Engineered Nanoparticles and Their Identification Among Natural Nanoparticles

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Abstract

The more nanotechnology develops, the more likely the release of engineered nanoparticles into the environment becomes. Due to a huge excess of natural nanoparticles, the identification and quantification of engineered nanoparticles pose a big challenge to analysts. Moreover, identification in a qualitative sense and quantification by mass concentration alone are not sufficient, because the potential environmental hazard arising from engineered nanoparticles is controlled by many other properties of the particles. We discuss the most important methods of fractionation and detection of both natural and engineered nanoparticles, with a focus on the chemical nature of the particles, particle concentration, and particle size. Analyses should not rely on only one method; instead, several complementary methods should, if possible, be used. Coupled techniques should be further developed and increasingly applied. Dedicated techniques that are tailored to the search for a particular sort of engineered nanoparticles are more promising than universal approaches that search for any engineered nanoparticles.

1. INTRODUCTION

Nanotechnology is expected to become one of the pillars of the next industrial revolution, and we will probably encounter engineered nanoparticles (ENPs) and all kinds of engineered nanomaterials much more frequently in the future. The spectrum of potential applications of nanoparticles is extremely broad; these applications include electronics, new technical materials, batteries, catalysts, water-purification systems, sporting goods, cosmetics and skin-care products, medical products for both diagnostics and therapy, paints, soil remediation materials, textiles, wound dressings, food, toothpastes, baby products such as pacifiers, and many others. The most important classes of ENPs are carbon nanotubes (CNTs); fullerenes; nanowires; TiO_2, ZnO, CeO_2, and silica nanoparticles; Fe(0), Ag(0), and Au(0) nanoparticles; and dendrimers (1–5). What happens with all these particles after they are used, that is, after they have been discarded? What does nature do with them? Can "nanowaste" have harmful effects on humans and other organisms, considering that toxicological tests have proven that certain ENPs are toxic at sufficiently high concentrations? Methods to identify the ENPs among the huge amounts of natural nanoparticles present in natural samples are necessary to answer such questions. They are also a prerequisite for introducing surveillance programs for ENPs in the environment. The methods and strategies that aid such are the subject of this review.

What does nano mean? What are nanoparticles? These questions are less trivial than they may seem. Several different definitions of a nanoparticle have been developed (e.g., References 5–10). Most authors consider a particle to be a nanoparticle if it has a length of 1 to 100 nm in at least one dimension. According to another definition, a nanoparticle, in addition to fulfilling this condition, has properties that differ from those of bulk materials of the same composition (11, 12). Such "nonbulk" properties may include a crystal structure different from that of the corresponding bulk material due to lattice relaxation effects; thermodynamic constants different from those of the bulk, such as higher solubility due to a disproportionately increased surface energy; or special optical and electrical properties due to quantum confinement (10, 13–17). According to Auffan et al. (11), such nonbulk properties are characteristic only of particles of less than approximately 30 nm.

The identification of ENPs among natural nanoparticles is not merely a matter of academic concern or an end in itself. Considering the potential hazard of ENPs to the environment and to humans, it is a task of great practical relevance. Moreover, the identification of these particles is not usually the ultimate goal of an analysis. Normally, the question behind the analysis pertains to the potential hazard. In contrast to the case of truly dissolved toxicants, the hazard of ENPs is not readily described by parameters employed in classical analytical chemistry or toxicology: the chemical identity of the substance in question and the mass concentration. Many additional properties of ENPs may influence the risk posed by a particular ENP in natural media. The list of the parameters (metrics) that need to be determined includes, but is not limited to, size, size distribution, shape, concentration, dispersion/aggregation, structure, chemical composition, surface area, surface charge, surface functionality, surface speciation, rates of desorption and dissolution, nature of coatings, and stability of coatings (3, 5, 7, 9, 18–23). The ultimate goal is a dosimetry in which the exposure or dose to humans, animals, plants, and so on is derived from both the concentration and the properties of the ENPs; in other words, some characterization of the particles must always be involved (4, 7, 18, 20, 24, 25). For predictive risk-assessment considerations on ENPs, the physicochemical behavior in the environment must also be taken into account, so such predictive considerations must be based on both toxicology and environmental chemistry. Our knowledge about both the toxicology of many ENPs (12, 19, 26–38) and their environmental behavior is already considerable (1, 2, 5, 15, 33, 39–52). However, we are far from obtaining a

consistent picture of the behavior of ENPs in nature and the risks they might cause, in part because of interactions between ENPs and natural nanoparticles (4, 30, 53), ENP coatings made of natural organic matter (15, 54, 55), coatings that originate from the production of the ENPs (21, 22), and surface functionalization that arises from either ENP production or environmental influences (3, 15, 21, 55–58), and because of the ability of the ENPs to act as carriers for contaminants (29, 40, 55, 59). Further complicating the issue is that the field of nanotechnology is developing, the release of known ENPs will increase, and new types of ENPs will appear.

We do not provide a comprehensive treatise on ENP analysis in environmental samples; doing so would be far beyond the scope of this review. There are many recent reviews of the analytics of ENPs in natural samples as a whole (2, 4, 5, 7, 14, 21, 22, 28, 60–62), on the analytics of individual types of ENPs (46, 63–66), and of individual analytical techniques for ENP analytics (8, 67–71). Furthermore, we restrict our considerations to liquid and solid samples (waters, sediments, soils, plants, food, etc.); samples from the atmosphere are excluded. We do so because (*a*) all ENPs released to the environment will—although the time they spend in the atmosphere may be considerable (72)—end up in soil or water and (*b*) there are more open questions for nongaseous samples than for gaseous ones (61, 73, 74).

2. PECULIARITIES OF ENGINEERED NANOPARTICLE ANALYTICS

Analyses of nanoparticles have several special features that differentiate them from analyses that do not have to distinguish between nanoparticulate and dissolved fractions or between nanoparticulate and coarse-grained fractions of the analyte. This is also true for ENPs.

2.1. Metrics of Interest

As discussed above, the qualitative detection of a particular type of ENPs is normally only a first step. Measurements of metrics that determine the potential dose, namely the risk posed by these ENPs, are also necessary. A simple metric, such as mass concentration, by itself is not sufficient for the estimation of this risk (2, 18, 21, 40). In Section 1, we list the relevant ENP parameters (there are other such lists). Considering the many types of ENPs in existence, it is not surprising that calls for prioritization of the metrics according to their importance in risk assessment and for classification of the ENPs according to their toxicological importance have arisen (9, 18, 23). Investigators are concerned that more and more characterization of the ENPs may result in a "paralysis by analysis" and may not support (but instead hinder) risk assessment (75).

Here, we restrict our considerations to three ENP parameters: chemical identity, particle-number concentration, and particle-size distribution. Doing so does not reflect a prioritization but the space constraints of this review. They readily demonstrate the problems and difficulties the analyst faces when identifying ENPs in natural samples.

However, even confining ourselves to these three parameters is not as straightforward as one might assume. Particle-number concentration is rather straightforward. Sometimes it is not easy to determine, but if correctly determined it provides an unambiguous piece of information about the particle population. Chemical identity is less straightforward. Most colloid-measuring techniques assume that the individual nanoparticles have a homogeneous composition. However, nanoparticles need not be homogeneous: Semiconductor quantum dots, for instance, consist of a core and a shell (1, 2). The most complex metric of the three selected is particle-size distribution. First, the parameter particle size is poorly defined, given that various measuring techniques yield differently defined particle sizes. Microscopic methods provide the projected area; other methods give the sphere-equivalent hydrodynamic particle diameter (Stokes diameter), the diameter of

gyration, or the equivalent spherical volume diameter (60, 76–78). Therefore, the term particle size must always be specified. Second, there are different types of particle-size distributions, such as the particle number–weighted, the particle volume–weighted, and the light intensity–weighted particle-size distributions (78, 79), that must also be considered. The figure in Section 3.3, below, gives an example of the dramatic differences between the light intensity–weighted and particle number–weighted particle-size distributions of the same particle collective.

2.2. Different Degrees of Difficulty

The difficulties the analyst faces depend on the sample type and the experimental context. Water samples are easier to analyze than soil samples or sediment samples. Samples from experiments that use deliberately added known ENPs, such as those that study (*a*) the colloidal stability of a certain type of ENP under environmental conditions (5, 54–56), (*b*) the behavior of a certain type of ENP in porous media (80–85), or (*c*) the toxicology of an ENP (29), are easier to analyze than samples containing unknown ENPs.

2.3. Prospective Inventories

Important questions for the analyst include the approximate analyte concentration to be expected and the type of sample matrices. A considerable fraction of the solid matter on Earth is in the size range of nanoparticles, and these natural nanoparticles normally occur in tremendous excess compared with ENPs (15, 17, 39, 60). Not much is known about the future concentrations of the miniscule ENP fractions expected in nature (7, 45, 63). **Table 1** estimates potential concentrations of ENPs (22). It is possible that the behavior of the tiny traces of the ENPs is controlled largely by the behavior of natural colloids.

3. METHODS OF NANOPARTICLE QUANTIFICATION AND CHARACTERIZATION

We give a short overview of the methods used to investigate nanoparticles. Researchers already have a great deal of experience with the behavior and the analytics of natural nanoparticles in the

Table 1 Predicted concentrations of engineered nanoparticles arising from consumer products (22)

	Water (μg liter^{-1})	Soil (μg kg^{-1})
Ag	0.010	0.43
Al_2O_3	0.002	0.01
Au	0.14	5.99
CeO_2	<0.0001	<0.01
Fullerenes	0.31	13.1
Hydroxyapatite	10.1	422
Latex	103	4,307
Organo-silica	0.0005	0.02
SiO_2	0.0007	0.03
TiO_2	24.5	1,030
ZnO	76	3,194

environment (86–90); most of the methods we refer to were developed for natural nanoparticles. Methods created especially for ENPs are indicated as such. Descriptions of the methods are reduced to a minimum; for details, see Literature Cited. Our focus is on a discussion of the advantages and disadvantages of the methods and the problems one is faced with when using them.

3.1. Sampling and Sample Pretreatment

Representative samples should be taken, and longer storage should be avoided for colloid samples (7, 14, 91–93). Sample pretreatment should aim for the right balance between reducing the complexity of the sample and maintaining its representativeness (69). Normally, the goal is to remove coarse components without perturbing the analyte particles. This goal can be achieved through, for instance, settling, mild centrifugation, and filtration through filters of relatively large pore size. Particle enrichment can also be achieved through split-flow thin-cell fractionation (94). An alternative is extraction, in which the nanoparticles of interest are enriched in a second liquid (95–99). Extraction is a technique used especially for ENPs. Sample pretreatment is usually more complex for solid samples than for aqueous ones.

3.2. Particle Fractionation

The purpose of particle fractionation is to achieve spatiotemporal separation of the particles. The easiest way to perform such separation is through microfiltration and ultrafiltration; however, these techniques are often plagued by artifacts. A more powerful fractionation method is field-flow fractionation (FFF), whose subvariants include flow field-flow fractionation (FFFF), sedimentation field-flow fractionation, and thermal field-flow fractionation (7, 8, 60, 67, 69, 76, 100–111). Additional methods are size-exclusion chromatography (SEC) (5, 7, 112–114), capillary electrophoresis (CE) (71, 117–121), hydrodynamic chromatography (7, 61, 115, 116), gel electrophoresis (61, 71), isoelectric focusing (61), manipulation between immiscible solvent phases (61), photophoretic velocimetry (122, 123), and centrifugation and ultracentrifugation (60, 124–128). These techniques can be used to obtain fractions of separated nanoparticles that subsequently can be further investigated. However, most of these fractionation techniques can also be coupled with detectors that can trace the separated particles online.

Figure 1 shows fractograms of 10 chemical elements in a river sediment, which were taken by asymmetrical FFFF coupled with inductively coupled plasma mass spectrometry (ICP-MS) (110). FFFF separates the nanoparticles according to their hydrodynamic diameters (i.e., Stokes diameters). **Figure 1** demonstrates that aluminum, a representative of the clay fraction in the sediment, is bound to particles that are larger than those containing iron and titanium and that the trace metals are held in or on those iron-containing mineral particles of only a few tens of nanometers. **Figure 2** shows an example of CE in combination with UV detection (119). CE separates nanoparticles according to their charge-to-size ratios. This figure demonstrates that gold nanoparticles in five size classes ranging from 5 to 40 nm can be effectively separated. **Figure 3** illustrates an ultracentrifugation experiment on uranium(IV)-silica nanoparticles that was performed with a preparative ultracentrifuge; these particles were investigated because they may play a role in subsurface uranium transport (129). The centrifugates were analyzed by ICP-MS (see Reference 129 for details). On the basis of Stokes's law, one can conclude that the sphere-equivalent hydrodynamic particle diameters are no larger than 20 nm and that there is a relatively broad size distribution below 20 nm. Almost all the uranium is removed through sufficiently strong centrifugations, which indicates that in this sample almost all the uranium was in a colloidal form.

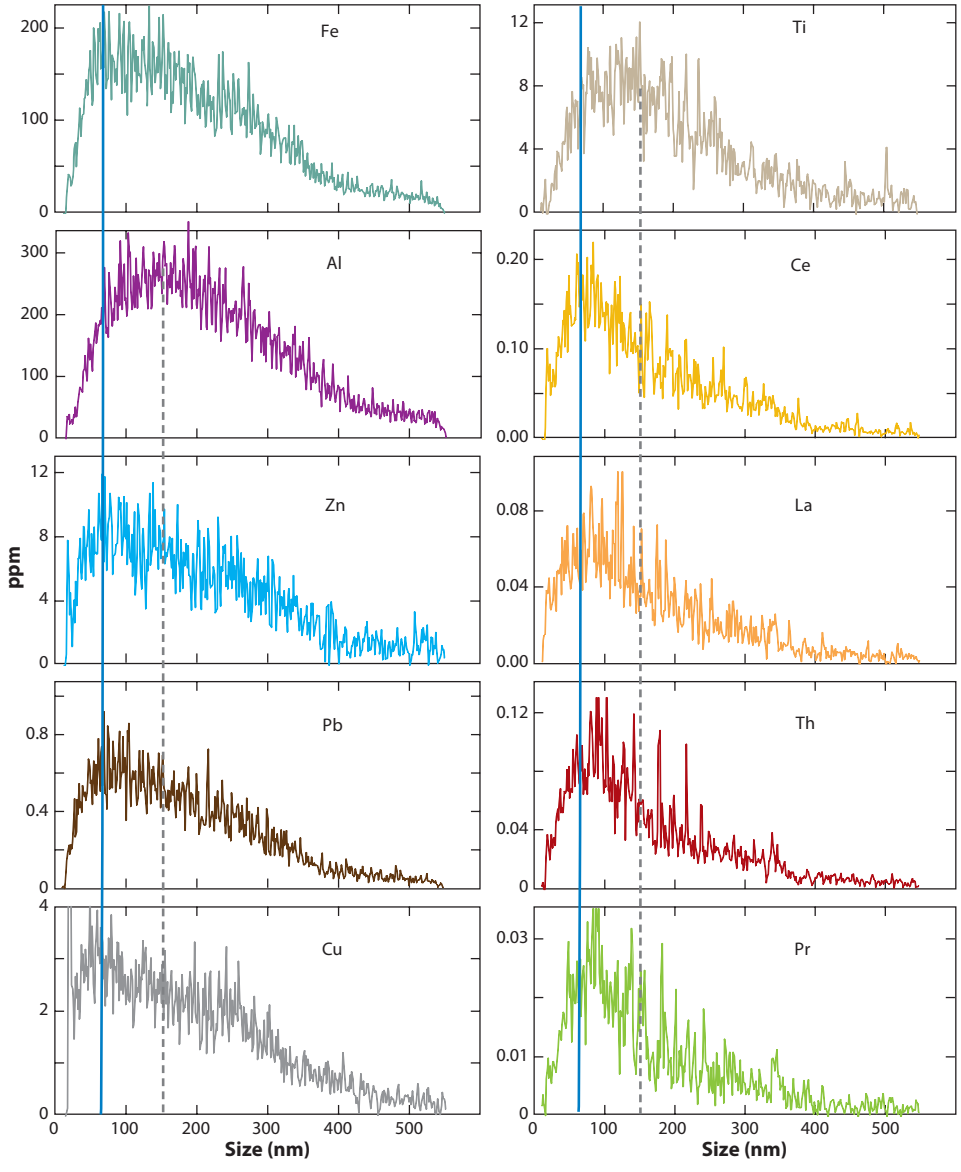

Figure 1

Results of asymmetrical flow field-flow fractionation coupled with inductively coupled plasma mass spectrometry for selected elements in a riverbed sediment. The solid blue line represents the peak maximum for iron (Fe), and the dotted gray line represents the peak maximum for aluminum (Al). Reproduced from Reference 110 with permission from CSIRO.

FFF is probably the most versatile and promising nanoparticle fractionation technique for ENPs in natural samples, although it is relatively cumbersome and highly complex. Comprehensive evaluations of the advantages and disadvantages of FFF have been performed (7, 8, 67, 69). CE has higher inherent separation efficiency, provided that the nanoparticles under study carry electric charge (121). However, the interpretation of data is more complex for CE than for other

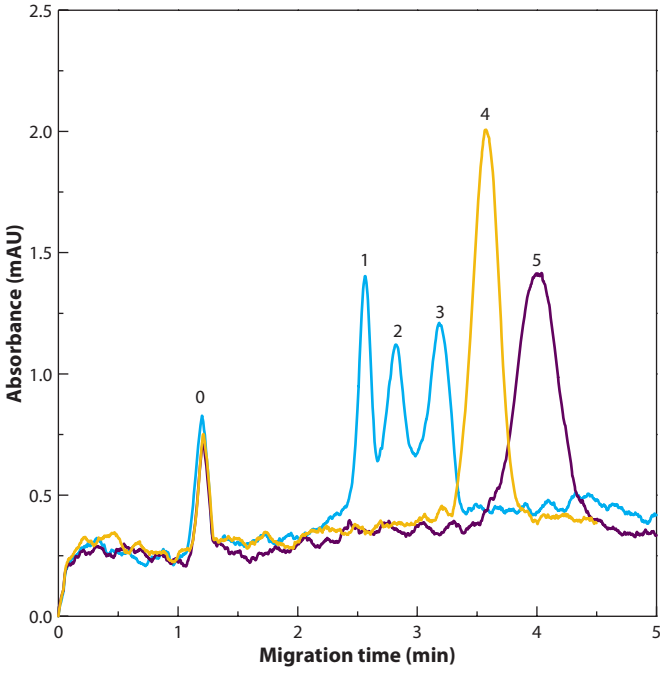

Figure 2

Electropherograms of five differently sized gold nanoparticles in buffer solution at an applied voltage of 18 kV. Peaks: *0*, electrophoretic flow; *1*, *2*, *3*, *4*, and *5*, 5.0-nm, 10.0-nm, 21.5-nm, 30.2-nm, and 41.2-nm gold nanoparticles, respectively. Reproduced from Reference 119 with permission from Elsevier.

techniques (21). Ultracentrifugation also has a very high inherent size resolution (124, 125); this technique is currently underrepresented in environmental nanoparticle analytics. Ultracentrifugation is not free of systematic errors (hydrodynamic nonideality and particle-particle interaction due to the differential settling), but it does not suffer from the artifacts of chromatographic or chromatography-like techniques, such as interactions between the analyte and the stationary phase and shear degradation (SEC) or problems arising from preconcentration, dilution in the channel, particle-membrane interactions, and washing of the particles, which results in reequilibration because of a change in chemistry (FFF).

3.3. Particle Detection and Characterization

The simplest detection methods of particulate matter are turbidometry and nephelometry (81, 108), which provide semiquantitative information on the presence or absence of particles. Particle-size information (hydrodynamic particle diameter) can be obtained through dynamic light scattering (DLS), also known as photon correlation spectroscopy (PCS) (7, 68, 77, 79, 124, 126, 130–132). Photodiode recordings of the light scattered by the particles in a laser beam serve as the input for calculating the autocorrelation function of the scattered light-intensity fluctuations. The faster the autocorrelation function decays to its baseline, the faster (i.e., smaller) are the particles. The particle size is derived from the diffusion coefficient through use of the Stokes-Einstein equation. DLS is very powerful for studying monomodal particle populations of relatively narrow particle-size distributions. In more complex particle systems, masking problems and problems with the deconvolution of the autocorrelation functions can easily ruin the measurements, as was

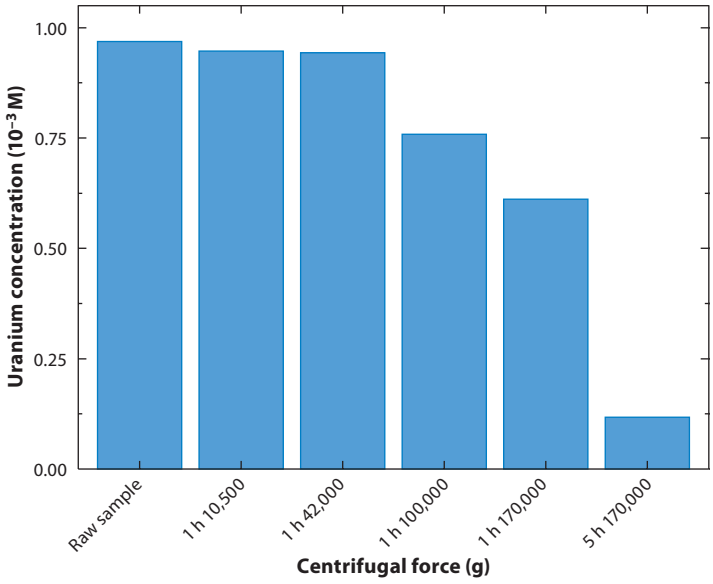

Figure 3

Ultracentrifugation series on a suspension of uranium(IV)-silica colloids. Uranium concentration is 1×10^{-3} M; silica concentration is 3×10^{-3} M. 1-h centrifugations at accelerations of up to 42,000 g are unable to remove significant fractions of the uranium. Each additional increase in centrifugal acceleration results in a further decrease in uranium concentration. Reproduced from Reference 129 with permission from Elsevier.

found for the above-mentioned sample of uranium(IV)-silica nanoparticles. DLS measurements of these colloids yielded a particle size of several hundred nanometers, a result that was repeatedly measured on the same sample over years and indicated a stable colloid. However, as illustrated in **Figure 3**, ultracentrifugation showed that the majority of the particles were <20 nm in size. Thus, the noninvasive technique (DLS) seems to contradict the size-characterization results according to the more invasive ultracentrifugation technique.

A more detailed investigation was performed to explain this apparent discrepancy. **Figure 4** shows the autocorrelation function of a sample of uranium(IV)-silica colloids. **Figure 4*a*** gives the corresponding CONTIN deconvolution (133) as the light intensity–weighted particle-size distribution. **Figure 4*b*** shows a transformation of the light intensity–weighted particle-size distribution of the raw sample into the number-weighted particle-size distribution. The latter size distribution does not agree with the ultracentrifugation result. Therefore, the particles were fractionated by a relatively mild centrifugation prior to PCS. **Figure 4*c*,*d*** provides the centrifugate's light intensity–weighted and number-weighted particle-size distributions. The latter reveals that most of the particles have a diameter of <20 nm; that is, the PCS result is in reasonable agreement with the particle-size determination obtained by ultracentrifugation. Similar masking problems, which are attributable to the strong dependence of scattered-light intensity on particle size, have also been reported for environmental nanoparticles such as iron(III) hydroxy sulfate particles in acid mine drainage (134) and for ENPs such as quantum dots in aqueous suspension (51). Thus, DLS results should always be thoroughly scrutinized for accuracy, and plausibility tests should be performed.

Another light-scattering technique is static light scattering (SLS) (79, 135), which measures the intensity of the scattered light of a nanoparticle suspension according to its dependence on

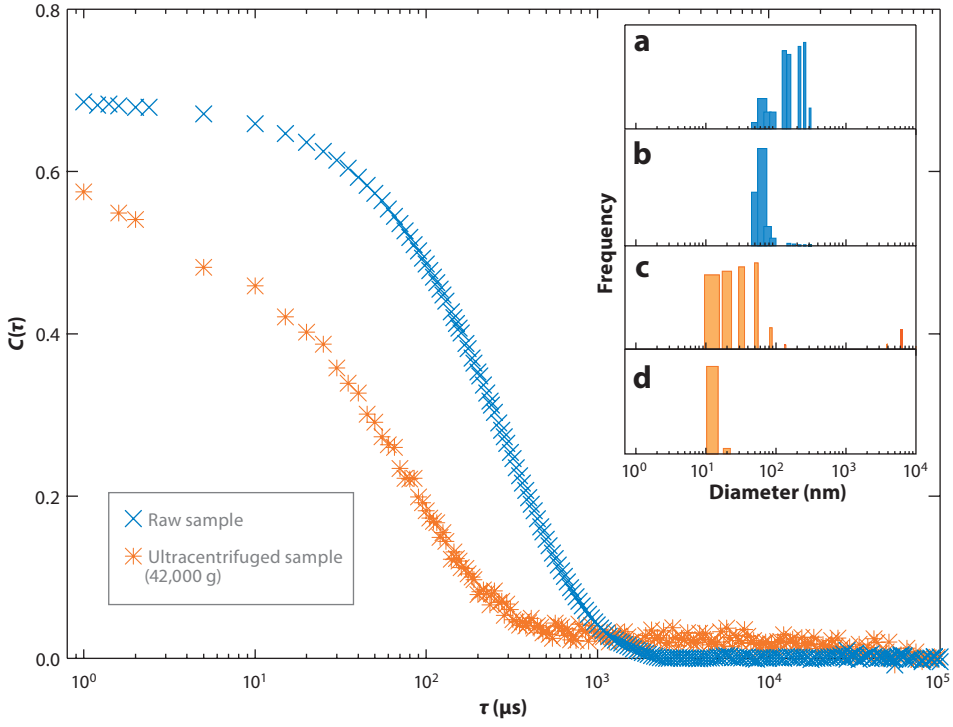

Figure 4

Influence of ultracentrifugation on the autocorrelation function, $C(\tau)$, of a suspension of uranium(IV)-silica colloids. The uranium concentration is 1×10^{-3} M; the silica concentration is 3×10^{-3} M. The first delay time was 1 μs, and the last delay time was 100 milliseconds. The insets show CONTIN deconvolutions of the autocorrelation functions. (*a*) The light intensity–weighted particle-size distribution of the raw sample. (*b*) The number-weighted particle-size distribution of the raw sample. (*c*) The light intensity–weighted particle-size distribution of the centrifugate. (*d*) The number-weighted particle-size distribution of the centrifugate. Reproduced from Reference 129 with permission from Elsevier.

the scattering angle. This technique provides information about the particles' molecular weight, the radius of gyration of the particles, and particle conformation.

Nanoparticle-tracking analysis is a relatively new method of light scattering that permits the determination of particle-size distribution and, to some extent, particle-number concentration (77, 136–142). Because of its physics, this technique is less prone to masking problems. However, it has been widely criticized on the grounds that too many adjustments and settings have to be chosen by the operator, which results in too much subjective influence on the results of the measurement (7, 60, 137, 139).

Laser-induced breakdown detection (LIBD) is a colloid detection method that uses plasma formation in the focus of a pulsed laser beam (143–148). The laser beam energy is adjusted such that no breakdown events are produced in the solvent of the colloidal solution (water), but breakdowns occur as soon as a nanoparticle enters the focus. Information about particle-number concentration and average particle size (**Figure 5**) can be obtained; in a more sophisticated version of LIBD, information about particle-size distribution can also be obtained (148). The lower particle-size detection limit is approximately 10 nm, and the lower particle-concentration limit is in the parts per billion–to–parts per trillion range. This concentration limit is unprecedented. LIBD is a highly

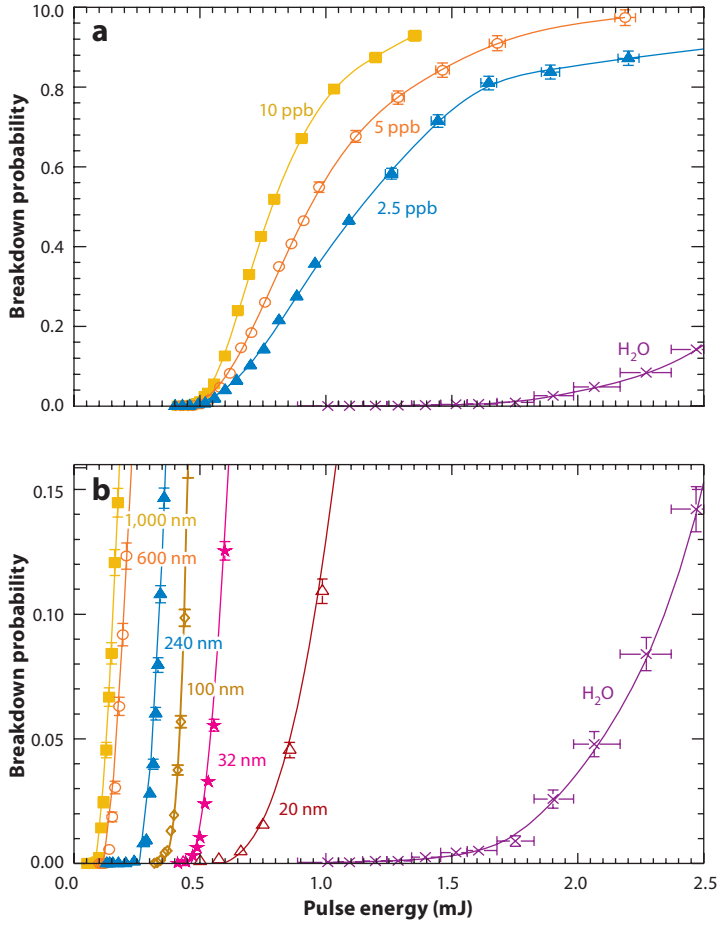

Figure 5

Laser-induced breakdown detection on polystyrene reference particles: breakdown probability as a function of the laser-pulse energy. (*a*) While the breakdown threshold remains unchanged, the slope of the curves changes with the colloid concentration (particle size, 32 nm). (*b*) The threshold of these curves increases with decreasing particle size. Reproduced from Reference 147 with permission from Elsevier.

specialized method that is not yet commercially available. Investigators have recently attempted to use LIBD to measure the particle contents of drinking waters (149–152).

For quantum dots, fluorescence spectroscopy can provide specific particle-related information (i.e., average particle size) because of the effects brought about by quantum confinement (4, 15, 60, 61). Similarly, for gold and silver nanoparticles, such information can be obtained through UV-visible spectrometry on the basis of surface plasmon resonance effects (113, 153–158). The size of gold nanoparticles has also been detected through matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (66, 159). Near-infrared fluorescence (NIRF) spectroscopy can provide structural information, such as the chiral wrapping angle, and the diameter distribution of single-walled carbon nanotubes (SWCNTs) (160).

An interesting method applied to metal and metal oxide nanoparticles is single-particle ICP-MS (136, 161–164). Whereas classical ICP-MS cannot differentiate between the dissolved and particulate species of an element, single-particle ICP-MS can. The flashes of the individual

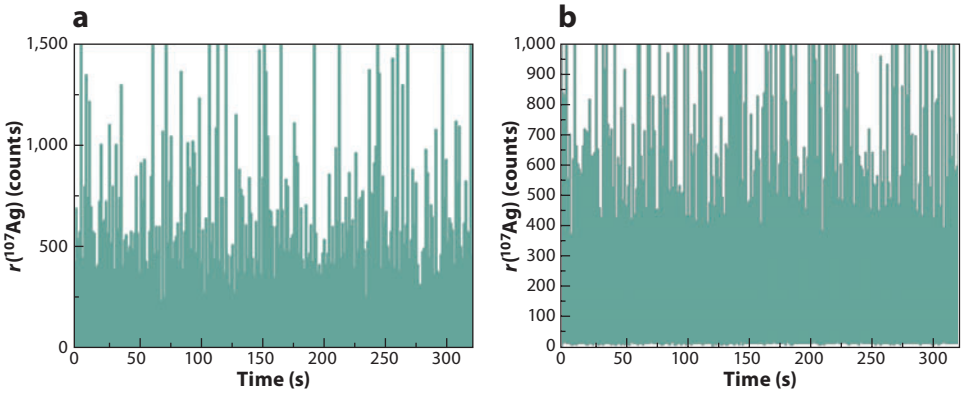

Figure 6

Single-particle inductively coupled mass spectrometry. ^{107}Ag time scans of (*a*) a 113-nm silver (Ag) nanoparticle suspension of 800 ng liter^{-1} and (*b*) a mixture of truly dissolved Ag(I) and 80-nm Ag nanoparticles. The Ag concentration was 300 ng liter^{-1} of each species. Reproduced from Reference 163 with permission from the Royal Society of Chemistry.

particles are measured according to their dependence on time. **Figure 6*a*** depicts a time scan of a 113-nm silver particle suspension. **Figure 6*b*** shows a scan of a mixture of 80-nm silver particles and truly dissolved silver. The admixture of dissolved silver increases the background, but the nanoparticles are still clearly detectable (163).

3.4. Coupled Techniques

As discussed above, most particle-fractionation methods are also methods of particle characterization. FFFF and ultracentrifugation also provide information about the particle's sphere-equivalent hydrodynamic diameter (Stokes diameter), d_h; sedimentation FFF provides information about the equivalent volumetric diameter (based on buoyant mass); and CE yields the size-to-charge ratio. These metrics are derived from the retention times of the particles during fractionation. To measure the retention times, appropriate detectors must be coupled to the fractionation techniques, yielding so-called hyphenated methods. Such detectors, such as refractive index detectors, UV detectors, and ICP-MS and ICP-OES detectors, may not discriminate between dissolved and particulate components of the sample (67, 78, 119, 165, 166). However, other detectors, such as multiangle laser light-scattering detectors, may provide a particle-related signal (105). The latter type of coupled systems can be very powerful because they may overcome the drawbacks and limitations of the individual methods. On the one hand, fractionation may become more reliable, given that particle detectors enable more effective checking and control of the fractionation process. On the other hand, fractionation may improve particle characterization because it simplifies the particle system, that is, makes it less polydisperse.

In the most straightforward case, the detector coupled to the fractionation system is based on turbidometry, as used in commercial analytical centrifuges (127) and ultracentrifuges (125), or on nephelometry, as employed by von der Kammer et al. (108) for an FFFF channel. Several groups of authors have coupled an SLS detector (in addition to a UV detector) to an FFFF system (67, 76, 100, 102, 103, 111, 167, 168). In this combination, information from the SLS detector about the diameter of gyration, d_g, is added to information from the FFFF retention time about the hydrodynamic diameter, d_h. The factor $\rho = d_g/d_h$ indicates to what extent the particles differ

from an ideal homogeneous sphere [$\rho = 0.775$ for a sphere; $\rho > 1$ for a prolate ellipsoid; $0.775 < \rho < 1$ for an oblate ellipsoid (79)]. This process seems to work even for nanoparticles that greatly deviate from an ideal sphere, such as CNTs (105). SLS has also been coupled to SEC (114).

FFFF and DLS have been combined to size C_{60} fullerene particles (168a). Both FFFF and DLS provide information about the hydrodynamic diameter, d_h, and DLS can be used to verify the result derived from the retention time. However, in this study the DLS measurement replaced the calculation of d_h from the retention time because DLS failed due to the C_{60} particles' nonideal retention behavior.

The combination of FFFF and LIBD (169, 170) also eliminates the drawbacks of the individual methods. FFFF overcomes the limits of LIBD in determining particle-size distributions by separating the particles, whereas the high sensitivity of LIBD counteracts the detection problems often caused by FFFF due to sample dilution. The combination of FFFF and single-particle ICP-MS is also a promising approach (164).

Coupling need not be limited to one or two detectors. It should be possible to determine, in a single analysis, the concentration of the particles, their size distribution, the chemical composition, the shape factor ρ, the charge (ζ potential), and so on (8). However, the success of such analyses will always depend to some extent on the type of particles under study and the matrix of the sample.

3.5. Nanoparticle Visualization

Microscopy yields the most direct information about the size, size distribution, and shape of the nanoparticles. The most common microscopic methods are scanning electron microscopy (SEM), transmission electron microscopy (TEM), and atomic force microscopy (AFM) (4, 7, 14, 60, 61, 77, 124, 171, 172). **Figure 7** presents two TEM images as examples. Because all microscopic techniques are invasive to some degree, a drawback of these techniques is the risk of changes occurring in particle properties during sample preparation. The most invasive microscopic method is electron microscopy. WETSEM® and similar techniques reduce sample-preparation

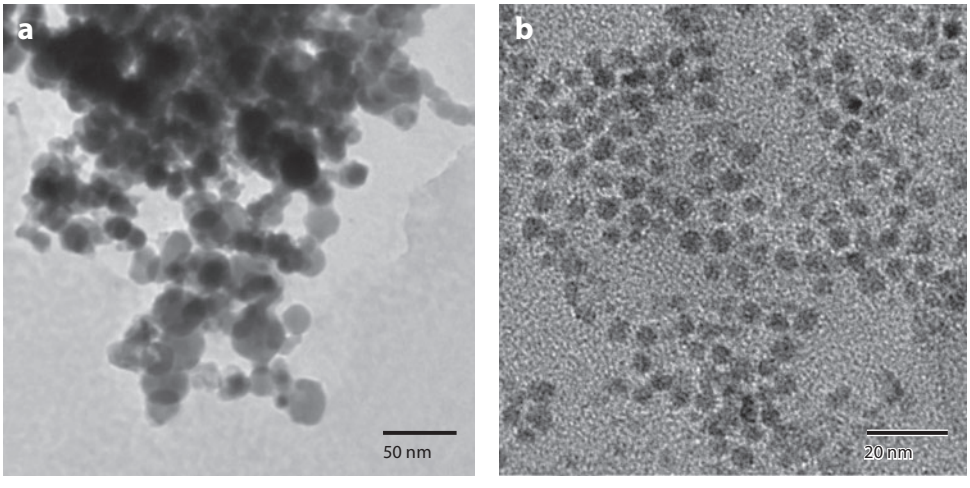

Figure 7

Transmission electron microscope images. (*a*) Loosely aggregated ZnO nanoparticles in the presence of fulvic acid. Reproduced from Reference 77 with permission from the American Chemical Society. (*b*) CdTe quantum dots. Reproduced from Reference 51 with permission from Elsevier.

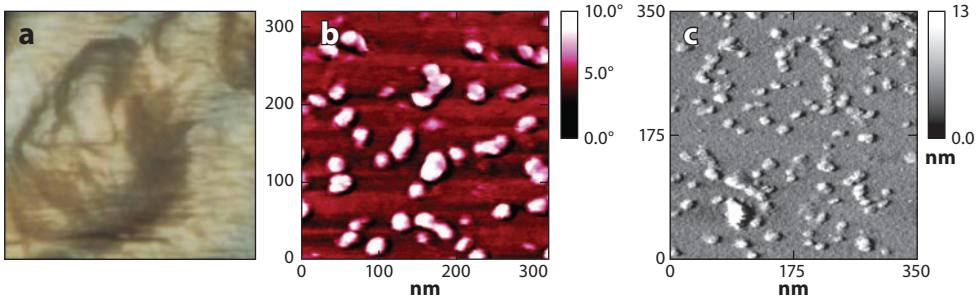

Figure 8

Atomic force microscope (AFM) images of humic acid (*a*) prepared through the evaporation of humic acid solution in air (image size, 488 nm × 488 nm). Reproduced from Reference 174 with permission from Springer. (*b*) AFM images prepared through spin-coating of humic acid solution in air. Reproduced from Reference 175 with permission from Wiley. (*c*) AFM images of humic acid scanned in water in a liquid cell. Reproduced from Reference 176 with permission from Elsevier.

artifacts but provide lower resolution. Even in the case of the relatively noninvasive AFM, it is critical to avoid sample-preparation artifacts. **Figure 8** provides three examples of attempts to study humic acid by use of AFM. Whereas evaporation of a humic acid solution in air (173, 174) causes the formation of unspecific structures on the underlying surface, spin-coating in air (175) and working in water in a liquid cell (176) lead to the resolution of the individual molecular units of the material. To our knowledge, **Figure 8*b*,*c*** represents the first successful visualizations of individual humic acid molecules by AFM. Investigators should consider artifacts such as those depicted in **Figure 8*a*** when using AFM to visualize ENPs made of soft matter (dendrimers). More sophisticated microscopic techniques that provide chemical images and that are only minimally invasive include X-ray spectroscopy with synchrotron radiation (177–180), laser scanning anti-Stokes Raman scattering (CARS) microscopy (181), tip-enhanced CARS microscopy (182), and tip-enhanced Raman spectroscopic microscopy (183).

A general drawback of microscopic techniques is the small amount of sample that can normally be imaged and analyzed; this limitation makes statistical validation of the results difficult. One can obtain reliable conclusions on the whole particle population of a sample only when very many particles are counted and measured. Thus, there is a need for automation and development of suitable image-analysis software, which would enable the characterization of millions of particles (14, 21, 22, 45, 60, 61, 77, 124, 172).

3.6. Sensor Designs

The most recent method used to identify ENPs involves the detection of the ENPs by sensors (5, 70). Sensors are typically used for liquid samples. The sensors may be solids in contact with the sample or reagents suspended in the sample (comparable to the scintillator in liquid scintillation spectrometry for determining radionuclides). Typically, the response of the sensors is specific for one type of nanoparticle (which, however, cannot normally be detected without analyte enrichment before measurement). Such sensor designs appeared after the advent of ENPs, and the field is still in its infancy.

Carrillo-Carrión et al. (184) have presented an interesting example of an optical sensor for the detection of C_{60} fullerene; this sensor consisted of CdSe/ZnS quantum dots coated with *p-tert*-butylcalix[8]arene and took advantage of the specific host-guest chemistry of calixarenes (185). The interaction between the *p-tert*-butylcalix[8]arene–CdSe/ZnS complex and C_{60} quenched the

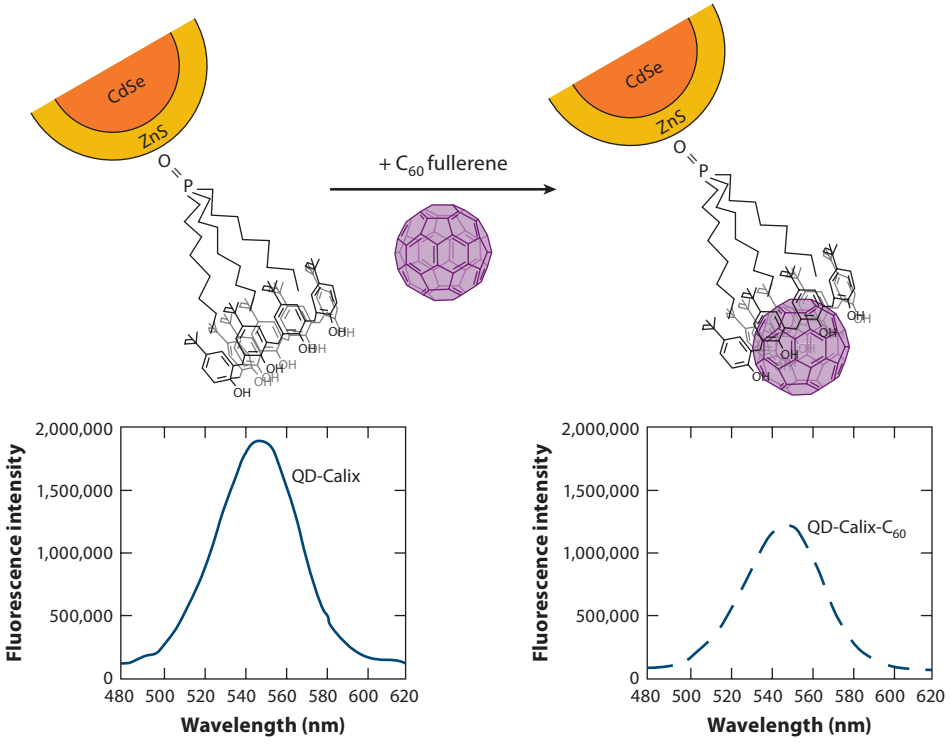

Figure 9

The interaction between a *p-tert*-butylcalix[8]arene–CdSe/ZnS complex and a quencher (C_{60} fullerene). Abbreviations: QD-Calix, O=P=calixarene; QD-calix-C_{60}, O=P=calixarene fullerene C_{60}. Reproduced from Reference 184 with permission from the American Chemical Society.

fluorescence of this complex; the concentration of C_{60} was derived from the degree of fluorescence quenching through the use of the Stern-Volmer equation. The sensor was suspended in toluene, and the fullerene nanoparticles were transferred from a relatively realistic sample (river water spiked with deliberately added C_{60}) into the toluene phase through repeated extraction. The authors reached a lower limit of detection of 5 μg^{-1} of fullerene (**Figure 9**).

Another type of sensor consists of biosensors. For instance, antibody-antigen recognition can be used for highly selective identification of ENPs, which has been demonstrated for gold nanoparticles with an antibody-coated electrode (186). A less specific but more toxicology-related biosensor is the dissolved oxygen sensor, which monitors the respiration of living cells and can thereby provide information about the cytotoxic effects of certain ENPs (70). Similarly, a more complex biological system such as a beating guinea pig heart (Langendorff heart) was used as a sensor to monitor the toxicology-related effects of ENPs (187).

4. SEARCHES IN NATURAL SAMPLES: DELIBERATELY ADDED ENGINEERED NANOPARTICLES

A special case of ENP identification among natural nanoparticles involves the detection of ENPs deliberately added to a system prior to an experiment. Several publications have reported analytical methods to isolate and quantify ENPs added to environmental media, including wastewater

treatment plant biosolids (97, 115, 188), surface water (190), aquatic sediments (98, 191), and terrestrial soil material (49, 192). The ability to quantify ENPs in a test matrix is essential for verification of the ENP concentrations to which organisms are actually exposed during toxicity studies. For example, the verification of applied doses may be particularly important for soil samples. Soils differ from fresh- and seawater in that the applied dose may overestimate the actual dose to soil biota, given that the solid phase provides a large sink for ENPs. As mentioned above, sample treatment is usually more complex for solid samples than for aqueous ones. The accurate detection of nanoparticles in soils or sediments requires that the nanoparticles be physically separated from the solid phase and dispersed into an aqueous suspension so that the above-discussed techniques can be used to identify them.

For example, the extraction of SWCNTs from spiked sediments into surfactant solutions (here, 2% sodium deoxycholate) facilitated, to a certain degree, the reduction of sample complexity and enhanced disaggregation of bundled SWCNTs prior to NIRF analysis (98). Additionally, ultracentrifugation was applied to concentrate sediment extracts containing SWCNTs, thereby improving the sensitivity of this method. Another method, chemothermal oxidation 375°C (CTO-375), was employed to isolate and quantify engineered CNTs in environmental matrices (192). As with soot, CNTs are generally resistant to the CTO-375 treatment step and are isolated and quantified as part of the fraction of soot. However, quantitative separation and identification of naturally produced soot and engineered CNTs were not possible.

An effective way to track ENPs when studying their interactions with natural nanoparticles (58, 193) or testing the uptake of ENPs in biological systems (194–196) is to label them. This technique is beneficial for fundamental studies on the fate and behavior of nanoparticles in complex environmental systems. It makes the particles of interest easily distinguishable and allows for highly sensitive detection in complex matrices at environmentally relevant nanoparticle concentrations. However, the application of labeled nanoparticles is limited to well-defined laboratory settings. Labeling methods that have previously been utilized for ENPs are radiolabeling with γ or β emitters (196–200), isotope labeling with stable isotopes (194, 195, 201), and fluorescence labeling through attachment of a dye to the particle surface (202).

The labeling process can be performed (*a*) during nanoparticle synthesis using a labeled precursor or (*b*) via postsynthesis manipulation. The appropriate label can be either attached to the particle surface (i.e., surface labeling) or integrated into the nanoparticle structure (i.e., so as to label the particle itself). However, labeling techniques are challenging and must be performed so as to avoid modification of the physical, chemical, and surface properties of the ENPs. For example, surface labeling modifies the surface properties of the particle to some extent and, thereby, alters its behavior in biological and environmental systems. Another critical factor that determines the applicability of surface-labeled ENPs is the stability of the ENP-label bonding under environmentally relevant conditions. To date, surface-labeled ENPs have been applied primarily in medical studies (203, 204). However, labeling the particles themselves is a better technique for testing ENPs. In this case, it is important to make sure that the physicochemical characteristics of the particles that determine their biological response are preserved (199, 205).

5. SEARCHES IN NATURAL SAMPLES: UNKNOWN ENGINEERED NANOPARTICLES

The discussion in Section 3 reveals that the methods of nanoparticle quantification and characterization in environmental samples are still developing. New techniques are appearing, and existing techniques are continuously being improved. Investigators agree that analyses should, if possible, be based not on a single method but rather on several complementary methods (4–7, 9, 14, 21, 22,

68, 77). In situ (i.e., minimally invasive) techniques are preferable (206), but there are analytical problems for which invasive methods are adequate. Many authors wish that the methods were standardized and that there were reference particles with which to verify methods (5, 7, 9, 18, 21, 22, 46, 50, 67, 207, 208). Concerning strategies for searching for ENPs, there is no single best method or combination of methods. The choice depends on the nature of the sample and on the information desired. In most cases, some pretreatment, such as the removal of coarse suspended matter from water samples, is necessary. For the pretreated sample, two approaches are typical:

1. use of a high-resolution method of particle fractionation (e.g., FFF) coupled with a less specific particle detector (e.g., light scattering) or
2. use of a less specific method of particle enrichment (e.g., extraction) and a highly specific method of particle detection (e.g., NIRF for SWCNTs or a sensor for fullerene).

Clearly, the second approach aims to detect only one particular type of ENP. Therefore, the first approach might be regarded superior because it seems more universal. However, both strategies struggle with the same inherent problem: They merely approach the solution from two different sides. On the one hand, the highly specific detection methods are, unfortunately, not as selective as one would hope; that is, enrichment or fractionation of the analyte remains a crucial step for approach 2. On the other hand, the performance of the methods of fractionation is high enough only when the methods are tailored to the needs of the search for a special ENP (63, 69). Therefore, both approaches 1 and 2 are normally successful only if applied to search for a particular sort of ENPs. Similar conclusions can be drawn for microscopic methods of searching for ENPs. It is the overwhelming excess of natural nanoparticles in environmental samples and the interaction between these nanoparticles and the ENPs that make the identification of ENPs such a challenge.

6. SUMMARY AND FUTURE PROSPECTS

The somewhat sobering conclusions drawn in the previous section must be taken into account when attempting to predict future development in the field of identifying ENPs in the environment. In the case of experiments with deliberately added ENPs (Section 4), searches are relatively easy—experimenters know which ENP is to be searched for because they know which ENP was added. However, for unknown ENPs (Section 5), the situation is not entirely different. Some authors hope that a "universal monitor" of ENPs can be developed for aerosols (18, 74, 209). However, adopting such a Swiss Army knife–type concept for liquid and solid samples could easily backfire. As discussed in Section 5, for liquid and solid samples the analyst should know which ENP is being searched for because otherwise he would be unable to optimize his measuring system and tailor it to the identification of a particular ENP suspected to cause environmental problems. In other words, the starting point should always be a well-defined search for a particular type of ENP, given that normally there are clues to the occurrence of a certain ENP in the environment, such as information about the existence of a production site of the ENP, the site of usage of the ENP (e.g., a wastewater treatment plant), and the occurrence of a transport accident. Such an analytical concept based on previous knowledge would significantly reduce the extent of surveillance programs for ENPs. Toxicological research also becomes important here. The more efficiently one can assess the toxicity or nontoxicity of individual ENPs to humans and the environment, the less monitoring of ENPs in the environment is necessary because one can focus on the truly dangerous ENPs.

Concerning fractionation methods, flow FFF, sedimentation FFF, CE, and—in combination with highly specific detection methods—liquid-phase extraction may be the most promising

techniques. Selection of the methods of detection, however, greatly depends on the type of sample and the type of ENP that is being searched for. Sensor designs, NIRF, and single-particle ICP-MS have good potential for searches for specific ENPs. Light-scattering techniques such as DLS, SLS, and possibly nanoparticle tracking analysis, which are less specific, will also continue to play an important role. In the monitoring of drinking water, LIBD may prove to be a very interesting method. Both fractionation and detection techniques will be increasingly widely used in direct combination (i.e., coupling). The potential for ultracentrifugation remains underutilized. In this case, further technical development is desirable; in particular, in situ detection of particles in samples of low particle concentration should be improved. Microscopic methods are also of interest for many types of samples. However, there is an urgent need for improvement in available image-analysis techniques. Analyses should not be based on only one method; rather, several complementary methods should be applied.

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LITERATURE CITED

1. Bhatt I, Tripathi BN. 2011. Interaction of engineered nanoparticles with various components of the environment and possible strategies for their risk assessment. *Chemosphere* 82:308–17
2. Farre M, Sanchis J, Barcelo D. 2011. Analysis and assessment of the occurrence, the fate and the behavior of nanomaterials in the environment. *Trends Anal. Chem.* 30:517–27
3. Helland A, Scheringer M, Siegrist M, Kastenholz HG, Wiek A, Scholz RW. 2008. Risk assessment of engineered nanomaterials: a survey of industrial approaches. *Environ. Sci. Technol.* 42:640–46
4. Ju-Nam Y, Lead JR. 2008. Manufactured nanoparticles: an overview of their chemistry, interactions and potential environmental implications. *Sci. Total Environ.* 400:396–414
5. Weinberg H, Galyean A, Leopold M. 2011. Evaluating engineered nanoparticles in natural waters. *Trends Anal. Chem.* 30:72–83
6. Baalousha M, Lead JR, von der Kammer F, Hofmann T. 2009. Natural colloids and nanoparticles in aquatic and terrestrial environments. In *Environmental and Human Health Impacts of Nanotechnology*, ed. JR Lead, E Smith, pp. 109–61. New York: Wiley
7. Hassellov M, Kaegi R. 2009. Analysis and characterization of manufactured nanoparticles in aquatic environments. In *Environmental and Human Health Impacts of Nanotechnology*, ed. JR Lead, E Smith, pp. 211–66. New York: Wiley
8. Lespes G, Gigault J. 2011. Hyphenated analytical techniques for multidimensional characterisation of submicron particles: a review. *Anal. Chim. Acta* 692:26–41
9. Stone V, Nowack B, Baun A, van den Brink N, von der Kammer F, et al. 2010. Nanomaterials for environmental studies: classification, reference material issues, and strategies for physico-chemical characterisation. *Sci. Total Environ.* 408:1745–54
10. Waychunas GA. 2001. Structure, aggregation and characterization of nanoparticles. *Nanopart. Environ.* 44:105–66
11. Auffan M, Rose J, Bottero JY, Lowry GV, Jolivet JP, Wiesner MR. 2009. Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. *Nat. Nanotechnol.* 4:634–41

12. Wiesner MR, Lowry GV, Jones KL, Hochella MF, Di Giulio RT, et al. 2009. Decreasing uncertainties in assessing environmental exposure, risk, and ecological implications of nanomaterials. *Environ. Sci. Technol.* 43:6458–62
13. Banfield JF, Zhang HZ. 2001. Nanoparticles in the environment. *Nanopart. Environ.* 44:1–58
14. Burleson DJ, Driessen MD, Penn RL. 2004. On the characterization of environmental nanoparticles. *J. Environ. Sci.* 39:2707–53
15. Christian P, von der Kammer F, Baalousha M, Hofmann T. 2008. Nanoparticles: structure, properties, preparation and behaviour in environmental media. *Ecotoxicology* 17:326–43
16. Hochella MF. 2002. Nanoscience and technology: the next revolution in the Earth sciences. *Earth Planet. Sci. Lett.* 203:593–605
17. Wigginton NS, Haus KL, Hochella MF Jr. 2007. Aquatic environmental nanoparticles. *J. Environ. Monit.* 9:1306–16
18. Abbott LC, Maynard AD. 2010. Exposure assessment approaches for engineered nanomaterials. *Risk Anal.* 30:1634–44
19. Krug HF, Wick P. 2011. Nanotoxicology: an interdisciplinary challenge. *Angew. Chem. Int. Ed.* 50:1260–78
20. Owen R, Handy R. 2007. Formulating the problems for environmental risk assessment of nanomaterials. *Environ. Sci. Technol.* 41:5582–88
21. Tiede K, Boxall ABA, Tear SP, Lewis J, David H, Hassellov M. 2008. Detection and characterization of engineered nanoparticles in food and the environment. *Food Addit. Contam.* 25:795–821
22. Tiede K, Hassellov M, Breitbarth E, Chaudhry Q, Boxall ABA. 2009. Considerations for environmental fate and ecotoxicity testing to support environmental risk assessments for engineered nanoparticles. *J. Chromatogr. A* 1216:503–9
23. Warheit DB. 2008. How meaningful are the results of nanotoxicity studies in the absence of adequate material characterization? *Toxicol. Sci.* 101:183–85
24. Maynard AD, Aitken RJ, Butz T, Colvin V, Donaldson K, et al. 2006. Safe handling of nanotechnology. *Nature* 444:267–69
25. Shatkin J. 2008. *Nanotechnology Health and Environmental Risks*. Boca Raton: CRC
26. Apte SC, Rogers NJ, Batley GE. 2009. Ecotoxicology of manufactured nanoparticles. In *Environmental and Human Health Impacts of Nanotechnology*, ed. JR Lead, E Smith, pp. 267–305. New York: Wiley
27. Baroli B. 2010. Skin absorption and potential toxicity of nanoparticulate nanomaterials. *J. Biomed. Nanotechnol.* 6:485–96
28. Farre M, Gajda-Schrantz K, Kantiani L, Barcelo D. 2009. Ecotoxicity and analysis of nanomaterials in the aquatic environment. *Anal. Bioanal. Chem.* 393:81–95
29. Handy RD, von der Kammer F, Lead JR, Hassellov M, Owen R, Crane M. 2008. The ecotoxicology and chemistry of manufactured nanoparticles. *Ecotoxicology* 17:287–314
30. Klaine SJ, Alvarez PJJ, Batley GE, Fernandes TF, Handy RD, et al. 2008. Nanomaterials in the environment: behavior, fate, bioavailability, and effects. *Environ. Toxicol. Chem.* 27:1825–51
31. Menard A, Drobne D, Jemec A. 2011. Ecotoxicity of nanosized TiO_2. Review of in vivo data. *Environ. Pollut.* 159:677–84
32. Nel A, Xia T, Madler L, Li N. 2006. Toxic potential of materials at the nanolevel. *Science* 311:622–27
33. Peralta-Videa JR, Zhao L, Lopez-Moreno ML, de la Rosa G, Hong J, Gardea-Torresdey JL. 2011. Nanomaterials and the environment: a review for the biennium 2008–2010. *J. Hazard. Mater.* 186:1–15
34. Poland CA, Duffin R, Kinloch I, Maynard A, Wallace WAH, et al. 2008. Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. *Nat. Nanotechnol.* 3:423–28
35. Scown TM, van Aerle R, Tyler CR. 2010. Review: Do engineered nanoparticles pose a significant threat to the aquatic environment? *Crit. Rev. Toxicol.* 40:653–70
36. Stone V, Clift MJD, Johnston H. 2009. Human toxicology and effects of nanoparticles. In *Environmental and Human Health Impacts of Nanotechnology*, ed. JR Lead, E Smith, pp. 357–88. New York: Wiley
37. Warheit DB, Webb TR, Colvin VL, Reed KL, Sayes CR. 2007. Pulmonary bioassay studies with nanoscale and fine-quartz particles in rats: Toxicity is not dependent upon particle size but on surface characteristics. *Toxicol. Sci.* 95:270–80

38. Wiesner MR, Lowry GV, Alvarez P, Dionysiou D, Biswas P. 2006. Assessing the risks of manufactured nanomaterials. *Environ. Sci. Technol.* 40:4336–45
39. Bernhardt ES, Colman BP, Hochella MF Jr, Cardinale BJ, Nisbet RM, et al. 2010. An ecological perspective on nanomaterial impacts in the environment. *J. Environ. Qual.* 39:1954–65
40. Boxall ABA, Tiede K, Chaudhry Q. 2007. Engineered nanomaterials in soils and water: How do they behave and could they pose a risk to human health? *Nanomedicine* 2:919–27
41. Chen KL, Smith BA, Ball WP, Fairbrother DH. 2010. Assessing the colloidal properties of engineered nanoparticles in water: case studies from fullerene C_{60} nanoparticles and carbon nanotubes. *Environ. Chem.* 7:10–27
42. Gottschalk F, Nowack B. 2011. The release of engineered nanomaterials to the environment. *J. Environ. Monit.* 13:1145–55
43. Lin D, Tian X, Wu F, Xing B. 2010. Fate and transport of engineered nanomaterials in the environment. *J. Environ. Qual.* 39:1896–908
44. Lowry GV, Hotze EM, Bernhardt ES, Dionysiou DD, Pedersen JA, et al. 2010. Environmental occurrences, behavior, fate, and ecological effects of nanomaterials: an introduction to the special series. *J. Environ. Qual.* 39:1867–74
45. Nowack B, Bucheli TD. 2007. Occurrence, behavior and effects of nanoparticles in the environment. *Environ. Pollut.* 150:5–22
46. Isaacson CW, Kleber M, Field JA. 2009. Quantitative analysis of fullerene nanomaterials in environmental systems: a critical review. *Environ. Sci. Technol.* 43:6463–74
47. Mueller NC, Nowack B. 2008. Exposure modeling of engineered nanoparticles in the environment. *Environ. Sci. Technol.* 42:4447–53
48. Musee N. 2011. Nanowastes and the environment: potential new waste management paradigm. *Environ. Int.* 37:112–28
49. Petosa AR, Jaisi DP, Quevedo IR, Elimelech M, Tufenkji N. 2010. Aggregation and deposition of engineered nanomaterials in aquatic environments: role of physicochemical interactions. *Environ. Sci. Technol.* 44:6532–49
50. Richardson SD, Ternes TA. 2011. Water analysis: emerging contaminants and current issues. *Anal. Chem.* 83:4614–48
51. Torkzaban S, Kim Y, Mulvihill M, Wan J, Tokunaga TK. 2010. Transport and deposition of functionalized CdTe nanoparticles in saturated porous media. *J. Contam. Hydrol.* 118:208–17
52. Zhang Y, Chen Y, Westerhoff P, Hristovski K, Crittenden JC. 2008. Stability of commercial metal oxide nanoparticles in water. *Water Res.* 42:2204–12
53. Buffle J. 2006. The key role of environmental colloids/nanoparticles for the sustainability of life. *Environ. Chem.* 3:155–58
54. Hyung H, Fortner JD, Hughes JB, Kim JH. 2007. Natural organic matter stabilizes carbon nanotubes in the aqueous phase. *Environ. Sci. Technol.* 41:179–84
55. Schierz A, Zänker H. 2009. Aqueous suspensions of carbon nanotubes: Surface oxidation, colloidal stability and uranium sorption. *Environ. Pollut.* 157:1088–94
56. Cho H-H, Smith BA, Wnuk JD, Fairbrother DH, Ball WP. 2008. Influence of surface oxides on the adsorption of naphthalene onto multiwalled carbon nanotubes. *Environ. Sci. Technol.* 42:2899–905
57. Lee J, Kim M, Hong CK, Shim SE. 2007. Measurement of the dispersion stability of pristine and surface-modified multiwalled carbon nanotubes in various nonpolar and polar solvents. *Meas. Sci. Technol.* 18:3707–12
58. Schierz A, Englehart B, Moore A, Ferguson PL. 2009. Association of single-wall carbon nanotubes with natural particulate matter under estuarine conditions. *Am. Chem. Soc.* Abstr.
59. Prasse C, Ternes T. 2010. Removal of organic and inorganic pollutants and pathogens from wastewater and drinking water using nanoparticles—a review. See Ref. 89, pp. 55–79
60. Hassellov M, Readman JW, Ranville JF, Tiede K. 2008. Nanoparticle analysis and characterization methodologies in environmental risk assessment of engineered nanoparticles. *Ecotoxicology* 17:344–61
61. Howard AG. 2010. On the challenge of quantifying man-made nanoparticles in the aquatic environment. *J. Environ. Monit.* 12:135–42

62. Peters R, ten Dam G, Bouwmeester H, Helsper H, Allmaier G, et al. 2011. Identification and characterization of organic nanoparticles in food. *Trends Anal. Chem.* 30:100–12
63. Ferreira da Silva B, Perez S, Gardinalli P, Singhal RK, Mozeto AA, Barcelo D. 2011. Analytical chemistry of metallic nanoparticles in natural environments. *Trends Anal. Chem.* 30:528–40
64. Perez S, Farre ML, Barcelo D. 2009. Analysis, behavior and ecotoxicity of carbon-based nanomaterials in the aquatic environment. *Trends Anal. Chem.* 28:820–32
65. Suarez IJ, Rosal R, Rodriguez A, Ucles A, Fernandez-Alba AR, et al. 2011. Chemical and ecotoxicological assessment of poly(amidoamine) dendrimers in the aquatic environment. *Trends Anal. Chem.* 30:492–506
66. Yu L, Andriola A. 2010. Quantitative gold nanoparticle analysis methods: a review. *Talanta* 82:869–75
67. Baalousha M, Stolpe B, Lead JR. 2011. Flow field-flow fractionation for the analysis and characterization of natural colloids and manufactured nanoparticles in environmental systems: a critical review. *J. Chromatogr. A* 1218:4078–103
68. Brar SK, Verma M. 2011. Measurement of nanoparticles by light-scattering techniques. *Trends Anal. Chem.* 30:4–17
69. von der Kammer F, Legros S, Larsen EH, Loeschner K, Hofmann T. 2011. Separation and characterization of nanoparticles in complex food and environmental samples by field-flow fractionation. *Trends Anal. Chem.* 30:425–36
70. Sadik OA, Zhou AL, Kikandi S, Du N, Wang Q, Varner K. 2009. Sensors as tools for quantitation, nanotoxicity and nanomonitoring assessment of engineered nanomaterials. *J. Environ. Monit.* 11:1782–800
71. Surugau N, Urban PL. 2009. Electrophoretic methods for separation of nanoparticles. *J. Sep. Sci.* 32:1889–906
72. Niessner R. 2010. Nanoparticles acting as condensation nuclei—water droplet formation and incorporation. See Ref. 89, pp. 13–21
73. Charron A, Harrison RM. 2009. Atmospheric nanoparticles. In *Environmental and Human Health Impacts of Nanotechnology*, ed. JR Lead, E Smith, pp. 163–209. New York: Wiley
74. Maynard AD, Aitken RJ. 2007. Assessing exposure to airborne nanomaterials: current abilities and future requirements. *Nanotoxicology* 1:26–41
75. Hansen SF, Maynard A, Baun A, Tickner JA. 2008. Late lessons from early warnings for nanotechnology. *Nat. Nanotechnol.* 3:444–47
76. von der Kammer F, Baborowski M, Friese K. 2005. Field-flow fractionation coupled to multi-angle laser light scattering detectors: applicability and analytical benefits for the analysis of environmental colloids. *Anal. Chim. Acta* 552:166–74
77. Domingos RF, Baalousha MA, Ju-Nam Y, Reid MM, Tufenkji N, et al. 2009. Characterizing manufactured nanoparticles in the environment: multimethod determination of particle sizes. *Environ. Sci. Technol.* 43:7277–84
78. Baalousha M, Lead JR. 2007. Characterization of natural aquatic colloids (<5 nm) by flow-field flow fractionation and atomic force microscopy. *Environ. Sci. Technol.* 41:1111–17
79. Schurtenberger P, Newman ME. 1993. Characterization of biological and environmental particles using static and dynamic light scattering. See Ref. 86, pp. 37–115
80. Cheng XK, Kan AT, Tomson MB. 2005. Study of C_{60} transport in porous media and the effect of sorbed C_{60} on naphthalene transport. *J. Mater. Res.* 20:3244–54
81. Greswell RB, Rahman SH, Cuthbert MO, Tellam JH. 2010. An inexpensive flow-through laser nephelometer for the detection of natural colloids and manufactured nanoparticles. *J. Hydrol.* 388:112–20
82. Jaisi DP, Elimelech M. 2009. Single-walled carbon nanotubes exhibit limited transport in soil columns. *Environ. Sci. Technol.* 43:9161–66
83. Lecoanet HF, Bottero JY, Wiesner MR. 2004. Laboratory assessment of the mobility of nanomaterials in porous media. *Environ. Sci. Technol.* 38:5164–69
84. Liu X, O'Carroll DM, Petersen EJ, Huang Q, Anderson CL. 2009. Mobility of multiwalled carbon nanotubes in porous media. *Environ. Sci. Technol.* 43:8153–58
85. Wang P, Shi Q, Liang H, Steuerman DW, Stucky GD, Keller AA. 2008. Enhanced environmental mobility of carbon nanotubes in the presence of humic acid and their removal from aqueous solution. *Small* 4:2166–70

86. Buffle J, van Leeuwen HP, eds. 1992. *Environmental Particles*, Vol. 1. Boca Raton: Lewis
87. Buffle J, van Leeuwen HP, eds. 1993. *Environmental Particles*, Vol. 2. Boca Raton: Lewis
88. Frimmel FH, von der Kammer F, Flemming KC, eds. 2007. *Colloidal Transport in Porous Media*. Berlin/Heidelberg: Springer
89. Frimmel FH, Niessner R, eds. 2010. *Nanoparticles in the Water Cycle*. Berlin/Heidelberg: Springer. 239 pp.
90. Lead JR, Wilkinson KJ. 2007. Environmental colloids and particles: current knowledge and future developments. In *Environmental Colloids and Particles*, ed. KJ Wilkinson, JR Lead, pp. 1–15. New York: Wiley
91. Baumann T. 2010. Nanoparticles in groundwater—occurrence and applications. See Ref. 89, pp. 23–34
92. McCarthy JF, Degueldre C. 1993. Sampling and characterization of colloids and particles in groundwater for studying their role in contaminant transport. See Ref. 86, pp. 247–315
93. Perret D, Newman ME, Negre JC, Chen YW, Buffle J. 1994. Submicron particles in the Rhine River. 1. Physicochemical characterization. *Water Res.* 28:91–106
94. Giddings JC. 1985. A system based on split-flow lateral-transport thin (SPLITT) separation cells for rapid and continuous particle fractionation. *Sep. Sci. Technol.* 20:749–68
95. Benn TM, Pycke BFG, Herckes P, Westerhoff P, Halden RU. 2011. Evaluation of extraction methods for quantification of aqueous fullerenes in urine. *Anal. Bioanal. Chem.* 399:1631–39
96. Benn TM, Westerhoff P, Herckes P. 2011. Detection of fullerenes (C_{60} and C_{70}) in commercial cosmetics. *Environ. Pollut.* 159:1334–42
97. Farre M, Perez S, Gajda-Schrantz K, Osorio V, Kantiani L, et al. 2010. First determination of C_{60} and C_{70} fullerenes and *N*-methylfulleropyrrolidine C_{60} on the suspended material of wastewater effluents by liquid chromatography hybrid quadrupole linear ion trap tandem mass spectrometry. *J. Hydrol.* 383:44–51
98. Schierz A, Parks Ashley N, Ferguson PL. 2010. Detection of single-walled carbon nanotubes in environmental samples by field flow fractionation: NIR fluorescence spectroscopy. *Am. Chem. Soc.* Abstr. 241
99. Wei GT, Yang ZS, Lee CY, Yang HY, Wang CRC. 2004. Aqueous-organic phase transfer of gold nanoparticles and gold nanorods using an ionic liquid. *J. Am. Chem. Soc.* 126:5036–37
100. Baalousha M, von der Kammer F, Motelica-Heino M, Baborowski M, Hofmeister C, Le Coustumer P. 2006. Size-based speciation of natural colloidal particles by flow field flow fractionation, inductively coupled plasma-mass spectroscopy, and transmission electron microscopy/X-ray energy dispersive spectroscopy: colloids–trace element interaction. *Environ. Sci. Technol.* 40:2156–62
101. Baalousha M, von der Kammer F, Motelica-Heino M, Hilal HS, Le Coustumer P. 2006. Size fractionation and characterization of natural colloids by flow-field flow fractionation coupled to multi-angle laser light scattering. *J. Chromatogr. A* 1104:272–81
102. Baalousha M, von der Kammer F, Motelica-Heino M, Le Coustumer P. 2005. 3D characterization of natural colloids by FlFFF-MALLS-TEM. *Anal. Bioanal. Chem.* 383:549–56
103. Baalousha M, von der Kammer F, Motelica-Heino M, Le Coustumer P. 2005. Natural sample fractionation by F1FFF-MALLS-TEM: sample stabilization, preparation, pre-concentration and fractionation. *J. Chromatogr. A* 1093:156–66
104. Chun J, Fagan JA, Hobbie EK, Bauer BJ. 2008. Size separation of single-wall carbon nanotubes by flow-field flow fractionation. *Anal. Chem.* 80:2514–23
105. Gigault J, Le Hecho I, Dubascoux S, Potin-Gautier M, Lespes G. 2010. Single walled carbon nanotube length determination by asymmetrical-flow field-flow fractionation hyphenated to multi-angle laser-light scattering. *J. Chromatogr. A* 1217:7891–97
106. Gimbert LJ, Haygarth PM, Beckett R, Worsfold PJ. 2005. Comparison of centrifugation and filtration techniques for the size fractionation of colloidal material in soil suspensions using sedimentation field-flow fractionation. *Environ. Sci. Technol.* 39:1731–35
107. Hassellov M, von der Kammer F, Beckett R. 2007. Characterisation of aquatic colloids and macromolecules by field-flow fractionation. In *Environmental Colloids and Particles*, ed. KJ Wilkinson, JR Lead, pp. 223–76. New York: Wiley

108. von der Kammer F, Baborowski M, Friese K. 2005. Application of a high-performance liquid chromatography fluorescence detector as a nephelometric turbidity detector following field-flow fractionation to analyse size distributions of environmental colloids. *J. Chromatogr. A* 1100:81–89
109. Klein T, Niessner R. 1998. Characterization of heavy-metal-containing seepage water colloids by flow FFF, ultrafiltration, ELISA and AAS. *Microchim. Acta* 129:47–55
110. Plathe KL, von der Kammer F, Hassellov M, Moore J, Murayama M, et al. 2010. Using FlFFF and aTEM to determine trace metal-nanoparticle associations in riverbed sediment. *Environ. Chem.* 7:82–93
111. Zattoni A, Rambaldi DC, Reschiglian P, Melucci M, Krol S, et al. 2009. Asymmetrical flow field-flow fractionation with multi-angle light scattering detection for the analysis of structured nanoparticles. *J. Chromatogr. A* 1216:9106–12
112. Bauer BJ, Fagan JA, Hobbie EK, Chun J, Bajpai V. 2008. Chromatographic fractionation of SWNT/DNA dispersions with on-line multi-angle light scattering. *J. Phys. Chem. C* 112:1842–50
113. Liu F-K. 2007. SEC characterization of Au nanoparticles prepared through seed-assisted synthesis. *Chromatographia* 66:791–96
114. Porsch B, Welinder A, Korner A, Wittgren B. 2005. Distribution analysis of ultra-high molecular mass poly(ethylene oxide) containing silica particles by size-exclusion chromatography with dual light-scattering and refractometric detection. *J. Chromatogr. A* 1068:249–60
115. Tiede K, Boxall ABA, Wang X, Gore D, Tiede D, et al. 2010. Application of hydrodynamic chromatography–ICP-MS to investigate the fate of silver nanoparticles in activated sludge. *J. Anal. At. Spectrom.* 25:1149–54
116. Yegin BA, Lamprecht A. 2006. Lipid nanocapsule size analysis by hydrodynamic chromatography and photon correlation spectroscopy. *Int. J. Pharm.* 320:165–70
117. Celiz MD, Colon LA, Watson DF, Aga DS. 2011. Study on the effects of humic and fulvic acids on quantum dot nanoparticles using capillary electrophoresis with laser-induced fluorescence detection. *Environ. Sci. Technol.* 45:2917–24
118. Lin K-H, Chu T-C, Liu F-K. 2007. On-line enhancement and separation of nanoparticles using capillary electrophoresis. *J. Chromatogr. A* 1161:314–21
119. Liu FK, Lin YY, Wu CH. 2005. Highly efficient approach for characterizing nanometer-sized gold particles by capillary electrophoresis. *Anal. Chim. Acta* 528:249–54
120. Lopez-Pastor M, Dominguez-Vidal A, Ayora-Canada MJ, Simonet BM, Lendl B, Valcárcel M. 2008. Separation of single-walled carbon nanotubes by use of ionic liquid-aided capillary electrophoresis. *Anal. Chem.* 80:2672–79
121. Stewart DTR, Celiz MD, Vicente G, Colon LA, Aga DS. 2011. Potential use of capillary zone electrophoresis in size characterization of quantum dots for environmental studies. *Trends Anal. Chem.* 30:113–22
122. Helmbrecht C, Niessner R, Haisch C. 2007. Photophoretic velocimetry for colloid characterization and separation in a cross-flow setup. *Anal. Chem.* 79:7097–103
123. Helmbrecht C, Niessner R, Haisch C. 2011. Photophoretic velocimetry—a new way for the in situ determination of particle size distribution and refractive index of hydrocolloids. *Analyst* 136:1987–94
124. Bootz A, Vogel V, Schubert D, Kreuter J. 2004. Comparison of scanning electron microscopy, dynamic light scattering and analytical ultracentrifugation for the sizing of poly(butyl cyanoacrylate) nanoparticles. *Eur. J. Pharm. Biopharm.* 57:369–75
125. Colfen H. 2004. Analysis of nanoparticles <10 nm by analytical ultracentrifugation. In *Particle Sizing and Characterization*, ed. T Provder, J Texter, pp. 119–37. Washington, DC: Am. Chem. Soc.
126. Lange H. 1995. Comparative test of methods to determine particle-size and particle size distribution in the submicron range. *Part. Part. Syst. Charact.* 12:148–57
127. McFadyen P, Fairhurst D. 1993. High-resolution particle-size analysis from nanometers to microns. *Clay Miner.* 28:531–37
128. Scott D, Harding SE, Rowe AJ, eds. 2006. *Analytical Ultracentrifugation: Techniques and Methods*. Cambridge, UK: R. Soc. Chem. Publ.
129. Dreissig I, Weiss S, Hennig C, Bernhard G, Zänker H. 2011. Formation of uranium(IV)-silica colloids at near-neutral pH. *Geochim. Cosmochim. Acta* 75:352–67

130. Chu B. 2008. Dynamic Light Scattering. In *Soft-Matter Characterization*, Vol. 1, ed. R Borsali, R Pecora, pp. 335–72. Berlin: Springer
131. Filella M, Zhang JW, Newman ME, Buffle J. 1997. Analytical applications of photon correlation spectroscopy for size distribution measurements of natural colloidal suspensions: capabilities and limitations. *Colloids Surf. A Physicochem. Eng. Asp.* 120:27–46
132. Ford NC. 1985. Light scattering apparatus. In *Dynamic Light Scattering: Applications of PCS*, ed. R Pecora, pp. 7–58. New York: Plenum
133. Provencher SW. 1982. A constrained regulation method for inverting data represented by linear algebraic or integral equations. *Comput. Phys. Commun.* 27:213–27
134. Zänker H, Moll H, Richter W, Brendler V, Hennig C, et al. 2002. The colloid chemistry of acid rock drainage solution from an abandoned Zn-Pb-Ag mine. *Appl. Geochem.* 17:633–48
135. Wyatt PJ. 1993. Light scattering and the absolute characterization of macromolecules. *Anal. Chim. Acta* 272:1–40
136. Farkas J, Peter H, Christian P, Urrea JAG, Hassellov M, et al. 2011. Characterization of the effluent from a nanosilver producing washing machine. *Environ. Int.* 37:1057–62
137. Filipe V, Hawe A, Jiskoot W. 2010. Critical evaluation of nanoparticle tracking analysis (NTA) by NanoSight for the measurement of nanoparticles and protein aggregates. *Pharm. Res.* 27:796–810
138. Gallego-Urrea JA, Tuoriniemi J, Pallander T, Hassellov M. 2010. Measurements of nanoparticle number concentrations and size distributions in contrasting aquatic environments using nanoparticle tracking analysis. *Environ. Chem.* 7:67–81
139. Gallego-Urrea JA, Tuoriniemi J, Hassellov M. 2011. Applications of particle-tracking analysis to the determination of size distributions and concentrations of nanoparticles in environmental, biological and food samples. *Trends Anal. Chem.* 30:473–83
140. Malloy A, Carr B. 2006. Nanoparticle tracking analysis—the Halo^{TM} system. *Part. Part. Syst. Charact.* 23:197–204
141. Malloy A. 2011. Count, size and visualize nanoparticles. *Mater. Today* 14:170–73
142. Xu CS, Cang H, Montiel D, Yang H. 2007. Rapid and quantitative sizing of nanoparticles using three-dimensional single-particle tracking. *J. Phys. Chem. C* 111:32–35
143. Kim J-I, Walther C. 2007. Laser-induced breakdown detection. In *Environmental Colloids and Particles*, ed. KJ Wilkinson, JR Lead, pp. 555–612. New York: Wiley
144. Knopp R, Neck V, Kim JI. 1999. Solubility, hydrolysis and colloid formation of plutonium(IV). *Radiochim. Acta* 86:101–8
145. Opel K, Weiss S, Huebener S, Zänker H, Bernhard G. 2007. Study of the solubility of amorphous and crystalline uranium dioxide by combined spectroscopic methods. *Radiochim. Acta* 95:143–49
146. Scherbaum FJ, Knopp R, Kim JI. 1996. Counting of particles in aqueous solutions by laser-induced photoacoustic breakdown detection. *Appl. Phys. B* 63:299–306
147. Walther C, Bitea C, Hauser W, Kim JI, Scherbaum FJ. 2002. Laser induced breakdown detection for the assessment of colloid mediated radionuclide migration. *Nucl. Instrum. Methods B* 195:374–88
148. Walther C, Cho HR, Fanghanel T. 2004. Measuring multimodal size distributions of aquatic colloids at trace concentrations. *Appl. Phys. Lett.* 85:6329–31
149. Bundschuh T, Wagner T, Weber M, Koster R. 2004. Method of laser-induced breakdown detection and application examples. *Chem. Eng. Technol.* 27:377–82
150. Kaegi R, Ulrich A, Sinnet B, Vonbank R, Wichser A, et al. 2008. Synthetic TiO_2 nanoparticle emission from exterior facades into the aquatic environment. *Environ. Pollut.* 156:233–39
151. Latkoczy C, Kaegi R, Fierz M, Ritzmann M, Guenther D, Boller M. 2010. Development of a mobile fast-screening laser-induced breakdown detection (LIBD) system for field-based measurements of nanometre sized particles in aqueous solutions. *J. Environ. Monit.* 12:1422–29
152. Wagner T, Bundschuh T, Schick R, Koster R. 2004. Detection of aquatic colloids in drinking water during its distribution via a water pipeline network. *Water Sci. Technol.* 50:27–37
153. Amendola V, Meneghetti M. 2009. Size evaluation of gold nanoparticles by UV-vis spectroscopy. *J. Phys. Chem. C* 113:4277–85
154. Aryal S, Remant BKC, Narayan B, Kim CK, Kim HY. 2006. Study of electrolyte induced aggregation of gold nanoparticles capped by amino acids. *J. Colloid Interface Sci.* 299:191–97

155. Etchegoin PG, Le Ru EC. 2010. Basic electromagnetic theory of SERS. In *Surface Enhanced Raman Spectroscopy*, ed. E Le Ru, P Etchegoin, pp. 1–37. Weinheim, Ger.: Wiley
156. Stiles PL, Dieringer JA, Shah NC, Van Duyne RR. 2008. Surface-enhanced Raman spectroscopy. *Annu. Rev. Anal. Chem.* 1:601–26
157. Haiss W, Thanh NTK, Aveyard J, Fernig DG. 2007. Determination of size and concentration of gold nanoparticles from UV-vis spectra. *Anal. Chem.* 79:4215–21
158. Khlebtsov NG. 2008. Determination of size and concentration of gold nanoparticles from extinction spectra. *Anal. Chem.* 80:6620–25
159. Zhang Y, Shuang S, Dong C, Lo CK, Paau MC, Choi MMF. 2009. Application of HPLC and MALDI-TOF MS for studying as-synthesized ligand-protected gold nanoclusters products. *Anal. Chem.* 81:1676–85
160. O'Connell MJ, Bachilo SM, Huffman CB, Moore VC, Strano MS, et al. 2002. Band gap fluorescence from individual single-walled carbon nanotubes. *Science* 297:593–96
161. Degueldre C, Favarger PY, Rosse R, Wold S. 2006. Uranium colloid analysis by single particle inductively coupled plasma-mass spectrometry. *Talanta* 68:623–28
162. Degueldre C, Favarger PY, Wold S. 2006. Gold colloid analysis by inductively coupled plasma-mass spectrometry in a single particle mode. *Anal. Chim. Acta* 555:263–68
163. Laborda F, Jimenez-Lamana J, Bolea E, Castillo JR. 2011. Selective identification, characterization and determination of dissolved silver(I) and silver nanoparticles based on single particle detection by inductively coupled plasma mass spectrometry. *J. Anal. At. Spectrom.* 26:1362–71
164. Tuoriniemi J, Hassellov M. 2010. Detection of nanoparticles in the environment using field flow fractionation coupled to single particle ICP-MS. *Geochim. Cosmochim. Acta* 74:1060A
165. Delay M, Tercero Espinoza LA, Metreveli G, Frimmel FH, Niessner R. 2010. Coupling techniques to quantify nanoparticles and to characterize their interactions with water constituents. See Ref. 89, pp. 139–63
166. Plaschke M, Schafer T, Bundschuh T, Manh TN, Knopp R, et al. 2001. Size characterization of bentonite colloids by different methods. *Anal. Chem.* 73:4338–47
167. Roessner D, Kulicke WM. 1994. Online coupling of flow field-flow fractionation and multi-angle laser light scattering. *J. Chromatogr. A* 687:249–58
168. Thielking H, Roessner D, Kulicke WM. 1995. Online coupling of field-flow fractionation and multi-angle laser-light scattering for the characterization of polystyrene particles. *Anal. Chem.* 67:3229–33
168a. Isaacson CW, Bouchard D. 2010. Asymmetric flow field flow fractionation of aqueous C-60 nanoparticles with size determination by dynamic light scattering and quantification by liquid chromatography atmospheric pressure photoionization mass spectrometry. *J. Chromatogr. A* 1217:1506–12
169. Baik M-H, Yun J-I, Bouby M, Hahn P-S, Kim J-I. 2007. Characterization of aquatic groundwater colloids by a laser-induced breakdown detection and ICP-MS combined with an asymmetric flow field-flow fractionation. *Korean J. Chem. Eng.* 24:723–29
170. Thang NM, Knopp R, Geckeis H, Kim JI, Beck HP. 2000. Detection of nanocolloids with flow-field flow fractionation and laser-induced breakdown detection. *Anal. Chem.* 72:1–5
171. Leppard GG. 2008. Nanoparticles in the environment as revealed by transmission electron microscopy: detection, characterisation and activities. *Curr. Nanosci.* 4:278–301
172. Mavrocordatos D, Perret D, Leppard GG. 2007. Strategies and advances in the characterisation of environmental colloids by electron microscopy. In *Environmental Colloids and Particles*, ed. KJ Wilkinson, JR Lead, pp. 345–404. New York: Wiley
173. Namjesnik-Dejanovic K, Maurice PA. 1997. Atomic force microscopy of soil and stream fulvic acids. *Colloids Surf. A Physicochem. Eng. Asp.* 120:77–86
174. Osterberg R, Mortensen K, Ikai A. 1995. Direct observation of humic-acid clusters, a nonequilibrium system with a fractal structure. *Naturwissenschaften* 82:137–39
175. Mertig M, Klemm D, Pompe W, Zänker H, Bottger M. 1999. Scanning force microscopy of spin-coated humic acid. *Surf. Interface Anal.* 27:426–32
176. Plaschke M, Romer J, Klenze R, Kim JI. 1999. In situ AFM study of sorbed humic acid colloids at different pH. *Colloids Surf. A Physicochem. Eng. Asp.* 160:269–79

177. Haberstroh PR, Brandes JA, Gelinas Y, Dickens AF, Wirick S, Cody G. 2006. Chemical composition of the graphitic black carbon fraction in riverine and marine sediments at sub-micron scales using carbon X-ray spectromicroscopy. *Geochim. Cosmochim. Acta* 70:1483–94
178. Mitrea G, Thieme J, Guttmann P, Heim S, Gleber S. 2008. X-ray spectromicroscopy with the scanning transmission X-ray microscope at BESSY II. *J. Synchrotron Radiat.* 15:26–35
179. Thieme J, McNulty I, Vogt S, Paterson D. 2007. X-ray spectromicroscopy—a tool for environmental sciences. *Environ. Sci. Technol.* 41:6885–89
180. Thieme J, Gleber S-C, Sedlmair J, Rieger J, Niemeyer J, Coates J. 2010. X-ray spectromicroscopy studies of nanoparticles in aqueous media. See Ref. 89, pp. 103–15
181. Cheng JX, Jia YK, Zheng GF, Xie XS. 2002. Laser-scanning coherent anti-Stokes Raman scattering microscopy and applications to cell biology. *Biophys. J.* 83:502–9
182. Ichimura T, Kawata, S. 2010. Surface- and tip-enhanced CARS. In *Surface Enhanced Raman Spectroscopy: Analytical, Biophysical and Life Science Applications*, ed. S Schlücker, pp. 305–21. Weinheim, Ger.: Wiley
183. Schmid T, Messmer A, Yeo B-S, Zhang W, Zenobi R. 2008. Towards chemical analysis of nanostructures in biofilms. II. Tip-enhanced Raman spectroscopy of alginates. *Anal. Bioanal. Chem.* 391:1907–16
184. Carrillo-Carrión C, Lendl B, Simonet BM, Valcárcel M. 2011. Calix[8]arene coated CdSe/ZnS quantum dots as C_{60} nanosensor. *Anal. Chem.* 83:8093–100
185. Atwood JL, Koutsantonis GA, Raston CL. 1994. Purification of C_{60} and C_{70} by selective complexation with calixarenes. *Nature* 368:229–31
186. Chen Y-S, Hung Y-C, Chen K, Huang GS. 2008. Detection of gold nanoparticles using an immunoglobulin-coated piezoelectric sensor. *Nanotechnology* 19:495502
187. Stampfl A, Maier M, Radykewicz R, Reitmeir P, Gottlicher M, Niessner R. 2011. Langendorff heart: a model system to study cardiovascular effects of engineered nanoparticles. *Am. Chem. Soc. Nano* 5:5345–53
188. Tiede K, Boxall ABA, Tiede D, Tear SP, David H, Lewis J. 2009. A robust size-characterisation methodology for studying nanoparticle behaviour in "real" environmental samples, using hydrodynamic chromatography coupled to ICP-MS. *J. Anal. At. Spectrom.* 24:964–72
189. Deleted in proof.
190. Suarez B, Moliner-Martinez Y, Cardenas S, Simonet BM, Valcárcel M. 2008. Monitoring of carboxylic carbon nanotubes in surface water by using multiwalled carbon nanotube-modified filter as preconcentration unit. *Environ. Sci. Technol.* 42:6100–4
191. Quevedo IR, Tufenkji N. 2009. Influence of solution chemistry on the deposition and detachment kinetics of a CdTe quantum dot examined using a quartz crystal microbalance. *Environ. Sci. Technol.* 43:3176–82
192. Sobek A, Bucheli TD. 2009. Testing the resistance of single- and multi-walled carbon nanotubes to chemothermal oxidation used to isolate soots from environmental samples. *Environ. Pollut.* 157:1065–71
193. Zhang L, Petersen EJ, Huang Q. 2011. Phase distribution of ^{14}C-labeled multiwalled carbon nanotubes in aqueous systems containing model solids: peat. *Environ. Sci. Technol.* 45:1356–62
194. Dybowska AD, Croteau M-N, Misra SK, Berhanu D, Luoma SN, et al. 2011. Synthesis of isotopically modified ZnO nanoparticles and their potential as nanotoxicity tracers. *Environ. Pollut.* 159:266–73
195. Croteau MN, Dybowska AD, Luoma SN, Valsami-Jones E. 2011. A novel approach reveals that zinc oxide nanoparticles are bioavailable and toxic after dietary exposures. *Nanotoxicology* 5:79–90
196. Ferguson PL, Chandler GT, Templeton RC, Demarco A, Scrivens WA, Englehart BA. 2008. Influence of sediment-amendment with single-walled carbon nanotubes and diesel soot on bioaccumulation of hydrophobic organic contaminants by benthic invertebrates. *Environ. Sci. Technol.* 42:3879–85
197. Petersen EJ, Huang QG, Weber WJ. 2008. Bioaccumulation of radio-labeled carbon nanotubes by *Eisenia foetida*. *Environ. Sci. Technol.* 42:3090–95
198. Oughton DH, Hertel-Aas T, Pellicer E, Mendoza E, Joner EJ. 2008. Neutron activation of engineered nanoparticles as a tool for tracing their environmental fate and uptake in organisms. *Environ. Toxicol. Chem.* 27:1883–87
199. Gibson N, Holzwarth U, Abbas K, Simonelli F, Kozempel J, et al. 2011. Radiolabelling of engineered nanoparticles for in vitro and in vivo tracing applications using cyclotron accelerators. *Arch. Toxicol.* 85:751–73

200. Abbas K, Cydzik I, Del Torchio R, Farina M, Forti E, et al. 2010. Radiolabelling of TiO_2 nanoparticles for radiotracer studies. *J. Nanopart. Res.* 12:2435–43
201. Gulson B, Wong H. 2006. Stable isotopic tracing—a way forward for nanotechnology. *Environ. Health Perspect.* 114:1486–88
202. Kirchner C, Liedl T, Kudera S, Pellegrino T, Javier AM, et al. 2005. Cytotoxicity of colloidal CdSe and CdSe/ZnS nanoparticles. *Nano Lett.* 5:331–38
203. Deng X, Yang S, Nie H, Wang H, Liu Y. 2008. A generally adoptable radiotracing method for tracking carbon nanotubes in animals. *Nanotechnology* 19:075101
204. Cai D, Mataraza JM, Qin ZH, Huang ZP, Huang JY, et al. 2005. Highly efficient molecular delivery into mammalian cells using carbon nanotube spearing. *Nat. Methods* 2:449–54
205. Simonelli F, Marmorato P, Abbas K, Ponti J, Kozempel J, et al. 2011. Cyclotron production of radioactive CeO_2 nanoparticles and their application for in vitro uptake studies. *IEEE Trans. Nanobiosci.* 10:44–50
206. Zänker H. 2010. In situ measurements on suspended nanoparticles with visible laser light, infrared light, and X-rays. See Ref. 89, pp. 117–38
207. Aitken RJ, Hankin SM, Tran CL, Donaldson K, Stone V, et al. 2008. A multidisciplinary approach to the identification of reference materials for engineered nanoparticle toxicology. *Nanotoxicology* 2:71–78
208. Gordalla BC. 2010. Standardisation. See Ref. 89, pp. 207–31
209. Justino CIL, Rocha-Santos TA, Duarte AC. 2011. Sampling and characterization of nanoaerosols in different environments. *Trends Anal. Chem.* 30:554–67

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