Comparative characterization methods for metal oxide nanoparticles in aqueous suspensions

Characterization of nanoscale materials is an essential component of research to inform product development as well as industrial and public health policies; however, few studies have investigated currently available competing and complimentary analytical techniques for characterization of nanoparticles in suspensions. The goal of this study was to compare multiple characterization methods and resulting data for aqueous nanoparticle suspensions used in semiconductor manufacturing. It was determined that the Scanning Mobility Particle Sizer (SMPS) provides the most reliable sizing and particle counting data, while other methods are offer less precision, accuracy, or are more resource-intensive. For determining concentration, standard methods like ICP-OES and ICP-MS are very effective. At present, there is no single tool that can provide comprehensive characterization data for aqueous nanoparticle suspensions, and therefore a combined approach is necessary. It was also found that information presented on Safety Data Sheets for nanomaterials may differ from that captured through analysis of the corresponding product, further highlighting the need for a comparison of characterization methods. Future studies aiming to characterize nanomaterials in the environmental or other aqueous matrices will be benefit from the development of combined techniques or novel characterization tools.

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INTRODUCTION

Nanoscale materials are playing an increasing role in industrial production.[1,2] With mounting evidence that certain nanomaterials may have toxic properties,[3–6] entry of engineered nanoparticles into the environment and exposure of workers to engineered nanomaterials are increasing concerns for stakeholders including industry members, researchers, and government regulators.[7,8] It is important to develop characterization methods for these materials for both manufacturing purposes and for environmental, health, and safety research.[9]

At this time, such methods that exist are typically adapted from existing analytical chemistry methods often intended for very different applications. Some methods, like atomic force microscopy,[10] transmission electron microscopy, and scanning electron microscopy are excellent for analyzing individual nanoparticles with unparalleled resolution. Such methods have a rich history in particle analysis, both in industrial and health settings.[11–14] Unfortunately, such methods suffer from cost-intensive sample preparation and analysis. Additionally, effort has been made to adapt venerable analytical chemistry techniques such as optical emission spectroscopy,[15,16] mass spectrometry,[17,18] and dynamic light scattering[19,20] to analysis of nanoparticles, with varying degrees of success and certain characteristic limitations. However, progress continues at a steady pace, and is complemented by novel approaches either rooted in older methods, such as single particle mass spectrometry,[21,22] or completely new techniques such as scanning mobility particle sizing.[23,24]

The semiconductor industry utilizes aqueous nanoparticle-containing slurry for integrated circuit fabrication. These slurries are comprised of a mixture of water, nanoparticles, dispersants, surfactants, and acids or bases designed specifically for the materials comprising and deposited on the substrate (see Figure 1).

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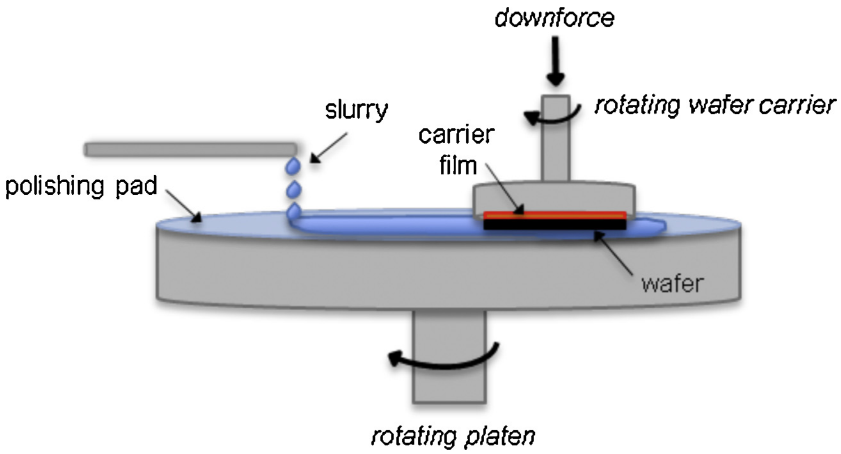

Figure 1. Semiconductor wafer polishing process schematic.[25] **The polishing process involves a wafer rotating on a carrier that is pressed against a polishing pad on a rotating platen. Abrasives used in the process are typically nanoparticles that are either dispersed in slurry or fixed onto the polishing pad.**

The most common nanoparticle abrasives currently used in industrial semiconductor manufacturing settings are silicon oxide (SiO_2, silica), aluminum oxide (Al_2O_3, alumina), and cerium (IV) oxide (CeO_2, ceria). These materials are used in a grinding process that selectively abrades a wafer to accomplish uniform thickness and low roughness. Abrasives used in the process are typically nanoparticles that may be either dispersed in slurry or fixed onto the polishing pad.

Characterization tools used to investigate nanoparticle-containing slurries may in some cases be applicable to environmental or wastewater samples as well, and thus help us better characterize potential environmental discharge or worker exposure to these materials. The goal of this study is to compare several characterization methods of nanoparticle-containing slurries and assess their relative results, difficulty in sample preparation, and potential reliability when confronted with unknown or mixed sample materials. This comparison will better enable selection of characterization not only for semiconductor manufacturers, but also for the toxicologists, medical researchers, and regulators, for whom a practical comparison of both the results and ease of implementation for such techniques are badly needed.[24–29]

MATERIALS AND METHODS

Nanoparticle Suspensions

Eight different nanoparticle-containing slurries were the focus of this study, each of which is used in commercial semiconductor manufacturing worldwide. The slurries were identified with letters indicating their primary nanoparticle component: AlO_x for alumina, SiO_x for silica, and CeO_x for ceria (IV), respectively, and numbers where multiple slurries contained the same primary nanoparticle component.

All slurry was kept at room temperature and, prior to any aliquotting, were either mechanically mixed or, for volumes under 500 mL, manually shaken vigorously for 30 s and then mixed using a vortex mixer for 30 s. Dissemination of small volumes (under 100 mL) was conducted by graduated pipette.

Scanning Electron Microscopy (SEM) and Energy-dispersive X-ray Spectroscopy (EDX)

Slurry samples were prepared for SEM by resuspension of nanoparticles through manual shaking of containers followed by high-speed vortexing for 1 min, dilution by 10° into HPLC-grade water, pipetting 1.5 μL of the dilution to a highly ordered pyrolytic graphite substrate mounted to stainless steel SEM stub by carbon tape, and drying ($\geq$3 h). Imaging was conducted using a LEO 1550 SEM with a Schottky field emitter source at 5 kV accelerating voltage, using a 30 μm aperture, at a working distance of 3–6 mm, with an InLens detector (acting as a 20 kV beam booster). Images obtained with LEO's proprietary software were analyzed manually to determine longest axial length and perpendicular axial length. Microsoft Excel and GraphPad Prism software were used for statistical analysis.

Samples prepared for SEM were analyzed by an EDX detector attachment for the LEO 1550 SEM at up to 20 kV accelerating voltage, using a 60 μM aperture, with a working distance of 15 mm at a 15° take-off angle. Elemental analysis of collected was conducted using Spirit software.

Dynamic Light Scattering (DLS)

Samples for DLS were diluted to approximately 100 μg/mL (assuming accuracy of where original mass fraction was assumed equal to that listed in the non-proprietary MSDS), followed by pipetting 1 mL to a cuvette for analysis. Size measurements were conducted by a Malvern Zetasizer system, assuming water properties for solvent parameters and taking 3 measurements with a minimum of 15 runs per measurement.

Single Particle Inductively Coupled Plasma-Mass Spectrometry (SP-ICP-MS) and Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES)

SP-ICP-MS and ICP-OES samples were prepared from slurries by dilution into HPLC water in parafilm-sealed screw-cap 50 mL polypropylene tubes. These samples were analyzed by PerkinElmer (Shelton, CT) using a Nexion 300 D SP-ICP-MS in single particle mode (final sample dilutions of 10^7–10^8) and an Optima 8300 ICP-OES (final dilution of about 10^2). Assay of selected materials (aluminum, silicon, and cerium) was conducted and reported to the research team. The research team multiplied the result by a correction factor derived from mass-ratios contributed by the oxide component of the metallic-oxide with the assumption of stoichiometric ratios (Al_2O_2, SiO_3, and CeO_2) to determine the concentrations of alumina, silica, and ceria (IV).

Scanning Mobility Particle Sizing (SMPS)

Samples were prepared for SMPS by 1:99 dilution into buffer (20 mM aqueous ammonium acetate at pH 8). Analysis was conducted by a TSI Scanning Mobility Particle Sizer Model 3080 acting to electrostatically filter particles before detection by a TSI Model 3772 Condensation Particle Counter. The SMPS was fed by a TSI 3480 Electrospray Aerosol Generator designed to deliver a constant 0.8 L/min air flow with a known loss. This was combined with a known rate of 135 s per scan, 103 size-bins per scan, a known capillary pressure drop, and system temperature to determine a correction function for SMPS efficiency of particle counts. Microsoft Excel and GraphPad Prism software were used for statistical analysis.

RESULTS AND DISCUSSION

Mass Concentration Analysis

Elemental composition, based on the metallic oxide indicated in the MSDS of the slurry, was first confirmed by EDX. While this data is not shown, spectra indicate that aside from occasional Group I and II peaks, the only significant metallic peaks were from aluminum, silicon, or ceria, and only the material indicated in the MSDS. This proved satisfactory evidence that mass concentration assessments would need only to assay the metals of interest.

Samples prepared yielded heterogeneous surface coverage (see Figure 2), creating alternating patches of bare area and multi-layered nanoparticle clusters. This is most likely an artifact of the drying process. Unfortunately, the high degree of heterogeneity undermines the ability to reliably use EDX data for quantitative characterization.

Instead, SP-ICP-MS and ICP-OES were employed for mass concentration assays. Mass spectrometry was selected due to its high accuracy, precision, high number of potential target analytes, large dynamic range, low detection limit, and reputation for reliability in these sorts of analyses.[30,31] ICP systems dissociate particles into constituent ions, which then yield a signal. While historically, ICP-MS was primarily used to analyze dissolved ionic concentrations, recent developments have yielded methods with a high efficiency of nanoparticle detection and quantification[17] as well as the application of such methods to complex matrices.[18] Analysis of aluminum, silicon, and cerium was conducted in each case. The oxygen content was not tested, but in each case a multiplier

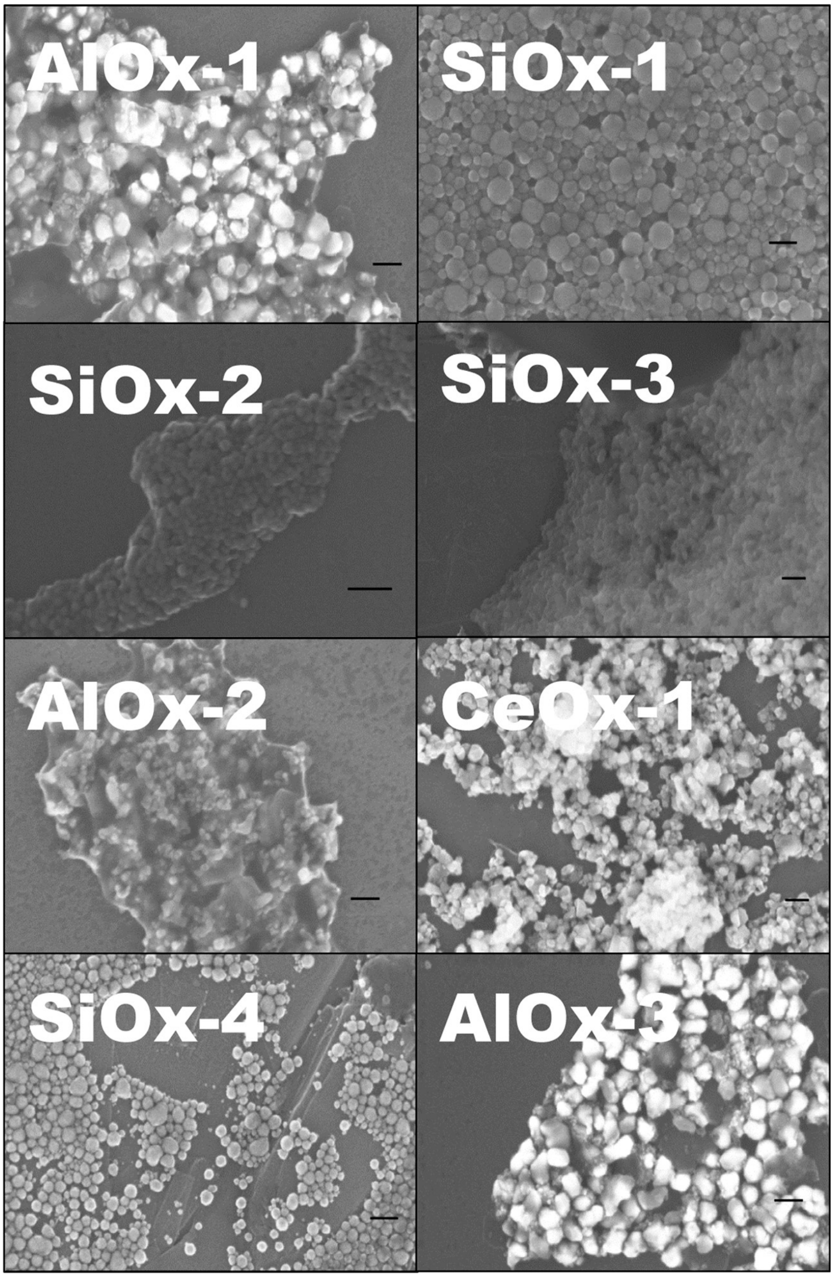

Figure 2. Slurry nanoparticle images via SEM. Scanning electron micrographs of nanoparticles contained in eight sample slurries. The inset letters indicate the slurry to which they are matched. Scale bars indicate 100 nm. Observe the shapes of the particles coincide with composition: elongated hexagonal particles observed in alumina, spherical particles observed in silica, and the cubic particles observed in ceria.

Table 1. Slurry Nanoparticle Concentrations.

Sample	Composition	SDS	SP-ICP-MS	ICP-OES
AlO_{x-1}	Alumina	<2%	1.8%	1.7%
AlO_{x-2}	Alumina	<5%	0.7%	0.7%
AlO_{x-3}	Alumina	<1.5%	0.9%[a]	1.0%[a]
SiO_{x-1}	Silica	<20%	21.3%	30.8%
SiO_{x-2}	Silica	<3%	5.3%	5.7%
SiO_{x-3}	Silica	12–30%	28.7%	25.6%
SiO_{x-4}	Silica	5%	14%	12.9%
CeO_{x-1}	Ceria (IV)	<5%	0.9%	0.8%

[a] SP-ICP-MS and ICP-OES measurements based on equipartition mixture of slurry.

was added to the measured metal concentration based on the portion of molecular mass contributed by the metal assuming ideal stoichiometry. Optical emission spectroscopy, like mass spectrometry, has a rich history in analytical chemistry and is being adapted to analyze nanomaterials[15] and is already showing promising results[16] on complex biological matrices, though it is still limited to analysis of total elemental content rather than analysis of specific particles. The results of this analysis are indicated in Table 1, which shows agreement between the SP-ICP-MS results and ICP-OES results. The correlation is significant ($R^2 > 0.9$) and the largest disagreement occurred in the most concentrated silicon samples. This indicates that ICP-MS for non-silicon slurry is a reliable assay method and may have utility for silicon slurries as well with additional method development.

It is important to note that there is a significant deviation in many cases between the indicated nanoparticle concentration on the SDS and the results from SP-ICP-MS and ICP-OES analysis. While most such SDS indicate a range or maximum concentration level, we found in the case of five of the eight slurries that the nanoparticle concentration exceeded the indicated amount. Notably, this was true only in the case of silica slurries, which might imply a systematic error on the part of the supplier. This could have implications for manufacturing, as well as environmental and safety studies based on these or similar materials. Regardless of the cause of the discrepancy, it reinforces the necessity of independent assays rather than reliance on manufacturer specifications.

Particle Sizing

Particles were sized by SEM, DLS, SMPS, and SP-ICP-MS. These results are presented in Table 2. We compared slurry characterization techniques, anticipating the potential application of these techniques for characterization of industrial materials and waste that may be discharged to the environment.

DLS continues to be one of the highest utility techniques in analyzing particulate suspensions since sample preparation is rapid and analysis is easy to automate. It has been shown to be accurate for nanoparticles with a hydrodynamic diameter less than 20 nm.[10] Its two most significant limitations, specifically the need for the analyte to be a single material of fairly uniform size,[10] are not problematic for slurry manufacturers, who typically intend to produce precisely such materials. However, both of these likely render DLS a poor choice for environmental samples, which are typically mixed in composition. Nonetheless, because DLS is a standard tool used in monodisperse colloidal particle sizing, it provides valuable data for comparison for this study.

SEM differs from other tools in that it is very difficult to automate to any degree and, rather than assessing size as a result of models derived from secondary phenomena, it produces images of particles which can then be measured directly. This theoretically provides the greatest degree of precision, though sample preparation is cost and time intensive as well as potentially leaving artifacts that affect measurement.[32] In reality, several things prevent this technique from being an optimal method of assessing particle size. It was observed that, in many cases, smaller particles tended to underlay layers of larger ones after drying, which would bias any measurement statistics. The formation of layers by particles partially obscures some particles and leads to measurement errors. Finally, the heterogeneity in surface coverage and thickness leads to non-uniform imaging parameters, and the researchers noted a propensity for larger particles to be more present in the surface layer, with smaller particles being more evident at edges of nanoparticle clusters or in more thinly layered areas. These effects create considerable difficulties in automation of imaging process and add uncertainty to manual measurement. Several methods are currently under investigation to aid in depositing higher numbers of particles per unit-area on the substrate while maintaining their separation from other particles to insure sizing accuracy. In spite of these difficulties, direct examination of these particles provides critical context for

Table 2. Slurry Nanoparticle Diameter.

Sample	DLS (nm)	SEM[b] (nm)	SP-ICP-MS (nm)	SMPS (nm)
AlO_{x-1}	57.81	63.9	64	61
AlO_{x-2}	100.1	N/A	35	48
AlO_{x-3}	56.19	71.5	30	74
SiO_{x-1}	24.22	49.5	110	54
SiO_{x-2}	14.96	16.5	111	22
SiO_{x-3}	61.84	29.7	114	100
SiO_{x-4}	25.13	28.6	111	41
CeO_{x-1}	64.30	35.0	28[a]	65

[a] SP-ICP-MS and ICP-OES measurements based on equipartition mixture of slurry.

[b] SEM diameter calculation was modeled on approximating particles as ellipses, and normalizing to the diameter of a circle with equal area to the ellipse.

the interpretation of other sizing methods that do not provide information on the particle shape, for example. As is observable in Figure 2, silica particles appear to be mostly spherical and thus there is no question as to the dimension of interest being reported by other methods. Ceria and alumina particles have a more complex structure, with their longest dimension between 1.3- and 1.5-times greater than the perpendicular direction. Morphological characteristics are significant in toxicology studies, where it is likely the smallest dimension that affects the entry of a particle into cells. Despite that, in order to facilitate comparison with other methods, SEM diameters in Table 2 have been calculated as appropriate to a sphere with equal area to an ellipse with diameters of the observed longest and shortest dimension. Additionally, while there are reasons to be concerned about SEM having a tendency to overestimate particle size, there are certain cases where the DLS system gives a significantly larger measurement than SEM, notably the case of SiO_{x-3}. One exception, SiO_{x-1}, had a larger range of particle sizes, which may result in more significant error due to the complications with measurement previously discussed. In such instances, there is the possibility that the DLS is assessing a small agglomerate of particles rather than a single particle, which provides potential clues as to the state of the particles in liquid (which may not, in fact, be monodisperse).

SP-ICP-MS functions by examining the areas of distinct peaks produced by a mass spectrometer when an individual particle passes through the ionizer, and then comparing that area with standards generated by known, differently sized particles of the same composition.[22] Thus, the instrument makes no assumptions about shape and assumes that particles will share the shape of the standard. When comparing the data with that provided by SEM or DLS, the results of the ICP-MS were generally quite different. All silica particles were found to be the same size, a result obviously contradicted by both DLS and SEM. Additionally, non-silica particles were generally indicated to be smaller than comparative DLS or SEM measurements. This cannot be attributed simply to the difference between the model deriving particle size and the measurement on which the parameter is based. It is possible that sample preparation results in agglomeration of nanoparticles to a fairly regular size that the detector cannot differentiate into component particles or that a complex etching process is occurring.[29] Consequently, SP-ICP-MS will need additional method development before it will be an adequate nanoparticle sizing instrument.

SMPS functions by the use of an electrostatic aerosol generator to create what are ideally single-particle droplets. These are dried, passed through an electrostatic filter to select a narrow size regime,[24] and then a new droplet of liquid is condensed around the particle by butanol to enable optical detection. Mathematical modeling normalizes for losses due to size-selectivity, pressure optimization, and other parameters, relating the detected number of particles back to the liquid flow through a capillary. The resulting sizes, indicated in Table 2, were larger than DLS except in one case, and at times differed more than the DLS measurement differed from SEM. Literature has indicated that similar effects can occur in comparisons with static light scattering, as a consequence of SMPS being able to handle a range of particle sizes, unlike DLS, which is adversely affected when the particle size in a sample is not highly uniform or, at least, described by a single Gaussian distribution.[24] However, the results are not highly dissimilar and, importantly, this method did not have difficulties analyzing specific materials, unlike SP-ICP-MS (and, in one case, SEM). This, along with the fact that the mode of particle detection in SMPS is material-independent indicates that the method may have unique utility in assessing mixed-material samples.

Particle Concentrations

SP-ICP-MS and SPMS also offer the opportunity to count the number of particles present and, by knowing the amount of liquid sampled, allow us to determine particles per unit volume. While from a chemical or manufacturing standpoint, it is often less important to know the exact number of particles than simply to determine results as a function of mass. However, there is increasing evidence that surface area of nanoparticles may be of greater toxicological concern than the total mass of material. Since a diminishing particle size correlates with increased numbers of particles and increased particle surface area for a given amount of mass, the question of the exact number of nanoparticles is directly relevant to health-related investigations.

Table 3 indicates these results of the SP-ICP-MS and SMPS assayed particles per unit volume. Unfortunately, we must treat the results of SP-ICP-MS as suspect, as we know from the sizing data that the SP-ICP-MS certainly misrepresents silica particle size and may be underestimating other metal oxides as well. If this is the case, we can expect significant underestimates of particle counts (as many smaller particles combine into fewer large ones in silica slurries, while in alumina or ceria slurries the smallest particles are fully dissolved[33]).

In contrast, raw SMPS yielded results that were both more consistent

Table 3. Slurry Nanoparticle Concentrations.

Sample	SMPS (particles/mL)	SP-ICP-MS (particles/mL)
AlO_{x-1}	2.79×10^{13}	29,472
AlO_{x-2}	1.84×10^{13}	148,960
AlO_{x-3}	2.40×10^{13}	244,833
SiO_{x-1}	1.61×10^{13}	75,401
SiO_{x-2}	6.32×10^{14}	45,764
SiO_{x-3}	2.48×10^{16}	98,558
SiO_{x-4}	3.13×10^{14}	51,416
CeO_{x-1}	5.01×10^{12}	96,421[a]

[a] SP-ICP-MS analysis based on equipartition mixture of slurry.

and vastly higher than those provided by SP-ICP-MS. One significant source was the presence of salts crystals that formed in the ammonium acetate buffer. These created significant and consistent signatures of particles in method blanks, the vast majority of which were below 7 nm. Initially, this was subtracted as a baseline, but it was then discovered that dilution of the slurry into the buffer created a highly variable number of additional particles under 12 nm. As insignificant numbers of particles were seen in this size range by any other assay, it was assumed these were artifacts and thus particles under 12 nm were eliminated from all calculations. This necessary step yielded consistent results over multiple replicate analyses of each slurry.

Many size-distribution histograms indicated a bimodal distribution, with the second peak occurring at a diameter twice the former. This indicates the possible formation of small agglomerates. However, no larger agglomerates were seen, indicating that particles are still primarily monodispersed.

After correction, SP-ICP-MS still yields particle counts on the order of 10^9 below those indicated by SMPS. SEM analysis, though not precisely quantitative, and with the previously mentioned propensity to underestimate or obscure particles, can provide a lower-bound of particles per μL of diluted slurry. The researchers estimate that a single μL of 100-fold diluted slurry in almost all cases contained in excess of 10^6 particles. Consequently, even this rough measure is sufficient to discount the results of SP-ICP-MS as impossibly low. Thus, the researchers believe the results of SMPS to be far more credible. Nonetheless, it is important that additional methods be developed to validate this technique.

CONCLUSIONS

The nanoparticle-containing slurry used by the semiconductor industry is a commercially relevant product whose particles may serve as a model by which to assess the efficacy of analytical methods for nanoscale materials. The increasing prevalence of nanomaterials makes versatile characterization a major interest to further research, particularly to environmental or health studies. This is significant for workers as well who may be using chemicals whose nanomaterial concentrations are incorrectly represented. Of the analytical instruments investigated in this study, no single instrument was capable of providing all of the characterization information that might be required by an environmental or health study. The most versatile instrument, the SP-ICP-MS, will require further method development before it can fill all these roles. Until that point, standard mass assay techniques like ICP-OES are effective, but must be combined with a method like SMPS to generate a complete understanding of particle sizing and particle concentrations. Finally, SEM and other direct visualization techniques will remain indispensable to any study in which the precise shape of a particle will have significant mechanistic implications, as there is not yet any instrument that can easily provide as thorough a representation of particle shape.

AUTHOR CONTRIBUTIONS

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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