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**Out of the Lab and into the Environment: The Evolution of
Single Particle ICP-MS Over the Past Decade**

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The detection, quantification and characterization of nanomaterials in the environment requires sensitive and selective analytical approaches. For the past two decades, single particle ICP-MS has demonstrated considerable advantages in environmental nanoanalysis, quantifying and sizing nanoparticles in complex environmental and biological matrices. The technique has continued to evolve beyond its initial scope of environmental nano-contaminants, to now explore nanogeochemical systems and processes. With these advances, multi-element particle populations can be delineated and the sources of nanoparticulates categorized *in situ*. New instrument hardware, software, and data analysis approaches have enabled a considerable expansion in the systems and particles capable of being studied. Future progress in the development of this technique will invariably lead to a deeper understanding of nanogeochemical dynamics.

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Out of the Lab and into the Environment: The Evolution of Single Particle ICP-MS Over the Past Decade

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The development and application of engineered nanomaterials has required pushing the boundaries of analytical instrumentation in order to detect, quantify and characterize the properties and behaviors of materials at the nanoscale. One technique, single particle ICP-MS, has stood apart for its ability to characterize and quantify inorganic nanomaterials at low concentrations and in complex environmental and biological media. For the past 20 years, this technique has matured significantly, with an ever-expanding scope of application. Where initially it was capable of analyzing precious metal nanoparticles in relatively pristine solutions, now it can be used to characterize multiple different NP populations of varying elemental and isotopic compositions. The types of materials analyzed now extend beyond traditional metallic NPs, with such varied materials as nanominerals, carbon nanotubes, biological cells, and microplastics. In this perspective, we examine the key developments in the past decade of spICP-MS and aim to provide a vision for what this field may look like 10 years from now. The study of nanoparticles, both natural and engineered, will continue to play a vital role in our understanding of climate change, anthropogenic impact, and biogeochemical cycling of nutrients and contaminants in a rapidly changing environment.

Nanotechnology needs nanometrology

Analytical instrumentation has almost always run parallel with advances in new technologies. In the case of engineered nanotechnology, first described in the mid-1950s¹, it wasn't until the invention of the scanning tunnelling electron microscope (1970s)² that the field began to truly take shape. The small size (1-100 nm in at least one dimension)³ and unique properties of nanomaterials (NMs) necessitates sensitive and selective instrumentation to characterize their properties and behavior. In this journal's inaugural issue, it was noted that careful and thorough characterization of nanomaterials is a necessary step in understanding their behavior and impacts.⁴

The growth of nanotechnology in the 1990s was a catalyst for the establishment of programs around the world to organize research dedicated to the study of NMs. In 1999 the National Nanotechnology Institute was created to facilitate the study of NMs and fill in gaps in the knowledge of their properties and behavior, as well as to expand upon their applications.⁵ Whether for assessing these unique properties or understanding their impact on human health and the environment, new analytical techniques and instrumentation were required. Prior efforts to quantify particulate concentrations were often based on crude separations between total and "dissolved" (i.e. < 450 nm) fractions. However, the properties of NMs arise from their size, necessitating a commensurate size measurement; while their concentration is

often best represented as a particle number concentration (PNC). Existing technologies for the characterization of nanoparticles (NPs) were often reliant on pre-separation by centrifugation or filtration, followed by light-based or microscopic methods of measurement, such as dynamic light scattering, transmission electron microscopy (TEM), or nano-tracking analysis. Some of these techniques lack sufficient sensitivity and resolution to capture specific NP particle size distributions (PSDs), and introduce artefacts that can obscure results, limiting their application for polydisperse and complex samples.⁶⁻⁸ Techniques such as TEM are frequently held up as the gold standard for nanomaterial size characterization, but are often limited by the low counting statistics and artefacts brought on by sample preparation.^{8,9}

The development of single particle-ICP-MS (spICP-MS) provided a breakthrough towards NM characterization, achieving comprehensive analysis of sub- $\mu\text{g/L}$ suspensions of NPs at predicted environmental concentrations. Early research in the field of single particle detection and characterization primarily focused on the analysis of metal-containing aerosols,¹⁰ first those generated by thermoionic emission in a sector field instrument,¹¹ and later the work by Kawaguchi et al.¹²⁻¹⁴ where the aerosols are introduced directly into an ICP plasma. One of the first instances of single liquid droplet measurements were performed by Olesik et al. utilizing microdroplet introduction of metal containing solutions in an effort to better understand space-charge effects in ICP instrumentation.^{15,16} The early 2000s papers by Degeuldre et al.^{6,7,17} represented a significant step forward in routine nanoanalysis, showcasing the mass-to-intensity relationship and the development of a particle size distribution, highlighting

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2 the potential of spICP-MS. In the 20 years since the publication
 3 of these articles, spICP-MS has become widely adopted among
 4 researchers performing nanoanalysis, registering over 1,400
 5 publications and 40,000 citations between the years 2004-2024
 6 (Web of Science), in fields ranging from environmental science,
 7 toxicology, and biochemistry.¹⁸ Even now it is continually
 8 evolving and seeing new growth in its capabilities.

9 The foundation of modern spICP-MS is the time-resolved
 10 analysis of transient signals produced from individual particle
 11 ionization events. Particle suspensions are introduced at
 12 sufficiently low particle number concentrations to prevent
 13 simultaneous detection of multiple particles (i.e. coincidence).
 14 Detected particle intensities are delineated from background
 15 signal through one of several methods that can involve iterative
 16 background subtraction,¹⁹ signal deconvolution,²⁰ and
 17 nominally setting a particle detection threshold.²¹ These
 18 particle intensities are then converted into mass according to
 19 an external calibration curve. Particle masses may then be
 20 converted into a size dimension if a geometry and density are
 21 assumed. The PNC can be determined by knowing the flow rate
 22 and a parameter known as the nebulization efficiency (η_{eff}
 23 , sometimes referred to as transport efficiency).²¹⁻²³

24 In the decade since the inaugural volume of this journal,
 25 new technologies and methods have been developed that have
 26 enabled the analysis of NPs in complex environmental and
 27 biological matrices, multi-element analysis, and reductions in
 28 size detection limits. The scope of analyses has also expanded
 29 beyond pristine, lab-generated samples with precious metal
 30 ENPs, and moved toward complex particle types (e.g. geogenic,
 31 naturally occurring NPs (NNPs)) and environmental matrices
 32 (e.g. wastewater, streams, biological fluids) as summarized in
 33 Figure 1. In this perspective, we aim to celebrate the evolution
 34 of spICP-MS analysis, identify the current knowledge gaps, and
 35 offer our insights into the future of this technique.

36 **Digging for Gold (and Silver)**

37 Initial publications in spICP-MS demonstrated considerable
 38 promise in quantifying and sizing dispersed NP populations. The
 39 reduction in dwell time from the conventional 100-200 ms to 10
 40 ms was an essential step to prevent multiple particle ionization
 41 events from being detected simultaneously. This had the
 42 additional virtue of operating at concentrations approximating
 43 that of expected ENP release scenarios (sub- $\mu\text{g}/\text{L}$). This
 44 analytical advancement came with other challenges, namely
 45 the limited dynamic range of PNCs that could be quantified, and
 46 elevated background signal from ionic species masking particle
 47 events.

48 These studies also focused primarily on method
 49 development for the detection, quantification, and
 50 characterization of pristine spherical NPs made of Au or Ag in
 51 deionized water.^{6-8,17,22-31} One of the most significant steps
 52 forward was in developing methods to approximate the
 53 nebulization efficiency by comparing the intensities of dissolved
 54 standards to a known particle size calibrant (usually gold
 55 nanoparticles). This then allowed for dissolved analyte
 56 standards to be used in calibrating the signal-to-mass
 57 relationship, permitting the analysis of a greater variety of
 58

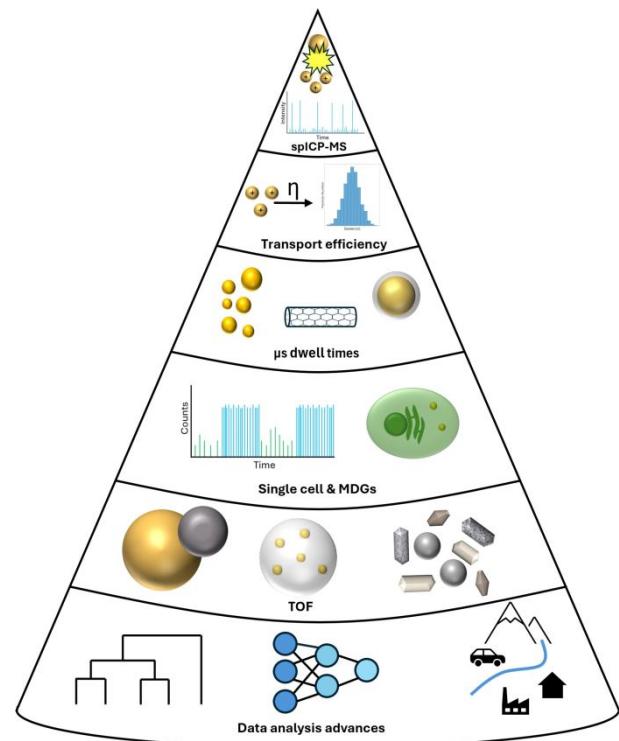


Figure 1. Overview of the advances and expanding scope of spICP-MS analysis over the last 10 years. Early spICP-MS studies were conducted primarily on spherical metallic NPs. Methods to determine the transport efficiency and automated background discrimination allowed for wide adoption of the technique. With the establishment of microsecond dwell times, dual-element analysis, core-shell particles and other NPs such as CNTs could be investigated. The utilization of microdroplet generators provided the next major advance of the field, addressing the lack of internal standards; while full consumption nebulization enabled the detection of NPs in biological cells. Development of sensitive spICP-TOFMS led to true multi-element analysis, greater ability to distinguish between mineral NNMs and ENMs, and has seen use in studies using NP-doped microplastics. The most recent progress in spICP-MS has been towards improvement in data analysis, with the inclusion of machine learning and hierarchical clustering; leading to advances in the ability to quantify and characterize geogenic NMs.

nanomaterial compositions without the need for external particle calibrants.²² Congruent with this development was also the expansion of commercially developed software capable of discerning particle events from background signal.^{20,32}

Early success with this approach was owed in part to the ability to manufacture precise shapes and sizes of these precious metals, while their widespread use in commercial products provided opportunities for environmental release case studies.^{17,33,34} The inevitable introduction of ENPs into the environment requires a thorough understanding of their fate and transport as well as their toxicological impacts. This shift towards environmental studies saw the first analyses in complex matrices, such as biological tissues,^{35,36} surface water,³⁷ tap water,³⁸ and waste water treatment plant influent and effluent.^{29,30}

These environmental release studies captured only a snapshot of the potential impacts of ENPs. Size detection limits for most elements missed particles <20-30 nm, which were predicted to be crucial sizes for environmental safety.^{8,23,26} Use of orthogonal techniques (e.g. field flow fractionation, hydrodynamic chromatography, and size exclusion chromatography) improved size fractionation and measurement of hydrodynamic diameter.^{28,39} However, analysis of NPs in complex matrices and high dissolved analyte

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3 background required new developments in instrument
4 sensitivity and detector electronics.

5 **Single particle goes mainstream**

6 Though precious metal NPs such as gold and silver were readily
7 detectable by spICP-MS, they constitute a small fraction of the
8 likely candidates for environmental release.⁴⁰ A much larger
9 contingent of NPs in commercial circulation are metal oxide
10 NPs, exploited for their unique mechanical, optical, and
11 electrical properties. In particular, TiO₂ and ZnO NPs are readily
12 released into the environment from a diverse range of activities
13 and products including food materials,⁴¹ sunscreens,^{42,43} and
14 paint.^{44,45} Some of these materials, such as ZnO and CuO,
15 dissolve in aqueous systems, leading to elevated dissolved ion
16 backgrounds that could mask particulate events in spICP-MS.
17 Consequently, new methods were developed to improve signal-
18 to-noise, including hyphenated techniques such as ion
19 chromatography-ICP-MS.⁴⁶

20 As instrument and detector electronics improved, the
21 advent of microsecond dwell times enabled a significant step
22 forward in the expansion of the linear range of PNCs that could
23 be quantified, and dramatically improved the signal-to-noise for
24 particle events amidst high dissolved background.^{32,47} By
25 dividing the particulate event across multiple dwell times, the
26 contribution of dissolved analyte signal relative to the particle
27 signal is diminished. Similarly, the contribution of isobaric
28 interferences (i.e. ArO⁺, N₂⁺) to the background signal were also
29 reduced, allowing for improved quantitation of common metal
30 oxide NPs such as SiO₂⁴⁸ and iron oxides.⁴⁹ Coincidence was
31 ameliorated by this move towards shorter dwell times, greatly
32 extending the range of PNCs that could be quantified.
33 Moreover, it opened a path toward analyzing multiple elements
34 in a given particle event through fast-switching dual-element
35 analysis by rapidly switching the quadrupole between analyte
36 masses to detect more than one element in a given particle
37 event.^{47,50-52}

38 This step forward in data quality and detection capability
39 saw an expansion in the scope of potential systems and NP
40 types that could be studied. Research began to move from
41 bench-top pristine studies into more representative
42 compartments such as streams,^{43,53} lakes,³⁷ and soils.⁵⁴ The
43 types of nanomaterials capable of being analyzed also
44 expanded to include carbon nanotubes (detected by their metal
45 impurity proxies^{55,56}) and silver nanowires being quantified in
46 *Daphnia magna* hemolymph.⁵⁷ Furthermore, spICP-MS also saw
47 the development of commercial software from major
48 instrument vendors,⁵⁸ bolstering the adoption of the technique,
49 that also led to various organizations producing standardized
50 methods for its application.⁵⁹

51 However, NP transport efficiency has long been a hurdle in
52 the analysis of larger particle sizes. Conventional nebulization
53 and aerosolization limits the size of droplets that reach the
54 plasma, with transport efficiencies often ranging between 2-
55 10%. Advances in sample introduction included the
56 development and application of total consumption nebulizers
57 and microdroplet generators (MDGs). Total consumption
58 nebulization facilitated the introduction of larger particles, as
59

60 well as cells and organisms in the nano- to micro-size range.^{25,60}
MDGs also improved on transport efficiency, and with the
61 eventual utilization of ICP-time-of-flight-MS (ICP-TOFMS)
62 would be used to address the problem of internal standards by
63 introducing a cesium sample uptake standard to better account
64 for instrumental drift and matrix effects.^{61,62}

65 Despite these leaps forward with microsecond dwell times
66 and single cell analyses, studies into nanomaterials were still
67 hampered by the quadrupole, incapable of reliably quantifying
68 more than one element at a time. For spICP-MS to evolve, the
69 limitations of the quadrupole mass analyzer had to be
70 overcome.

71 **Fewer Atoms and More Elements**

72 Arguably, one of the most significant advances in single particle
73 analysis came with the adoption of time-of-flight mass
74 analyzers. Though ICP-TOFMS had been demonstrated several
75 decades prior⁶³, faster data collection was needed to capture
76 the microsecond transient signals of single particle events.⁶⁴
77 The advantage of TOF is the ability to capture a near complete
78 atomic mass spectrum (7-250 m/z⁺) per dwell time. Early
79 applications of these instruments were the differentiation of
80 bimetallic core-shell particles^{26,29} and delineating natural clay
81 particles from engineered CeO₂ NPs.⁶⁵

82 Other advances in spICP-MS have been the utilization of
83 sector field instruments to improve on size detection limits and
84 isotopic quantification.^{20,66} There have also been efforts to
85 move single particle beyond the realm of solution-based
86 suspensions as researchers have started to incorporate laser
87 ablation sample introduction as a means to analyze
88 nanoparticles in solid samples.^{67,68}

89 With these advances, more representative environmental
90 samples, such as those from streams, rivers, agricultural
91 leachates, sea water, and biological tissues, can be explored.⁶⁹⁻⁷¹
92 Further enabled by the use of triple quadrupole, TOF, and
93 sector field mass analyzers, a greater diversity of NP types can
94 now be analyzed ranging from multi-element NPs to
95 heteroaggregates to nanominerals^{29,39,71-73} Much of this
96 progress is the result of both reducing the contribution of
97 isobaric interferences (ICP-QQQ-MS) and enabling quasi-
98 simultaneous multielement particle detection (ICP-TOF).
99 Advances in mass analyzers and detectors have greatly
100 expanded the dynamic range of analysis, achieving the
101 detection and quantitation of NPs as small as <10 nm.⁴⁶ It
102 should be noted however that despite the wider variety of
103 samples being analyzed, there are still no comprehensive
104 standardized procedures for sample storage and
105 transportation, reducing certainty that PSDs are the same when
106 measured in the lab as when initially sampled from the
107 environment.³⁹

108 **Mountains of Data**

109 As we come to the present state of spICP-MS, the most
110 significant advances are now being made in how we analyze our
111 data. spICP-TOFMS generates significant amounts of data, and
112 with that there is a need to parse out what the collected data
113 means. Some of the early approaches with multi-element data

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2 involved the use of machine learning (ML) models. In some
3 cases, supervised^{65,74} ML models have been employed where
4 samples from known sources or known compositions are used
5 as training datasets to identify and quantify unknown samples.
6 More recent approaches however have utilized unsupervised
7 ML models with hierarchical clustering analysis (HCA) to group
8 particles together based on similarities in their mass, elemental,
9 and isotopic ratios.^{75–78} The advantage in this approach is the
10 ability to analyze a given sample and delineate NP populations
11 into broad categories (e.g. natural, engineered, incidental) and
12 specific groups (i.e. mineral types). However, these approaches
13 require a great deal of care in how samples are collected,
14 stored, and extracted as these processes modify the
15 representativeness of the NPs analyzed with regards to their
16 environmental and biological state. Moreover, there is a need
17 to account for the well-described sources of uncertainty in
18 these measurements. For example, small NPs approaching the
19 size detection limit, with minor or trace elemental constituents
20 will invariably be subject to large uncertainties. This can lead to
21 suspect interpretation of spICP-TOFMS data. Recent studies
22 have begun to address this uncertainty in both fundamental and
23 applied aspects.^{79–81}

24 Despite the considerable amount of work still needed, it is
25 evident that spICP-MS has made significant strides from being a
26 technique only capable of measuring single-element, precious
27 metal NPs, to one that is now capable of identifying and
28 quantifying broad NP populations of varied composition amidst
29 challenging matrices.

30 **Where do we go from here? Foundations for the next 10 years of
31 spICP-MS**

32 Thus far we have highlighted the significant advances seen in
33 the past 10 years in many aspects of spICP-MS. As it stands, this
34 is a technique that can be routinely used by researchers to study
35 nanoscience across multiple disciplines. Given its widespread
36 use, some may consider spICP-MS to be “mature”. However,
37 there are still significant opportunities for improvement that
38 can be made in the future that will greatly expand the capability
39 of the technique. Here we provide our perspective on the most
40 promising developments that we believe will lead to new
41 applications and improved analytical capabilities. In our view,
42 future developments should accomplish the following: a) obtain
43 more information about the particles detected, and b) expand
44 the range of particle types and sizes that can be detected.
45 Although there are numerous disciplines that will benefit from
46 these improved capabilities, we focus here on earth and
47 environmental sciences, in keeping with the focus of this
48 journal. These disciplines are arguably the most complex to
49 study, and thus represent ideal systems to test emerging
50 nanoanalytical capabilities.

51 **Size matters: Hyphenated techniques**

52 There are many opportunities to advance spICP-MS by coupling
53 it with various analytical techniques. Although spICP-MS is often
54 used in reporting a size measurement, this is based on
55 inferences of a particle’s full elemental composition, geometry,
56

57 and density. Though spICP-TOFMS theoretically has the
58 capability to analyze the full mass range, and thus provide a
59 complete particle composition, this is practically impossible.
60 Light elements, particularly those that suffer from isobaric
61 interferences, make up many of the most abundant elements in
62 the Earth’s crust and are common constituents of ENPs (e.g.
63 oxygen in TiO_2). Thus, a comprehensive chemical composition
64 of most NPs (save for fully metallic NPs) cannot be accurately
65 determined. Other factors, such as a high dissolved background
66 or particle coincidence, can also increase the difficulty of
67 analyzing many types of natural (mineral) particles.

68 One way to overcome these limitations is to obtain a particle
69 size measurement prior to the particle entering the plasma.
70 There are many in-line, hyphenated techniques that may
71 accomplish this, among them asymmetrical flow field flow
72 fractionation (AF4) may be the most promising. AF4-ICP-MS has
73 been routinely applied to environmental samples to understand
74 size-resolved distributions of metals and is therefore a good
75 candidate in this approach.⁸² By coupling AF4 to spICP-MS, one
76 would be able to obtain the true particle size and the chemical
77 composition of each particle. This could help bridge the gap in
78 identifying ENPs and has been the focus of recent work on AF4-
79 spICP-TOFMS to identify composition, size, and shape of
80 ENPs.^{83,84} Future work to further refine the combination of
81 these techniques will likely lead to better characterization of
82 NPs. This strategy could also benefit spICP-TOFMS analysis of
83 NNP and incidental NPs (INPs) and would greatly improve
84 confidence in detection of specific mineral types. For example,
85 if a Zr-Si-Hf bearing particle was detected, one could then
86 compare the hydrodynamic radius obtained from AF4 to the
87 particle size calculated from the elemental composition and
88 assumption of a mineral phase (in this case, zircon). If the two
89 sizes agreed, then more confidence can be taken in the
90 chemistry of the nano-zircon grain.

91 Although AF4 may be a promising solution to improve
92 nanoanalysis, some limitations must be kept in mind. Namely,
93 the size measurement provided by AF4 is a) the hydrodynamic
94 size, and b) typically calibrated using plastic beads, neither of
95 which is representative of many NP types analyzed by spICP-
96 TOFMS. The former issue may be limited to small NPs where the
97 hydrodynamic diameter is appreciably different than the core
98 diameter. In general, AF4 method development is time
99 consuming compared to the relative ease of direct spICP-MS
100 analysis. However, this combination of techniques is likely to
101 prove useful for the right research areas.

102 In addition to AF4, other techniques could be used to
103 separate particle sizes prior to spICP-MS. Hydrodynamic
104 chromatography (HDC) or size exclusion chromatography (SEC)
105 are already routinely coupled to ICP-MS, and their use in
106 conjunction with spICP-MS has been explored.^{85,86} Other
107 approaches have recently been tested including differential

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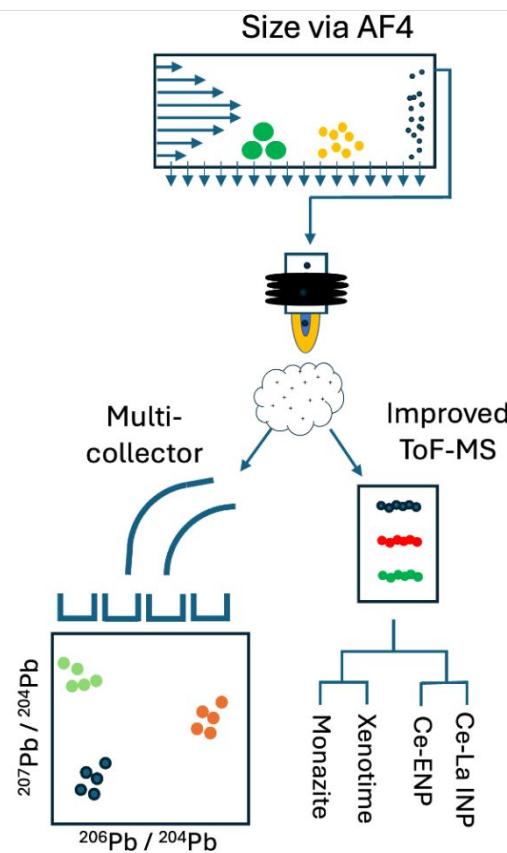
mobility analyzers (DMA) to fractionate particles by size, or ion exchange resins to remove ionic backgrounds.^{87,88} One particularly interesting approach in development is optofluidic force induction, which uses the force of a laser acting in opposition to flow in a microfluidic channel to trap and measure particle sizes.⁸⁹ In the coming decade, development and refinement of particle size analysis techniques will complement the improved capabilities of spICP-MS.

Go big, and small: Expanding the dynamic range of spICP-MS

The ultimate goal of spICP-MS is to analyze the full population of NPs in a given sample, and to completely characterize the composition of each NP. This is currently limited at both ends of the dynamic range of spICP-MS measurements (i.e. very small and very large particle sizes). Many studies have emphasized the need to detect smaller NPs, taking advantage of sector field instruments, or developing more sophisticated methods of discriminating particles from background.⁴⁶ Because most natural particle types follow a power-law number size distribution, the smallest particles are by far the most abundant by number, providing motivation for these efforts.^{76,90} As new ICP-MS models are introduced in the coming decade, improvements in ion transmission and detector design will increase sensitivity, facilitating the detection of smaller particles.

A related challenge in spICP-MS is the ability to detect trace elements in larger particles. The need for this type of measurement was first identified in pursuit of ENP fingerprinting. For example, if Nb is present in a Ti-bearing NP, it would more likely be classified as an NNP, rather than its TiO_2 ENP counterpart.⁹¹ Detecting large particles may be as important as the detection of small particles, especially for studies of NNPs, including nanominerals. Detection of large NPs would enable the quantification of trace elements at the part per million level in each nanomineral grain, which would allow for true mineral chemistry analyses. Furthermore, as larger particles are analyzed, their minor constituents will be present at higher amounts compared to smaller particles, lowering the uncertainty in their measurement.⁹² These two scenarios result in more precise mineral chemistry analysis of NPs, as well as improved characterization of INPs.

While lower size detection limits have been well established for many elements, discussion of upper size detection limits has largely been speculative. The upper limit of an spICP-MS measurement results from two sources: the maximum number of counts before the detector response becomes non-linear, and the physical limits on particle transport and vaporization in the plasma. The former results in an upper limit of a few hundred nm for most elements.⁸¹ It is possible that larger particles can be vaporized in the plasma, meaning the upper end of the microchannel plate dynamic range must be improved to characterize larger NPs. Alternative plasma torch orientations, with the torch downward-pointing, have been proposed which could lead to improved nebulization and larger particles being analyzed.⁹³ Future studies should determine the



- True anthropogenic fingerprints
- Radiogenic / stable isotopes
- Trace element mineral chemistry

Figure 2. Envisioning a hypothetical spICP-MS study, with several analytical developments. AF4 coupled online with spICP-MS provides a hydrodynamic radius to couple with elemental composition of single particles. The development of the MC-ICP-MS for single particle applications, and improvements in the dynamic range of the ICP-TOFMS will enable isotopic and trace elemental characterization of NPs.

upper limit of particle vaporization in the plasma, as this is likely to differ based on NM properties.

Isotopes: a true “fingerprint”?

The field of isotope geochemistry has proliferated in recent decades benefitting from high-resolution ICP-MS instrumentation.⁹⁴ New insights in geochemistry, cosmochemistry, and environmental chemistry are revealed through the measurement of both stable and radiogenic isotopes. The fields of isotope geochemistry and nanogeochimistry continue to gravitate toward each other, as spICP-MS measurements have recently been successful using multiple-collector (MC) ICP-MS.⁹⁵ The high resolution and simultaneous detection capabilities of the MC-ICP-MS have allowed the determination of precise isotope ratios in single particles.⁹⁶ However, the limiting factor is the data acquisition speed of the Faraday cups most commonly used as detectors in

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2 MC-ICP-MS. If this hurdle is overcome, spICP-ICP-MS could
3 revolutionize nanoanalysis. Rather than use an elemental
4 fingerprint to assign a source of an NP, an isotopic fingerprint
5 could be used; inherently a more robust marker for sources and
6 processes. Where no elemental fingerprint is possible (e.g. TiO_2
7 ENP), an isotopic fingerprint may be obtained. INPs produced
8 from industrial processes could likely be fingerprinted, allowing
9 for a more reliable method to trace their source. Isotopic
10 fingerprints in NNPs could also be exploited, with possible
11 applications in atmospheric science, mineral exploration, and
12 cosmochemistry.

13 It should be noted that isotopic measurements have been
14 performed using spICP-TOFMS, primarily in proof-of-concept
15 studies.^{97,98} Major differences in isotopic distributions can be
16 detected, but the per mil magnitude of most stable isotope
17 fractionations observed in many natural systems are not
18 currently detectable. Pb isotopic signatures may be the most
19 feasible application for spICP-TOFMS, especially with regard to
20 fingerprinting anthropogenic sources. Future development of
21 the ICP-TOFMS instrument should result in improved isotopic
22 measurements, which would be useful as the MC-ICP-MS is
23 prohibitively expensive for many applications.

24 **Go where the particles are: Natural and incidental nanomaterials**

25 spICP-MS owes much of its development to concern over the
26 environmental release of ENPs and their ecotoxicity. While
27 there is still strong interest in this topic, the state of spICP-MS
28 research has continued to broaden into a multitude of different
29 areas. A growing number of scientists are beginning to
30 investigate INPs and NNPs for various purposes across
31 geochemical and environmental sciences.^{76,99,100} The power of
32 spICP-TOFMS lies in its ability to fingerprint NPs based on the
33 presence and abundance of multiple elements. In this way, INPs
34 and NNPs are inherently better candidates for study compared
35 to ENPs, largely due to their multi-element composition.
36 Additionally, both INPs and NNPs are more abundant in Earth's
37 nanogeochemical cycle than ENPs; INPs are estimated to be 3-
38 30x more abundant, and NNPs are 100,000,000x more
39 abundant.¹⁰¹ Clearly, a major opportunity to advance
40 nanoscience using spICP-MS lies in these two domains.

41 Finally, many INPs can pose greater ecotoxicological
42 concerns than ENPs, as they often contain As, Pb, Cr, and other
43 toxic elements.^{102,103} Conversely, many ENPs are highly
44 insoluble (e.g. TiO_2 , CeO_2), and therefore may not be as
45 bioavailable.⁴⁰ With the analytical advancements described
46 above, future studies of NNPs and INPs will be highly successful.
47 Improved characterization of INPs will allow for better source
48 identification and tracing, as well as identifying their
49 ecotoxicological effects. Studies of NNPs may include nano-
50 mineral chemistry, radiometric dating of single particles to
51 advance geochronology, or cosmochemical applications such as
52 detection of micro-meteorites and interplanetary dust particles.
53 These represent just a few of the possible applications of spICP-
54 MS to NNP populations; the potential to study these highly
55 abundant and dynamic contributors to geochemical cycles is
56 almost unlimited.

5 In order to take full advantage of the improved analytical
6 capabilities described here, data processing and interpretation
7 must advance in parallel. In addition to regular software
8 updates from commercial instrument manufacturers, a number
9 of researchers have developed, or are developing in-house tools
10 to process spICP-TOFMS data. These software packages now
11 provide more flexibility in peak-finding parameters, and can
12 integrate new tools such as microdroplet calibration.^{104,105} Data
13 interpretation has progressed from proof-of-concept
14 approaches to web-based applications where spICP-TOFMS
15 datasets can be uploaded and interrogated by users.¹⁰⁶ These
16 advancements in data processing serve as a foundation for the
17 future of spICP-MS, and will continue to advance as the
18 technique matures.

Conclusions

19 The past several years of spICP-MS development have seen it
20 mature from a technique skilled in assessing ENP behavior in
21 pristine systems, to one now capable of analyzing entire NP
22 populations in complex biological and environmental matrices.
23 It has made significant strides in this maturation, with advances
24 in multiple aspects of the technique ranging from sample
25 introduction, mass analyzer configuration, and recently
26 sophisticated data analysis. This had led to an expansion in the
27 type of materials analyzed to now include biological cells,
28 nanominerals, and emerging contaminants (i.e. microplastics).

29 Despite all this progress, there are still considerable
30 research opportunities to further the advancement of this
31 technique. With continued improvements in detection
32 capabilities, isotopic fingerprinting, and improved sensitivity,
33 there are many areas into which this field can expand. As spICP-
34 MS gave us the tools to monitor ENP behavior in environmental
35 systems, we can now turn these tools toward looking at the
36 system itself, and better understanding complex
37 nanogeochemical cycles. The consistent pressure of
38 urbanization, resulting in new influxes of incidental
39 nanoparticulate exposure can also be better studied within the
40 context of human and ecological health outcomes. While the
41 progress in environmental nanoanalysis research can be
42 attributed to many analytical techniques, spICP-MS has proved
43 to be an invaluable tool that, with continued development, will
44 further illuminate our understanding of environmental
45 processes.

Author contributions

46 **A.J. Goodman:** Writing-review & editing, Writing-original draft. **B.F.**
47 **Benner:** Writing-review & editing, Writing-original draft. **M.D.**
48 **Montaño:** Writing, review & editing, Writing-original draft,
49 Conceptualization

Conflicts of interest

50 There are no conflicts to declare

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Data availability

No primary research results, software or code have been included and no new data were generated or analyzed as part of this perspective.

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‡ Footnotes relating to the main text should appear here. These might include comments relevant not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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5 Data availability

6 No primary research results, software or code have been included and no new data were generated or analysed
7 as part of this perspective.