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Keywords
additives, polymer, review, characterisation, spectrometry, polymers, mass, ambient, ionisation

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Ambient Ionisation Mass Spectrometry for the Characterisation of Polymers and Polymer Additives

Martin R. L. Paine[1*], Philip J. Barker[2], and Stephen J. Blanksby[1]

[1]ARC Centre of Excellence for Free Radical Chemistry and Biotechnology, School of Chemistry, University of Wollongong, Wollongong NSW 2522, Australia

[2]BlueScope Steel Research, PO Box 202, Port Kembla NSW 2505, Australia

*Corresponding author

Mr Martin Paine

ARC Centre of Excellence for Free Radical Chemistry and Biotechnology

School of Chemistry, University of Wollongong

Wollongong NSW 2522

Australia

Ph: +61 2 4221 5943

Fax: +61 2 4221 4287

Email: mpaine@uow.edu.au

Abstract

The purpose of this review is to showcase the present capabilities of ambient sampling and ionisation technologies for the analysis of polymers and polymer additives by mass spectrometry (MS) while simultaneously highlighting their advantages and limitations in a critical fashion. To qualify as an ambient ionisation technique, the method must be able to probe the surface of solid or liquid samples while operating in an open environment, allowing a variety of sample sizes, shapes, and substrate materials to be analysed. The main sections of this review will be guided by the underlying principle governing the desorption/extraction step of the analysis; liquid extraction, laser ablation, or thermal desorption, and the major component investigated, either the polymer itself or exogenous compounds (additives and contaminants) present within or on the polymer substrate. The review will conclude by summarising some of the challenges these technologies still face and possible directions that would further enhance the utility of ambient ionisation mass spectrometry as a tool for polymer analysis.

Keywords: Synthetic Polymer; Polymer additive; Ambient mass spectrometry; Direct analysis; Hindered amine light stabiliser (HALS); Surface analysis.

1. Introduction

Whether it is determining the molar mass distributions, quantifying associated additive compounds, or characterising the chemical composition of synthetic polymers; mass spectrometry has delivered in terms of providing a powerful and sensitive tool to meet each of these demands. Several reviews outlining the advances in polymer mass spectrometry have recently appeared [1-4]. Within the field of polymer mass spectrometry (MS), but also the greater mass spectrometric community, there is a drive to increase the versatility of MS

methods and to widen the range of their application. There are three major avenues one can take to increase the capability and versatility of mass spectrometry: (i) technological advancement of the analyser and detector components of the instrument, (ii) allowing MS to be undertaken outside the laboratory environment through instrument miniaturisation and portability, and (iii) broadening the range of samples amenable to MS analysis through the development of direct ionisation techniques or "ambient ionisation" mass spectrometry. Due to the ever increasing complexity of synthetic polymer materials being produced and the growing diversity of chemical additives formulated therein, it stands to reason that developments pertaining to avenue (iii) would potentially have the largest impact in the field of polymer MS and hence form the subject of this review.

The ability to directly sample solid material in its native-state using ambient ionisation techniques can provide complementary information to conventional methods. For instance, many contemporary ionisation sources rely on digestion and/or extraction of analytes into the solution phase followed by direct infusion, *e.g.*, electrospray ionisation (ESI). Digestion/extraction is necessary to obtain information about the bulk composition of certain samples but can limit the analyst's ability to derive spatial information on analyte distribution in 2- or 3-dimensions. Traditional extraction-based methods for polymer and polymer additive analysis also tend to rely on chromatographic separation. Chromatography aids in reducing sample complexity and offers the potential for quantitation [5-12]. However, chromatographic separations can increase analysis times considerably and, in the case of gas chromatography (GC), suitable only for volatile compounds [13-18]. Conversely, methods that retain spatial distribution of analytes by probing solid samples in their native state, such as matrix-assisted laser desorption ionisation (MALDI), require stringent operating conditions involving the application of matrices to the sample substrate with ions typically produced under vacuum at pressures of 10 mTorr or less. The heightened amount of sample

preparation and necessity to break and re-equilibrate the low pressure environment can also place a heavy burden on analysis times. Generally, polymer substrates and formulations are relatively homogeneous placing a greater emphasis on high throughput capabilities rather than analyte distribution analysis via MS imaging. Though in certain applications, valuable insight can be gained from depth profiling experiments or assessing lateral migration of analytes within polymer substrates, particularly when characterising the weathering of materials under different in-service conditions. In the following sections of this review, the application of ambient ionisation techniques for the analysis of polymers and polymer additives are grouped according to the desorption process employed as listed in Table 1.

Table 1. List of techniques and references reporting ambient mass spectrometric analysis of synthetic polymers and polymer additives.

Class of desorption	Technique[a]	References	Applications[b]
Liquid extraction	DESI	[19-28]	• PEG, PTMG, PAM, PPG, PMMA, PMS, PDMS, PUR, and polyglycol esters characterisation • HALS additives in polyester and PP • Diphenylamines in PTFE • Insecticides on polyester bednets • 2,4-dichlorophenoxyacetic acid analogues on poly(propylmethacrylate) MIP's
	EASI	[28-30]	• Organo-functionalised silane and siloxanes • Phenothiazines on methacrylic MIP's
	LESA	[31, 32]	• HALS additives in polyester • Polyester degradation products • Lipids on hydrogel contact lenses
	Paint spray	[33]	• HALS additives in polyester
Thermal desorption	DART	[34-39]	• Phthalates detected in PVC and plastic toys • Detection of stabilisers in PP and PE • Tackifier additives detected in synthetic rubber and acrylic adhesives

			• (See also Table 2)
	TM-DART	[24]	• Insecticides on polyester bednets
	FAPA	[40, 41]	• IR, PEG, PET, PS, PBS, POM, and POM copolymer characterisation • Phthalate plasticisers detected in PVC
	ASAP	[42-44]	• PEG and PS characterisation • PP characterisation and stabiliser identification • Erucamide and stabilisers in PET and PET degradation products
	DP-APCI	[45]	• Amphiphilic copolymer network analysis
	PADI	[46]	• PMMA, PET, PLA, and PTFE characterisation
	DAPPI	[47]	• Human metabolites, pharmaceuticals, and toxic compounds detected on PDMS
Laser ablation	AP-MALDI	[48-51]	• PEG and ethoxylated surfactant characterisation • PEG eluting from a LC column
	ELDI	[52]	• PEG, PPG, and PMMA characterisation
	LAESI	[102]	• PEG 400

[a] AP-MALDI, atmospheric pressure-matrix assisted laser desorption ionisation; ASAP, atmospheric solids analysis probe; DART; direct analysis in real time; DAPPI, direct atmospheric pressure photoionisation; DESI, desorption electrospray ionisation; DP-APCI, direct probe-atmospheric pressure chemical ionisation; EASI, easy ambient sonic-spray ionisation; ELDI, electrospray-assisted laser desorption ionisation; FAPA, flowing atmospheric pressure afterglow; LAESI, Laser ablation electrospray ionisation; LESA, liquid extraction surface analysis; PADI, plasma-assisted desorption/ionisation; TM-DART, transmission mode-direct analysis in real time.

[b] HALS, hindered amine light stabiliser; IR, *cis*-poly(isoprene); MIP, molecularly imprinted polymer; PAM, polyacrylamide; PBS, poly(butanediol succinate); PDMS, poly(dimethylsiloxane); PE, poly(ethylene); PEG, PET, poly(ethylene terephthalate); poly(ethylene glycol); PLA, poly(lactic acid); PMMA, poly(methylmethacrylate); PMS, poly(α-methylstyrene); POM, poly(oxymethylene); PP, poly(propylene); PPG, poly(propylene glycol); PS, poly(styrene); PTFE, poly(tetrafluoroethylene); PTMG, poly(tetramethylene glycol); PUR, polyurethane; PVC, poly(vinyl chloride).

2.1 Extraction-based ambient ionisation mass spectrometry

Ionisation techniques utilising solvents to facilitate the extraction/desorption process are the most widespread among ambient sampling methods. Solid-liquid extraction-based techniques enjoy their popularity due to the relatively simple instrumentation involved and the ease with which they can be coupled to existing commercial ESI-based mass spectrometers: one of the most commonly used ionisation methods in mass spectrometry. The first reported ambient ionisation/sampling method for MS was desorption electrospray ionisation (DESI) which relies on an extraction-based mechanism [27]. Since the initial study by Cooks and co-workers, DESI has been regarded as the flagship ambient ionisation method with the majority of publications within ambient ionisation mass spectrometry during the 2009-2011 period [53]. This is also true for the number of publications involving polymer research with 10 of the 31 research articles sourced for this review. The DESI process is illustrated in Figure 1 and promotes analyte desorption through a pneumatically assisted electrospray directed at the sample surface. The fine mist of charged microdroplets generated by the spray emitter wets the surface forming a dynamic solid-liquid interface and it is here that rapid extraction of analytes into the thin solvent film occurs [54]. The continual barrage of microdroplets impacting the solvent layer combined with pneumatic forces shear away charged droplets from the surface. These plumes of secondary droplets contain dissolved analyte that splash towards the inlet of the mass spectrometer [54]. From there solvent evaporation and droplet fission processes result in gas-phase analyte ions analogous to mechanisms that dictate ESI [55].

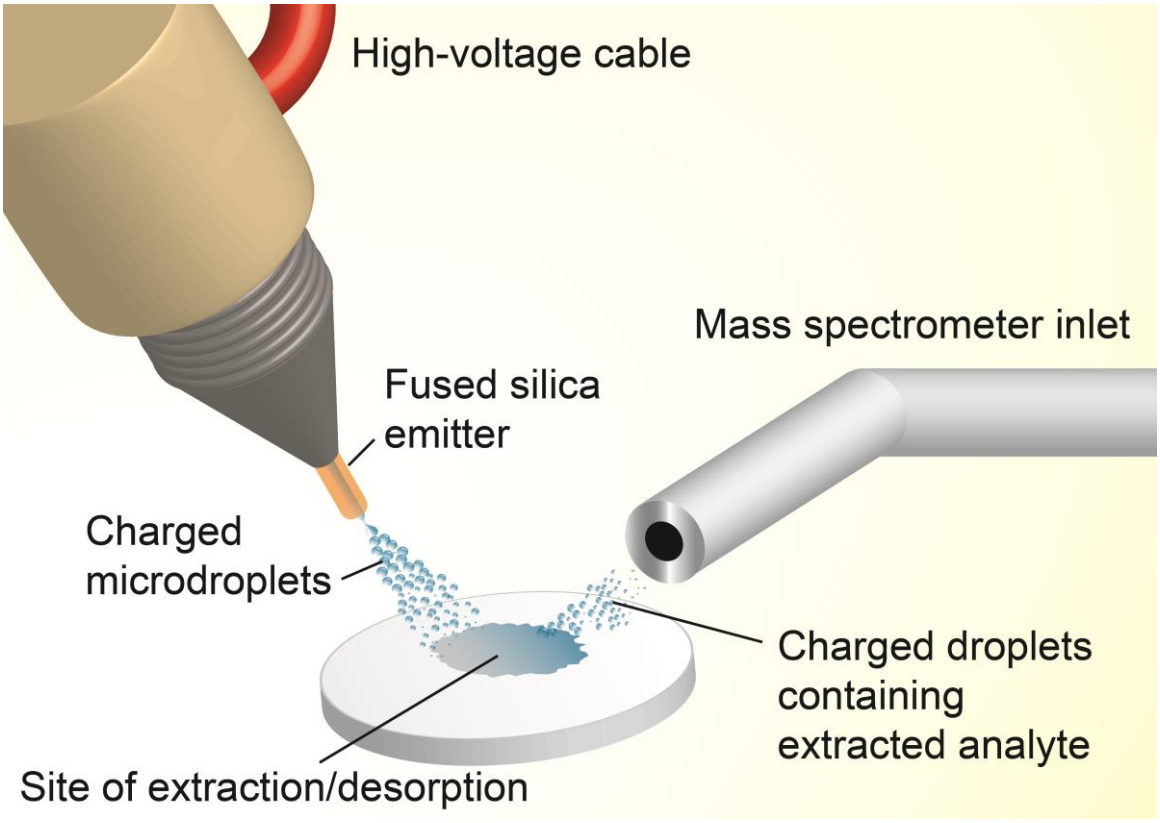

Figure 1. An illustration of the desorption electrospray ionisation (DESI) process where a pneumatically assisted electrospray generates a fine mist of charged microdroplets directed at the sample. Upon continual wetting of the surface, analytes are extracted into a thin solvent film and desorption occurs by microdroplets impacting the solvent layer producing secondary droplets containing dissolved analyte that splash towards the mass spectrometer inlet.

2.2 Characterisation of polymers by extraction-based methods

In 2006, Nefliu *et al.* published the first example of DESI being applied to synthetic polymers: poly(ethylene glycol) (PEG), poly(tetramethylene glycol) (PTMG) and polyacrylamide (PAM) with average molecular weights up to 3000 $g.mol^{-1}$ [28]. Condensed phase polymers deposited on to paper surfaces were detected in positive-ion mode (and PAM also in negative-ion made) using methanol:water (1:1) as the spray solvent and a linear ion trap mass spectrometer with a mass range of *m/z* 2000. DESI analysis of solid PEG produced

spectra that closely resembled the mass spectra acquired by ESI of PEG in solution. Both the number average molar mass (Mn) and molecular weight averages calculated from the DESI-MS data were in good agreement with expected values [56]. The analysis of PTMG and PAM proved to be more difficult due to their incompatibility with the DESI solvents leading to inefficient desorption, particularly with the more hydrophobic PTMG.

Jackson *et al.* took this one step further and applied DESI with various spray solvent mixtures to a range of 'real world' samples. They reported the detection of PEG spraying methanol containing 0.1% v/v formic acid, poly(proplylene glycol) (PPG) and poly(methyl methacrylate) (PMMA) spraying methanol with lithium bromide (5 mg/mL), and poly(α-methyl styrene) (PMS) spraying methanol with silver nitrate (5 mg/mL). In each case, methanolic solutions containing the polymer were deposited onto matt-finished cardboard surfaces and allowed to dry. Oligomers from the cyclic trimer to tridecamer of poly(dimethyl siloxane) (PDMS) were also detected directly from a pharmaceutical tablet using methanol/water (1:1) containing 0.1% formic acid as the solvent spray [57]. Tandem mass spectrometry (*i.e.*, DESI-MS/MS) experiments were also carried out, providing structural information and identifying the end group chemistry of the polymers investigated.

In a follow up publication by the same group, more accurate structural information was obtained for a series of polyglycol esters and ethers by incorporating tandem MS experiments and peak assignment software. Solutions of each PEG sample were deposited onto matt-finished cardboard surfaces, allowed to dry, and detected using DESI with methanol:water (1:1) as the spray solvent. Microstructural characterisation of PEG dibenzoate, PEG monooleate, PEG butyl ether, PEG diacrylate, and PEG *bis*(2-ethylhexanoate) (M_n < 800 g.mol^{-1}) was achieved through cationisation with different Group I metal ions (Li^+, Na^+, K^+, Rb^+, and Cs^+) by the addition of the appropriate salts to the solvent

spray. Li^+ adduct ions provided the most informative product-ion spectra, exhibiting more product ion peaks than other cation adduct precursor-ions tested [58].

A very useful application that ambient ionisation techniques have always been associated with is the rapid monitoring of qualitative changes to material as a function of various exposures or treatments. An example of this is the bulk analysis of polyurethane (PUR) films by ESI and direct surface analysis by DESI that investigated the degradation products observed upon irradiation with an electron beam to simulate ageing of the polymer within waste storage [19]. Comparison between ESI and DESI for bulk and surface analysis of PUR after irradiation showed that the same degradation species are observed for bulk analysis and confirmed the homogeneity of the PUR irradiation. Slight differences were observed at the surface of the films with the authors attributing those to degradation products that could react after irradiation with atmospheric oxidants [19]. The study also provided a thorough optimisation of the DESI spray parameters used during the experiments noting that a much higher gas flow rate and spray voltage were needed for maximising PUR signal intensities compared to PEG. Higher gas flow rates and spray voltages promoted smaller droplet sizes which enhanced desolvation efficiency and generated droplets with higher velocity, producing more secondary droplets upon impact.

DESI mass spectra can become too complex to interpret due to multiple charge states when the polymer molecular weight increases, but advances in high-resolution mass analysers are broadening the molecular weight range accessible by this technique by resolving different oligomers from higher charge states. A study reporting the use of DESI coupled with an Orbitrap mass spectrometer demonstrated the effectiveness of this configuration for the characterisation of various industrial synthetic polymers with masses ranging from 500 $g.mol^{-1}$ to more than 20 000 $g.mol^{-1}$ [23]. A range of average molecular weight PEG (620, 1080, 1470, 4120, 7100, 11840, and 22800 $g.mol^{-1}$), PPG (1200 and 2000

g.mol^{-1}), PMMA (855, 1970, and 2710 g.mol^{-1}), PDMS (770, 1200, and 2000 g.mol^{-1}), and copolymers of ethylene and propylene glycol standards were investigated. For the homopolymers, number average molecular weight (M_n), weight average molecular weight (M_w), and polydispersity index (PDI) were calculated from DESI-Orbitrap MS data. These calculated values were compared with the more established and well characterised gel permeation chromatography (refractometric detection) and MALDI-time of flight (TOF) MS techniques [59]. For the homopolymers (except in the case of PMMA), molecular weights of polymers deduced from DESI-Orbitrap MS were slightly superior to those deduced from MALDI-TOF MS and were in good agreement with the GPC data.

In the case of copolymers (Fig. 2), ions with a charge state > 1 caused overlapping peaks that were unable to be discriminated – even with the high resolving power (100,000) of the Orbitrap mass analyser and the help of deconvolution software. PEG was also detected from two commercially available cosmetic products as examples of complex matrices. Diluted samples of the two cosmetic products were spotted onto a hydrophobic substrate and analysed by DESI, revealing the presence of sodium and potassium adducts of PEG [23]. The authors conclude by making a critical comparison of DESI-Orbitrap versus MALDI-TOF for the mass spectrometric analysis of low molecular weight synthetic polymers. On the one hand, DESI offers a much simpler experimental set-up – once the spray solvent and surface composition are optimised – by operating at atmospheric conditions and without the need of matrix application. DESI also has an ionisation mechanism akin to ESI and is therefore prone to generating multiple charge states. The higher charge states observed effectively increases the mass range beyond the 4 kDa limit of the orbitrap analyser. However, spectral complexity eventually reaches a limit as deconvolution of multiple charge states and oligomers becomes challenging requiring substantially more post-acquisition data processing than MALDI-TOF data, capable of mass-resolved spectra up to 70 kDa and beyond [23, 59]. These results

highlight some of the major limitations with DESI and, to a greater extent, most solid-liquid extraction based techniques in that they suffer from the same problems experienced with ESI analysis of polymers. Problems such as the inability to generate higher charge states in low-polarity solvents, overlapping peaks and discrimination among different molecular weight oligomers have to be considered when higher molecular weight polymers are investigated.

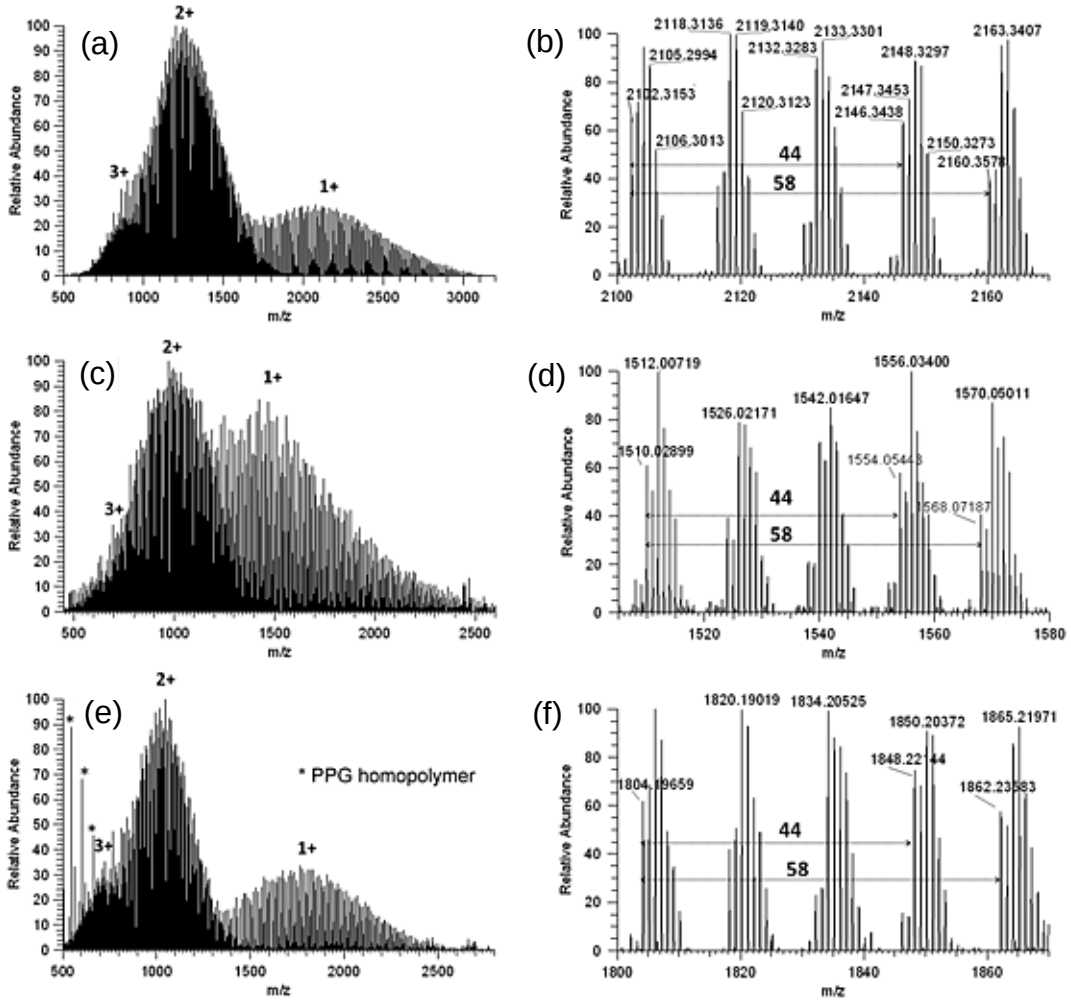

Figure 2. DESI-Orbitrap spectra (positive-ion mode) of three PEG/PPG copolymers: (a) whole spectrum of random PEG/PPG 2500 copolymer, (b) zoom in the *m/z* 2100 - 2170 mass range of the spectrum (a), (c) whole spectrum of PEG-PPG-PEG 1900 copolymer, (d) zoom in the *m/z* 1500 - 1570 mass range of the spectrum (c), (e) whole spectrum of PPG-PEG-PPG 2000 copolymer, (f) zoom in the *m/z* 1800 - 1870 mass range of spectrum (e). The figure is adapted from ref. [23] with kind permission of John Wiley and Sons and is an example of complex spectra caused by overlapping ion signals.

An alternative extraction-based approach is easy ambient sonic-spray ionisation (EASI) [60], formerly known as desorption sonic spray ionisation (DeSSI) [61]. EASI is an ambient adaptation of sonic spray ionisation [62, 63] and is considered to be one of the simplest ambient ionisation techniques to implement [64]. The technique is very similar to DESI, the major difference being a higher nebulising gas pressure is used to form small droplets rather than a high voltage applied to the spray solvent. With EASI, the solvated analytes are ionised due to a non-statistical charge distribution within the micro-droplets [62]. Removal of the high voltage requirement is not only advantageous for instrumentation simplification but also eradicates electrochemical or oxidative processes occurring at the source that might otherwise drive unwanted chemistry [65].

This technique has been employed for the real-time monitoring of polymerisation reactions occurring on surfaces in the open atmosphere. Commercially available nanofilm products (NFPs) consisting of 1% solutions of hydrolysates and condensates of 1H, 1H, 2H, 2H-perfluorooctyl triisopropoxysilane in 2-propanol (NFP-1) and hexadecyl triethoxysilane in ethanol (NFP-2) were applied to glass, filter paper or cotton surfaces and monitored over time by EASI-MS [30]. The organo-functionalised silane and siloxane compounds present in NFP-1 and -2 form thin films on surfaces by self-organisation that involve a series of hydrolysis and condensation reactions during evaporation of the solvent [66]. Consumption of the monomers and the formation of heavier oligomers could be observed directly by continuously scanning the surface over time. Interactions with the EASI spray itself was found to have only a minimal impact on the rate of polymerisation [30].

2.3 Analysis of additives, adsorbents and contaminants by extraction-based methods

Equally as important as characterising the bulk material of synthetic polymers is evaluation of the chemical additives that render the polymeric material commercially viable.

The qualitative and quantitative measure of additives such as stabilisers, plasticisers, and flame retardants directly by mass spectrometry from the bulk polymer material represents the ideal technique for rapid analysis of synthetic polymers yet there have been limited studies reported in this area. The limiting factor that impeded progress in this area was the inability of ambient ionisation techniques to successfully extract the additive from the bulk material without destroying or severely altering the physical nature of the polymer substrate, *e.g.*, milling the polymer. Reiter, Buchberger, and Klampfl [26] were able to facilitate additive extraction using DESI by rapidly heating the polymer samples with a heat gun (400 °C) for up to 5 s – enough to liberate the analyte without substantially deforming the substrate. A series of laboratory prepared poly(propylene) samples containing the stabilisers Chimassorb 81, Tinuvin 328, Tinuvin 326, and Tinuvin 770 in concentrations between 0.02 % and 0.2 % (w/w) were analysed with the aid of the heat gun. Signal intensities from extracted ion chromatograms were used to construct calibration curves, giving R^2 values of 0.994 or better. Using these calibration curves, the amounts of stabiliser present in an in-ground swimming pool liner and commercially available poly(propylene) (PP) granules were calculated by DESI-TOF-MS analysis. The DESI results were compared with traditional quantitative methods including high-performance liquid chromatography with detection by ultraviolet (UV) absorption (HPLC-UV) and thermal desorption- (TDS) GC-MS and deemed to be in "excellent accordance" [26].

An alternative to heating the sample is to exploit the solubility properties of the polymer investigated. Recently, *in situ* detection of the stabiliser Tinuvin 123 within a cross-linked thermoset polyester-based surface coating by DESI-MS was accomplished by a simple and easy pre-treatment involving acetone vapour [25]. Prior to DESI-MS analysis, the samples were placed in a standard laboratory glass desiccator that had the desiccant replaced with a small volume of acetone. The polymer sample was placed such that it was not

physically wet by the acetone rather the acetone vapour present in the enclosure was enough to swell the polymer and dissolve/mobilise the stabiliser from the bulk polymer material to the surface. Exposure to the acetone vapour for 1 minute was enough to afford detection by DESI-MS and was shown not to disturb the morphology of the sample nor the lateral distribution of the analyte [25]. Coupled with a linear ion-trap mass spectrometer, DESI-MS^n experiments were conducted that enabled the characterisation of specific structural changes occurring as a result of the elevated curing temperatures associated with the surface coating production and after exposure to simulated weathering [25].

These initial findings led to a broader follow-up study using the aforementioned DESI-MS method to investigate the major structural changes occurring to ten hindered amine light stabilisers (HALS) in cross-linked thermoset polyester-based surface coatings including; Tinuvin 770, 292, 144, 123, 152, NOR371; Hostavin 3052, 3055, 3050, and 3058 [67]. HALS containing a 2,2,6,6-tetramethylpiperidine functionalised at the piperidinyl nitrogen all gave indications of undergoing *in situ* conversion to the corresponding secondary piperidine (*N*-H) moiety during thermal and/or photodegradation of the polymer, a finding that has implications for understanding the mechanism(s) via which HALS additives stabilise polymers, especially in high temperature applications [67].

DESI has also been employed for the desorption and analysis of non-volatile pyrolysis products of PEG and biological samples directly from the pyrolysis probe [22]. DESI-MS data were in agreement with analyses of non-volatile pyrolysis products by ESI-MS or MALDI-MS, which were pyrolysed off-line, required sample extraction/solubilisation, and in the case of MALDI, the use of a matrix compound and a cationising agent [22].

An interesting example where DESI provides selective extraction of small molecules from polymeric material is in the reported detection of nitrated derivatives of the diphenylamine stabilizer: dinitro-, trinitro-, and tetranitrodiphenylamine, from

poly(tetrafluoroethylene) (PTFE) [21]. PTFE seals became visibly discoloured over time when used in the storage of double-base propellants consisting of nitrocellulose, nitroglycerin, and stabiliser. The nitrated derivatives of diphenylamine preferentially absorbed to the PTFE liner of double-base propellants due to changes in their solubility as the propellants aged. Such changes went undetected when extracts from the seals were analysed by HPLC [21] but when the PTFE seals were analysed directly by DESI as shown in Figure 3(a), nitrated diphenylamine additives present after 6 days of aging were readily detect (Fig. 3b).

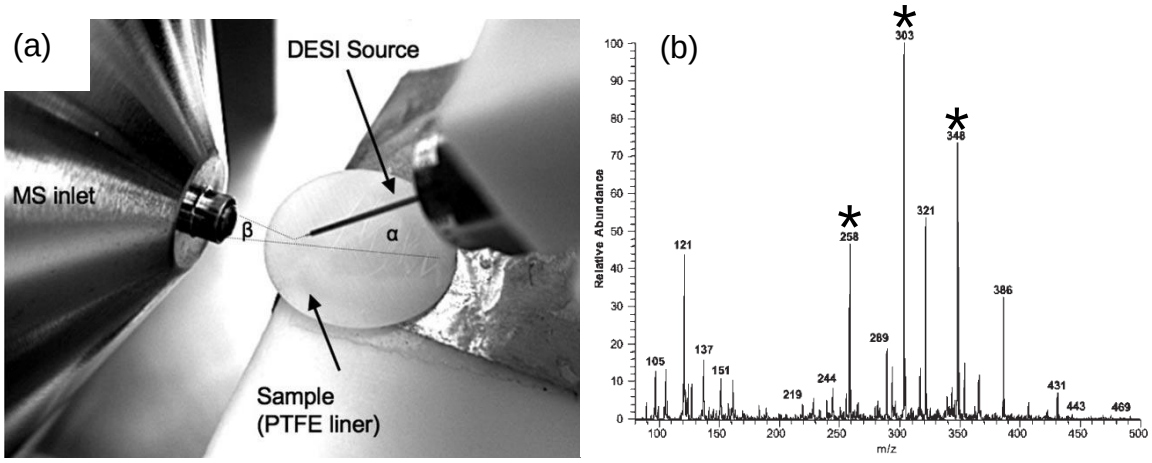

Figure 3. (a) A photograph of the experimental set-up for the DESI-MS analysis of poly(tetrafluoroethylene) (PTFE) with the incident (α) and collection (β) angles set at 50 ° and 10 °, respectively. (b) DESI analysis of the PTFE liner after aging for 6 days. Detection of ions at *m/z* 258, 303 and 348, denoted by (*), were later identified as nitrated derivatives of the diphenylamine additive. The figure is adapted from ref. [21] with kind permission of John Wiley and Sons.

'Transmission-mode' DESI is an alternative to the conventional DESI configuration where specific types of sample can be analysed rapidly without rigorous optimisation of spray distances or angles [68]. This modified configuration directs the electrospray towards a porous or mesh-like sample with a zero degree angle between the electrospray tip, sample, and capillary inlet of the mass spectrometer. Transmission mode DESI (TM-DESI) is obviously not applicable to solid materials, but is designed to simplify the sample preparation process for liquid samples deposited on a substrate [68]. A particularly interesting example of the use of TM-DESI is the application to the analysis of a polyester bednet treated with the insecticide deltamethrin (16 $mg.m^{-2}$) for malarial control [24]. TM-DESI was used in this instance as a comparative measure for the assessment of transmission-mode direct analysis in real time (TM-DART) – DART will be discussed in a following section. Under the

conditions tested, TM-DART's limit of detection (LOD) was 0.5 $mg.m^{-2}$, providing better sensitivity than TM-DESI (LOD = 8 $mg.m^{-2}$) primarily due to the larger sampling diameter of TM-DART. However, the smaller sampling diameter of TM-DESI made it possible to analyse one bednet fibre at a time, therefore providing complementary information to TM-DART by evaluating the spatial distribution of the insecticide [24].

The design of smart polymer substrates capable of selective separation of components from complex matrices has resulted in their use in many applications. One example of a smart polymer in use is the selective extraction of analytes by molecularly imprinted polymers (MIPs). A poly(propylmethacrylate) MIP formed with 2,4-dichlorophenoxyacetic acid (2,4-D) as the template was used for the extraction of this analyte and four chemical analogues from tap and river water. Following the selective extraction, performing DESI on the MIP surface allowed rapid detection of the analytes – free from matrix interferences – by mass spectrometry [20]. The detection of 2,4-D was linear from 0.005 up to 0.50 $mg.L^{1}$, and then levelled off due to saturation of the active sites of the MIP. EASI has also been employed for the detection of five phenothiazines (chloropromazine, perphenazine, trifluprom azine, thioridazine and prochlorperazine) from an MIP [29]. The phenothiazine compounds were selectively adsorbed from urine samples by a chlorpromazine-imprinted methacrylic polymer and quantified using MIP-EASI-MS at a limit of quantitation (LOQ) *ca*. 1 mM [29].

Liquid extraction surface analysis (LESA) is a commercially available liquid-solid extraction technique descended from an in-house ambient surface sampling probe first constructed by Wachs and Henion in 2001 [69]. The key to the success of this technique lies in the formation of a liquid microjunction created between the sample surface and the sampling probe when the probe is within ~ 1 mm to the surface. This is achieved through adaptation of the commercially available Advion NanoMate chip-based infusion nanoelectrospray system that uses a robotic pipette tip and has also recently been

implemented in its continuous flow form by Prosolia. Accurate control of the dispensation height and solvent volume allow formation of liquid-surface microjunctions that extract analytes into small volumes of solvent before being aspirated back into the pipette tip, ready for introduction to an ionisation source (Fig. 4) [70]. Creating the liquid microjunction can be difficult on rough, wettable, or absorbent surfaces and represents the greatest limitation of this technique. Generally, LESA works best on flat, homogeneous and hydrophobic surfaces that facilitate the stabilisation of the liquid microjunction: making it highly suitable for many synthetic polymer applications.

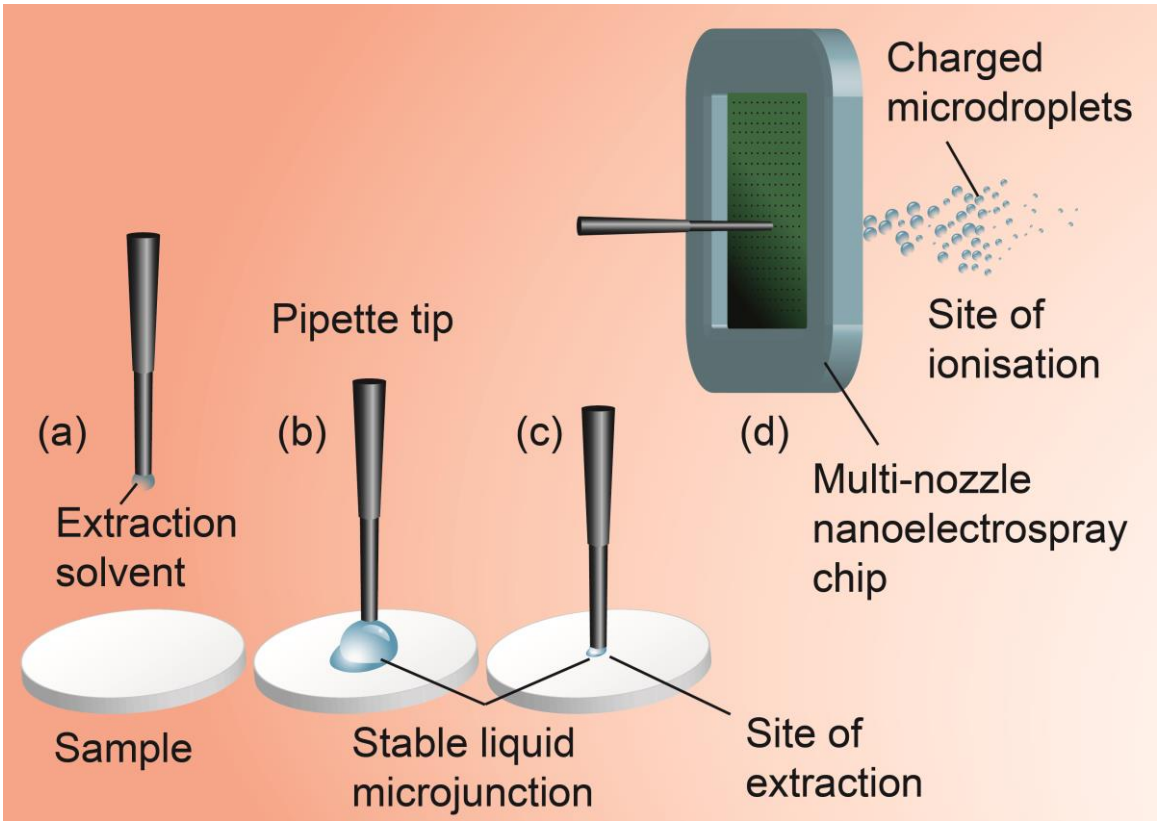

Figure 4. An illustration of the liquid extraction surface analysis (LESA) process. (a) A robotically controlled, disposable pipette tip aspirates a small volume of solvent into the tip. (b) The pipette tip is positioned above the sample and dispenses a portion of the solvent, forming a liquid microjunction with the sample. (c) The solvent containing the extracted analyte is re-aspirated back into the pipette tip. (d) The pipette tip docks with a nanoelectrospray chip nozzle and the extraction solvent sprayed forming a mist of charged microdroplets.

The first reported use of LESA-MS for the analysis of synthetic polymers involved the *in situ* characterisation of stabilised and unstabilised thermoset, polyester-based surface coatings [31]. The high extraction efficiency aided by the controlled solid-liquid extraction process allowed for thermoset polymers to be interrogated without any sample pre-treatment or preparation prior to analysis. The detection of the additive Tinuvin 123 and its associated

degradation products directly from stabilised coatings under ambient conditions was fast, simple, and highly reproducible as the technique is fully automated. The analysis of unstabilised coatings of the same composition after exposure to four years of outdoor field testing revealed elevated levels of melamine (1,3,5-triazine-2,4,6-triamine) present on the surface. The detection of melamine was supported by the comparison of LESA-MS/MS spectra to that reported for authentic melamine. The detection of melamine on the degraded sample also correlated with changes in the coatings visual appearance, *i.e.*, powder-like deposits on the surface, indicative of polymer blooming. These visual changes may be directly attributable to the presence of melamine as a degradation product concentrating at the surface or may be indirectly responsible as an association with one or more other components, possibly an organic acid, capable of forming a hydrogen donor-acceptor complex [31].

LESA is not only adept at investigating analytes within polymers but can also target material residing on the surface of polymers through judicious selection of the extraction solvents. This can help reduce spectral complexity and signal suppression from polymer contaminants and leachables. An interesting example of selective analysis of surface material on a polymer substrate is the lipid profiling of biological material deposited on worn contact lenses [32]. The biofouling of contact lenses can cause major discomfort to those who wear them yet little is known about (i) the chemical nature of the biological material deposited, and (ii) how the composition of the silicon hydrogel that constitutes the contact lens affects this deposition. Employing LESA with tandem mass spectrometry enabled the selective detection of different lipid classes and the construction of lipid profiles of biological samples and off surfaces. By comparing the lipidome of tear film secretions and meibum extracts to those from worn contact lens surfaces, lipid molecular species representing all major classes present in the human tear film were identified as being present on the hydrogel [32].

Thanks to the improvements in sensitivity of modern instrumentation, analysts have greater freedom to create new ionisation sources or modify existing equipment 'in-house'. Such modifications have the potential to increase experimental flexibility and broaden the range of substrates amenable to mass spectrometric analysis. An example of a very simple modification to a commercial ionisation source is the analysis of thermosetting paints on conductive surfaces by paint spray MS. Paint spray MS was inspired by the paper spray [71, 72] and leaf spray [73] ionisation methods developed by Cooks, Ouyang and co-workers. The paint spray method can be coupled with any mass spectrometer with an atmospheric pressure ion-source interface; requiring only a voltage applied to the wet substrate for generation of an ion signal (Fig. 5) [33]. Paint spray mass spectrometry shares characteristics of ESI and ambient ionisation methods but does not require pneumatic assistance to transfer the analytes to the gas phase. Analyte desorption is achieved by liquid extraction of analytes at or near the surface, and a high electric field is used to facilitate ionisation. The paint spray source was constructed by simply attaching a high-voltage power supply directly to the investigated sample using a crocodile-clip and a flow of solvent from a pipette, which in this case was chloroform:methanol (2:1) containing 0.1 % formic acid (v/v). Paint spray MS was reported for the qualitative analysis of four stabilisers (Tinuvin 770, 292, 123, and 152) present within polymer-based surface coatings on conductive metal surfaces [33].

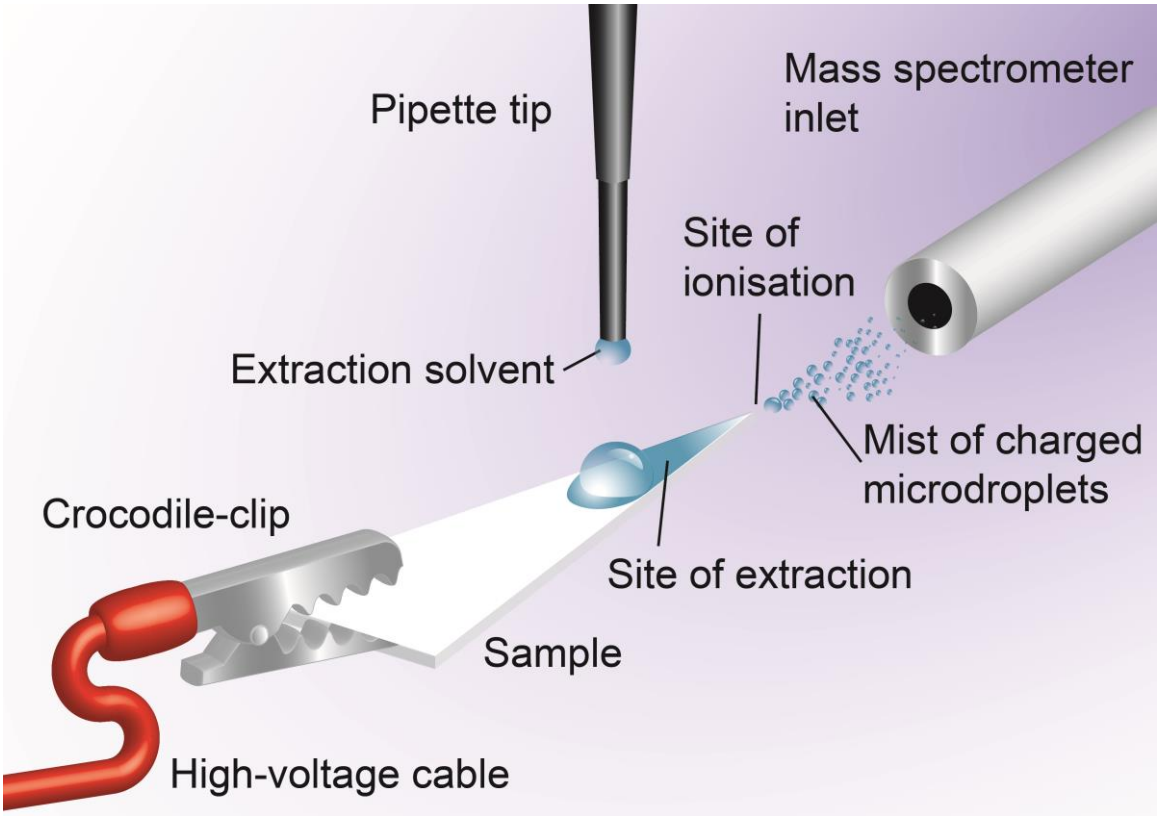

Figure 5. An illustration of the paint spray ionisation process where analyte desorption is achieved by liquid extraction and a high voltage applied to the substrate creates a Taylor cone at the edge of the sample. The result is a mist of charged microdroplets containing the analyte, emanating from the sample towards the mass spectrometer inlet.

3.1 Thermal- and plasma-desorption ambient ionisation mass spectrometry

Promoting analytes into the gas-phase from solid and liquid samples can sometimes be achieved simply through heating of the sample. Passing a flow of heated gas over the sample or by placing the sample onto a heated probe are the most common methods for thermal desorption. Due to the involvement of a heated gas stream, thermal desorption methods are usually coupled with atmospheric pressure chemical ionisation (APCI) [74, 75]. Chemical ionisation makes thermal desorption techniques amenable to a wider range of

analyte polarities compared to extraction-based methods such as DESI and are particularly useful for low polarity compounds. Plasma-based methods are presented here under the category of thermal desorption but do not use heat exclusively as the desorption process. Plasma-based techniques are generally limited to analytes of molecular mass < 1000 Da, however, heating of the plasma or coupling with a heated sample probe can extend the accessible mass range [76]. These attributes make thermal/plasma-based techniques ideal for polymer additive analysis and thermal degradation monitoring but less useful for the characterisation of higher mass, polydispersed polymers.

3.2 Characterisation of polymers by thermal- and plasma-desorption methods

In a study focusing on low molecular weight synthetic polymers, the use of an atmospheric solids analysis probe (ASAP) provided a fast and efficient method of identification of PEG (M_n = 1430 g.mol^{-1}) and poly(styrene) (PS) (M_n = 1770 g.mol^{-1}), directly from the solid polymer material [44]. ASAP can be accomplished with a simple modification to an APCI source with desorption of material arising from either a heated nitrogen gas stream or from directly heating the probe itself. Ionisation of the thermally vaporised sample then occurs by corona discharge under standard APCI conditions with solids, as well as liquid samples, being analysed in seconds [77]. Employing ASAP-MS, PEG was observed as protonated oligomers while PS, a non-polar polymer that is difficult to analyse by MALDI or ESI, was found to form radical cations. The key instrument parameter in optimising this experiment was the additional heat from gas flowing over the probe that aided desorption. At 600 °C, the heated flow of nitrogen gas was sufficient to desorb the heavier oligomers for ionisation. Ion fragmentation caused by in-source dissociation increased spectral complexity but could be minimized by optimising the sampling cone voltage and gas temperature. Fortuitously, in-source dissociation resulted in cleavage of the

C–C and C–O backbone bonds, in contrast with the exclusive C–O bond cleavage observed by tandem mass spectrometry. This in-source fragmentation thus provided increased structural information on the polymer through a series of pseudo-MS^2 type experiments.

The ability to ramp the N_2 gas temperature also provides an extra degree of experimental flexibility. At 600 °C, many small organic molecules have already desorbed [78] allowing temporal separation of the polymer from chemical noise. If the polymer is not the target analyte, ion suppression by abundant oligomers can be reduced by maintaining the desorption gas at lower temperatures [79]. It should be noted however, that the gas temperature does effect the polymer ion distribution therefore average molecular weight or polydispersity calculations using ASAP-MS could be unreliable [44].

The combination of ASAP and travelling wave ion mobility MS (TWIM-MS) has recently been reported as an alternative approach for the simultaneous characterisation of polymers and additives. TWIM is a post-ionisation separation method based on low-voltage waveforms pushing the ions across a gas-filled ion guide. Temporal separation of isobaric ions is achieved as drift times through the TWIM cell change as a function of charge (z), mass (m), and collision cross-section (Ω) of the ions [80]. TWIM-MS has already proven to be a useful tool for synthetic polymers analysis [81-83] and the coupling of ASAP with TWIM-MS offers a fast, simple method of ionising hydrocarbon species that are often difficult to analyse. Afonso and co-workers using ASAP-TWIM-MS were able to characterise commercial PP samples and identify unknown stabilisers that were present without prior separation steps as illustrated in Figure 6 [43]. For a PP sample where no stabilisers were detected, a different pattern of pyrolysis residues was observed associated with changes due to polymer degradation. The comparison of stabilised versus non-stabilised PP pyrolysis residues using this method could provide further insight into stabiliser activity and polymer degradation [43].

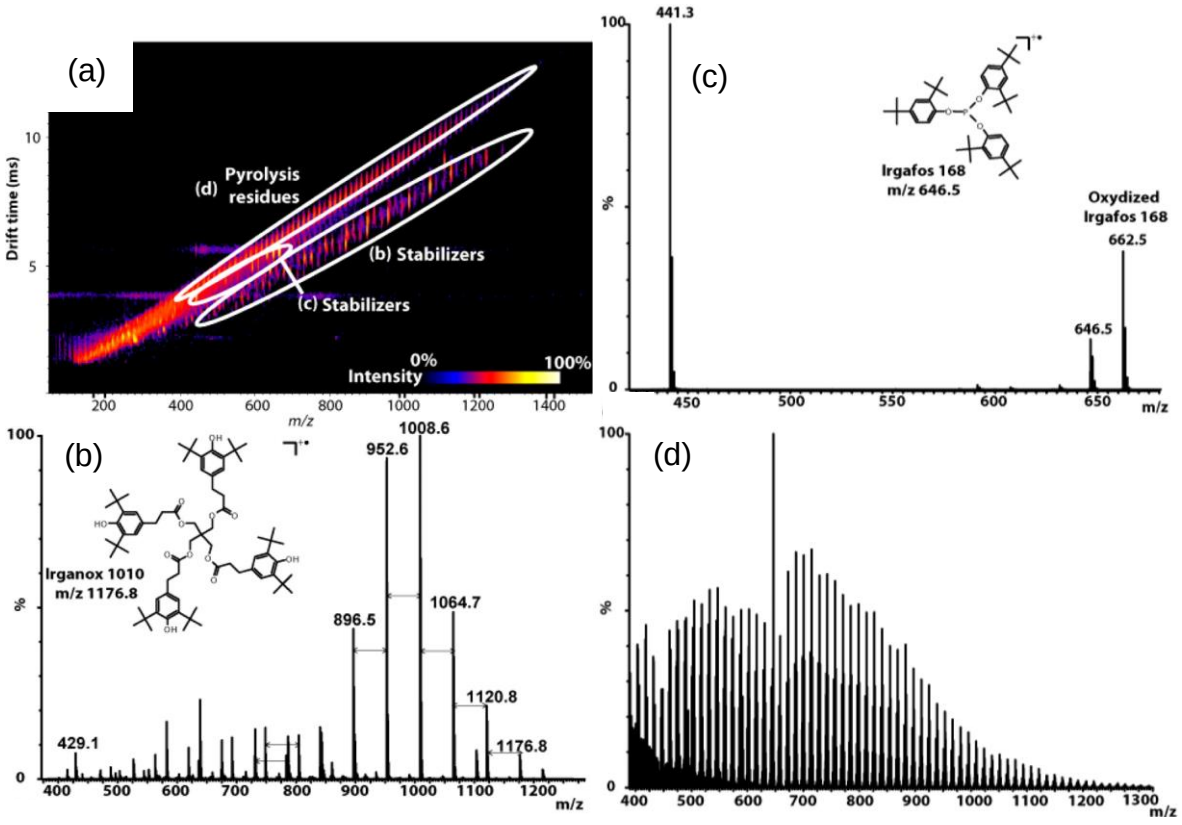

Figure 6. ASAP-TWIM-MS results of a commercially available PP pipette tip. (a) *m/z*-drift time plot and the extracted mass spectra obtained, respectively, for (b) Irganox 1010, (c) Irgafos 168, and (d) PP pyrolysis products. The figure is adapted from ref. [43] with kind permission of the American Chemical Society.

Direct probe-atmospheric pressure chemical ionisation (DP-APCI) [45] is a thermal desorption technique almost identical to ASAP, the only difference being that DP-APCI involves slow heating of samples using the probe to cause gradual degradation and volatilisation of their constituents according to their intrinsic thermal stabilities. This differs from ASAP, which generally relies on energetically excited species and heat associated with the gas stream or flash pyrolysis from rapid heating of the probe. DP-APCI produces more background noise and less reproducible spectra than direct pyrolysis mass spectrometry, which operates under vacuum. However, carrying out the analysis at atmospheric pressure

may provide more useful information about the thermal properties of materials as it is more similar to a classic thermogravimetric analysis [45, 84, 85]. Four amphiphilic copolymer networks (APCN's) were investigated by Wesdemiotis and co-workers using DP-APCI. The polymers consisted of various amounts of hydrophilic poly(*N*,*N*-dimethyl acrylamide) (PDMAAm) and hydrophobic PDMS domains to form graft copolymers. Two of the networks were cross-linked with a poly(methylhydrosiloxane) (PMHS) and the other two were blends of a polyurethane and the PDMAAm-PDMS graft. DP-APCI experiments carried out on these APCN's were able to provide information about the nature of the hydrophobic and hydrophilic components present and could readily distinguish between copolymers with different comonomer compositions, cross-linked copolymers, and copolymer blends with similar physical properties [45]. The experiments were dominated by ions below 1000 Th, being unable to detect larger oligomers, however, the dependence of DP-APCI mass spectra on temperature does provide insight into the thermal stability of the different domains within the copolymer.

Flowing afterglow-atmospheric pressure glow discharge (FA-APGD) – also known as flowing atmospheric pressure afterglow (FAPA) – is a plasma-based technique where the sample is spatially separated from the plasma discharge and ionisation of the analyte takes place in the ambient air region between the plasma source and the mass spectrometer [86, 87]. Direct analysis of liquid and solid (soluble or insoluble) bulk polymers and granulates is possible and introducing the samples to the gas stream outside the discharge chamber overcomes problems of discharge instability and memory effects while allowing for rapid, high-throughput analyses (< 30 s per sample) [86-88]. The unfiltered afterglow allows ionisation of lower polarity analytes but also complicates mass spectra with a greater number of background ions and different adduct species [89]. In the analysis of synthetic polymers, two studies have been reported that were both restricted to an accessible mass range below

m/z 500. The limited *m/z* range was due to the inability to thermally desorb larger molecules and constitutes a major limitation of this technique, making it unsuitable for molecular weight determination and differentiation of polydispersed polymers [40, 41].

Using FA-APGD-MS, the homopolymers *cis*-poly(isoprene) (IR), PEG, and poly(ethylene terephthalate) (PET) were identified by monomer units and fragments ions without any sample preparation. In combination with principle component analyses (PCA), differentiation of three natural polymers; pectin, amylopectin, and cellulose, was achieved quite remarkably as the three differ only by their glycosidic linkage. The technique was also applied to commercial PVC-based food wrapping material where the detection and identification of the phthalate plasticisers, DEHP and DBP was demonstrated [40]. In a similar study, a homemade heating apparatus positioned directly below the APGD source was used to volatilise the samples into the atmospheric afterglow region. The technique described as thermal assisted-atmospheric pressure glow discharge mass spectrometry (TA-APGD-MS) decouples the desorption and ionisation steps and allows for a more accurate control of thermal degradation products generated for analysis. Polymer samples including homopolymers of PS, poly(butanediol succinate) (PBS), and poly(oxymethylene) (POM) as well as POM copolymers, were directly characterised and thermal degradation products of these synthetic polymers identified by tandem mass spectrometry [41].

Plasma-assisted desorption/ionisation (PADI) consists of generating a non-thermal radio frequency-driven atmospheric pressure plasma and directing it onto the surface of the analyte as illustrated in Figure 7 [90]. The result is a “cold” plasma with an operating temperature close to that of the ambient surroundings, which is particularly useful for thermally sensitive samples. The plasma plume of PADI has a sub-millimetre diameter, offering comparable spatial resolution to extraction-based techniques (*cf*. LESA) and its visibility makes optimising source geometries much easier [90]. Four different polymers,

PMMA, PET, poly(lactic acid) (PLA), and PTFE were able to be detected by PADI-MS. Characteristic ions for all four polymers were observed in negative-ion mode whereas only PMMA and PLA were detected as positive ions. The upper mass limit of detection was assigned as polymer fragment ions of PTFE at *m/z* 1200 [46].

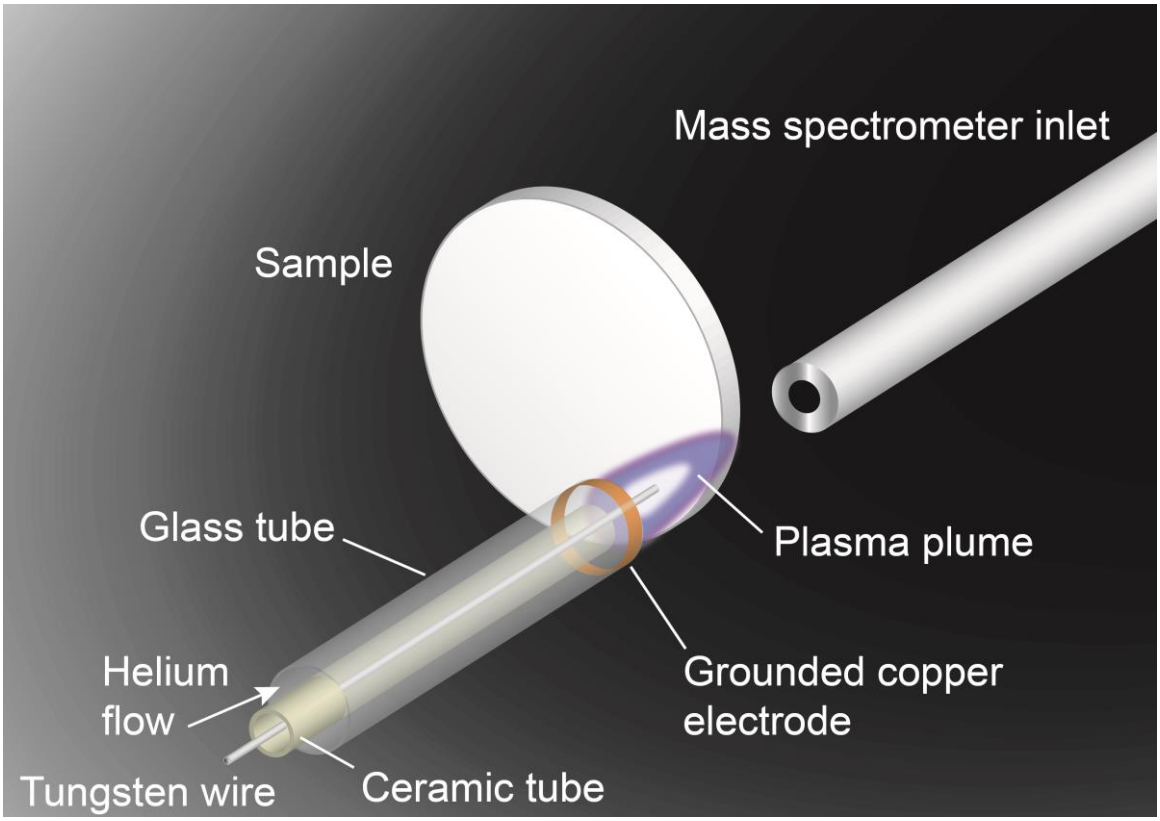

Figure 7. An illustration of the plasma-assisted desorption/ionisation (PADI) process where a low temperature, non-thermal plasma consisting of positive and negative ions, electrons, and excited state species is utilised. The plasma is in contact with the sample in close proximity to the mass spectrometer inlet.

3.3 Analysis of additives, adsorbents and contaminants using thermal- and plasma-based methods

Additives used in polymeric food-contact materials are subject to regulation due to the possibility of their migration into foods. The US Food and Drug Administration, concerned with the development of analytical techniques capable of high-throughput screening, evaluated direct analysis in real time (DART) for its ability to screen food-packaging material for the presence of 13 common additives including; plasticizers, anti-oxidants, colorants,

grease-proofers, and ultraviolet light stabilizers [34]. DART involves the creation of a high-voltage plasma by introducing a flow of gas to a coronal discharge inside a ceramic flow cell. This gas stream can be heated if desired and exits the source through another grid-electrode that neutralises counter ions and repels sample ions [76]. The additives detected by DART are listed in Table 2 by their common abbreviation or commercial name as these products are often formulated within polymers as complex mixtures of several compounds. For each additive, the type of polymeric materials they were successfully sampled from is also listed. The most abundant and characteristic ion detected in each case (Table 2) was assigned from the analysis of standard solutions of each additive by the same method. As the analyses were performed on a triple quadrupole mass spectrometer, comparison of product-ion spectra provided further supporting evidence for direct additive detection. The DART source parameters were optimised for *bis*(2-ethylhexyl) phthalate (DEHP) except for the DART gas stream temperature which was generally increased (between 200 – 450 °C) as the molecular weight of the additive increased. In all cases, the additives were unambiguously detected in the packaging materials yet method sensitivity and linearity were reported to be difficult to establish. These difficulties were due to the large effect that sample positioning relative to the DART source and the mass spectrometer inlet had on signal intensities – a 0.1 mm change in sample position was enough to reduce the signal by nearly one order of magnitude [34].

Table 2. List of food-packaging materials and the additives detected from them by DART-MS [34].

Class of additive	Additive name	Material detected from	Dominant ion detected	
			m/z	ion identity
Plasticiser	DEHA	PVC	371.3	$[M+H]^+$
	DEHP	PVC	391.3	$[M+H]^+$
	ESBO	PVC	992.8	$[M+H_3O]^+$
UV stabiliser	Chimasorb 81	HDPE	327.2	$[M+H]^+$
	Tinuvin 234	PET	448.2	$[M+H]^+$
Colorant	Uvitex OB	HDPE	431.2	$[M+H]^+$
	Blue 15b	PS	576.1	$[M+H]^+$
	Yellow 110	PS	642.8	$[M+H]^+$
Grease proofer	diPFAoAA	Paper	489.0	M^-
	diPAPS	Paper	889.0	M^-
Antioxidant	Irganox 1076	HDPE, LDPE, PP	531.5	$[M+H]^+$
	Irgafos 168	HDPE, LDPE, PP	647.5	$[M+H]^+$
	Irganox 1010	HDPE	1196	$[M+H_3O]^+$

Rothenbacher and Schwack also employed DART for the rapid identification of polymer additives directly from glass jar lid gaskets [36] and in a separate study, additives from toys and childcare articles [37]. In PVC-based gaskets, DART analysis was able to identify phthalates, fatty acid amides, tributyl O-acetylcitrate, dibutyl sebacate, *bis*(2-ethylhexyl) adipate, 1,2-diisononyl 1,2-cyclohexanedicarboxylate, acetylated mono- and diacylglycerides, epoxidised soybean oil, and polyadipates, with an LOD less than or equal to 1 % w/w of polymer [36]. In toys, an LOD of 0.05% was obtained for benzyl butyl phthalate, diisononyl phthalate, and DEHP. For dibutyl phthalate (DBP), di-*n*-octyl phthalate and diisodecyl phthalate, the LOD was 0.1% [37]. This aligns with the Council Directive 76/769/EEC of the European Commission that restricts the use of DEHP, DBP, or benzyl butyl phthalate in toys and childcare articles at concentrations of greater than 0.1% w/w and equivalent if the articles can be taken into the mouth by children for diisononyl phthalate, diisodecyl phthalate, or di-n-octyl phthalate [91]. The sensitivity of DART-MS in both cases makes it an attractive candidate for high-throughput screening for both food packaging and products produced for children. Unfortunately, under these experimental conditions, most samples rapidly decomposed due to the high gas stream temperatures (200 – 450 °C) making the technique unsuitable for non-destructive control screening.

In a study by Haunschmidt *et al.* [38], it was demonstrated that DART-MS is capable of the detection of 21 commercially available stabilising agents directly from a model polymer system. The additives Tinuvin 234, 326, 327, 328, 770; Irgafos 38, 126, 168; Irganox E201, PS 800, PS 802, 1010, MD 1024, 1035, 1076, 1081, 1330, 3114; Chimassorb 81; PEP 36, and HP 136, were added in various mixtures to PP at a concentration of 10 mg of each stabiliser in 5 g of base polymer. Without any sample pre-treatment, each stabiliser was detected directly from the PP plaques and identified by accurate mass measurements obtained using a TOF mass analyser. In addition, DART-MS allowed for the fast identification of

some additive degradation products generated during polymer compounding and processing [38]. By comparing the signal intensities of the stabiliser precursor and its related degradation products over systematic changes in processing conditions, semi-quantitative trends could be inferred.

In a similar type of study, the role played by the stabilizer Irgafos 168 in retarding thermal and photo-oxidation of industrial poly(ethylene) (PE) was monitored *in situ* by DART-TOF-MS [39]. Accurate mass measurements obtained for degradation products of both Irgafos 168 and PE directly from the polymer showed that under thermal treatment the stabiliser reduced degradation by decomposing the generated hydroperoxides or by limiting the formation of peroxide radicals by trapping the oxygen present into the bulk of the polymer [92]. Under UV light exposure, the stabiliser acts as a common antioxidant according to the mechanisms described above but also through homolytic P–O bond cleavage may also be able to trap harmful, propagating free radicals [39].

DART-MS has also been reported for the analysis of tackifier additives in synthetic rubber and acrylic adhesive matrices [35]. This was deemed particularly useful as the tackifier resins play a critical role in adhesive products and are commonly comprised of multi-component mixtures that are difficult to fully extract and analyse. Four key classes of tackifier resins were characterised (rosin, terpene phenolic, poly(terpene), and hydrocarbon resins) allowing complete pressure-sensitive adhesive (PSA) products containing two or three of these tackifiers to be analysed. Analysis times were less than 10 mins per sample and by using the three most abundant characteristic ion signals, the tackifiers could be identified when present in the adhesive material at concentrations as low as 0.1 % (w/w) [35].

The ASAP method can also be used for the detection of exogenous compounds and is particularly appealing because of its ease of use, sensitivity, and speed of analysis [42, 77]. As an example of the sensitivity, detection of erucamide present on a piece of PET fabric

only required rubbing the closed end of a clean melting point tube over the material and inserting it into the source [42]. When a small fibre of this polymeric material was introduced into the source and the temperature ramped from 100 °C to 400 °C not only was erucamide detected but also Irganox 1076 and 3114, Irgafos 168 and oxidized Irgafos 168. At temperatures above 500 °C, degradation products indicative of the polymer itself were observed including the cyclic trimer of PET at *m/z* 577 [42]. Water stored in PET bottles also tested positive for the presence of cyclic PET oligomers that were assumed to have leached from the container. ASAP was also able to detect palmitic acid and possibly bisphenol A from a new polycarbonate (nalgene) bottle and identify a carpet fibre as being Nylon-6 by observing characteristic cyclic oligomers [42].

Desorption atmospheric pressure photoionisation (DAPPI) is a technique that can be used to ionise both polar and completely non-polar analytes. The DAPPI experimental set-up is similar to DESI, in that a pneumatically assisted solvent spray is directed at a samples surface. The difference being that with DAPPI, desorption of analytes is a thermal process as the nebulising gas is heated (250-350 °C) and is highly dependent on the thermal conductivity of the sampling surface [93]. Ionisation still takes place in the gas phase but is promoted by the use of a UV lamp and not by the application of a high-voltage to the solvent line as is the case with DESI [93]. Vaikkinen *et al.* have reported a method employing DAPPI-MS for the direct analysis of pieces of PDMS used as a solid phase extraction media. Human metabolites, pharmaceuticals, and toxic compounds all ranging in polarity, were extracted to PDMS from spiked waste water and urine samples [47]. Combining solid-phase extraction onto PDMS with direct analysis by DAPPI-MS greatly reduced the background ion signals, circumventing the complexity of the matrices without laborious, time-consuming separative clean-up protocols. Additional selectivity towards different analytes could be achieved by varying the solvents used for both the DAPPI spray and the treatment of the

PDMS prior to the extraction. The authors also suggested that it may be possible to shorten the extraction time and reach even lower detection limits by changing the dimensions of the PDMS extraction material [47].

4.1 Laser ablation/desorption ambient ionisation mass spectrometry

Ambient sampling techniques involving laser irradiation of samples are traditionally less popular than solvent extraction-, thermal- or plasma-based desorption methods due to the requirement for specialised equipment and the necessity for additional safety precautions. It can also be difficult to sample unusual shapes and sizes while containing possible reflections of the laser light. In most cases, the ionisation source needs to be at least partially enclosed for safety, which removes some of the inherent advantages of ambient ionisation MS. Nevertheless, laser ablation/desorption-based ambient ionisation techniques have found useful application in polymer analysis and are thus included in this discussion.

In contrast, atmospheric pressure MALDI (AP-MALDI) employs an ion source external to the mass analyser and, being operated at ambient temperature and pressure, is not held to such restrictions. AP-MALDI does suffer from reduced ion transfer efficiencies as compared to conventional vacuum MALDI (vMALDI) but they can be bolstered by pneumatic assistance with a coaxial gas flow and voltages applied to the target plate [50, 94, 95]. Even with the reduced ion transmission there are some advantages to AP-MALDI. These include the ease in which AP-MALDI sources can be coupled to MS instruments capable of analysing atmospheric pressure ions and simplified sample handling. There is also evidence that AP-MALDI produces ions with lower internal energies than those produced by vMALDI due to collisional cooling at atmospheric pressure [96]. AP-MALDI is therefore considered to be a softer ionisation technique than vMALDI and ideal for the analysis of non-covalent complexes or fragile analytes [97].

4.2 Characterisation of polymers and additives by laser ionisation/desorption methods

The first reported use of AP-MALDI for the analysis of synthetic polymers was by Creaser *et al.* [48] as part of an investigation into the capability of an AP-MALDI quadrupole ion trap (QIT) instrument to provide structural information from MS^n experiments. Combinations of α-cyano-hydroxycinnamic acid (CHCA), 2-(4-hydroxyphenylazo)benzoic acid (HABA), and 6,7-dihdroxycoumarin (esculetin) with Li^+, Na^+, or K^+ cationising agents all yielded spectra containing PEG ions. Spectra recorded using 2,5-dihydroxybenzoic acid (DHB) as the matrix exhibited low signal-to-noise ratios for PEG ions and the matrix 6-aminothiothymine (6-ATT) did not yield PEG ions at all. The use of esculetin with lithium hydroxide as the matrix additive was deemed to be the most effective combination for PEG analysis by AP-MALDI in terms of signal intensity and lowest abundance of $[PEG + matrix - H + 2metal]^+$ ions relative to $[PEG + metal]^+$ ions. Using Li^+ as the cationising agent, highly informative tandem mass spectra were observed for PEG 1500 that were not possible with Na^+ or K^+ cationisation [98].

Using a similar AP-MALDI-QIT configuration, experiments were carried out on a series of commercially available telomeric ethoxylated surfactants; Surfynol 440, 465, and 485 [51]. The increasing Surfynol values indicate increasing amounts of ethoxylation on a backbone of 2,4,7,9-tetramethyl-5-decyne-4,7-diol (Surfynol 104). The results obtained from collision-induced dissociation (CID) experiments using the QIT gave better signal to noise, improved mass resolution on the fragments, and improved mass accuracy of the fragments compared to previous vMALDI-TOF-MS and post-source decay (PSD) results [51, 99]. Tandem mass spectra also identified analyte matrix clusters with sodiated DHB that were isobaric with the ethoxylated telomers and allowed the identification of unassigned peaks from previous MALDI PSD experiments. MS^3 experiments now accessible with a QIT demonstrated that some of the ions detected contained multiple matrix cluster species.

Like conventional vMALDI, AP-MALDI can be coupled to liquid delivery systems for post-separative analysis by MS [49]. An HPLC-AP-MALDI configuration is far removed from an *in situ* analysis of a polymer sample but does highlight the versatility afforded by AP-MALDI in analysis of both solid- and liquid-phase samples (previously separated or not). Using a nitrogen laser (337 nm) focused at the exit of a static fused silica capillary illustrated in Figure 8(a), Zenobi and co-workers [49] were able to show the intact Na^+ cationised oligomer distribution of 1 mM PEG1000 eluting from a HPLC column (Fig. 8b). The mobile phase consisted of a liquid matrix, *N*-(4-methoxybenzylidene)-4-butylaniline (MBBA) and methanol (1:1). The analysis was not limited to the use of liquid matrices as mass measurements were also possible using dissolved solid matrices, *e.g.*, α-cyano-4-hydroxycinnamic acid (HCCA).

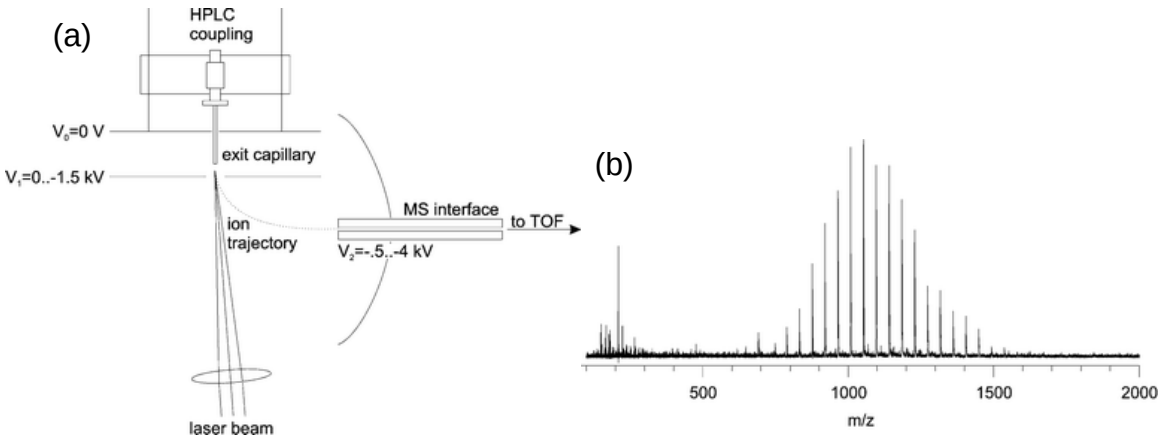

Figure 8. (a) A schematic of the flow injection setup. The liquid is connected by a HPLC coupling to the ionisation source, the laser is focused to the end of the exit capillary and the liquid analyte/matrix mixture is desorbed/ionised. The ions are guided by electric fields to the interface of the mass spectrometer. (b) Positive-ion mode flow injection AP MALDI mass spectra of a 1 mM PEG 1000 solution in *N*-(4-methoxybenzylidene)-4-butylaniline:methanol (1:1) at a flow rate of 5 µl min^{-1}. The figure is adapted from ref. [49] with kind permission of The Royal Society of Chemistry.

In a report by the methods developers, the applicability of electrospray-assisted laser desorption/ionisation (ELDI) was demonstrated through the analysis of various chemical components on the surfaces of different solids and dried liquids under ambient conditions [52]. ELDI involves irradiating samples with a pulsed laser and entraining the ablated material in an electrospray ionisation plume directed at the mass spectrometer inlet where post-desorption ionisation occurs [100, 101]. One of the many examples reported was the characterisation of synthetic polymer standards. One drop of PPG1000, PEG1500, and PMMA1300 standard solutions were deposited onto a sample plate, allowed to dry, and analysed directly by ELDI-MS. Only singly charged ion series were observed for PPG1000

and PMMA1300, but both singly and doubly charged ions from PEG1500. The ELDI mass spectra obtained were comparable to conventional ESI-MS and MALDI-MS spectra [52].

Laser ablation electrospray ionisation (LAESI) is another technique – similar to ELDI – that combines laser ablation with electrospray ionisation [102]. The major difference between ELDI and LAESI is that the latter employs a mid-infrared laser (2940 nm) whereas the former typically uses UV wavelengths (~ 337 nm) for irradiation. This means that LAESI relies heavily on the presence of water in the substrate for the ablation of material into the electrospray plume. To the best of the authors' knowledge the only reported use of LAESI for the analysis of synthetic polymers or polymer additives is within the patent claim for the LAESI invention [103]. The claim reports the use of LAESI for the detection of a drug compound directly from the pharmaceutical tablet and in doing so inadvertently identified PEG 400 and its derivatives from the solid material. The LAESI technology would be well suited for the analysis of polymer additives accumulating in biological tissues and may also find application in the characterisation of hydrogels (and/or additives contained in them) due to the high water content of these materials.

5. Future Perspectives and Challenges

Ambient ionisation approaches are advantageous not just because of speed and the ability to interrogate objects with non-standard and irregular shapes but because the desorption and the ionisation of the analyte can be decoupled depending on the application. For instance, an analyst may choose an extraction method when focused on exogenous compounds (additives, adsorbents or contaminants) within a polymer, a laser desorption method when spatial information is required (both lateral and depth resolution), or a thermal desorption method to interrogate the structure of the polymer itself. The ability to tailor the desorption and ionisation events independently, depending on the application, constitutes a

major strength of ambient ionisation technologies and affords the user great versatility. Classical ionisation methods, although robust, do not share the same flexibility.

There are challenges associated with ambient ionisation approaches that currently limit their use and require further development. Reliable quantitation still remains the greatest challenge and although there are examples of successful quantitative analyses, they are highly dependent on the experimental set-up. The numerous degrees of freedom that provide ambient ionisation sources with their versatility also make it difficult to achieve the reproducible sampling required for quantitation. Technologies that automate part of the sampling procedure (*e.g.*, LESA) are helping to overcome this challenge but further method development is needed. The introduction of internal standards can also limit the quantitative ability of many ambient ionisation approaches. In particular, how one adds an exogenous compound to a complex matrix (particularly solid matrices) changes its recovery and possibly affects the recovery of the analyte and so care must be taken to control for such variables. For some applications, overwhelming spectral complexity can make spectra too difficult to interpret and peak assignment inaccurate. Higher resolution mass analysers can help deconvolute spectra but in the absence of sufficient mass resolution there are alternatives that are currently being explored. Again, finding the right combination of desorption and ionisation through experimentation can enhance the ion signals of interest while actively suppressing chemical noise. Another option is the post-ionisation separation of ions by ion mobility. Such methods provide an additional dimension of selectivity, able to reduce background noise and potentially separate isobars or even isomers prior to mass spectrometric analysis. However, the simplest method for increasing selectivity is tandem mass spectrometry. Using mass filtering techniques, for example, precursor-ion and neutral loss scanning using a triple quadrupole mass analysers, allows for selective detection of ions containing similar structural motifs from complex matrices.

Taken together, the diverse array of ambient desorption/ionisation technologies and the power of modern mass spectrometers provide an exciting and extensive tool-box for the contemporary polymer analyst.

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