PERSPECTIVE

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The signal-to-noise issue in mass spectrometric analysis of polymers

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Mass spectrometric approaches to polymer analysis become increasingly ineffective as the average molecular weight of the polymer increases. Why? The reasons are several-fold, and apply to both ESI and MALDI: the distribution of signal over an increasing number of different species, even for distributions of narrowest possible dispersity; each unique species has its own intensity broadened over a widening range of m/z values as polyisotopic contributions become more significant; individual signal width becomes larger as m/z increases; and solubility properties and solvent adducts can limit the analytical signal for polymer analysis. For MALDI analysis there is an additional reason: effective sample preparations require a certain weight percentage, causing the concentration of polymer in the matrix to drop. All these factors conspire to cause a signal-to-noise problem that fundamentally limits the ability of mass spectrometry to determine molecular weight distribution for high mass polymers.

Introduction

The stochastic nature of any polymerization process results in it producing molecules of differing mass and composition.[1,2] Thus, unlike with most biomolecules, there is a lack of homogeneity in a synthetic homopolymer that gives rise to it having both a molar-mass distribution (MMD) and a distribution of end-groups.[3] This is further complicated in copolymer systems, which additionally show chemical composition distribution and functionality distribution.[4] Characterization of MMD and composition is therefore often the first step in the analysis of polymeric materials. Historically, methods of characterization were based on indirect properties such as light scattering and intrinsic viscosity, which provide limited chemical information about the polymer and only an average molar mass. End-group titration analysis provides some compositional information, allowing the estimation of molar mass in low mass polymers, and giving clues about the mechanism adopted in synthesis.[2,3] NMR spectrometry is also readily used to provide information on polymer structure including conformational analysis,[5–8] micellar structure[9] and crystalline morphology,[10,11] all of which can be correlated with mechanical behavior. Due to the nature of NMR, the information gained still only yields an average of the polymer characteristics.[8]

Among the many techniques used for polymer analysis, mass spectrometry (MS) is one of the most recently developed but has rapidly become one of the most prominent. Using only minute amounts of sample, detailed information on polymer composition and structure can be gleaned from mass spectra of a wide variety of polymers.[3] The advent of soft-ionization techniques, in particular electrospray ionization (ESI) and matrix assisted laser desorption/ionization (MALDI), has driven much research into optimizing mass spectrometric techniques for polymer analysis.[12,13] A comprehensive study by Ladavière and colleagues compared the ability of ESI and MALDI to ionize polystyrene carrying labile end-groups from reversible-deactivation radical polymerization, showing that different doping salts result in significantly more intact end-groups being detected when using ESI.[14] Significant fragmentation was observed in both ionization techniques, with the cationization salt found to play a key role in its extent. Koster and colleagues carried out end-group and mass determination of poly(oxyalkyne)s in the range 400–8000 Da with ESI performed on a Fourier-transform ion-cyclotron resonance mass spectrometer (FTICR-MS), utilizing the multi-charge states observed in ESI for increased accuracy.[15] However, mass discrimination remains a key disadvantage with ESI for high-mass polymer samples owing to the charge-state distribution complexity of ESI spectra,[8,12–16] as will be discussed in this article. Solvent systems also have a significant effect on ESI polymer analysis, with solvent adducts shown to split the mass peaks and reduce the overall signal.[17]

On the other hand, MALDI MS of polymeric systems shows significantly increased detection of intact mass fragments up to a molecular weight of 30 kDa generated almost exclusively

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as singly charged ions.[14,16,18–21] However, whether using MALDI or ESI, polymer chemists using MS to characterize their materials usually are disappointed to observe the progressively poorer quality of their data as the average molecular weight (MW) gets higher and/or the distribution gets broader.[16,22–26] While MALDI MS is a well-established analytical tool for biomacromolecules,[27–29] which typically exhibit narrow molar mass distributions, complications arise with synthetic polymers owing to their much broader molecular mass distributions.[18] Precision in quantitative analysis is not fully understood, due to a number of complicating factors that typically affect high m/z regions.[21,30,31]

This perspective provides an explanation for this phenomenon of poor MS data for high molecular weight polymers based on some simple physical limitations. Fundamentally, mass spectrometric techniques rapidly run into a signal-to-noise (S/N) issue as the signal becomes distributed over more m/z values. The sources of this S/N problem are several-fold;

these various factors that conspire to prevent polymer chemists obtaining good results from mass spectrometric studies at high molecular weights are presented in what follows.

First, we give a real example of the signal-to-noise problem. The MALDI-ToF-MS spectra in Fig. 1 are reproduced from the work of van Herk and co-workers,[32] involving styrene bulk polymerization with times of 0.02 s (top) to 1 s (bottom) between initiation-inducing laser pulses. This is a characteristic representation of polymer analysis by MALDI which we will use as reference for further discussion of the S/N problem, which we stress applies equally where ESI is used. The resulting spectra in Fig. 1 reach maxima at approximately 2400, 4000, 15 000 and 70 000 Da. Note the stark diminution of spectral quality as m/z increases.

Discussion

Isotope pattern contributions

Isotope patterns are analytical fingerprints that aid in the characterization of a polymer. This typically involves computing theoretical isotope patterns that are matched to the measured mass spectra. For low molecular mass oligomers (<5000 Da), isotopic resolution can typically be achieved with a mass measurement accuracy of better than 100 ppm.[25] As the mass of a polymer increases, the isotope peaks of an oligomer become difficult to resolve.[15,25,33,34] Consider the isotope pattern of the styrene oligomer $H(C_2H_3Ph)_nH$ (H assumed as the end groups for simplicity), where we will use n values corresponding closely to the peaks in each of the Fig. 1 spectra. For $n = 23$ ($m/z = 2397.4$ Da for $z = 1$, Fig. 2a) the pattern is considerably more complex than that observed for a low molecular weight ion, thanks principally to the contributions from ^{13}C (1% natural abundance) and somewhat less from ^{2}D (0.015% natural abundance). The ion current from the formation of a single species is therefore distributed across ~7 peaks instead of mostly just one. This acts to greatly diminish the S/N. For $n = 39$ ($m/z = 4063.8$ Da for $z = 1$, Fig. 2b), the pattern gets broader yet, distributed across ~10 peaks with even more contributions from ^{13}C and ^{2}D. For $n = 145$ ($m/z = 15\,103.6$ Da for $z = 1$, Fig. 2c), the resolution is insufficient to provide an isotope pattern at all, although one may still distinguish some shoulders resulting from the pattern. For $n = 605$ ($m/z = 63\,012.0$ Da for $z = 1$, Fig. 2d) there is no overt evidence of isotope pattern, for the curve is smooth and broad, with full-width of over 20 Da at half-maximum (for the full envelope). All isotope patterns were calculated using open source tools from http://www.chemcalc.org.[35]

All modelled spectra here are presented at a resolution of 10 000, which determines the so-called FWHM, $i.e.$ full width at half maximum. For example, at an m/z value of 1000 an individual peak will have a width of $m/z = 0.1$ at half of its height. In Fig. 2c this means each isotopomer signal has a width of 1.5 Da at half-height, explaining why the isotope pattern may no longer be distinguished. The resolution used here is typical of a research-grade MALDI-TOF instrument, though high-end
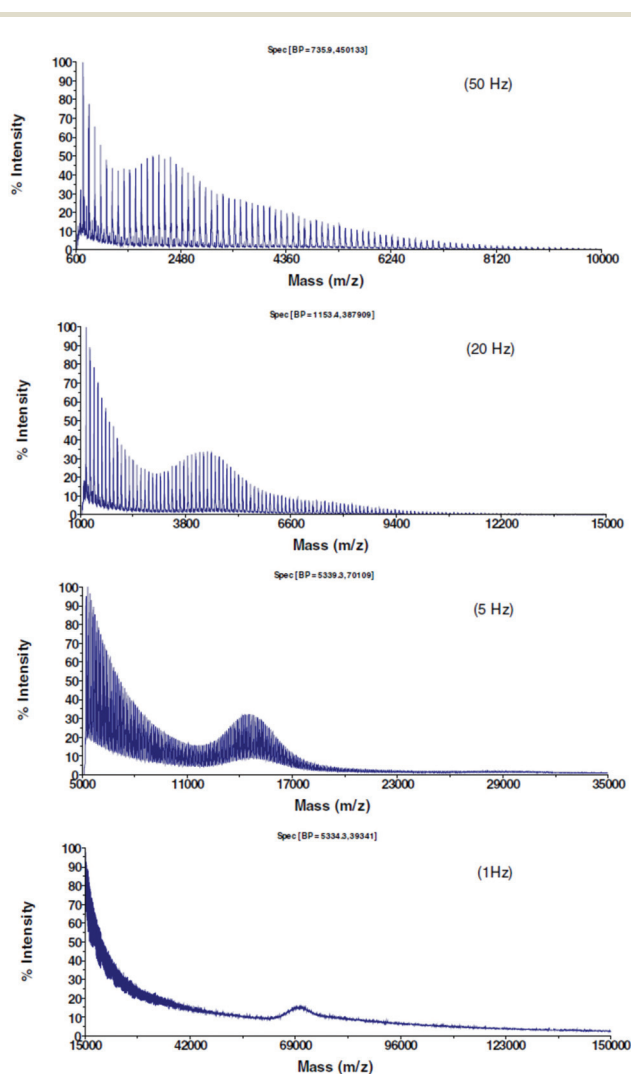

Fig. 1 MALDI-ToF-MS mass spectra from bulk styrene pulsed-laser polymerization. Reprinted with permission from ref. 32. Copyright 2003 American Chemical Society.
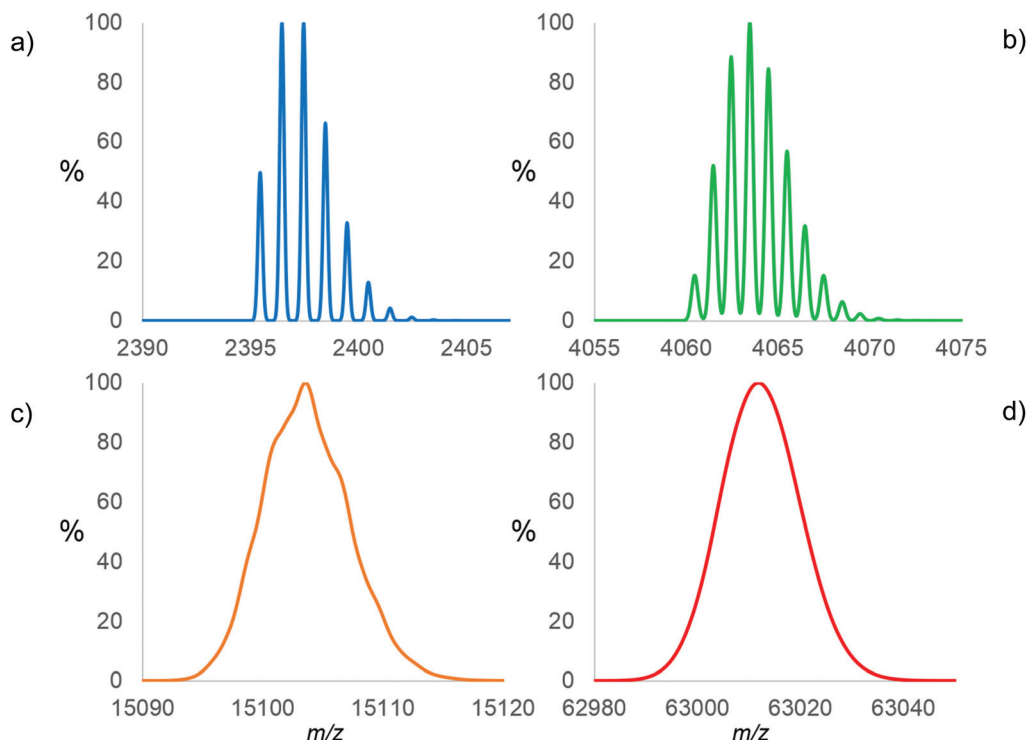
Fig. 2   Isotope patterns for $H(C_2H_3Ph)_nH$, where n = 23 (blue, (a)), 39 (green, (b)), 145 (orange, (c)) and 605 (red, (d)). All are plotted with a simulated resolution of 10 000 (FWHM). Isotopic envelope widths are m/z = 8 Da, 11 Da, 21 Da and 47 Da respectively.

modern instruments are capable of considerably higher resolution. Even though these calculations are purely meant to be illustrative, one sees that they correspond closely to the situation observed in Fig. 1.

The above representation, plotted as it is on increasing x-axis widths and normalized to a maximum of 100% for the most abundant peak in the spectrum, is deceptive. It suggests the principal difference between the signals is simply resolution. A better indication of what the isotope pattern does to the signal-to-noise is generated if we present all 4 plots overlapping each other and with the same total peak area. This is Fig. 3, and it tells a different story.

Fig. 3 shows clearly how the signal from higher molecular mass polymers gradually slumps into the baseline from isotopic contributions alone. This is reflected in the isotopic envelope widths, which are m/z = 8 Da, 11 Da, 21 Da and 47 Da for n = 23, 39, 145 and 605 respectively, as calculated using (both here and elsewhere in this article) the criterion of intensity being greater than 1% of the highest intensity peak of the envelope.[36] When one considers that n = 605 – the largest polymer simulated here – is actually quite small for commercial polystyrene (PS), one sees that MS for high polymers can never be what it is for oligomers. It is important to stress that this is for two separate reasons, both of which give rise to stronger effects as m increases: (1) The constant resolution means that FWHM becomes larger as m increases, which leads to broadening of individual peaks so that they cannot be distinguished, as shown in Fig. 2 and 3. (2) What Fig. 3 addition-
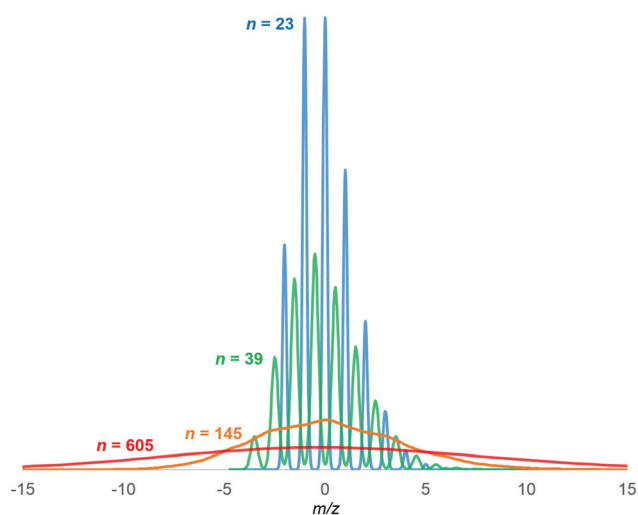

Fig. 3   Isotope patterns for $H(C_2H_3Ph)_nH$, where n = 23 (blue, $m/z \approx$ 2400 Da), 39 (green, $m/z \approx$ 4000), 145 (orange, $m/z \approx$ 15 000) and 605 (red, $m/z \approx$ 63 000), plotted with a simulated resolution of 10 000 (FWHM), recentered at an m/z value of 0, and giving each trace the same total peak area.

ally makes clear is how there is a greater multitude of individual peaks spread over a broader range of m as m increases. This is because the larger the number of atoms in a molecule, the greater will be the number of different isotopes that can be present.

In relation to point (2), there are several things that it is instructive to realize: (i) It only takes $n = 13$ for a PS molecule to contain 104 carbon atoms, which means that even at this relatively small size there will already be a spread of isotopomers across a MW range of 104 Da (*i.e.*, from 0 ^{13}C up to 104 ^{13}C), which is the mass of a styrene unit. Although the probability of having ^{13}C for all carbons is vanishingly low, this nevertheless makes the point that even at $n = 13$ there is already in-principle mixing of the m of molecules with different n. As n increases into the hundreds and then thousands, the probability of an envelope spreading beyond 104 Da (a repeat unit) in width becomes higher and higher, until one literally cannot distinguish polymers of different n mass spectrometrically, because the envelopes for successive n will overlap. This is implicit in the results of Fig. 3. (ii) The nature of Pascal's triangle acts to overcome low probabilities relatively quickly as the number of entities increases. For example, the abundance of ^{13}C may be small at 1%, but it only requires there to be 100 carbon atoms (*i.e.*, $n \geq 13$) for it to be more probable to have one ^{13}C than to have zero. This explains why the all ^{12}C left-edge of an isotope pattern relatively quickly becomes of low intensity as n increases (see Fig. 2). Furthermore, it is also Pascal's triangle that gives rise to there being a greater multitude of molecules with different m as n increases.

Point (2) is relevant for all polymers, and the magnitude of the effect depends on what atoms are present. Most polymers are dominated by ^{13}C contributions to isotopic complexity, but other common elements also add to the broadness of these envelopes. For example, nitrogen has contributions from ^{15}N (0.4%), oxygen from ^{17}O (0.04%) and ^{18}O (0.20%), and chlorine from plentiful ^{37}Cl (24%) to go with the more abundant ^{35}Cl (76%). The latter makes poly(vinyl chloride) (PVC) interesting. For example, Fig. 4 shows that the pattern for an oligomer of PVC with just 23 repeat units is already significantly broader than the equivalent PS pattern (*cf.* Fig. 2a and 3) thanks to the isotopic richness of Cl.

With regard to the two forces giving rise to broad MS signals as m increases, it is important to point out that factor (2) is part of the inherent nature of polymers, and thus applies to all methods of analysis. For example, the spread of m for a specific chain length is equally present in carrying out size-exclusion chromatography (SEC), it's just that this technique never operates with resolution in hydrodynamic volume that translates into anything near a mass resolution of 1 Da (in fact, except for small oligomers, SEC cannot even resolve successive repeat units), and so this broadening effect never enters consideration. Therefore, one should not think of this as being a weakness of MS methods, but rather one should regard the individual molecular identification that is possible at low m as being a unique strength. On the other hand, factor (1) – increasing FWHM as m increases – is an MS instrumental factor. But of course, other methods have instrumental broadening too. Most notably, SEC has column broadening, which in fact operates on a $\log m$ rather than (linear) m scale. This means SEC broadens over an exponentially increasing range of m as m increases, making it a far stronger effect than in MS.

In this section we have discussed how isotopic contributions give rise to the problem of diminishing S/N with increasing mass in MS. We will now describe how there are additional complicating features causing this problem.

Oligomeric and polymeric distributions

The identification of molecular properties is often the first step in the analysis of a polymer, with mass spectrometry providing substantial information in such investigation. This includes identification of monomer unit and end-groups,[37,38] tracking of catalyst activity in the polymerization process,[39,40] and estimations of composition for complex copolymer systems.[41–44] Crotty and colleagues have extensively reviewed the application of MS and tandem techniques for probing synthetic polymer architecture of simple linear homopolymers through to complex copolymer systems.[45] The estimation of molar masses and molar mass distributions is also of primary interest in polymer characterization.[23] Contrary to proteins, which exhibit uniform chain lengths, synthetic polymers exhibit significant dispersity with mass ranges over many thousands.[3] As MALDI mass spectrometry was originally developed for proteins, its extension to synthetic polymers has not been as straightforward, owing to the aforementioned dispersity of synthetic polymers.

Initial reports of molar mass and molar mass distributions determined for low-mass synthetic polymers using MALDI MS showed reasonable agreement with conventional methods such as viscometry, SEC and light scattering for samples with dispersity <1.2, which of course is narrow.[1,23] For samples pos-
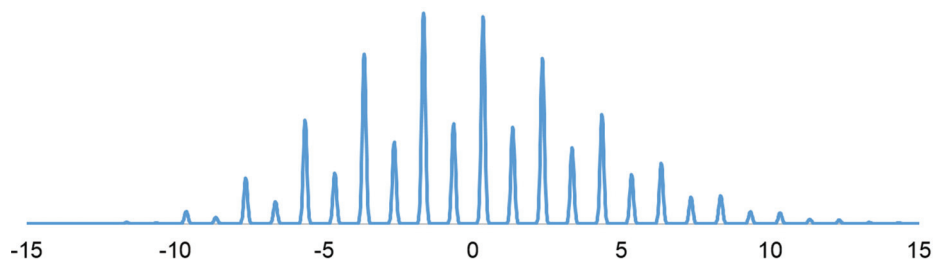

Fig. 4 Isotope pattern for H(C$_2$H$_3$Cl)$_n$H where $n = 23$, plotted with a simulated resolution of 10 000 (FWHM) and recentered at an m/z value of 0 (actually $m/z = 1439.5$ Da) for consistency with Fig. 3. The isotopic envelope width is $m/z = 22.1$ Da.

sessing broader dispersity, reported molar mass values showed significant underestimation.[46] This issue of broader dispersity, which is intrinsic to the polymerization process,[3] is more pronounced with higher molar mass polymers. This is because these generally produce a lower signal response, resulting in a lower S/N, due to the signal intensity being distributed over a larger number of species of different degrees of polymerization, as will be explained. This problem can be mitigated by separation of polymer samples using chromatography methods prior to mass analysis,[16] but this is rarely done.

We can illustrate this inherent limitation of mass spectrometric analysis of synthetic polymers by looking again at polystyrene. Bulk PS is typically synthesized in batch reactors through chain polymerization resulting in dispersity of roughly 2.[47] We will make our point by assuming something far narrower than this, namely the narrowest that can be achieved without further chromatographic separation, which is a Poisson distribution, as can be obtained by high purity anionic polymerization[3] and nearly obtained by various forms of reversible-deactivation radical polymerization. In Fig. 5 we present Poisson distributions for PS with average degree of polymerization 23, 39, 145 and 605, the same as the n values in Fig. 2 and 3 (although note that these previous calculations were for truly uniform polymers, whereas now each calculation is for a distribution of n). The new distributions in Fig. 5 are the absolute best that can be achieved by standard synthesis; the reality is always broader distributions, as for example seen

in Fig. 1 (where in fact the peaks are approximately Poisson distributions, but there is a lot of polymer in addition to this).

Again, when plotted with different x and y axes, these distributions are deceptive. Resetting them such that they are all overlaid and have the same total area, we get the different picture of Fig. 6. In appraising this it is important to remember that dispersity reflects standard deviation relative to the mean. This explains why the broadest distribution has the lowest dispersity: although the standard deviation is larger, the mean is larger to an even greater extent, and so the ratio of the two values is smaller.

We can estimate how much the signal intensity at a given m/z value will be compromised from a combination of isotopic broadening and oligomeric distributions. The (average) $n = 605$ example in Fig. 6 has a central intensity 1/4 that of the (average) $n = 23$ distribution due to a wider oligomeric distribution, while Fig. 3 shows a 1/20 intensity ratio for the same n due to isotopic broadening. This means the amount of signal for a PS ion at $m/z = 60\,000$ Da is about 1/80 of that of a PS ion at 2500 Da. The falloff in intensity at any given m/z value due to these two effects alone is therefore quite dramatic, and it will be even more dramatic where polymerization gives rise to constant dispersity (*cf.* Fig. 5). For example, the common situation of the most-probable distribution, which has dispersity of 2, gives standard deviation that is equal to average size. This means that there is large increase in the number of species as average size increases.
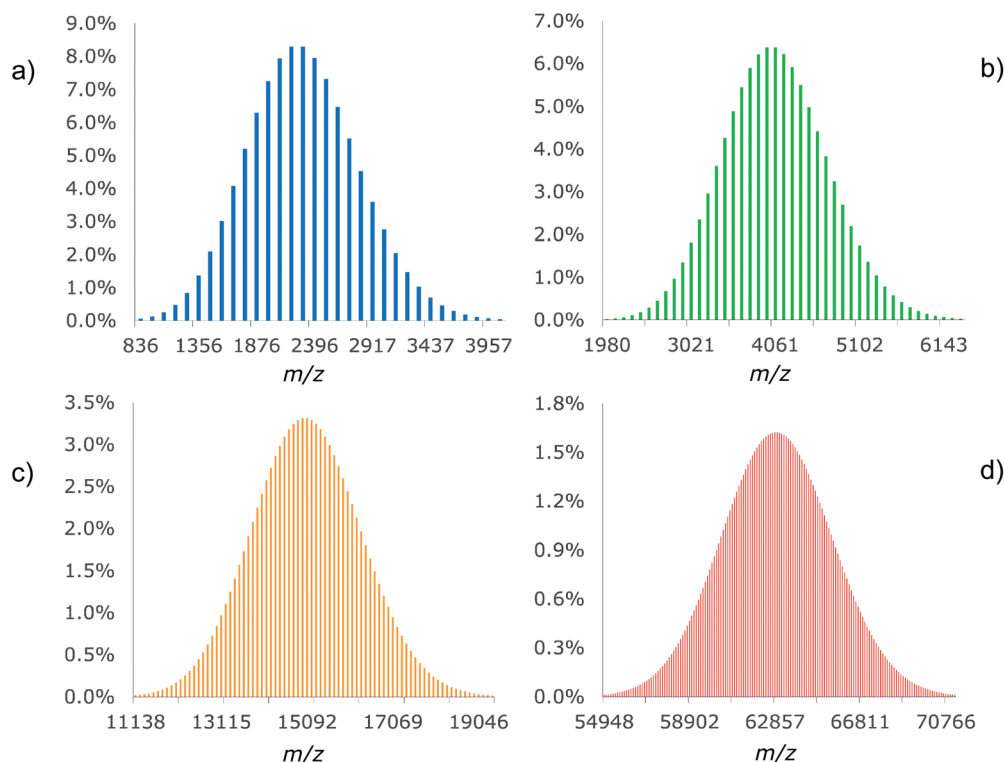

Fig. 5 Poisson distributions for polystyrene with average degree of polymerization 23 (blue, (a)), 39 (green, (b)), 145 (orange, (c)) and 605 (red, (d)). These distributions have dispersity of 1.04, 1.03, 1.007 and 1.002 respectively, and peak widths of m/z = 2913.8, 3746.3, 7492.5 and 15 401.3 Da respectively.
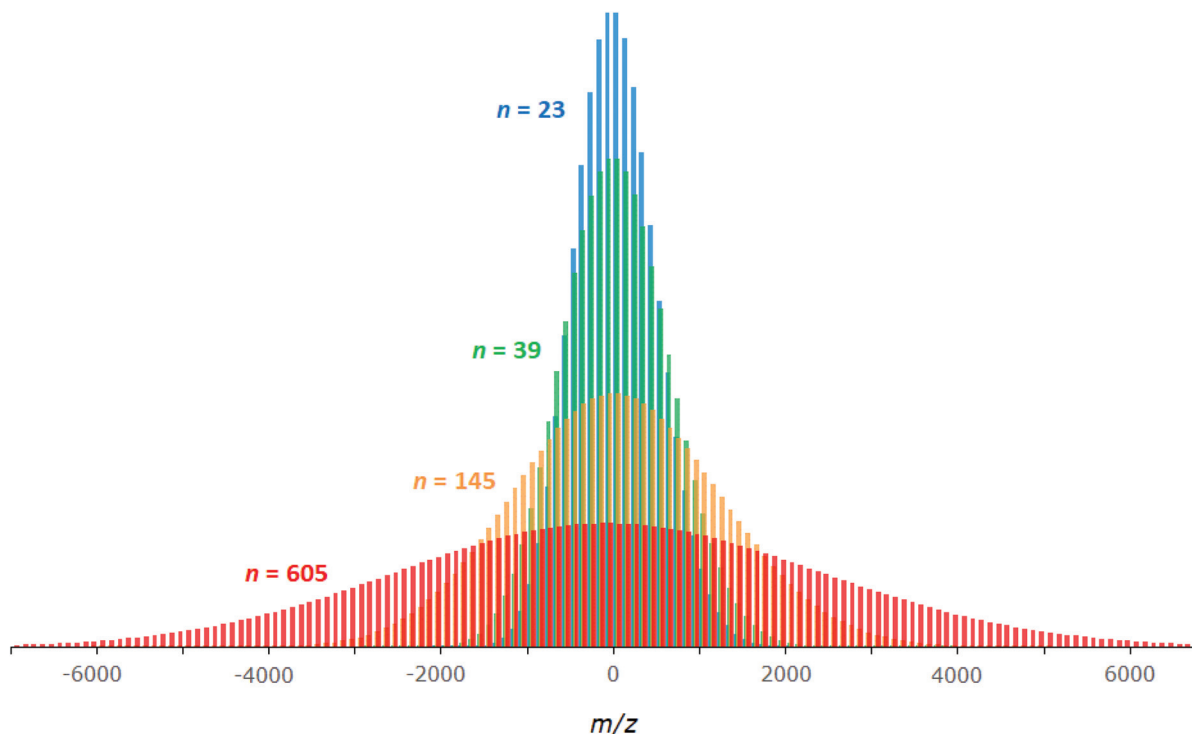
Fig. 6 The Poisson distributions from Fig. 5, overlaid and with the same total intensity (summed heights) (meaning each trace has the same total peak area), and recentered at an m/z value of 0.

Ionization method-specific considerations: MALDI

MALDI mass spectrometers make use of intense pulses of laser light that induce vaporization of a co-crystallized mixture of a matrix (typically an organic acid with a UV chromophore) and analyte molecules.[48] Ionization occurs in the resulting energetic plume, with singly-charged ions being the lucky survivors of what is a complex and rapid process. There are a number of factors that affect the spectral intensity of a polymer, many of which are related to its molecular weight, and which are responsible for the molecular weight distributions for high molecular weight polymer samples (especially those with high dispersity) disagreeing with results from other quantitative methods.[49–53] These factors include the following.

Molar considerations. At a given power, the laser removes essentially the same amount of material in a single pulse (because the matrix is in great excess, and it is responsible for the energy absorption). If the matrix : analyte (M/A) weight ratio remains constant, this means that the concentration of individual polymer molecules in the plume is inversely proportional to the molecular weight of those molecules. As such, for the same amount of matrix and analyte material ablated, fewer high molecular weight polymer ions will be present in the ionized plume (note that this is simply a concentration effect, and is separate to any effect of m on ionization efficiency). Attempting to remedy this problem simply by boosting the polymer concentration when preparing the sample is not necessarily productive, as now explained.

Matrix : analyte (M/A) weight ratio. These are typically in the range $100:1$ to $10^6:1$.[48,54] This ratio tends to increase with polymer size, with more matrix required to act as a dispersant, desorber, and ionization agent for each analyte molecule.[55] Increasing M/A ratios also act to minimize multimer formation.[31] Investigations into the effect of M/A ratio on a MALDI analysis have shown diminishing returns for higher M/A for larger polymers.[31,56] As M/A increases beyond an experimentally determined "Goldilocks zone" for each polymer sample, there is less analyte signal (as there is less analyte available for ionization). At the other extreme of the "Goldilocks zone", low M/A ratios (and hence higher concentrations of analyte in the matrix) show decreasing ion intensity at lower masses, with significantly broader distributions shifted towards higher m/z.[57] This leads to an overestimation of number-average MW for a non-uniform polymer sample, where the higher mass components reach co-crystallization point before lower mass components.[31]

Cation affinity. Higher mass oligomers may have higher proton or cation affinity, where their probability of undergoing cationization in the MALDI plume is increased due to having more sites for the cation to associate with.[46,48,57]

Sample preparation. High mass oligomers in high concentration solutions have an increased tendency for polymer precipitation to occur prior to matrix co-crystallization.[25,58] Matrices usually tolerate only a certain percentage of analyte before co-crystallization fails, leading to altered polymer distribution in the ionized plume.[25] Most preparative protocols call

for a particular weight of sample for optimal performance,[54] with the most common sample preparation method being the "dried droplet" (DD) method.[12,25,59] The DD method remains the most widely used MALDI sample preparation method, given its relatively simple preparation steps that are applicable to many different sample types. It involves depositing droplets of dissolved matrix and analyte onto a target plate, with co-crystallization occurring as the solvent evaporates.[23] However, uneven droplet distribution causes irregular crystallization and heterogeneous distribution, leading to mass distributions in the ionized plume that may not accurately represent the distribution in the analyte, and thus making quantitative analysis difficult.[59,60] Other sample preparation methods have attempted to improve on this limitation, including the forced dried droplet method,[59] solvent-free methods,[61–63] freeze vacuum-drying method,[64] and electrowetting-assisted drying.[65] Although these methods show improved crystal homogeneity, they often require more preparation time and additional instruments in order to generate homogeneous microcrystal distribution.[12] On the other hand, it also should be mentioned that developments in automated chemistry have also led to improvements in consistency and reductions in the time required for sample preparation.[66,67]

Laser energy. Studies of different molecular masses of the same type of polymer have indicated that higher molecular masses require higher laser energies for efficient ionization.[68,69] However, increasing the laser energy produces the desired effect only to a certain extent, after which mass discrimination becomes a noted consequence. Using laser energy above an experimentally determined optimal point for each polymer type showed no further advantage of increasing the peak areas for high molecular mass components.[69] The excess laser energy instead causes fragmentation, seen with a shift to lower m/z values and broader low molecular mass distributions. The intensity of doubly charged peaks also increases, further complicating the spectral analysis.[46,69]

Noise. MALDI noise mostly arises from matrix clusters,[70] and the abundance of these drops off with increasing molecular weight (*e.g.* see Fig. 1, in which the baseline becomes lower and lower with increasing molecular weight). Other sources of chemical noise (impurities, fragments, aggregates, *etc.*) will similarly drop off with greater molecular weight. As such, the S/N problem should experience some mitigation from decreasing noise at high molecular weight.

Mass discrimination at the detector

Whether MALDI or ESI is being used, differences in detector response may be observed for oligomers of different mass, and this will result in biasing of the MMD. Microchannel plates (MCPs) can give lower responses for high-mass ions due to poor ion-to-electron conversion for heavy, low-velocity ions,[71] although correcting for this effect is possible.[72] Ion-conversion dynode detectors exhibit less mass bias, with lower mass ions exhibiting slightly lower responses.[73]

Ionization method-specific considerations: ESI

Electrospray ionization mass spectrometry (ESI-MS)[74] involves a solution containing ions of interest pumped through a charged capillary. A spray of fine droplets results, which are desolvated in a warm bath gas to the point that ions are released into the gas phase. ESI-MS is sometimes used to characterize lower molecular weight oligomers,[38,75] but it is complicated even further than MALDI because the signal is additionally distributed across multiple charge states and/or ionizing additives.[48] For example, as shown in Fig. 7, an oligomeric phosphaalkene provides 4 series of ions in two different charge states, in which each series arises from the oligomers associating with either $[Ag_2]^{2+}$, $[Ag_3]^{3+}$, $[Ag_3Cl]^{2+}$ or $[Ag_4Cl]^{3+}$.[76]

The inherent entanglement of chains in high mass polymers also presents a challenge to obtaining high quality ESI mass spectra. This entanglement inhibits the droplet fission process as the solvent evaporates and oligomers acquire charge.[48] An investigation of droplets in the ESI process revealed bimodal particle size distribution, with a significant large-particle component reflecting an inhibition of droplet fission.[77] Evidence for entanglement has shown decreased sensitivity for samples at higher concentration, an effect that may also be attributed to competition for available charge.[78] This decreased sensitivity is also observed at relatively low initial sample concentrations, with oligomer entanglement occurring early in the evaporation process, limiting the fission process necessary to generate single-chain particles. Detection of such entangled clusters is therefore limited by the m/z range of the spectrometer. These additional complications are why ESI-MS in general has a lower mass range for polymers (currently <10 kDa) than does MALDI-MS (<30 kDa), which has the additional advantage of preferentially producing singly-charged ions.[13,16,18,25] Other ionization techniques are limited in their ability to move high molecular weight materials into
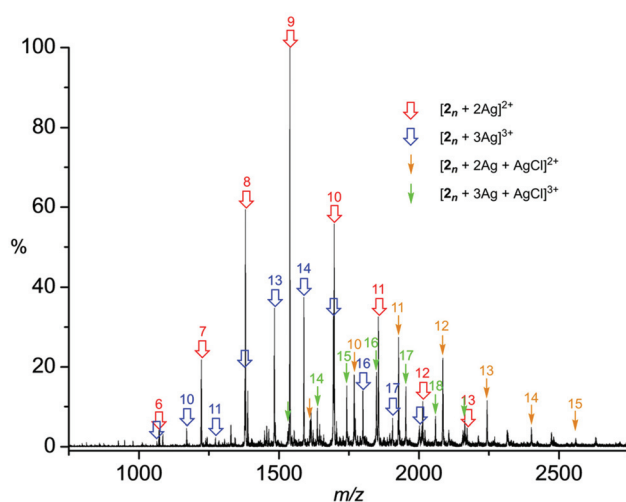

Fig. 7 Positive ion ESI-MS of oligomerized phosphaalkene, recorded in acetonitrile with the addition of $AgNO_3$.[76]

the gas phase at all, which is why only ESI and MALDI are used for MS analysis of polymers.

Conclusions

Every analytical method has strengths and weaknesses. With mass spectrometric analysis of polymers, two groundbreaking strengths were immediately evident: (1) the high-resolution separation of non-uniform samples so that individual species could be 'visualized' according to their precise MW; and (2) the lack of need for calibration *via* narrow-dispersity polymer samples of known MW. Because of these strengths, polymer scientists naturally became excited about the possibility of realizing the Holy Grail of easy, accurate determination of molecular weight distribution for any sample of polymer. This paper has explained how this will not be possible due to various weaknesses of MS methods, most notably signal-to-noise issues that are unavoidable as MW increases, and ionization bias.

Understanding the source of the signal-to-noise problem helps us propose solutions, some practical, some not. An example of the latter: it is unlikely a polymer chemist is going to employ ^{13}C-depleted monomer for their reactions for the sake of better mass spectrometric results! But they will at least know that polymers containing polyisotopic elements (*e.g.* PVC, with Cl) are much less likely to produce good mass spectrometric results. Because S/N is a problem, running longer experiments will help, as S/N increases in proportion to the square root of the number of scans. Chemists will know to expect better MS results for their polymers when dispersity is low (or where mass selective separation has been performed prior to analysis, *e.g.* by chromatography), as this means the ion current is spread over fewer species. Experimenting with the matrix and solvent compositions or tuning the laser energy for better ionization conditions may also provide opportunity for better quality analysis of high molecular mass samples. And finally, the lower the average molecular weight of the polymer, the better the mass spectrometric results are likely to be. All these traits should be clear from the discussion that has been presented.

On a positive note: mass spectrometric innovation continues to be exceptionally vibrant. Instrumentation is in a process of continuous development, and better machines (increased sensitivity, higher resolution, lower noise) and experimental methodologies (sample preparation, matrices, ionization methods, MS/MS methods) will lead to the limits of what is possible in mass spectrometric polymer characterization being continuously extended. Furthermore, the issues discussed here in no way detract from the strengths of MS methods for polymer analysis. In fact these strengths are so profound that MS has rapidly become an almost essential tool for polymer characterization, much like NMR in organic chemistry: workers use MS to confirm the chemical identity of their polymers (which even for high MW samples is still possible from the low MW portions of the distribution) and SEC to determine average MW and dispersity. SEC will never be able to subsume the role of MS, but it is at least conceivable that MS could subsume the role of SEC.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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