger Au NCs like $\text{Au}_{144}(\text{SR})_{60}$ and $\text{Au}_{130}(\text{SR})_{50}$, and also showed that the extent of fragmentation is specific to the charge state of the cluster ions⁸⁹. CID of mixed-ligand-protected cluster, $[\text{Au}_{11}(\text{PPh}_3)_8\text{X}_2]^+$ ($\text{X} = \text{Cl}, \text{C}\equiv\text{CPh}$), showed competing fragmentation channels involving sequential loss of PPh_3 and $\text{Au}_x(\text{PPh}_3)$ ⁹⁰.

The extent of fragmentation also depends on the internal energy distribution of the ions, and hence CID studies were used to understand the stabilities of the cluster ions. Taking $\text{Ag}_{29}(\text{SR})_{12}$, $\text{Ag}_{25}(\text{SR})_{18}$, and $\text{Ag}_{44}(\text{SR})_{30}$ NCs as examples, Chakraborty et al. demonstrated that the predominant fragmentation pathways of these NCs involved the loss of $\text{Ag}_5(\text{SR})_6^-$, $\text{Ag}(\text{SR})^-$, or $\text{Ag}_2(\text{SR})_3^-$ fragments⁹¹. By using survival yield analysis and comparing the values of $E_{\text{com}50}$ ($E_{\text{com}50}$ is center-of-mass energy corresponding to 50% dissociation of the cluster), the stabilities of these clusters were compared (Fig. 9a), and the order of gas-phase stability $[\text{Ag}_{29}(\text{SR})_{12}]^{3-} > [\text{Ag}_{25}(\text{SR})_{18}]^- > [\text{Ag}_{44}(\text{SR})_{30}]^{3-}$ was similar to that observed in the solution phase.

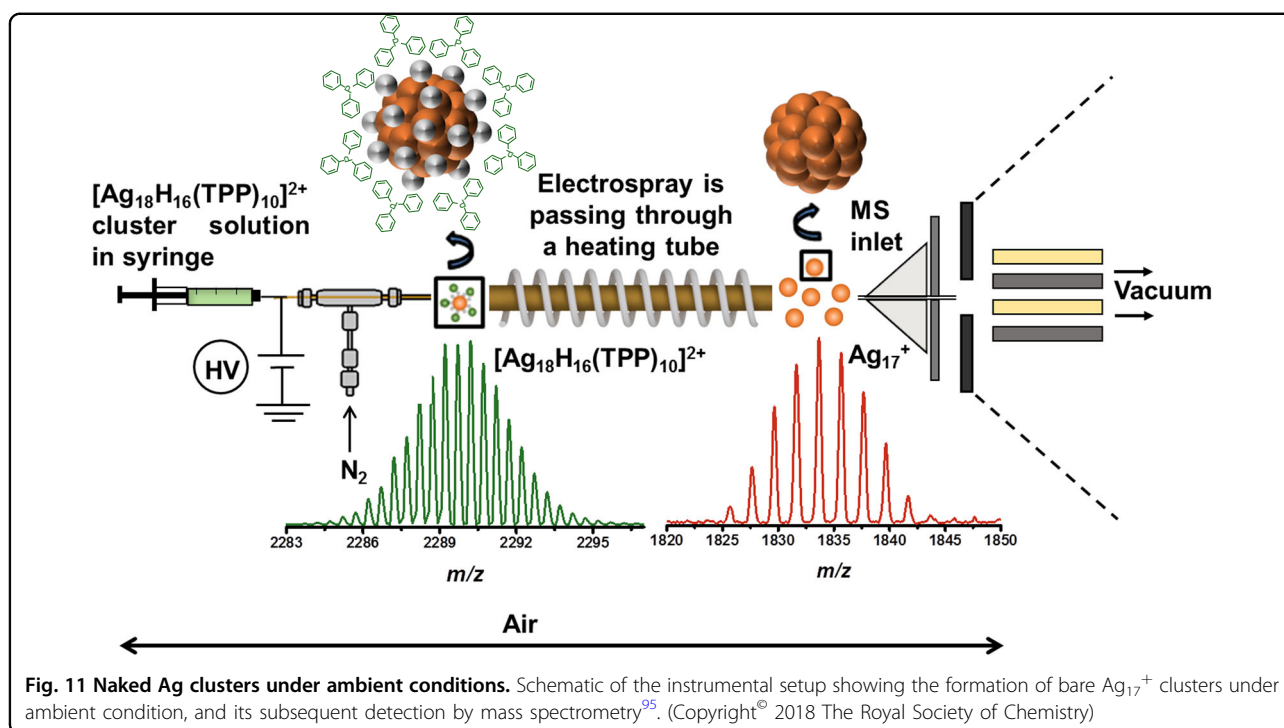
Another technique that can be effectively used to study the energetics and kinetics of the fragmentation process is surface-induced dissociation (SID). In this process, mass-selected ions are collided with a surface (usually Au surfaces protected by monolayers of alkanethiols) and impact induced activation leads to dissociation. In comparison with CID, SID is a more convenient technique to extract thermodynamic parameters of the cluster ions, as here the applied CE can be varied through a large range to observe a small change in the threshold internal energies of large ions. Using SID, Johnson et al. quantified the stability and ligand-binding energies of small TPP-protected Au clusters, $\text{Au}_7\text{L}_6^{2+}$, $\text{Au}_8\text{L}_6^{2+}$, $\text{Au}_8\text{L}_7^{2+}$, and $\text{Au}_9\text{L}_7^{2+}$ ⁹². Collision energy-resolved fragmentation curves revealed that $\text{Au}_8\text{L}_6^{2+}$ cluster was more stable toward dissociation (Fig. 9bi). SID enabled the quantitative estimation of the threshold energies and activation entropies of fragmentation. It also enabled to understand the kinetics of fragmentation by determining the microcanonical rate constants for the different fragmentation pathways (Fig. 9bii) and hence determining the kinetically and thermodynamically favored pathways. Moreover, taking $\text{Ag}_{11}(\text{SG})_7^{7-}$ clusters as an example, Baksi et al. showed that CID and SID of the clusters occurred through different pathways. SID produced more fragments compared with CID, and charge stripping from 3- to 2- and 1- charge states of the cluster ions occurred⁸⁰.

While both CID and SID produces a lesser number of fragments, extensive fragmentation can be observed by ultraviolet photodissociation (UVPD) as observed in the case of $\text{Au}_{25}(\text{pMBA})_{18}$ and $\text{Au}_{36}(\text{pMBA})_{24}$ NCs⁹³. UVPD on these clusters using $\lambda = 193$ nm involved high-energy fragmentation pathways and cleavage of Au-S and C-S



bonds. When the cluster ions were exposed to multiple laser pulses, a series of bare Au cluster ions were formed by sequential evaporation of neutral Au atoms (Fig. 10).

Recently, Ghosh et al. showed that the bare cluster ion, Ag_{17}^+ , can be produced selectively by CID of $[Ag_{18}(TPP)_{10}H_{16}]^{2+}$ clusters and by further increasing the



collision energy, a series of Ag_n^+ ($n = 1-17$) clusters may be produced^{63,94}. In a similar manner, $[\text{Ag}_{25}(\text{DPPE})_8\text{H}_{22}]^{3+}$ and $[\text{Ag}_{22}(\text{DPPE})_8\text{H}_{19}]^{3+}$ were also used as precursors for bare Ag clusters⁹⁴. In a recent study by Jash et al., electro sprayed $[\text{Ag}_{18}(\text{TPP})_{10}\text{H}_{16}]^{2+}$ clusters were passed through a heated tube, whereby all the ligand layers were desorbed leading to the formation of Ag_{17}^+ under ambient conditions, and the product ions were subsequently detected by MS (Fig. 11)⁹⁵.

Spectroscopy on the mass-selected gas-phase cluster ions

The electronic properties of the NCs are probed experimentally by optical and electrochemical studies in solution. However, these experimental results are influenced by the solvents and the counter ions present in solution. So, there is a need to directly probe the energy levels of the isolated cluster ions in vacuum. Anion PES is usually used to determine HOMO–LUMO gaps and EAs. Such studies have been done for bare Au_n^- clusters⁹⁶. Recently, Hirata et al. performed PES on isolated $[\text{Au}_{25}(\text{SC}_{12}\text{H}_{25})_{18}]^-$ ions by coupling a magnetic bottle-type photoelectron spectrometer with a TOF mass spectrometer⁹⁷. Schematic of the instrumental setup used for the study is presented in Fig. 12a. The photoelectron spectrum of $[\text{Au}_{25}(\text{SC}_{12}\text{H}_{25})_{18}]^-$ showed two bands, A and B (Fig. 12b), corresponding to electron detachment from 1P superatomic and Au 5d orbitals localized on the core Au atoms. The vertical detachment

energy (VDE) and adiabatic electron affinity (AEA) of $[\text{Au}_{25}(\text{SC}_{12}\text{H}_{25})_{18}]^-$ was determined to be 2.5 eV and 2.2 eV, which corresponds to the values of E_{top} and E_{th} in the photoelectron spectrum (Fig. 12b), respectively. Hamouada et al. studied photoexcitation of $[\text{Au}_{25}(\text{SG})_{18-6}\text{H}]^{7-}$, where the yield of electron detachment as a function of the laser wavelength gave the gas-phase optical action spectra, which was found to be similar to the solution-phase spectrum⁹⁸. Daly et al. studied the photofragmentation and VUV photoionization of $[\text{Ag}_{10}\text{D}_8\text{L}_6]^{2+}$ NCs in the gas phase by coupling a linear ion trap mass spectrometer with a beamline of synchrotron, capable of producing high flux of photons that could be tuned in the entire VUV range⁹⁹. Upon photoexcitation of $[\text{Ag}_{10}\text{D}_8\text{L}_6]^{2+}$, a number of photofragments were produced, such as $[\text{Ag}_{10}\text{D}_8\text{L}_6]^{3+}$, $[\text{Ag}_{10}\text{D}_8\text{L}_5]^{2+}$, $[\text{Ag}_{10}\text{D}_8\text{L}_4]^{2+}$, $[\text{Ag}_9\text{D}_8\text{L}_4]^{2+}$, and $[\text{AgL}_2]^+$. The ionization onset of $[\text{Ag}_{10}\text{D}_8\text{L}_6]^{2+}$ was determined from the onsets in the yield of $[\text{Ag}_{10}\text{D}_8\text{L}_6]^{3+}$ as a function of photon energy. Two ionization onsets were determined as ~ 9.3 eV and ~ 10.6 eV, which might be due to removal of electrons from orbitals of different energy levels. In another study, authors from the same group performed VUV and UV spectroscopy on $[\text{Ag}_{14-n}\text{Cu}_n(\text{C}\equiv\text{CtBu})_{12}\text{X}]^+$ ($X = \text{Cl}$ and Br) cluster ions⁸³. The ionization onsets of the cluster ions were determined to be ~ 8.8 eV, and this was similar for all the ions, irrespective of the nature of halides or the extent of Cu doping (Fig. 12c). Photofragmentation of the same

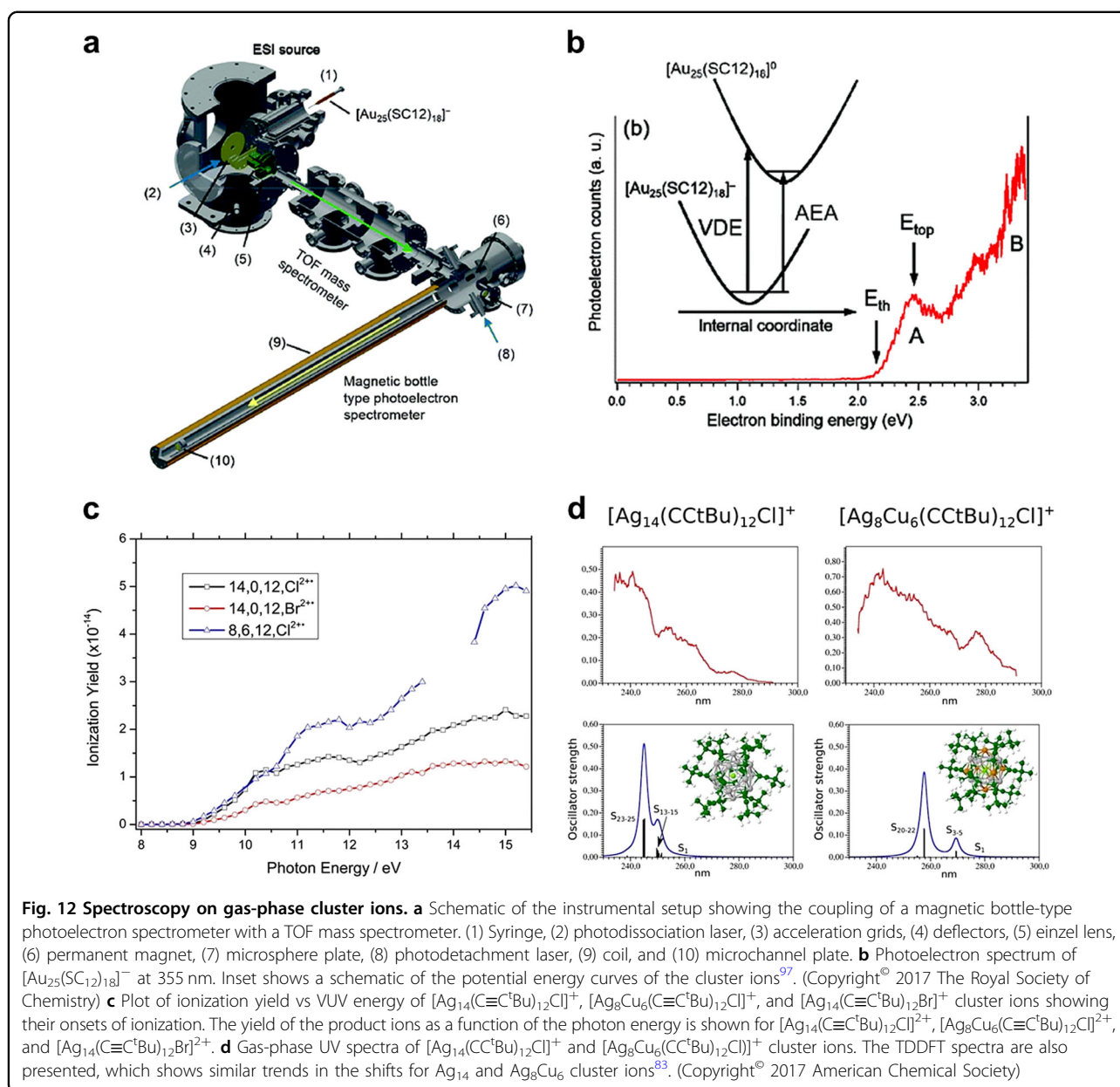


Fig. 12 Spectroscopy on gas-phase cluster ions. **a** Schematic of the instrumental setup showing the coupling of a magnetic bottle-type photoelectron spectrometer with a TOF mass spectrometer. (1) Syringe, (2) photodissociation laser, (3) acceleration grids, (4) deflectors, (5) einzel lens, (6) permanent magnet, (7) microsphere plate, (8) photodetachment laser, (9) coil, and (10) microchannel plate. **b** Photoelectron spectrum of $[\text{Au}_{25}(\text{SC}_{12})_{18}]^-$ at 355 nm. Inset shows a schematic of the potential energy curves of the cluster ions⁹⁷. (Copyright© 2017 The Royal Society of Chemistry) **c** Plot of ionization yield vs VUV energy as a function of the photon energy is shown for $[\text{Ag}_{14}(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Cl}]^+$, $[\text{Ag}_8\text{Cu}_6(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Cl}]^+$, and $[\text{Ag}_{14}(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Br}]^+$ cluster ions showing their onsets of ionization. The yield of the product ions as a function of the photon energy is shown for $[\text{Ag}_{14}(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Cl}]^{2+}$, $[\text{Ag}_8\text{Cu}_6(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Cl}]^{2+}$, and $[\text{Ag}_{14}(\text{C}\equiv\text{C}^t\text{Bu})_{12}\text{Br}]^{2+}$. **d** Gas-phase UV spectra of $[\text{Ag}_{14}(\text{CC}^t\text{Bu})_{12}\text{Cl}]^+$ and $[\text{Ag}_8\text{Cu}_6(\text{CC}^t\text{Bu})_{12}\text{Cl}]^+$ cluster ions. The TDDFT spectra are also presented, which shows similar trends in the shifts for Ag_{14} and Ag_8Cu_6 cluster ions⁸³. (Copyright© 2017 American Chemical Society)

clusters were studied in the wavelength range of 235–291 nm by coupling a laser with the ion trap. The plot of photofragmentation yield as a function of the wavelength of the radiation gave the UV spectra of the cluster ions in the gas phase (Fig. 12d). The experimental optical absorption spectra were also in accordance with TDDFT calculations (Fig. 12d).

Resolving the solution-phase growth and nucleation of clusters

Apart from such studies on gas-phase cluster ions, MS also proved to be powerful in unveiling complex

solution-phase phenomena. Understanding the mechanism of nucleation and growth of clusters in solution has always remained challenging. In 2012, Yu et al. reported the size controlled growth of Au_{25} NCs where they slowed down the reduction rate by using CO as a mild reducing agent¹⁰⁰. By using MALDI MS, the authors demonstrated that a mixture of Au_{10-15} NCs was produced within 5 min of reaction, followed by the formation of Au_{16-25} NCs over a period of 40 min, which finally size focussed to Au_{25} NCs after 24 h. However, due to fragmentation, only the core masses could be identified, and no information was obtained about the ligand shell of the intermediate

products. More recently, in 2014, in another report from the same group, ESI MS was used to trace all the stable intermediates involved in the formation of Au₂₅ clusters starting from Au thiolates. This study showed that the formation of Au NCs occurred by a 2e hopping process, which involved a fast reduction step followed by slow interconversion and size focussing steps¹⁰¹. All the intermediates involved in the process were detected by ESI MS, and the changes in the solution composition with gradual growth of the NCs were also in accordance with the changes in the optical absorption features (Fig. 13). Similar studies have been reported by the same group where ESI MS was used to understand the steps involved in the process of conversion of Au₂₅ to Au₄₄ NCs¹⁰². Isoelectronic conversion from [Au₂₃(SR)₁₆]⁻ to [Au₂₅(SR)₁₈]⁻ NCs was also studied by ESI MS. Careful mass spectrometric analysis of the system revealed the size-conversion reaction as [Au₂₃(SR)₁₆]⁻ + 2 [Au₂(SR)₃]⁻ → [Au₂₅(SR)₁₈]⁻ + 2 [Au(SR)₂]⁻¹⁰³. Based on HRMS measurements, Chen et al. have recently formulated a balanced equation for the stoichiometric synthesis of Au₂₅(SR)₁₈ NCs as, 32/x [Au(SR)]_x + 8e⁻ = [Au₂₅(SR)₁₈]⁻ + 7 [Au(SR)₂]⁻¹⁰⁴. Similar studies have also been done to understand the growth of silver clusters like [Ag₁₇(SPh-^tBu)₁₂]³⁻ and [Ag₄₄(SPh-^tBu)₃₀]⁴⁻¹⁰⁵, and step-by-step mechanism of ligand exchange induced cluster conversion reactions, e.g., the conversion from Ag₄₄ to Ag₂₅ clusters and vice versa¹⁰⁶.

Reactions between nanoparticles

Inter-cluster reactions are an emerging area in the field of NCs¹⁰⁷. Krishnadas et al. demonstrated the reaction between Au₂₅(FTP)₁₈ and Ag₄₄(FTP)₃₀ NCs, which produces a mixture of alloy clusters in solution^{108,109}. Exchange of Au–Ag atoms between the clusters were observed by using MALDI and ESI MS (Fig. 14a, b). In case of reaction between clusters protected by different ligands like Au₂₅(PET)₁₈ and Ag₄₄(FTP)₃₀, ligand exchanges were also observed in MS. In another report from the same group, the authors demonstrated reaction between Au₂₅(SR)₁₈ and Ag₂₅(SR)₁₈ clusters leading to the formation of alloy clusters Ag_mAu_n(SR)₁₈ (n = 1–24) (Fig. 14c)¹¹⁰. The authors also detected a dianionic intermediate, [Ag₂₅Au₂₅(SR)₃₆]²⁻ (Fig. 14d) at the early stages of the reaction, which provided better insights into the mechanism of such reactions. Salassa et al. used MALDI MS and NMR spectroscopy to show that monolayers of clusters are dynamic in nature, and inter-cluster ligand exchanges can occur during collision between the NCs¹¹¹. Using isotopically pure silver clusters made of ¹⁰⁷Ag and ¹⁰⁹Ag, Chakraborty et al. studied rapid isotopic exchange in silver clusters by HR ESI MS and found that the solution-state exchange dynamics of the clusters is similar to that occurring in water (H₂O + D₂O = 2HDO)¹¹².

Supramolecular chemistry of monolayer-protected noble metal NCs

MS has also been used for exploring supramolecular chemistry of clusters. Chakraborty et al. studied supramolecular functionalization of [Ag₂₉(BDT)₁₂]³⁻ clusters with fullerenes (C₆₀ and C₇₀) by HR ESI MS (Fig. 15a)¹¹³. The authors also used CID studies to gain further insights into the nature of the interaction and IM–MS (Fig. 15b) to study the structure of the adducts. Mathew et al. studied supramolecular functionalization of [Au₂₅(SBB)₁₈]⁻ clusters with cyclodextrins (CD), the adducts [Au₂₅(SBB)₁₈ ∩ CD_n]⁻ (n = 1–4) were characterized by using MALDI and ESI MS (Fig. 15c)¹¹⁴. Recently, Nag et al. separated isomers of the inclusion complexes [Ag₂₉(BDT)₁₂ ∩ CD_n]³⁻ (n = 1–6) (Fig. 15d) by using IM–MS¹¹⁵. Two isomers were observed for n = 2, 3, and 4 while no isomerism was observed in the case of n = 1, 5, and 6 complexes, suggesting similar behavior to that observed in octahedral transition metal co-ordination complexes.

Liquid chromatography (LC) -MS

Characterization, analysis, and separation of mixtures of clusters by chromatography have been pursued for long¹¹⁶. Some of the recent developments include directly coupling chromatographic techniques to MS. Black et al. coupled reversed-phase chromatography with mass spectrometry and separated gold clusters of varying core sizes from their mixtures¹¹⁷. The same group also coupled capillary LC to ESI and separated Au₁₀₄L₄₅, Au₁₃₀L₅₀, Au₁₃₇L₅₆, and Au₁₄₄L₆₀ clusters from their mixtures (Fig. 16a)¹¹⁸. In another report, isomers of Ag₂₉(LA)₁₂ (LA = (R)-α lipoic acid) clusters were separated using LC–MS (Fig. 16b)¹¹⁹.

Toward nanoparticles

Though the atomically precise NCs have been extensively characterized by MS, plasmonic NPs are not atomically precise, and determination of their exact composition still remains challenging. Recently, with the tremendous advancement in instrumentation and using a combination of ESI, LDI, and MALDI MS, it has been possible to assign approximate composition to some such plasmonic NPs, e.g., Au₃₃₃(SR)₃₉⁵³, Au_{~500}(SR)_{~120}¹²⁰, Au_{~940}(SR)_{~160}¹²¹, etc. NPs. Recently in 2017, the crystal structure of a plasmonic NP, Au₂₇₉(SPh-^tBu)₈₄ was reported¹²². MS measurements also revealed the composition in accordance with the crystal structure. Even larger NPs, Au_{~1400}¹²³ with a mass of ~300 kDa (Fig. 17a) and Au_{~2000}¹²⁴ with a mass of ~400 kDa (Fig. 17b) were recently characterized by MALDI MS.

Mass spectrometry as a tool for materials synthesis

Electrospray as a method of ionization has also been used for organic synthesis^{125,126}. While synthesis of new molecules

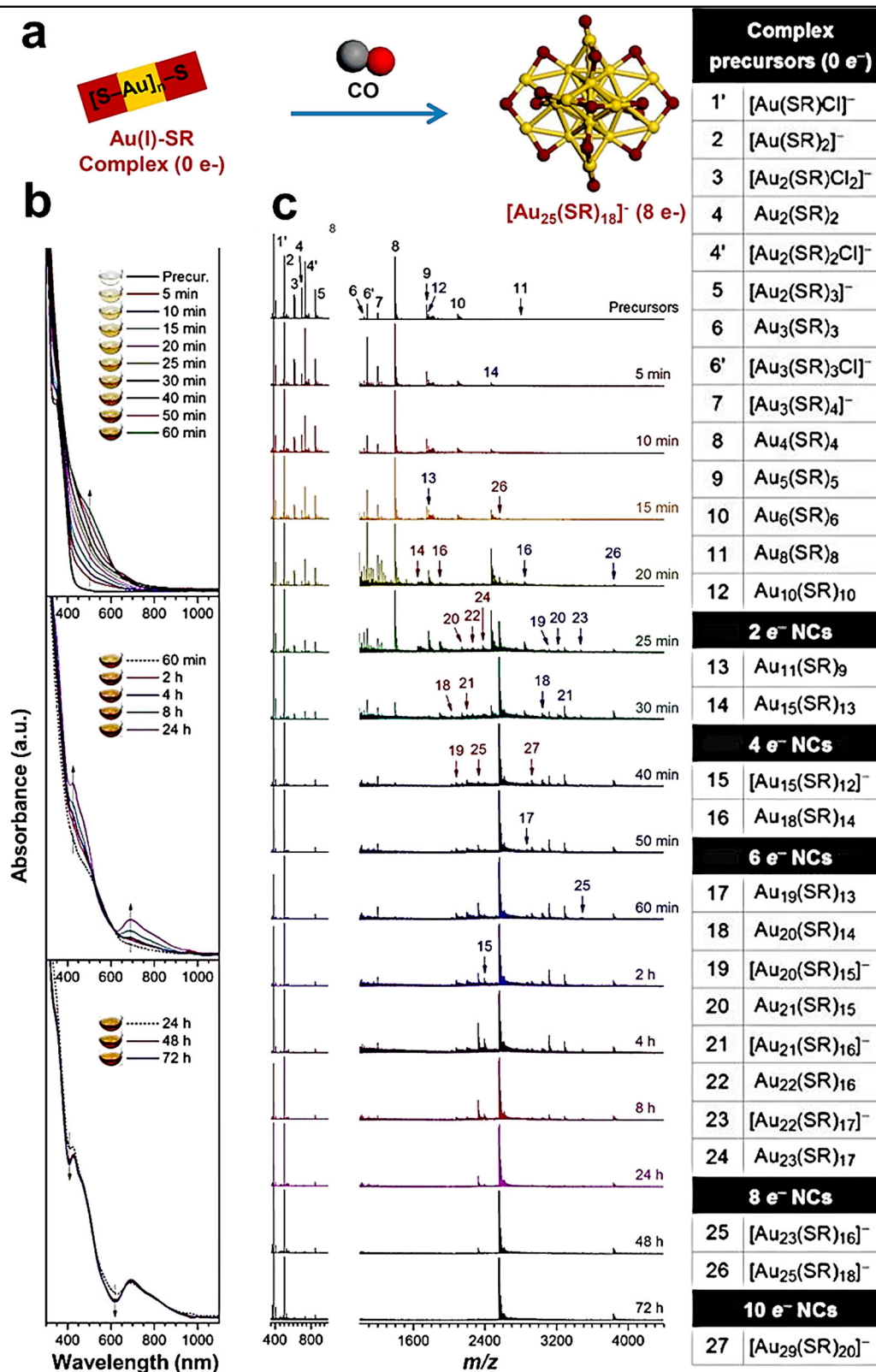


Fig. 13 ESI MS showing stepwise growth of Au₂₅(SR)₁₈ clusters. **a** Reaction scheme showing the formation of Au₂₅(SR)₁₈ clusters from Au thiolates under the mild reducing environment of CO. **b** Time-dependent UV-vis spectra, and **c** ESI MS during the formation of Au₂₅(SR)₁₈ clusters from Au thiolates. ESI MS shows detection of several intermediate species (numbered 1–27), which are listed in the table presented on the right¹⁰¹. (Copyright © 2014 American Chemical Society)

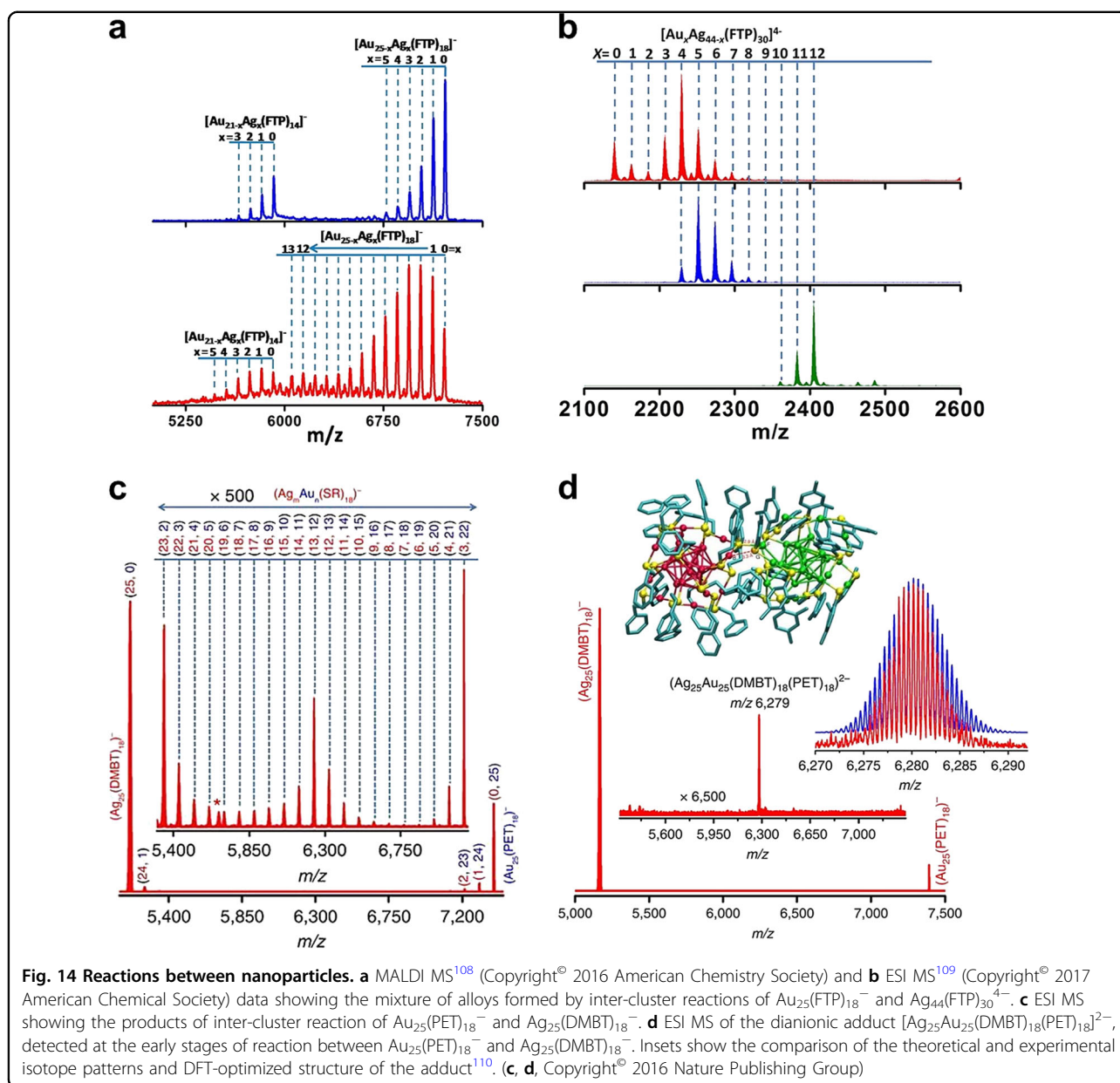


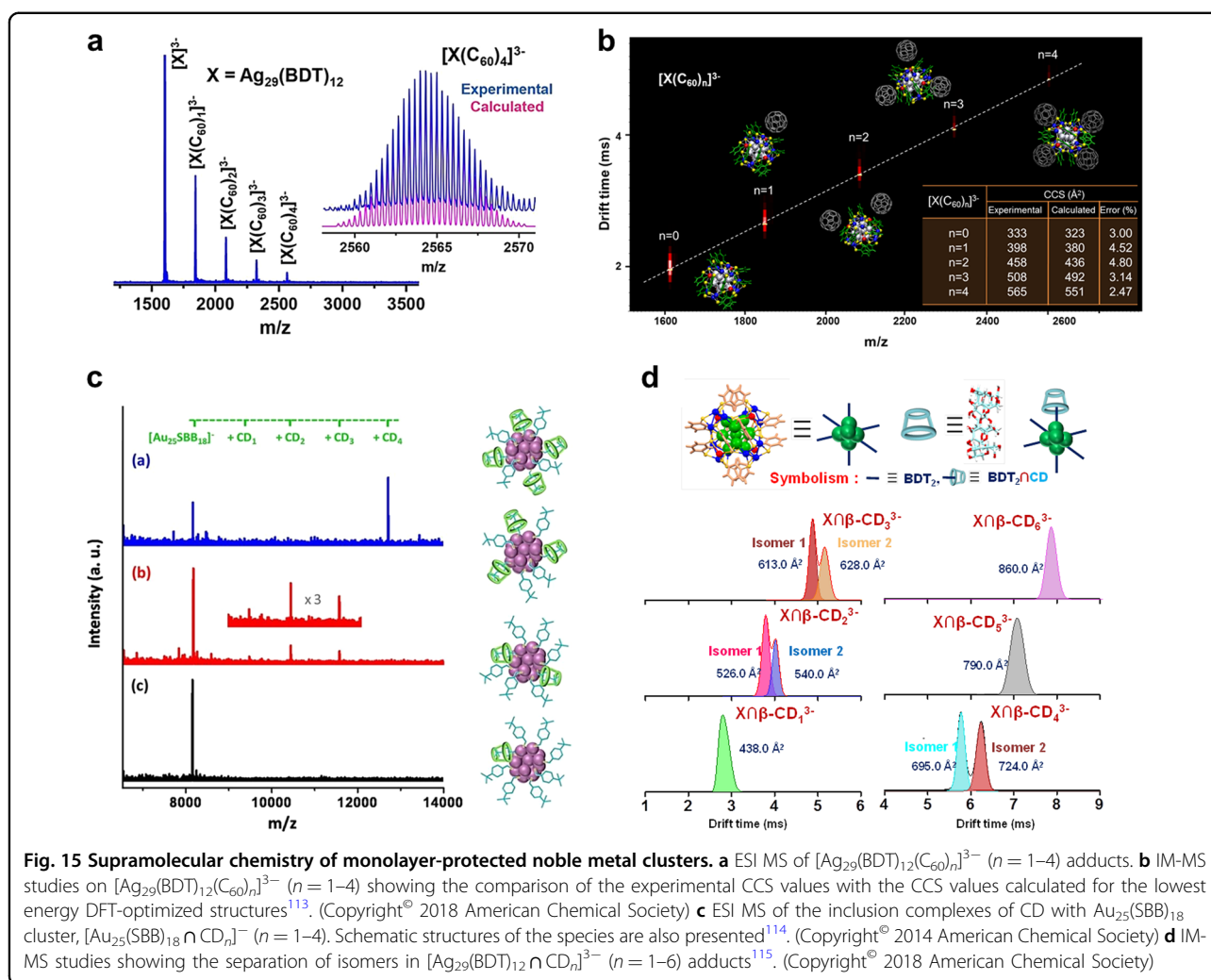
Fig. 14 Reactions between nanoparticles. **a** MALDI MS¹⁰⁸ (Copyright© 2016 American Chemistry Society) and **b** ESI MS¹⁰⁹ (Copyright© 2017 American Chemical Society) data showing the mixture of alloys formed by inter-cluster reactions of $\text{Au}_{25}(\text{FTP})_{18}^-$ and $\text{Ag}_{44}(\text{FTP})_{30}^{4-}$. **c** ESI MS showing the products of inter-cluster reaction of $\text{Au}_{25}(\text{PET})_{18}^-$ and $\text{Ag}_{25}(\text{DMBT})_{18}^-$. **d** ESI MS of the dianionic adduct $[\text{Ag}_{25}\text{Au}_{25}(\text{DMBT})_{18}(\text{PET})_{18}]^{2-}$, detected at the early stages of reaction between $\text{Au}_{25}(\text{PET})_{18}^-$ and $\text{Ag}_{25}(\text{DMBT})_{18}^-$. Insets show the comparison of the theoretical and experimental isotope patterns and DFT-optimized structure of the adduct¹¹⁰. (**c, d**, Copyright© 2016 Nature Publishing Group)

in sprays was observed before, bulk synthesis of molecules with which characterization is possible was not attempted earlier. Using a home-built nano-electrospray source, Sarkar et al.¹²⁷ showed that spraying an aqueous solution of silver acetate (AgOAc) over a TEM grid, resulted in the formation of 1D nanowire structures of Ag NPs (Fig. 18). The precursors for the formation of the nanostructures were ions. Such studies unfold new routes of synthesis of materials using mass spectrometric interfaces¹²⁷.

Conclusions and future perspectives

In conclusion, we have presented how MS has enriched the field of materials science; in particular, the field of

monolayer-protected atomically precise NCs. From the discussion presented above, it becomes clear that MS has developed into a powerful tool for materials characterization, and it is expected to expand further in the future. MS as a technique is capable of building new interfaces which connects itself with independent disciplines. This has produced GC-MS, LC-MS, and their variations. New hyphenated methodologies and their power to understand structural details would expand further in the coming years. Combined with automation, synthesis of materials of atomic precision is expected to produce greater throughput in precision manufacture. Newer methods, utilizing the properties of molecular solids, and molecular building



blocks such as infrared (IR) absorption will be important to study molecular interactions on such materials. Interfaces such as ion chromatography or PES could be built with the mass spectrometer, which can produce new information related to structural changes and associated electronic structure. As the science of the noble metal clusters is enriched by MS, a thorough study on these systems also reveals their potential to be used as mass spectrometric standards¹²⁸. Due to their high efficiency of ionization, distinct isotope patterns, stable intensities, and high m/z values, they can be used as calibrants for mass spectrometers. This might help in overcoming the limitations of the lack of proper calibrants in the high mass range, and especially in the negative ion mode¹²⁸.

Gas-phase IR in combination with IM-MS has recently gained importance in revealing the structural details of proteins. It has also proved to be powerful in understanding the geometries of other molecules such as the aggregates of protoporphyrin IX where IR spectroscopy confirmed that the pairing of carboxylic groups occurred during the

formation of the stacked conformations¹²⁹. Moreover, IM-MS in combination with IR has also been used in understanding the structures of isomers of small molecules like the N-protonated and O-protonated forms of benzocaine¹³⁰, and structures of serine octamers¹²⁹. In a similar manner, such studies may be extended in the case of clusters as well. Gas-phase IR can give more insights into the structure of the isomers or polymers of clusters. It can also be helpful for understanding interactions in the case of supramolecular adducts of clusters.

Spectroscopy and dynamics of trapped clusters ions, produced inside the mass spectrometer, can present new insights into their electronic structure. Trapped ion electron diffraction may be used for determining structures of noble metal NCs. Other possibilities include studies such as trapped ion laser-induced fluorescence. Spectroscopy of isolated cluster ions like electron detachment spectroscopy, PES, and single-particle fluorescence may be explored for a wide range of ligand-protected clusters. Such studies may even be done on

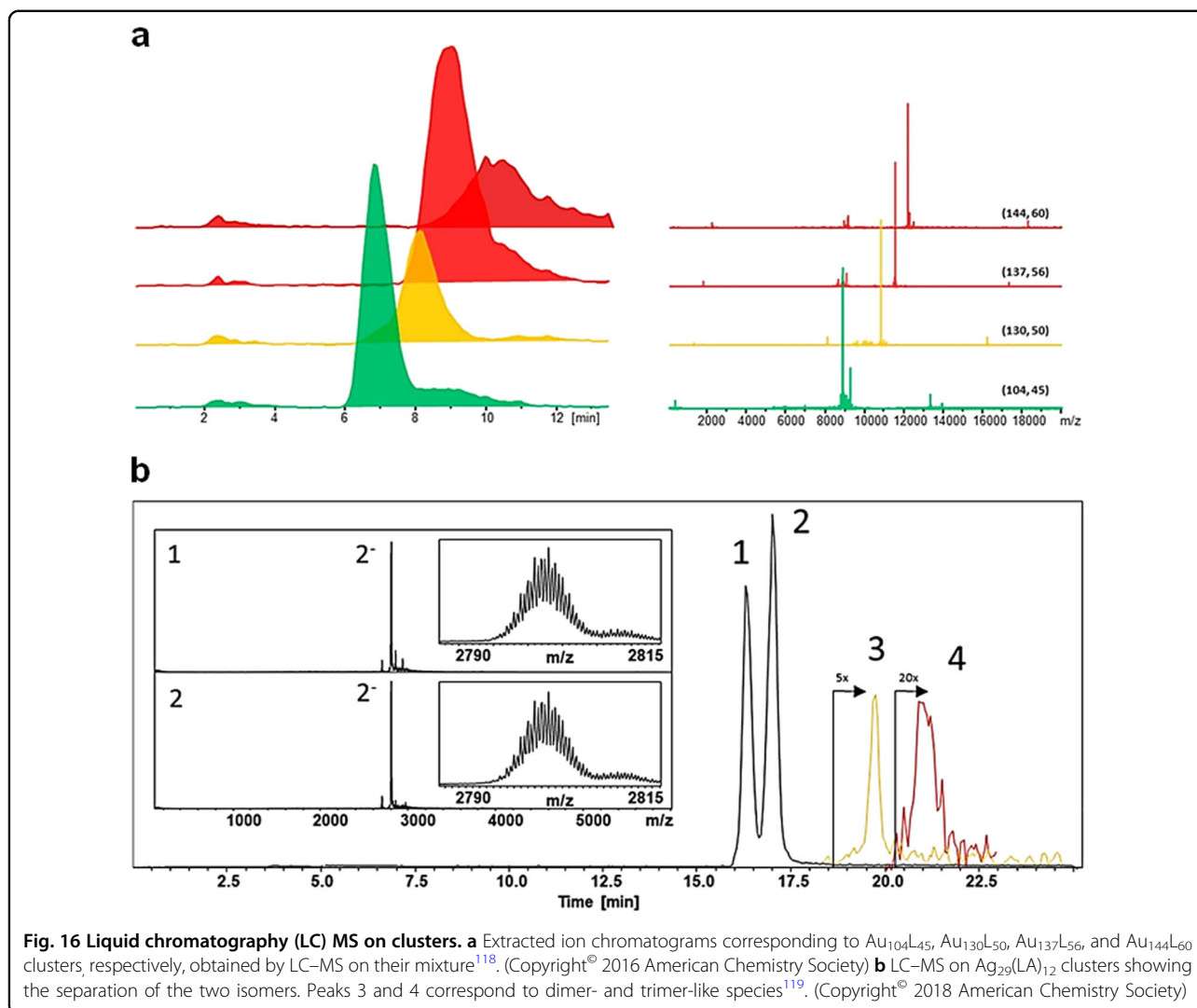


Fig. 16 Liquid chromatography (LC) MS on clusters. **a** Extracted ion chromatograms corresponding to $\text{Au}_{104}\text{L}_{45}$, $\text{Au}_{130}\text{L}_{50}$, $\text{Au}_{137}\text{L}_{56}$, and $\text{Au}_{144}\text{L}_{60}$ clusters, respectively, obtained by LC–MS on their mixture¹¹⁸. (Copyright© 2016 American Chemistry Society) **b** LC–MS on $\text{Ag}_{29}(\text{LA})_{12}$ clusters showing the separation of the two isomers. Peaks 3 and 4 correspond to dimer- and trimer-like species¹¹⁹. (Copyright© 2018 American Chemistry Society)

specific isomers of the clusters to obtain isomer-specific properties. Catalysis of isolated cluster ions may be studied. Ion soft landing may be used to deposit ligand-protected cluster ions on specific substrates.

Extensive studies can also be done with clusters synthesized in macromolecular templates like proteins¹³¹, DNAs¹³², etc., which are of particular interest because of their biocompatibility. Till now, most of the protein-protected clusters are mainly characterized by MS due to the difficulty in their crystallization. Though this aspect has not been discussed in detail in this review, enormous literature exists on the use of MS in understanding their composition, mechanism of growth, etc.^{131,133}. MS has always been effective in revealing structural details of proteins. In a similar way such studies can be extended to clusters synthesized in protein templates.

With such enormous possibilities, the proliferation of MS into materials science could make it an indispensable

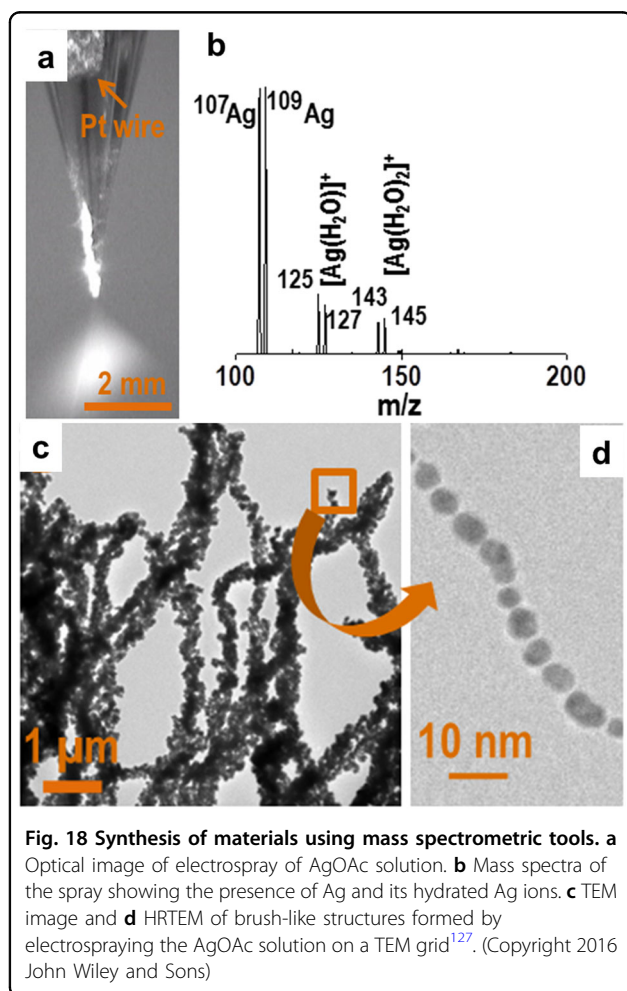
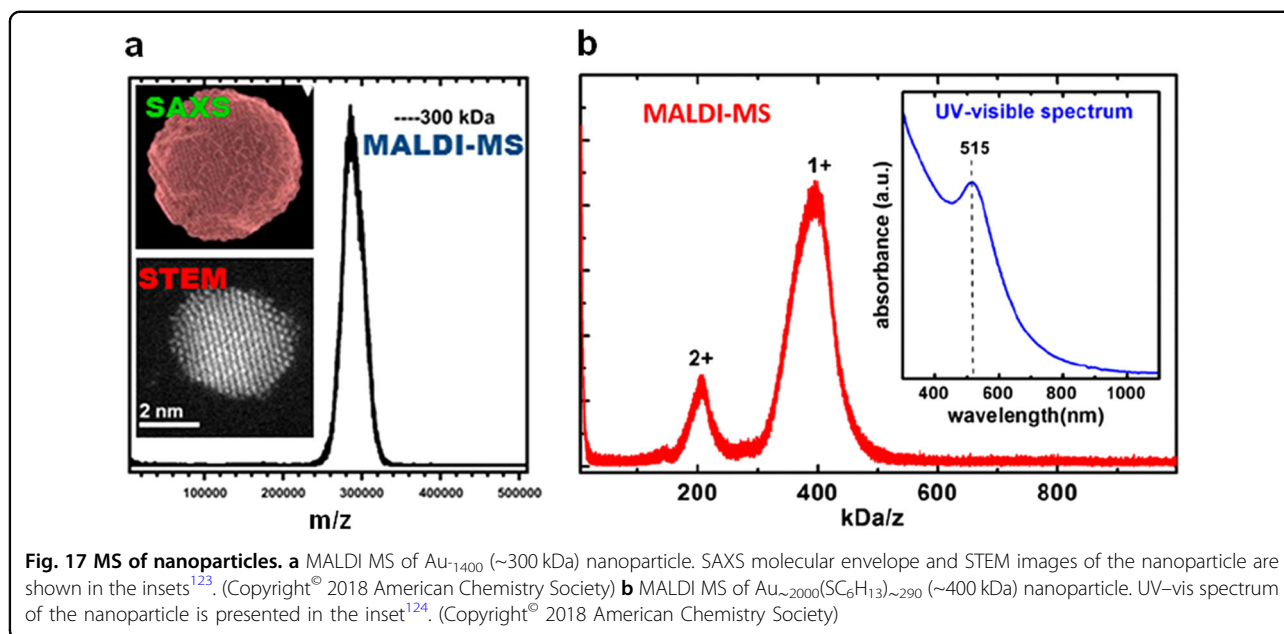
tool in that branch of science as has happened with TEM. This would produce new demands for instrumentation, associated interfaces, calibration standards, and associated needs. Expanding the limits of mass spectrometry in mass range and resolution would push traditional analytical methods further. Depending on the properties of such materials, possibilities to do catalysis, IR spectroscopy, fluorescence spectroscopy, and electron diffraction in mass spectrometers, as discussed above, could expand our understanding of phenomena to even greater detail.

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Conflict of interest

The authors declare that they have no conflict of interest.

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