Separation and quantification of quantum dots and dissolved metal cations by size exclusion chromatography–ICP-MS

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ABSTRACT

The prevalence of engineered metallic nanoparticles within electronic products has evoked a need to assess their occurrence and fate within environmental systems upon potential release of these nanoparticles. Quantum dots (QDs) are mixed-metal nanocrystals with the smallest of particle sizes (2–10 nm) that readily leach heavy metal cations in water, potentially creating a co-occurrence of nanoparticle and dissolved metal pollutants. In this report, we develop a size exclusion chromatography–inductively coupled plasma–mass spectrometry method (SEC-ICP-MS) for the rapid separation and quantification of ~5-nm-sized CdSe/ZnS QDs and dissolved Cd\(^{2+}\) and Zn\(^{2+}\) cations in water. The SEC-ICP-MS method provided a wide chromatographic separation of CdSe/ZnS QDs and dissolved Cd\(^{2+}\) and Zn\(^{2+}\) cations only when using the smallest SEC column pore size available and an eluent composition that prevented loss of metals to column polymer surfaces by using a surfactant to ensure elution of QDs (ammonium lauryl sulfate) and a complexing ligand to ensure elution of metal cations (ethylenediaminetetraacetate). Detection limits were between 0.2 and 2 µg L\(^{-1}\) for Cd\(^{2+}\) and Zn\(^{2+}\) among dissolved cation and QD phases, and ranges of linearity covered two to three orders of magnitude. Gold nanoparticles of sizes 5, 10, 20 and 50 nm were also effectively separated from dissolved Au\(^{3+}\) cations, illustrating the method applicability to a wide range of nanoparticle sizes and compositions. QD and dissolved metal concentrations measured by SEC-ICP-MS were comparable to those measured using the more conventional method of centrifugal ultrafiltration on split samples for dissolved and total metals. The applicability of the SEC-ICP-MS method to environmental systems was verified by measuring QDs and dissolved metals added to samples of natural waters. The method was also applied to monitoring CdSe/ZnS dissolution kinetics in an urban river water. The SEC-ICP-MS developed here may offer improved automation for characterising heterogeneous suspensions containing >1 µg L\(^{-1}\) heavy metals.

1. Introduction

With the projected market for nanomaterial-based products lasting in billions of dollars annually, management of these products and their waste will inevitably pose challenges...
to environmental health, particularly when nanomaterials are released through product disposal or industrial waste streams. Therefore, numerous studies have explored the environmental fate of engineered nanoparticles (Nps) [1–3], with particular concerns on their detection, transformation and quantification in water.[4–6] Detection and quantification of metallic Nps may be challenging for the smallest of sizes (2–10 nm) due to insufficient size detection limits, interference by their dissolved metal cations or matrix effects. Within this small size range are quantum dots (QDs), which are mixed-metal nanocrystals used for their extraordinary semiconducting and photoelectronic properties [7], and elemental silver (Ag Nps) and gold (Au Nps), which are used in biocidal [8] and biological [9] applications, respectively.

QDs and Ag Nps may partially dissolve and release metal cations (e.g. Cd\(^{2+}\), Zn\(^{2+}\), In\(^{2+}\), Ag\(^{+}\)) when present within water closely resembling natural conditions.[10–16] Laboratory studies have shown that both the QDs and the leached metal cations can induce toxic effects to aquatic organisms.[3,13,14,15,17] In fact, experiments with cadmium-based QDs exposed to algae [15] and zebra fish [14] have identified different biological effects or bioaccumulation extents caused by the leached Cd\(^{2+}\) compared with intact QDs. Therefore, the co-occurrence and co-threat of Nps and their dissolved metal cations drives a need to quickly and accurately characterise waters with both metals in both solid and dissolved forms.

The goal of this work is to develop an improved method for rapid and simultaneous separation and quantitation of <10-nm-sized QDs and their dissolved metal cations within aqueous suspensions utilising inductively coupled plasma–mass spectrometry (ICP-MS) and an inline separation of solid and dissolved phases via chromatography. The new chromatography-ICP-MS method is then evaluated and compared with the conventional pre-filtration ICP-MS technique for its capabilities to separate QDs and dissolved metals. The conventional method for measuring both phases involves a pre-measurement separation step using filtration membranes which are small enough to prevent passage of QDs during sample processing but allows filtration of dissolved solutes, and these steps may include centrifuge ultrafiltration [17–19] or filtration followed by ultracentrifugation [13]. In this method, a sample containing QDs and dissolved solutes is split into two volumes: one is fully digested with acid and measured by ICP-MS for total metals concentration, the other is filtered and measured for dissolved concentrations, and QD concentration is estimated by difference. Depending on the number of samples, this approach, however, may become time- or labour-consuming, uses expensive filter devices and requires two measurements.

The need for centrifuge ultrafiltration sample preparation could possibly be circumvented by use of revised sample introduction techniques that can separate detected signals generated by Nps and dissolved metals. Chromatographic-based sample introduction techniques show some promise for separating <20 nm Nps and their dissolved cations prior to detection with ICP-MS or UV absorbance. Reversed-phase chromatography with C18 columns has demonstrated some separation between Ag Nps and dissolved Ag\(^{+}\) [20] as well as Au Nps and dissolved, low-molecular-weight Au complexes [21], but the observed resolution between the two chromatographic peaks is usually fairly close, with retention times differing by <1 min and the dissolved peak often eluting with the tailing of the Np peak. Soto-Alvaredo et al. [20] did show improved resolution between 10 nm Ag Np and dissolved Ag\(^{+}\) peaks in a C18 column for dilute
suspensions when fetal bovine serum was added, and this matrix additive caused proteins to sorb to the Ag Nps, to increase the Ag Np hydrodynamic size and to decrease Ag Np retention time. Separation of Nps of different sizes within C18 columns was thought to occur mainly by the size exclusion process, with smaller-sized Nps eluting later than larger ones that are less hindered by the smallest pores in the column media. Correspondingly, others have examined the usefulness of size exclusion chromatography (SEC), which typically contains pore sizes smaller than C18 columns, for Np size separation. SEC is capable of sorting a wide range of Au Np sizes [22–24] or a small-size range of QDs [25–28], but particles close in size usually remain fairly blended and close in elution time, and better sorting may be achieved with recycling Nps through multiple column paths over ~60 min [23,25] or with very slow flow rates [28].

However, coupling SEC with ICP-MS for the determination of both Nps and dissolved metal cations has not yet been demonstrated. Directly testing the behaviour of dissolved metal cations with SEC was not performed in the above studies, and this is likely partly due to the potential of cation loss to column media surfaces caused by electrostatic attraction between cations and the slightly negatively charged polymers. Electrostatic attraction between Ag$^+$ and C18 media was overcome by inducing negative Ag-thiosulfate complexes [20], and electrostatic interactions between Nps and SEC polymers are usually mitigated by carrying in the eluent polar ligands [26] or ionic surfactants [20,21]. Hydrodynamic chromatography, which is based on separating colloids using a parabolic flow velocity profile as opposed to size exclusion, was also demonstrated to distinguish between ~5 nm Au Nps and dissolved Au without significant dissolved Au loss to the column, although peak retention time resolution was only 0.28 min [29]. Coupling SEC and ICP-MS for engineered Np and dissolved cation separation and quantification has not been described yet to the best of our knowledge.

Ultimately, we hypothesised there exists a potential to separate ~5 nm Nps and their dissolved metal cations under the most conducive relationship between Np hydrodynamic size, column pore size and eluent composition. To the best of our knowledge, there are no reports that have fully separated and quantified <10 nm metallic Nps and dissolved metal cations by chromatographic-ICPMS methods, nor have performance evaluations (detection limits, range of linearity, recovery) been fully addressed in the studies that report partial separation of QDs. This work solves the problems of co-elution and cation loss to column media by using a column that maximises separation and an eluent that maximises analyte recovery, ensuring simultaneous quantification of both Np and dissolved phases. The objectives of this work were therefore (i) to develop an SEC-ICP-MS method to separate and quantify QDs and their dissolved metal cations within water samples, and (ii) to demonstrate the suitability of this method for examining QDs in natural and treated waters. An improved method for the simultaneous measurement of CdSe/ZnS QDs and dissolved Cd$^{2+}$ and Zn$^{2+}$ was established using an SEC column with the smallest obtainable pore size to achieve the greatest possible size-based separation of the two forms. Au is also used as a model metallic Np, chosen because of its poor solubility and thereby greater resistance to dissolution during study. Operational parameters and method limitations were determined. In addition, suitability of the SEC-ICP-MS method was applied to observing CdSe/ZnS QD within environmentally relevant waters from natural settings and treated municipal wastewater effluent.
2. Experimental

2.1. Materials

Suspensions of CdSe/ZnS and InP/ZnS QDs with a core/shell structure, a nominal size of 5 nm (full size range of 4–10 nm), and stabilised with mercaptoundecanoic acid (a carboxylic acid) were supplied at a nominal concentration of 1.0 mg mL\(^{-1}\) (NN-Labs, Fayetteville, AR, USA). A multi-element solution containing dissolved Zn\(^{2+}\), Cd\(^{2+}\) and In\(^{3+}\) (10 mg L\(^{-1}\) in 2% HNO\(_3\) acid) and a dissolved Au solution (100 mg L\(^{-1}\) Au\(^{3+}\) in 2% HCl, as HAuCl\(_4\)) were obtained from High Purity Standards (USA) and used for calibration purposes. Monodispersed suspensions of Au Nps with diameters of 5 ± 2 nm, 10 ± 3 nm, 20 ± 3 nm and 50 ± 4 nm, stabilised with polyvinylpyrrolidone (PVP) on their surfaces were supplied at a nominal concentration of 50 mg L\(^{-1}\) (nanoComposix, San Diego, USA). Dilutions of these suspensions and solutions were prepared using deionised water (>18 M\(\Omega\)) and, when solution pH control was necessary, trace metal grade HNO\(_3\) (67–70%, Fisher), NH\(_4\)OH (28–30%, VWR, USA), or MOPS buffer (3-(N-morpholino)propan sulfonic acid, 99%, ACROS) were used. Other compounds used within analyses included ethylenediaminetetraacetic acid (EDTA, 99+%, Johnson Matthey Electronics, USA), citric acid (99.5%, Fisher), ammonium lauryl sulfate (ALS) (30% solution, MP Biomedicals, USA), formaldehyde (37%, ACROS) and hydrochloric acid (37%, ACROS).

2.2. ICP-MS analysis

A Bruker aurora M90 ICP-MS equipped with a quadrupole mass analyser, a Micromist nebulizer and a Scott double-pass spray chamber was used for Au, Cd, Zn and In detection and quantification. Important instrument settings such as plasma position, optic electronics and argon gas flow rate were optimised as needed. Typical instrument settings are listed in Table S1 in the Appendix.

In order to determine the metal composition present in CdSe/ZnS QDs, suspensions of QDs with varying concentrations (10–200 µg L\(^{-1}\) as QDs according to the vial label) were prepared, split into two samples and measured for total and dissolved Zn\(^{2+}\) and Cd\(^{2+}\). Total metal concentration was measured by ICP-MS after digesting the suspensions with HNO\(_3\), and dissolved metal concentrations were measured after filtering samples with centrifuge ultrafiltration using Millipore Amicon ultra-4 centrifugal filter concentrators with ultracel 3 regenerated cellulose membranes and a nominal molecular weight cut-off of 3000 Da. Significant dissolved Zn\(^{2+}\) but no dissolved Cd\(^{2+}\) were found in the QD stock solution, so QD-Zn\(^{2+}\) (0.14 mg mL\(^{-1}\)) and QD-Cd\(^{2+}\) (0.30 mg mL\(^{-1}\)) were calculated by subtracting dissolved concentrations from total concentrations. The quantification of S and Se was not performed because detection of these elements at our QD concentrations requires introduction of O\(_2\) and H\(_2\) respectively to the Ar plasma which was not possible at the time of measurement. O\(_2\) is necessary to form SO (m/z 48) because S (m/z 32) is indistinguishable from ambient O\(_2\) (m/z 32), and H\(_2\) is necessary to demolish plasma-generated \(^{40}\)Ar–\(^{38}\)Ar dimers for Se detection (m/z 78). All other ways of measuring Se m/z signals produced noisy machine response and held detection limits too high for much of the QD concentration range studied here.
2.3. **SEC-ICP-MS analysis**

Separation of nanoparticulate and dissolved metals using SEC-ICP-MS was done using suspensions of either the 5 nm Au Nps, the CdSe/ZnS QDs or the InP/ZnS QDs, each with their corresponding dissolved metal cations. Au Nps and QD stock suspensions were prepared daily by adding aliquots of purchased suspensions to a 20 mM MOPS solution (pH 7.0) to a final metal concentration of 1 mg L\(^{-1}\). Dissolved cadmium and zinc stock solutions were prepared by dissolving zinc sulfate (ZnSO\(_4\).7H\(_2\)O) and cadmium sulfate (3CdSO\(_4\).8H\(_2\)O) salts in deionised water to a final concentration of 400 mg L\(^{-1}\). Dissolved Au solutions were prepared by adding an aliquot of acidified Au\(^{3+}\) stock solution to a solution of 20 mM MOPS and 5 mM EDTA to a final concentration of 1 mg L\(^{-1}\), and then increasing pH to 7.0 using NaOH solution. The order of addition of the chemicals matters when making the dissolved Au solution, and adding acidic Au\(^{3+}\) solution to a solution of EDTA and MOPS at pH 7.0 does not lead to stable dissolved Au species but rather Au precipitates. All stock suspensions were stored at 4°C to suppress agglomeration and sonicated for 30 s before use. Samples were prepared by adding aliquots of Nps stock suspensions and dissolved metal solutions to 20 mM MOPS solution (pH 7.0) and analysed immediately.

SEC was carried out using a Varian liquid chromatography unit comprised of a Varian prostar autosampler and pump. Separation was achieved using a TOSOH Bioscience TSK-GEL BioAssist G25WXL column (5 µm particle size and 12.5 nm pore size, 7.8 mm inner diameter × 30 cm length, total volume 14.3 mL, pH range 2.5–7.5) and a mobile phase of 20 mM citrate buffer, 5 mM EDTA complexing ligand, 4 mM ALS surfactant and 20 mg L\(^{-1}\) formaldehyde biocide. Eluent pH was adjusted to be in the range of 6.2–6.8. Mobile phase was delivered with a 1 mL min\(^{-1}\) flow rate, and injection volume was 50 µL. The void volume was determined as 5.5 mL based on elution times of polystyrene sulfonate polymers with known molecular weights, which was close to the void volume reported by the column manufacturer (5.7 mL). All connections and the injection loop were PEEK. The coupling was achieved by directly connecting the column outlet to the nebulizer of the ICP-MS instrument.

SEC-ICP-MS measurements were conducted with the instrument equipment described above and tuned to optimised operation parameters (Table S1). Element detection was performed by monitoring the 197-Au\(^{+}\) isotope for Au and, 66-Zn\(^{+}\) and 114-Cd\(^{+}\) isotopes with isotopic abundances of 27.9% and 28.7% for zinc and cadmium, respectively. Instrument dwell time was 10 ms. Chromatograms for samples containing both QDs and dissolved metals were processed for peak areas with Galaxie (version 1.9.302.952; Agilent, Wilmington, DE, USA) software. Standard curves were plotted to relate peak areas and metal mass concentration. Instrument detection limit (IDL) was defined as three times the noise of the baseline signal created during analysis of a sample containing low concentration of QDs and dissolved metals. The method detection limit (MDL) was determined by multiplying the t-test value at the 99% confidence level and the standard deviation of seven replicate measurements of low concentrations of QDs and dissolved metals. Per cent relative standard deviation (RSD) was calculated by dividing the standard deviations of four replicate measurements by the mean measurement. These replicate measurements were performed for a range of concentrations spanning 1–200 µg L\(^{-1}\).
2.4. Comparison of SEC-ICP-MS and centrifuge ultrafiltration

Suspensions containing CdSe/ZnS QDs and dissolved Cd\textsuperscript{2+} and Zn\textsuperscript{2+} were prepared in 20 mM MOPS buffer at pH 7.0, and the QD and dissolved metals concentrations were measured both by SEC-ICP-MS as described above and by ICP-MS with a centrifuge ultracentrifugation preprocessing step. Both methods were performed on the same day as suspension preparation to minimise any QD dissolution. For the centrifuge ultrafiltration method, samples were processed in triplicate using Millipore Amicon ultra-4 centrifugal filters. EDTA with final concentration of 0.1 µg L\textsuperscript{-1} was added before centrifugation with a speed of 8000 rpm for 30 min. The EDTA was found to be necessary to form negatively charged metal–EDTA complexes with the dissolved metal cations to prevent cation loss by binding to oxygen functional groups on the cellulose membranes. Concentrations of dissolved metal cations were determined by measuring the filtrate on ICP-MS. Total concentrations of metals (QDs plus dissolved cations) in the original suspension were determined after digestion with HNO\textsubscript{3}. QD-phase metal concentrations were then calculated by subtracting dissolved concentrations from total concentrations.

2.5. Characterisation of natural and treated waters

Water samples were obtained from the lower basin of the Charles River (Boston, MA), a well in southeastern Connecticut, and the secondary effluent of a municipal wastewater treatment plant in northeastern Connecticut. Approximately 200 mL of water was obtained using acid-washed and water-rinsed polycarbonate bottles and stored at 4°C until analysis. All samples were filtered through a 13 mm 0.2 µm PTFE syringe filter prior to use. In order to detect and quantify common anions (Cl\textsuperscript{-}, SO\textsubscript{4}\textsuperscript{2-}, NO\textsubscript{3}\textsuperscript{-}, PO\textsubscript{4}\textsuperscript{3-}, F\textsuperscript{-}) present in the water samples, ion chromatography was carried out using a Dionex ICS-5000 liquid chromatography unit with a RFIC Ion Pac AS20 column (4 x 250 mm) and a KOH eluent at a 1 mL min\textsuperscript{-1} flow rate. Common cations (Na\textsuperscript{+}, K\textsuperscript{+}, Mg\textsuperscript{2+}, Ca\textsuperscript{2+}) and trace metals (Mn\textsuperscript{2+}, Cd\textsuperscript{2+}, Mn\textsuperscript{2+}, Fe\textsuperscript{3+}, Sr\textsuperscript{2+}, Ba\textsuperscript{2+}) were measured by ICP-MS as described above. Dissolved total organic carbon (TOC) was measured with a Shimadzu TOC-L CPH/CPN analyser. Bicarbonate concentrations were estimated from alkalinity titration to pH 4.2 using 0.1 mM HCl.

3. Results and discussion

3.1. Separation of QDs and dissolved metal cations by SEC-ICP-MS

Separation of QDs and dissolved metals was explored using high-pressure SEC coupled to ICP-MS. Because all SEC and C18 columns reported in the literature for Np-cation separation held 100 nm pore size [20,21,26,30] but exhibited <1 min separation in retention time, our approach was to use a much smaller SEC pore size (12.5 nm) in order to increase the separation in retention time well beyond 1 min which allows more definitive peak integration. These prior studies using SEC columns also used UV [21,26] detection, and ICP-MS allows simultaneous measurement of multiple metals. Rapid separation of Nps and dissolved metal cations was indeed made possible using SEC and specific eluent conditions. Figure 1 presents a typical chromatogram obtained from
SEC-ICP-MS analysis for a suspension containing 100 µg L$^{-1}$ CdSe/ZnS QDs and 100 µg L$^{-1}$ dissolved Cd$^{2+}$ and Zn$^{2+}$, partially dissolved 100 µg L$^{-1}$ InP/ZnS QDs, and 1 µg L$^{-1}$ Au Nps of various diameters with 1 µg L$^{-1}$ dissolved Au$^{3+}$. Small changes in dissolved peak retention times are attributed to effects of prior column cleaning. Small second peaks for dissolved Au$^{3+}$ may be caused by a second configuration of Au complexes with EDTA or Cl$^{-}$ ligands. Small dips observed after dissolved Zn peaks may be a result of a re-equilibration of baseline Zn present from leached HPLC instrument parts.

SEC-ICP-MS chromatograms for suspensions of 100 µg L$^{-1}$ CdSe/ZnS QDs with 100 µg L$^{-1}$ dissolved Cd$^{2+}$ and Zn$^{2+}$, partially dissolved 100 µg L$^{-1}$ InP/ZnS QDs, and 1 µg L$^{-1}$ Au Nps of various diameters with 1 µg L$^{-1}$ dissolved Au$^{3+}$. Small changes in dissolved peak retention times are attributed to effects of prior column cleaning. Small second peaks for dissolved Au$^{3+}$ may be caused by a second configuration of Au complexes with EDTA or Cl$^{-}$ ligands. Small dips observed after dissolved Zn peaks may be a result of a re-equilibration of baseline Zn present from leached HPLC instrument parts.

Figure 1. SEC-ICP-MS chromatograms for suspensions of 100 µg L$^{-1}$ CdSe/ZnS QDs with 100 µg L$^{-1}$ dissolved Cd$^{2+}$ and Zn$^{2+}$, partially dissolved 100 µg L$^{-1}$ InP/ZnS QDs, and 1 µg L$^{-1}$ Au Nps of various diameters with 1 µg L$^{-1}$ dissolved Au$^{3+}$. Small changes in dissolved peak retention times are attributed to effects of prior column cleaning. Small second peaks for dissolved Au$^{3+}$ may be caused by a second configuration of Au complexes with EDTA or Cl$^{-}$ ligands. Small dips observed after dissolved Zn peaks may be a result of a re-equilibration of baseline Zn present from leached HPLC instrument parts.
the larger molecules (here the surfactant- and PVP-coated Nps) to elute first at around 350 s and the dissolved metal–EDTA complexes to elute later around 650 s due to retention within the smallest size pores. Detection of all the metal cations within the QDs (i.e. Zn$^{2+}$, Cd$^{2+}$ and In$^{2+}$) is possible simultaneously, but Se and S detection would require sample re-runs using introduced H$_2$ and O$_2$ gases, respectively, with our instrument. For one measurement, the overall run time of 15 min with no sample pre-treatment is shorter and less labour-intensive than the required sample processing by centrifuge ultrafiltration and its subsequent measurements.

Elution of Nps occurred only when a surfactant was available within the eluent, and here ALS was chosen instead of the often-used sodium dodecyl sulfate [21] to avoid Na$^+$ contamination within the ICP-MS. ALS concentration (4 mM) was kept well below 10 mM which is an approximate critical micelle concentration for similar surfactants [31]. ALS, with a negatively charged hydrophilic head and a hydrophobic 12-C tail, presumably coats both the column media and suspended QDs and prevents adhesion through electrostatic repulsive forces. Similarly, metal cations eluted only when EDTA was provided in the eluent. The formation of metal–EDTA complexes, with negative charge, minimised sorption of the metal cations to the slightly negatively charged column media by way of electrostatic repulsion. Citric acid at pH 6.0–7.0 was provided to maintain the pH high enough to ensure metal–EDTA complex formation and below the upper limit of the column (pH 7.5). Small variations in ALS, EDTA and citric acid concentrations did not significantly affect retention times for Nps or dissolved cations, but column cleaning procedures (e.g. washing with DI water) were observed to temporarily shorten retention time of dissolved phase metals.

Interestingly, Ag Nps and dissolved Ag$^+$ were not effectively quantified with this method due to poor formation of an Ag$^+$ peak. Although Ag Nps did manage to elute, our pH 6.0–7.0 eluent conditions were not conducive to EDTA complex formation with dissolved Ag$^+$ which requires higher pH between 8.0 and 10.0, and a dissolved Ag$^+$ peak was broad with significant tailing (Figure S1). This analytical method would, therefore, need an SEC column with higher allowable pH conditions in order to be applicable for dissolved and nanoparticulate silver, and with alkaline conditions the eluent must ensure prevention of dissolved metals precipitating as metal hydroxides which could result in artefacts suggestive of Nps. Alternatively, a ligand that forms negative complexes with Ag$^+$ at pH 6.0–7.0 such as thiosulfate [20] could possibly replace EDTA for elution of Ag$^+$. Other metal cations that may not form EDTA complexes at pH 6.0–7.0 are Rb$^+$ and Cs$^+$ [32]. Considering the typically weak complexes that alkali metals (e.g. Na$^+$, K$^+$) form with organic ligands, dissolved Rb$^+$ and Cs$^+$ within environmental samples may not be detectable by SEC.

Using Au Nps also allows us to test a wide range of Np sizes to be separated from dissolved metal cations. Au Nps between 5 and 50 nm were all separated from dissolved Au$^{3+}$ (Figure 1) and held similar Np retention times around the total exclusion time of 5.5 min (330 s). The Nps are apparently minimally retained during flow through the column, which would be expected for Nps with sizes greater than the column pore size of 12.5 nm. This SEC method could, therefore, be applied to measurement of heterogeneous aqueous Np suspensions with a variety of Np sizes.
and compositions to determine total Np concentrations and total dissolved cation concentrations. An upper limit to Np sizes may exist in which pore clogging could occur, but this was not explored here. However, it is likely not possible to determine individual concentrations of different size Nps using this SEC method due to incomplete separation of Au Nps. A small trend in Au Np size and retention time is in fact noted in Figure 1: retention time slightly increased for decreasing Au Np diameter according to 50 nm (330 s), 20 nm (344 s), 10 nm (348 s) and 5 nm (353 s). But separating all four Au Np sizes within one suspension was not possible due to co-elution of the 20, 10 and 5 nm sizes (Figure S2). Sorting the smallest of Np sizes into more well-defined peaks could be performed by SEC using longer durations within columns, such as by recirculating flow within multiple columns [23,25], and this configuration could be amended with our approach to improve Np size resolution and characterisation in the presence of dissolved metals. Np size distribution could also be improved using a lower flow rate or optimised surfactant concentration [22].

In fact, a single reverse-phased HPLC column (Restek Viva C18, Bellefonte, PA, USA) has also demonstrated good separation of QDs based on size and hydrophobicity of QD capping agents while using a methanol-based eluent and UV detection at much slower flow rate [28]. However, this method cannot be adapted to our ICP-MS due to incompatibility of organic solvents with ICP-MS detection. Nevertheless, we tested whether a reverse-phase C18 HPLC column with aqueous eluent without alcohol (the SEC eluent) could also separate CdSe/ZnS QDs and dissolved Cd$^{2+}$ and Zn$^{2+}$. A Luna C18 column (150 mm length, 4.6 mm diameter, 5 µm particle size) with similar pore size (10 nm) as the SEC column (12.5 nm) was chosen to most closely maintain small pore size. Co-elution of QD and dissolved metals was observed using the C18 column with SEC eluent conditions (Figure S3), suggesting the specific SEC polymer media configuration is required with our mobile phase described above.

Because of the possibility that analyte loss could occur during chromatography by potentially irreversible interactions of Nps and metal–EDTA complexes with the column media surfaces, metal recovery after elution was checked. Various suspensions of 100–1000 µg L$^{-1}$ CdSe/ZnS QDs and 100–400 µg L$^{-1}$ dissolved Cd$^{2+}$ and Zn$^{2+}$ were injected into the column and then collected at expected elution times, with a 200 s window around each peak time to ensure maximum collection. The collected volumes were recorded, acidified to digest any QDs, measured for Cd and Zn mass by ICP-MS and compared to initially injected Cd and Zn mass to determine per cent recovery. Average recoveries of Cd in the QD phase and the dissolved phase were 97% and 108%, respectively, indicating little loss, if any, of Cd to column media. Recovery of Zn in the QD phase was 102%, but the measured amount for Zn in the dissolved phase was a little less at 87%. Recovery of Zn was determined by subtracting a background Zn signal in the eluent, presumably due to leaching of Zn from HPLC tubing and internal components, and this contamination could be a source of error for quantifying Zn-containing Nps such as CdSe/ZnS or ZnO. Quantification of Zn-free QDs, such as CdTe/CdSe, may not be affected. Nevertheless, measured recoveries are similar to or greater than those reported for Ag Nps after elution with a C18 column [20]. The eluent chemistry is, therefore, considered favourable for near complete elution of both Np and dissolved metal phases.
3.2. **SEC-ICP-MS standard curves and detection limits**

In order to determine the concentration range of linear instrument response for the SEC-ICP-MS method, suspensions containing 0.1–200 µg L$^{-1}$ Nps and dissolved cations were analysed and standard curves were plotted (Figure 2). Both multi-elemental CdSe/ZnS QDs and 5 nm elemental Au were evaluated, and concentrations on the $x$-axis refer to elemental concentrations, which for QDs were calculated using QD-phase metal concentrations estimated in the purchased stock vial. Suspensions were analysed immediately after preparation in order to minimise any dissolution of QDs. For dissolved Cd$^{2+}$ and Zn$^{2+}$, the chromatographic method shows a range of linearity with good correlation ($R^2 > 0.99$) exists for concentrations less than the chosen maximum of 200 µg L$^{-1}$ (Figure 2a). Zn atoms show less instrumental response compared to Cd under our instrument conditions, as indicated by a significantly smaller slope. Linearity was also observed for Cd and Zn in the QD phase (Figure 2b). The QD Cd and Zn slopes are similar (within 10%) to the slopes observed for dissolved Cd and Zn, and this indicates that QDs behave similarly to their dissolved metal cations during the transport, nebulization, ionisation and detection process. The small discrepancy in instrumental response could be due to uncertainty in QD metal composition determination or possibly due to slight dissolution of the ZnS coating and redistribution of Zn during analysis.

![SEC-ICP-MS standard curves](image)

**Figure 2.** SEC-ICP-MS standard curves for suspensions containing either 5 nm CdSe/ZnS QDs with dissolved Cd$^{2+}$ and Zn$^{2+}$ (a, b) or 5 nm Au Nps with dissolved Au$^{3+}$ (c, d). Insets for Au standard curves at low concentrations are provided. Slopes and regression coefficients of linear regression lines are indicated.
To further test the notion that the smallest of Nps should behave similarly to dissolved cations during SEC measurement, ranges of linearity were also determined for Au, whose Au Nps contain only one element and resist dissolution at pH 7.0. Similar to Cd, 5 nm Au Nps and dissolved Au$^{3+}$ show similar slopes here within 15% (Figure 2c,d) [33].

The lowest concentrations applicable for SEC-ICP-MS were determined by calculating MDLs based on peak integration for replicate measurements and IDLs based on background noise (Table 1). MDL values were consistently slightly larger than IDL values, as expected. CdSe/ZnS QDs could effectively be detected down to metal concentrations of about 1–2 µg L$^{-1}$. The MDL values for the Cd and Zn dissolved phases were approximately twofold to fourfold lower than those for QDs. This could be due to more consistent and uniform chromatography – and therefore quantification – for dissolved solutes compared to the Nps. Cd held lower MDLs than Zn owing to its greater sensitivity in our instrument. Our IDL values (0.1–2.0 µg L$^{-1}$) and RSD values (3.2–6.3% measured at 3 µg L$^{-1}$ dissolved Zn and Cd) for dissolved Cd$^{2+}$ and Zn$^{2+}$ are similar to the IDL (0.3 µg L$^{-1}$) and precision (9.7%, measured concentration not provided) observed in another SEC-ICP-MS method that examined dissolved As(III) complexation with humic acids [34]. Soto-Alvaredo et al. (2013) [20] also reported similar detection limits for Ag$^{+}$ (0.12 µg L$^{-1}$) and 10 nm Ag Nps (0.08 µg L$^{-1}$) analysed by HPLC-ICP-MS with a C18 column. Elemental Au showed MDLs an order of magnitude lower than Cd despite similar sensitivities in the standard curves. RSDs measured for several suspensions in the mass concentration range of 1–200 µg L$^{-1}$ were mainly between 3% and 5% in value but at times as high as 8%, showing fairly good reproducibility.

The SEC-ICP-MS method developed here appears applicable for QD metal concentrations approximately ≥1 µg L$^{-1}$, although sub-µg L$^{-1}$ detection may be possible for elemental metal Nps such as Au. Environmental water samples with <1 µg L$^{-1}$ concentrations would, therefore, require acid digestion and quantification by the more conventional sample introduction via peristaltic pump to ICP-MS. MDLs for dissolved Cd$^{2+}$, Zn$^{2+}$ and Au$^{3+}$ by conventional ICP-MS were between 0.02 and 0.50 µg L$^{-1}$ and were 10–50-fold lower than those for SEC-ICP-MS. Separating dissolved metal cation detection from QD metal detection in this case would require a pre-filtration step. IDL and MDL values for chromatographic methods are expected to be not as sensitive as ICP-MS due to partial analyte dilution during flow through the column. However, detection limits for the SEC method here could be improved with larger injection volumes which deliver greater mass to the detector. The column diameter (here,

### Table 1. SEC-ICP-MS instrument detection limits (IDLs), method detection limits (MDLs) and relative standard deviations (RSDs) of suspensions containing 5 nm Au Nps and dissolved Au$^{3+}$, or 5 nm CdSe/ZnS QDs and dissolved Cd$^{2+}$ and Zn$^{2+}$.

| Method     | Phase | Au IDL (µg L$^{-1}$) | Au MDL (µg L$^{-1}$) | Au RSD (%) | Cd IDL (µg L$^{-1}$) | Cd MDL (µg L$^{-1}$) | Cd RSD (%) | Zn IDL (µg L$^{-1}$) | Zn MDL (µg L$^{-1}$) | Zn RSD (%) |
|------------|-------|---------------------|----------------------|------------|---------------------|----------------------|------------|---------------------|---------------------|------------|
| SEC-ICP-MS | Dissolved | 0.10                | 0.12                 | 0.3–1.3    | 0.1                  | 0.2                  | 3.2–6.3    | 0.5                  | 1.0                  | 5.1–10     |
|            | Nps    | 0.10                | 0.14                 | 2.3–4.5    | 0.3                  | 3.0                  | 1.6–7.0    | 0.5                  | 10                   | 2.6–8.0    |
| ICP-MS     | Dissolved | 0.01                | 0.02                 | 0.1–3.5    | 0.01                 | 0.04                 | 0.6–5.3    | 0.05                 | 0.5                  | 0.8–7.6    |

Note: Statistics measured for dissolved cations only by conventional ICP-MS are also listed.
7.8 mm, a fairly large size for mass spectrometry applications) could also be decreased which lessens analyte dilution and peak broadening prior to detection, although column capacity would be lessened as well.

3.3. **Separation of QD and dissolved metals by SEC-ICP-MS versus centrifuge ultrafiltration**

In order to evaluate our new SEC method in comparison to the more conventional method with centrifuge ultrafiltration preprocessing, several suspensions containing both CdSe/ZnS QDs and dissolved Cd\(^{2+}\) and Zn\(^{2+}\) were prepared and analysed concurrently by the two methods. **Figure 3** shows the measured concentrations of Cd and Zn in aqueous suspensions containing (a) dissolved metal cations and (b) CdSe/ZnS QDs, comparing performance by SEC-ICP-MS and by first separating QD and dissolved metals using centrifuge ultrafiltration followed by ICP-MS.
the dissolved phase (a) and the QD phase (b) plotted as determined by separation via SEC or centrifuge ultrafiltration. The performance of the two methods is in close agreement as indicated by the proximity of the measured concentrations to the 1:1 line of equality. For the measurement of dissolved zinc, a slight overestimation was observed by the centrifuge ultrafiltration method, and this could be due to partial dissolution of the outer ZnS shell by EDTA ligands during the long (30 min) processing time, a possible artefact that could be minimised using shorter centrifuging times. Dissolved cadmium concentrations measured by centrifuge ultrafiltration were also slightly underestimated compared to SEC-ICP-MS. Sorption loss of Cd$^{2+}$ and Zn$^{2+}$ to ultrafiltration membranes was not considered to be an important cause based on near-100% recovery of dissolved Cd$^{2+}$ and Zn$^{2+}$ cations after centrifugation with EDTA present in a separate solution without QDs (Table S2).

Measurements of Cd and Zn within QDs using SEC-ICP-MS were, therefore, nearly identical to those performed using centrifuge ultrafiltration for the studied concentration range. Additionally, a negligible amount of metals from QDs was found to pass through the centrifuge ultrafiltration membranes during sample processing of a QD suspension without dissolved cations, indicating near-complete retention of QDs by these membranes, and no significant false-positive detection of metals in the filtrate at low QD concentrations. Table S3 shows measured dissolved Cd$^{2+}$ and Zn$^{2+}$ after centrifuging suspensions of 50, 100 and 200 µg L$^{-1}$ QDs, and no Cd$^{2+}$ was detected in the filtrate, although residual Zn$^{2+}$ from the QD stock solution was noticeable at high QD concentrations. SEC-ICP-MS is consequently considered comparable to, and can be operated in place of, the method of sample splitting and processing by centrifuge ultrafiltration for Np suspensions with metals concentration >1 µg L$^{-1}$.

3.4. Separation of CdSe/ZnS QDs and dissolved metals in environmental waters

After establishing analysis capabilities with prepared laboratory solutions of defined composition, a brief test was performed to verify the ability of SEC-ICP-MS to separate and quantify both phases in environmentally relevant waters. Waters from different environmental sources were selected to obtain different compositions, and consequently, possibly different interferences. These included an urban river (Charles River), a moderately hard groundwater and a secondary effluent from a municipal wastewater treatment plant. Measured water quality parameters for common solutes appear in Table 2. Solution pH was near 7.0 for all waters, but Na$^+$, HCO$_3^-$ and TOC concentrations varied widely depending on source. Both CdSe/ZnS QDs (~1000 µg L$^{-1}$ as QDs) and dissolved metals (~400 µg L$^{-1}$) were spiked and immediately analysed.

SEC-ICP-MS chromatograms in Figure 4 show both phases are readily separated for all source waters. No significant differences in retention times for both peaks were noted. Moreover, the concentrations measured by SEC-ICP-MS were similar among the Charles River water and municipal wastewater, varying only by about 8% maximum (Table 2). The close values reveal good reproducibility for measurements in natural and treated waters with fairly similar water qualities. The groundwater sample, though, held significantly different (up to 50%) measured metals concentrations among the waters. We attribute this variation to the higher bicarbonate
concentrations present in the groundwater, which can influence metal speciation through metal–ligand complex formation or carbonate solid precipitation. In fact, equilibrium modelling using visual Minteq software (version 3.1, KTH Royal Institute of Technology, Stockholm, Sweden) was performed using the measured water quality parameters in Table 2, and the simulation for groundwater predicts the formation of cadmium carbonate and zinc carbonate dissolved complexes and solid precipitates under the conditions listed. It is, therefore, possible that bicarbonate ions caused the decrease in measured QD-Cd and QD-Zn through ligand-promoted dissolution and perhaps carbonate solid precipitation which decreased QD metals’ quantification. No significant carbonate complexes or solids were observed within model simulations for the Charles River water or the municipal wastewater, but chloride complexes (CdCl⁺, CdCl₂ and ZnCl⁺) are expected to coexist with the free metal cations.

Table 2. Measured water quality parameters for samples from Charles River water, groundwater and municipal wastewater.

| Water quality parameter | Charles River | Groundwater | Municipal wastewater |
|-------------------------|--------------|-------------|---------------------|
| pH                      | 6.9          | 7.7         | 6.8                 |
| Major ions (mM)         |              |             |                     |
| Cl⁻                    | 4.6          | 4.2         | 2.8                 |
| F⁻                     | <DL          | 1.5         | <DL                 |
| SO₄²⁻                  | 0.4          | <DL         | 0.3                 |
| NO₃⁻                   | 0.05         | 0.06        | 0.3                 |
| PO₄³⁻                  | <DL          | <DL         | 0.8                 |
| HCO₃⁻                  | 1.1          | 4.1         | 1.0                 |
| Na⁺                    | 3.3          | 8.6         | 0.2                 |
| K⁺                     | 0.2          | 0.1         | 0.3                 |
| Mg²⁺                   | 0.6          | 0.01        | 0.3                 |
| Ca²⁺                   | 0.7          | 0.01        | 0.6                 |
| TOC (mg/L)              | 6.9          | ND          | 4.6                 |
| Trace elements (µg L⁻¹) |              |             |                     |
| Zn²⁺                   | 5.4 ± 1      | 2.3 ± 0.02  | <DL                 |
| Cd²⁺                   | <DL          | <DL         | <DL                 |
| Mn²⁺                   | 25           | <DL         | 4                   |
| Fe³⁺                   | 224          | 9           | 224                 |
| Sr²⁺                   | <DL          | 3           | <DL                 |
| Ba²⁺                   | 60           | 4           | 32                  |

Measured concentrations after addition of 1000 µg L⁻¹ QDs and 400 µg L⁻¹ dissolved metal cations (µg L⁻¹)

|          | Charles River | Groundwater | Municipal wastewater |
|----------|---------------|-------------|----------------------|
| QD Cd²⁺  | 295           | 184         | 292                  |
| QD Zn²⁺  | 93            | 40          | 86                   |
| Dissolved Cd²⁺ | 396 | 478 | 375               |
| Dissolved Zn²⁺ | 388 | 414 | 418               |

Measured concentrations after addition of 30 µg L⁻¹ QDs and 10 µg L⁻¹ dissolved metal cations (µg L⁻¹)

|          | Charles River | Groundwater | Municipal wastewater |
|----------|---------------|-------------|----------------------|
| QD Cd²⁺  | 27.7 ± 0.3    | 30.3 ± 0.9  | 28.2 ± 0.5           |
| QD Zn²⁺  | 28.1 ± 1.0    | 32.5 ± 2.0  | 27.9 ± 1.5           |
| Dissolved Cd²⁺ | 12.5 ± 0.6 | 12.6 ± 0.5  | 13.1 ± 0.5          |
| Dissolved Zn²⁺ | 12.4 ± 0.4 | 11.9 ± 0.2  | 12.7 ± 0.6           |

Notes: <DL, less than detection limit; ND, not determined.

The high concentration of carbonate species interfered with TOC measurements and prevented reliable, reproducible measurements. Prevalent anions and cations are reported. Trace metals Zn and Cd are included to show background concentrations of these elements. Water samples were exposed to the atmosphere for several days prior to analysis, so dissolved oxygen was not measured and assumed to be close to values predicted by equilibrium with atmospheric O₂.
In a second spike experiment, QDs and dissolved metal cations were added to the three waters at lower concentrations, ~30 µg L⁻¹ and 10 µg L⁻¹ cations, in order to further test phase separation and quantification in the SEC method. The QD and dissolved metal phases still separated and eluted at expected elution times (Figure S4). Mean values of concentrations were similar across all metals for each water (Table 2), showing good method reproducibility for natural samples and likely no carbonate precipitation problems as in the high concentration condition. Visual Minteq simulations did not predict any solid formation within the three waters at this low QD and dissolved cation conditions.

In order to further investigate applicability of the SEC-ICP-MS technique for utility in QD dissolution studies, the method was applied to monitor metals in the QD phase and in the dissolved phase upon release within two batch reactors. Each batch reactor contained 1000 µg L⁻¹ of CdSe/ZnS QDs within a 2.0 mL polypropylene autosampler vial, and injections to SEC-ICP-MS were made periodically over just less than 4 days. Charles River water was first chosen in order to explore the fate of QDs upon potential release to a typical urban river system, and 4 days is close to the residence time in the lower Charles River basin which may host human activity, calculated assuming a flow velocity of 2 cm s⁻¹ [35] and reach length of 7 km. A second reactor with 20 mM MOPS buffer solution at the same pH 7.0 was also operated as a control without natural dissolved solutes. Figure 5 shows QD and aqueous phase metal composition of Cd

Figure 4. SEC-ICP-MS chromatograms of CdSe/ZnS QDs (~1000 µg L⁻¹ as QDs) and dissolved metal cations (~400 µg L⁻¹) that were added into samples of municipal wastewater, Charles River water and groundwater. Measured water quality parameters are presented in Table 2.
and Zn as calculated by percentage for both samples over time. Significant release of both Zn and Cd is apparent in this short time within the Charles River water, with almost 50% of Zn and 20% of Cd dissolving (Figure 5a). In addition, it can be seen that Zn is released earlier than Cd, suggesting that Zn present in the outer ZnS shell starts dissolving before Cd present in the CdSe core. Some Cd is released before the entirety of the ZnS shell is dissolved, and this could be explained either by shell crevasse formation that exposes the CdSe core or by preferential and complete dissolution of the smallest QD sizes. Significantly less dissolution is observed in the control reactor at the same pH, with only 10% of Zn and no Cd dissolving (Figure 5b). Enhanced dissolution in the natural water sample is tentatively attributed to the presence of ligands that can complex Zn and Cd and increase their solubility, particularly chloride, bicarbonate and natural organic matter (Table 2).
Finally, the phase distribution profiles for QD metal release and dissolved metal formation appear fairly linear over time. Constant rates of transformation are usually indicative of zero-order kinetics, but here both a zero-order and a first-order rate law with respect to all metals concentrations could well fit the experimental data with correlation coefficients $R^2 > 0.98$ (Figure S5). Consequently, the plots provide insufficient information to whether the dissolution rate is limited by a mass transfer step (typical for zero-order kinetics) or not. Further experimentation is needed to identify the processes controlling ZnS and CdSe dissolution within the unique nanosized, bi-mineral lattice environment of QDs, and these processes could be driven by metal solubility, sulfide and selenide oxidation, or metal complexation with inorganic ligands, siderophores or organic matter. Metallic Np dissolution is often described with complex kinetics [10,36], especially if redox reactions and diameter changes are involved. The SEC-ICP-MS method developed here can help simplify Nps dissolution studies by allowing smaller batch reactor volumes and more automated analyses.

The main advantage of SEC-ICP-MS is a simultaneous quantification of both solid and dissolved phases within only one injection and no sample preparation step. SEC consequently provides a more automated approach compared to using pre-filtration steps to separate dissolved metals from suspensions followed by two measurements (dissolved and total digested metals) which could be more labour intensive. The two measurements might also result in less precision in determining solids concentration by error propagation calculation or if multiple processing steps become sources of error. Additionally, centrifuge ultrafiltration tubes large enough to process the approximately 2–3 mL QD suspension volume for ICP-MS measurements can bring a high material cost per sample (e.g. ~$12 per tube at the time of writing). For analysing very large numbers of suspensions, though, the improved automation offered by SEC would need to be considered against possibly longer ICP-MS analysis time and Ar gas consumption, and the conventional pre-filtration method may be more economical [19].

QDs are finding increased use in light-emitting technologies for electronic displays and in photovoltaics for solar energy harvesting. The SEC-ICP-MS method may be applicable for monitoring QD and dissolved metals presence where QDs are mass-produced, such as in production waste liquids, or where nano-enabled products are recycled or disposed of, such as in landfills. Upon disposal, the organic polymers or inorganic substrates that hold collections of QDs may slowly break down and release nanoparticulate and dissolved metals. The longevity of QDs in soil or leachate environments might depend on capping agent type and its lability to detachment, and more resilient coatings may be engineered in the future. The role of soil organic matter, soil minerals and dissolved natural organic matter in protecting whole QDs or promoting their dissolution needs to be explored. Within soil column studies, QDs were found to preferentially attach to top soil, but some mass was transported through soil pores as Nps and dissolved cations [37]. QDs were also shown to readily attach to silica surfaces, and attachment depends on water chemistry [38]. Adsorbed humic and fulvic substances can also influence QD surface charge and fluorescence [39]. Our results of slow, partial dissolution over 4 days in a natural water indicate that detecting intact
QDs within environmental settings may be time sensitive, but leached metals such as Cd and Zn should still be observable.

Overall, the SEC-ICP-MS method developed here can serve as a complementary approach within a suite of analytical techniques for Np characterisation in water matrices. Here we demonstrate SEC can separate dissolved metals from Nps with sizes <20 nm, a capability that is not possible with single-particle ICP-MS that has an Np size detection limit of ~20 nm for some metals such as Au and Ag [40]. Dissolved metal cations may also interfere with the detection of Np by single-particle ICP-MS by altering signal-to-noise ratio, and this interference is not present with SEC-ICP-MS. Field flow fractionation is another separation method that can provide important size distribution information for metallic Nps including QDs [41], but obtaining accurate information on dissolved metals can be challenging if at all possible, requiring a second quantification method. Finally, online separation by SEC may be connected to other detection devices, such as UV absorption or fluorescence, which can give information on UV-absorbing compounds such as natural organic matter or organic micropollutants in addition to metals detection by ICP-MS [34,42]. This method could also be amended to include assessment of organic matter interactions with diverse metals in natural water samples [43] or biological tissues [44]. Metal cations may readily bind to organic matter functional groups or be present within proteins or other bio-macromolecules. With broad size distributions and molecular weights up to 10,000 Da, these organic molecules could be separated within an SEC column over a wide range of elution times between the elution of Nps and metal–EDTA complexes [45]. The metals associated with various size fractions could potentially be identified [43], although within our eluent the EDTA may strip organic matter-bound metal cations during analysis.

4. Conclusions

Mixed-metal QDs may be problematic to detect and quantify in environmental or waste waters by conventional methods owing to their <10 nm diameter size, interference by their dissolved metal cations or interference from other dissolved constituents. We have developed an SEC-ICP-MS method for the rapid and simultaneous quantification of dissolved metal cations and QDs with sizes <10 nm. This method overcomes prior challenges in chromatographic separation of Nps and dissolved metals. First, complete chromatographic resolution of each phase is ensured by using the smallest of SEC column pore sizes that produces about 5 min separation in retention times, avoiding the problem of co-elution or peak overlap sometimes observed with C18 columns. Second, near complete recovery of both QDs and dissolved metal cations is ensured by preventing any significant loss of analytes to column media through use of surfactants and EDTA complexing ligands within eluent. Quantification of suspensions with CdSe/ZnS QDs and dissolved Cd$^{2+}$ and Zn$^{2+}$ cations by the SEC-ICP-MS method were comparable to the conventional method of first separating dissolved cations by centrifuge ultrafiltration and separately measuring dissolved metals and total acidified (QD plus dissolved) metals. However, the observed SEC-ICP-MS MDLs of 0.8 μg L$^{-1}$ Cd$^{2+}$ and
2 μg L\(^{-1}\) \(\text{Zn}^{2+}\) for CdSe/ZnS QDs were about 4–20-fold greater than those of standard ICP-MS (0.04 μg L\(^{-1}\) \(\text{Cd}^{2+}\) and 0.5 μg L\(^{-1}\) \(\text{Zn}^{2+}\)). The SEC-ICP-MS method may, therefore, be limited to analysis of water samples with suspensions of Nps with ~1 μg L\(^{-1}\) level amounts or more, and the pre-filtration and digestion methodology may be more applicable to the most dilute of suspensions with sub-μg L\(^{-1}\) metal concentrations. This method is not applicable, though, to obtaining size distribution information for Np sizes between 1 and 20 nm. SEC-ICP-MS is well-suited for laboratory settings for examining Np behaviour in water, particularly for dissolution kinetics. Here, CdSe/ZnS QDs were observed to leach ~50% \(\text{Zn}^{2+}\) and 20% \(\text{Cd}^{2+}\) over 4 days within natural river water contained within a 2 mL HPLC autosampler vial. The small injection volume (50 µL) at each sample time point and, therefore, small batch reactor volume could lead to significant cost savings when studying expensive nanomaterials (e.g. ~$200/mL for water-soluble CdSe/ZnS QDs at the time of writing). SEC-ICP-MS could occupy a niche in Np analysis by offering a facile way to simultaneously quantify the smallest of Np sizes and their dissolved metals.

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