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Direct and Indirect Toxic Effects of Engineered Nanoparticles on Algae: Role of Natural Organic Matter

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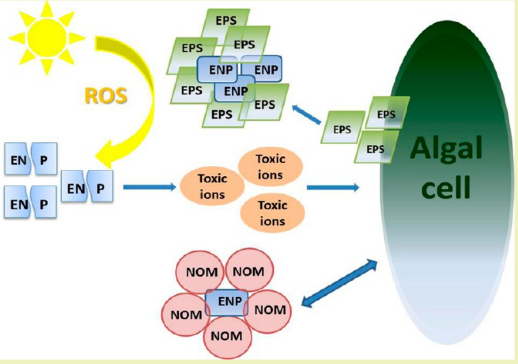
ABSTRACT: In order to assess the overall risk posed by engineered nanoparticles (ENPs), the biological effects of this emergent pollutant to aquatic ecosystems must be evaluated. We present findings from studies conducted with a diversity of ENPs (metallic, quantum dots) on a variety of freshwater and marine algae (phytoplankton) illustrating both their direct and indirect effects. We show that in general, while the surface properties of ENPs govern their aggregation behavior and ionic strength controls their dissolution, exopolymeric substances (EPS) produced by algae determine their potential to be toxic and thereby movement through the water column and food web. The production of EPS reduces the impact of ENPs (bioavailability and toxicity) and/or their ions on cellular activities of algae. It does not however directly reduce the aggregation and/or solubility of ENPs but rather affects their stability. Complicating understanding of these interactions is the great assortment of surface coatings for ENPs. This perspective is intended to highlight our current knowledge and the need for future research particularly focused on determining the fate and transport of ENPs in the aquatic environment.



KEYWORDS: *Engineered nanoparticles, Phytoplankton, Toxicity, Metals, Exopolymeric substances, Nanomaterials, Quantum dots*

INTRODUCTION

Engineered nanoparticles (ENPs) are arguably the most important products of nanotechnology whose benefits and drawbacks are believed to well exceed those of the industrial revolution.[1−4] These novel materials are used in diverse areas such as electronics, biomedicine, pharmaceuticals, cosmetics, environmental analysis and remediation, catalysis, and material sciences. Applications that directly benefit the environment include nanotechnologies for site remediation and wastewater treatment and air and water purification.[5−7] While the total global investment in nanotechnologies was around $10 billion in 2005, today it is estimated that the annual value for all nanotechnology-related products will be closer to $1 trillion.[4,8] Nanotechnologies are estimated to have impacted $251 billion across the world economy in 2009. This is estimated to grow to $2.5 trillion by 2015.[9,10]

ENPs are used herein to refer to nanoparticles that are designed and intentionally produced, with generally more narrowly defined sizes and composition than natural and unintentionally produced nanoparticles (e.g., black carbon). ENPs can be classified into five groups based on their chemical composition and functions: (i) carbon nanotubes and related products such as fullerenes, (ii) metal-containing products (including metal oxides), (iii) semiconductor nanocrystals (e.g., quantum dots; CdSe/ZnS and InGaP/ZnS), (iv) zerovalent metal products (e.g., zerovalent iron), and (v) dendrimers.[11] The size of these ENPs (1−100 nm in at least one dimension) lies somewhere between that of individual molecules and the corresponding bulk materials of the same chemistry. The physicochemical properties (e.g., redox potential, coagulation rates, and dissolution rates) of ENPs are very different from those of larger particles composed of the same basic elements. ENPs have generally high reactivity and surface area and tunable optical and other properties.[12−15]

Because of their widespread use in consumer products, it is inevitable that these emergent pollutants (nanowaste) will find their way into aquatic, terrestrial, and atmospheric environments, with the consequent potential health and/or environmental effects.[1,16−28] Despite an increasing number of studies, their fate and behavior in the environment remains largely

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unknown, especially in aquatic ecosystems.[29−34] In this perspective, we examine the environmental behavior and ecotoxicity of ENPs to algae—both direct and indirect effects. Algae in the surface ocean account for about half of all the global photosynthetic activity,[35,36] making them a major driving force in the sequestration of CO_2 from the atmosphere. Of this photosynthetic production, 40−60% is released back into the ocean as exopolymeric substances (EPS) into the dissolved organic carbon (DOC) pool, contributing to the primary marine carbon reservoir.[37−42] The recent discovery that ∼10% of the DOC pool can assemble to form porous microscopic gels that are readily colonized and metabolized by marine bacteria has opened a novel lens to view carbon cycling in the oceans.[39,42−48] Microgels serve as an important nutritional source for the marine food web in the deep ocean, raising the possibility of ENPs impacting higher-level organisms, from protozoa to metazoa.[49]

In 2008, Navarro et al.[50] published an article summarizing the then state of the art knowledge of the ecotoxicity of ENPs on algae, plants, and fungi. There was surprisingly little known at the time about the effect of ENPs on algae.[51−53] The number of articles has since risen exponentially, and today the nanotoxicity of ENPs has been studied intensively. Their small size endows ENPs with unique physicochemical characteristics and versatile applications, but it is these characteristics that ultimately associated with their adverse biological effects, such as inhibition of photosynthesis, changes in behavior and self-development, reproduction at the macroscopic level, and lipid, protein, and DNA oxidation at the molecular level in a wide variety of organisms.[18,19,54,55] While the unintended environmental impacts still remain largely unknown, we now know that the hydrophilicity/hydrophobicity of ENPs is a key factor controlling their ability to reach coastal waters, as well as their bioavailability and biological uptake.[11,19,32,34,56,57]

BEHAVIOR OF ENPS IN AQUATIC ENVIRONMENTS

While ENP surface properties affect their aggregation behavior in the aquatic environment, their dissolution is dependent on (i) ionic strength (∼0.0015 mol kg^{-1} in freshwater to ∼0.72 mol kg^{-1} in seawater), (ii) the presence of various surface coatings (amine, carboxyl, other, or none), and (iii) the presence of and the composition of EPS or natural organic matter (NOM), including but not limited to those produced by algae.[11,19,50] The interactions between freshwater, estuarine, and marine algae and these materials is highly diverse. For instance, considering the electrostatic interactions, ENPs are expected to be more soluble in freshwater with lower pH and are more likely to aggregate in high ionic strength seawater.

Aggregation and deposition (attachment) are two interrelated processes that ultimately determine the distribution and fate of ENPs in water. The limited research suggests that the principle for colloidal fluid transportation may also apply to ENPs in many cases. Thus, ENP deposition/aggregation can be defined as a two-step process of particle transport followed by attachment.[58] Transport of ENPs may be dominated by convection and diffusion, whereas attachment is controlled by the total interaction energy between two objects. The collision frequency (transport) can be largely described by Smoluchovsky's equations, while the collision event that results in aggregation/deposition mostly follows the DLVO theory.[59−64] ENP transport and fate in the environment is dependent not only on physical parameters, such as temperature, ionic strength, pH, particle concentration, and size,[29,58,63,65,66] but also on the relative hydrophobicity/hydrophilicity of ENPs,[19,67−69] which is not described by DLVO theory.

NOM can add a level of complexity beyond the scope of the DLVO theory. Although ENPs tend to form aggregates in aquatic environments, especially when the ionic strength is high, NOM can both increase their stability by coating their surface with negative charges and by steric repulsion[39,42,70] or decrease stability through a variety of mechanisms, including bridging[71] and pearls-on-a-string formation.[70] With increased ENPs stability by NOM, more and more ENPs may remain suspended such that there will be an increased likelihood of interactions with aquatic organisms.[67,68,72−76] Given that ENPs will aggregate or interact (bind) with NOM, their sorption to algal cells may be expected.[77,78] There is a considerable deal of study required in order to understand the fundamental processes and mechanisms of the interactions between ENPs and the aquatic environments, particularly ENPs' aggregation, deposition, and mobilization behavior. Given the importance of primary productivity and nutrient cycling by algae and the potential for trace metals associated with metal-containing ENPs (e.g., CdSe quantum dots) to be biotransferred and biomagnified in the food chain,[11,57,78,79] the toxicity of metal-containing ENPs specifically requires a focused effort if we are to better predict their fate as well as their biological effects.

CAPPING AGENTS/SURFACE COATINGS

The surface properties of ENPs are one of the most important factors governing their stability, mobility, and/or aggregation into larger particles and deposition in aquatic systems.[80−82] Stable suspensions of ENPs (e.g., particles rather than aggregates) are in fact a prerequisite for efficient interactions with algae. Great efforts have recently been made toward improving the water stability of ENPs by utilization of surface coatings that alter the solubility, surface charge, and thus their relative hydrophilicity/hydrophobicity.[83−85] Surface properties of metal oxide ENPs are also determined by their acidity constants and zero point of charge.[86−89] Nonmetallic ENPs such as carbon nanotubes and fullerenes have hydrophobic surfaces and are not readily dissolved in water. In order to solubilize these ENPs, they must first be surface functionalized with polar groups.

Capping agents protect ENPs from degradation, change their properties (by the addition of catalytically active species, various drugs, and/or specific binding sites), and/or may prevent aggregation due to either charge or steric stabilization mechanisms. Capping agents may be organic molecules, polymers, biological molecules, or carriers of specific functionalities.[13,90] For example, metallic ENPs are usually coated with inorganic or organic compounds (e.g., amine, citrate, cysteine, carbonate) or surfactants (e.g., sodium dodecyl sulfate).[80] In some cases, the surface coatings on ENPs have been observed to eliminate ENP toxicity to various organisms, from bacteria to human skin keratinocytes.[33,91,92] Possible explanations include a reduction of ENP dissolution and/or a reduction in direct interactions between nanoparticles and organisms.

Given that capping agents are an integral component of many ENPs, the consideration of ENPs behavior without understanding the chemistry of the capping agent will lead to misunderstandings of their properties and/or misinterpreting the findings of toxicity studies. Further, these physicochemical modifications in the relative hydrophilicity/hydrophobicity of

ENPs likely alter the potential interactions between ENPs, algae, and NOM, which will ultimately cause changes in the fate and transport behavior of ENPs in the aquatic environment as well as in aquatic organisms.

■ ROLE OF NATURAL ORGANIC MATTER

As a ubiquitous component of aquatic systems, NOM (including EPS) may influence the surface speciation and charge of ENPs and thus affect their aggregation/deposition properties. Buffle et al.[71] distinguished three groups of NOM compounds based on their biophysical properties: (i) rigid biopolymers, including the polysaccharides and peptidoglycans produced by algae or bacteria, (ii) fulvic compounds mostly from terrestrial sources, originating from the decomposition products of plants, and (iii) flexible biopolymers composed of aquagenic refractory organic matter from a recombination of microbial degradation products. While it is thought that rigid biopolymers can induce aggregation/deposition through gel formation,[39,42,70] the latter two groups may work by modifying the particle or its surface charge due to their high surface charge density.[93] While dispersed particles will be destabilized when their surface charge is nearly neutralized, their stability can also be increased due to electrostatic or steric repulsion.[34,77,94] The interactions between ENPs and NOM will most likely determine the fate of ENPs in aquatic systems. The formation of larger aggregates by high molecular weight NOM compounds will favor the removal of ENPs into sediments, thereby *decreasing* their bioavailability. By comparison, solubilization by natural surfactants such as lower molecular weight NOM compounds will *increase* their mobility and thereby their bioavailability.

EPS excreted from bacteria and algae are polysaccharide-rich anionic colloidal biopolymers critical for the formation of marine gels, marine snow, and biofilms, as well as for colloid and trace element scavenging and for providing protection against virus infection.[39−42,70,95] EPS from biofilms have been categorized as (i) inactive (neutral polysaccharides), (ii) sorptive (charged and hydrophobic polymers), (iii) active (enzymes), (iv) surface active (amphiphilic polymers), (v) informative (recognition/specificity or genetic information), and (vi) nutritive (sources of carbon, nitrogen, phosphorus). EPS from free-living algae and bacteria have not yet been fully characterized or categorized to the same extent but can be expected to have similar functions and/or properties. Theoretically, EPS can stabilize ENPs dispersions or induce their aggregation. In this way, EPS may either exacerbate or reduce the direct toxicity of ENPs to aquatic organisms.[69,74−76,96] EPS may also provide abundant binding ligands for the trace metal ions released from metal-containing ENPs, reduce their accumulation, or change their subcellular distribution in cells and thus influence the indirect effects of ENPs.[19] EPS production has been shown to increase in algae upon exposure to ENPs, contributing to detoxification mechanisms.[68,73,74] The high production of EPS may not only protect algae against stress conditions such as those induced by ENPs but also play an important role in the biogeochemical cycling of trace metals released in the ocean. Consequences include but certainly are not limited to a change in nutrient utilization by free-living microbes in the water column and sinking rates.[45,48,97]

NOM−ENP interactions are undoubtedly colloid, pollutant, and species specific. NOM excreted by aquatic organisms may provide a feedback response, altering ENPs toxicity. For example, fulvic acids helped disperse TiO_2 ENPs in freshwater systems in the absence of Ca^{2+} or phosphate.[98] This was also the case for Ag-ENPs in artificial seawater due to their high surface charge density.[74] Chen et al.[69] found that as little as 10−100 ppb of polystrene ENPs released into the aquatic environment can cause significant changes of the EPS-assembly kinetics and increase the equilibrium microgel sizes of EPS produced by the green alga *Ankistrodesmus angustus* (Chlorophyta) and the diatoms *Amphora sp.* and *Phaeodactylum tricornutum* (Bacillariophyta). Hydrophobic ENPs induced significant acceleration of EPS assembly, even under Ca^{2+}-free conditions. Results showed that ENPs bound to the hydrophobic domains on the EPS serve as cross-linkers for the microgel matrices (low binding energy <50 kJ/mol). Various functional groups distributed on dissolved organic matter (DOM) polyelectrolyte chains and charges on chain surfaces serve as binding sites. The divalent Ca^{2+} ions surrounding the DOM polymers can serve as cross-linkers to hold polymer chains together to stabilize the DOM polymer chains through electrostatic interactions.[43] For amphiphilic polymer chains, such as those produced by certain algae, hydrophobic domains can act as the binding sites to promote polymer matrix (gel) formations.[42,47,69,99]

Dynamic laser scattering was used to monitor the assembling kinetics of DOM/particulate organic matter (POM) by measuring changes in particle size as a function of time.[69,100] DOM microgels typically reached an equilibrium size (4−6 μm) within ∼60 h, but in the presence of 10 ppb 23 nm polystyrene hydrophobic ENPs, gel formation was accelerated by 200%. ENPs in filtered seawater medium with different surface modifications (positive charge, negative charge, no charge) showed similar DOM assembly acceleration and microgel equilibrium sizes. However, when the experiment was repeated using lake water as the medium, the sizes of the gels at equilibrium were similar, but the DOM assembly kinetics were dependent on the surface charge on the ENPs: amine functionalized > no charge > carboxyl functionalized. It was hypothesized that the differences observed were caused by the high ionic strength of seawater relative to the negligible concentration in lake water. Ions surrounding ENPs may shield the charges on the surface. As a result, high concentration ions may reduce the electrostatic interactions between marine DOM and ENPs. These observations highlight the important roles of electrostatic interactions and aquatic environments in ENPs−DOM assembly.[69,100] Hence, interactions between ENPs and DOM not only depend on the properties of ENPs but also on the properties of DOM.

■ DIRECT VERSUS INDIRECT TOXIC EFFECTS

Direct toxic effects of ENPs on organisms are primarily determined by their chemical composition and surface reactivity. Indirect effects are those caused by physical restraints or the release of toxic ions (e.g., from metallic ENPs) or from the production of reactive oxygen species (ROS). The latter is thought to lead to incremental cellular responses classified as defense, pro-inflammatory effects (in plant and animal cells), and cytotoxicity.[18,19,34,91,101] Toxicological effects of ENPs may include (i) oxidative stress and inflammation related to production of ROS, depletion of glutathione, and accumulation of oxidized glutathione in response to ROS production; (ii) protein denaturation, membrane damage, DNA damage, immune reactivity, and the formation of foreign body

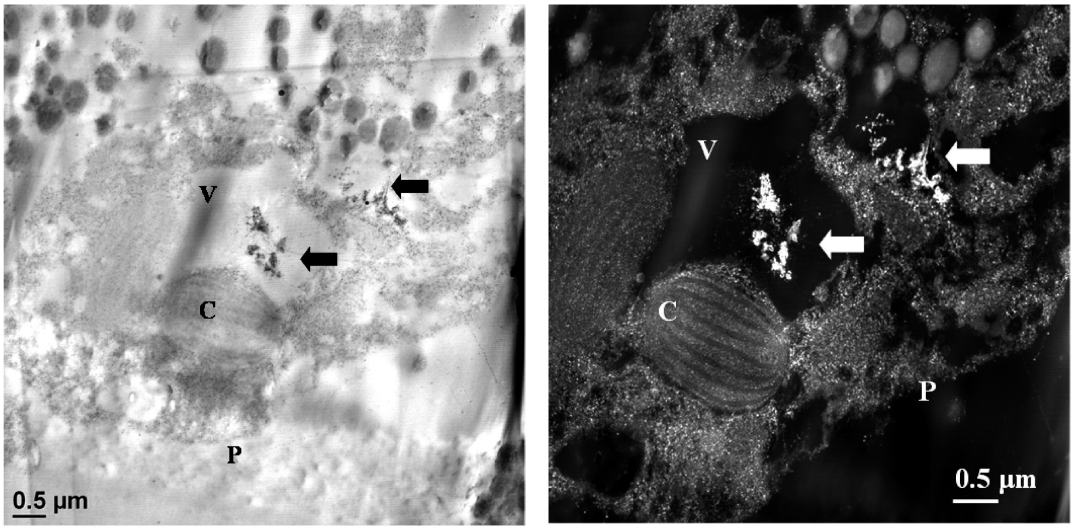

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Figure 1. Transmission electron microscope (a) and Z-contrast dark-field scanning transmission electron microscope (b) images of a single *Ochromonas danica* cell in the Ag-ENP addition (92.7 μM) treatment.[76] Arrows indicates the locations of Ag-ENP inside the cells, which was further confirmed by energy dispersive X-ray spectrum. The letters "P" represents the plasma membrane of the cell, "V" means vacuole, and "C" is chloroplast.

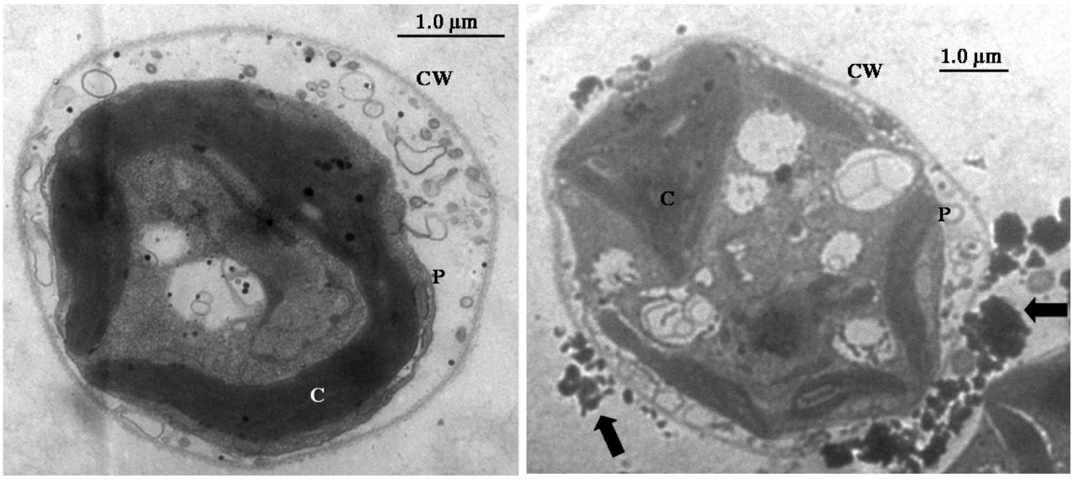

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Figure 2. Transmission electron microscope images of *Chlamydomonas reinhardtii* in the presence of (a) 100 mg L^{-1} well-dispersed polyacrylate-coated TiO_2 nanoparticles or (b) their bare counterparts that aggregated easily in the WC medium.[114] Arrows indicate the attachment of bare TiO_2-ENP on the cell surface, which was further confirmed by energy dispersive X-ray spectrum. No polyacrylate-coated TiO_2 nanoparticles were found either on the cell surface or inside the cells. The letters "CW" represents the cell wall, "P" means the plasma membrane, and "C" is chloroplast.

granulomas;[17−19,26,27,34,102] and (iii) a reduction or loss in photosynthetic activity in algae and plants.[50,53,57,74−76,103]

Metallic ENP dissolution has been found to affect algal growth in three ways. First, metallic ENPs dissolve in the bulk media, releasing their metal ions which then diffuse to the algal surface, leading to deleterious toxic effects after internalization.[74,75] Second, ENPs within the diffusion layer of algal cells or attached to the algal cell surface may dissolve. This would then provide additional metal ions directly to the algae. This may be what was found by Navarro et al.[53] in which case Ag-ENPs were found to be more toxic than $AgNO_3$ (based on the free Ag^+ concentrations in the media $[Ag^+]_F$). This toxicity can be reduced or eliminated by the presence of cysteine (a strong Ag^+ binding ligand). Third, metallic ENPs may enter algal cells directly and liberate metal ions once inside the cells (Figure 1). In this scenario, the $[Ag^+]_F$-based EC_{50} will be lower for Ag-ENPs compared to Ag^+ addition treatments only. This was observed in a study that found Ag-ENPs located inside cells of a freshwater algal species.[76] It is however unclear whether Ag-ENPs inside cells directly inhibited algal growth and other activities (e.g., photosynthesis) or indirectly by the release of Ag^+ internally. Once inside algal cells, there is a potential for both biotransference and biomagnification of metals to higher trophic levels. While many trace metals (elements) have a nutritive role (e.g., Fe, Mn), others are toxic (e.g., Ag) or have unknown functions despite being present in cells (e.g., Cd).[79,104,105] Some trace metals maybe nutritive at low concentrations but become toxic when over accumulated (e.g., Cu or Zn).[52,75,106]

In recent years, other toxicity mechanisms of metallic ENPs have been investigated, including to what extent dissolution plays a role. While this is a major factor in some cases,[17,52,74,78,107] in others the adverse impacts of ENPs could not be completely explained by their metal ion release.[108,109] Further, the toxicity of some metallic ENPs has been found to be light-dependent (e.g., TiO_2), becoming more toxic under irradiation,[51,110] whereas others (e.g., CeO_2) have antioxidative effects.[111] In a recent review of bioaccumulation studies, Hou et al.[112] found that daphnia, fish, aquatic worms, and earthworms are the most commonly studied ecological receptors in freshwater systems. Current evidence suggests that ENP accumulation is generally low in fish and earthworms with a logarithmic bioconcentration factor ranging from 0.85−3.43 (L kg^{-1}). Hou et al.[112] concluded that ENPs accumulated at the lower trophic levels can transfer to higher trophic level animals with the degree of biomagnification dependent on the specific food web investigated.

A further consideration is that ENPs themselves may serve as pollutant carriers (indirect effect). In this manner, ENPs may enhance or reduce the bioavailability of other toxic substances to algae.[50,78,112] Supporting such concerns, Yang et al.[113,114] recently showed the interactions between classical pollutants (Cd^{2+}), ENPs (TiO_2-ENP), and the green alga *Chlamydomonas reinhardtii* (Chlorophyta) (Figure 2). They found that TiO_2-ENPs could alleviate the inhibitive effects of Cd^{2+} on the green alga. Cd^{2+} adsorption by TiO_2-ENPs decreased its ambient free ion concentration and its intracellular accumulation in the cells as well as its toxicity. Other studies have also shown that TiO_2-ENPs can remove heavy metals (Pb, Cd, Cu, Zn, and Ni) from water.[115,116] Given these findings, the carrier effects of ENPs should also be considered.

SPECIFIC EXAMPLES ILLUSTRATING INTERACTIONS BETWEEN ENPS AND ALGAE

Silver Nanoparticles (Ag-ENPs). Engineered nanoparticles of silver (Ag-ENPs), believed to be the most commercialized nanomaterial, are extensively used as bactericides or fungicides and have found versatile applications in diverse products like household appliances, cleaners, clothing, cutlery, children's toys, and coated electronics,[117−120] as well as in coatings of medical equipment such as catheters, infusion systems, and medical textiles.[121,122] Because of their extensive applications, Ag-ENPs have been extensively studied.[31,123−132] This is also the case for ZnO-ENPs; both of which can enter coastal marine environments through sewer overflows and surface runoff given their numerous applications.[133] Ironically, what makes Ag-ENPs so valued in consumer products, that is, their significant antibacterial properties, is also the cause of their inherent toxicity to microbes in the environment.[34,132,134] Ag-ENPs have been shown to increase antibacterial activity of antibiotics such as vancomycin and amoxicillin when used on bacteria such as *Staphylococcus aureus* and *Escherichia coli*.[128] Although the high ionic strength of seawater may prevent a large-scale dispersion of ENPs in the marine environment, NOM, such as fulvic acid, humic substances, and thiols that have surfactant and binding qualities, has been shown to control their solubilization and dispersion. NOMs have reduced the potential toxicity of Ag-ENPs and/or stabilize Ag-ENP suspensions, especially in coastal areas.[74,94]

In addition, particle surface area (triangular plates, spherical, and rod shaped) is an important factor determining antibacterial properties as well as the extent and kinetics of particle dissolution.[125−127,135] A good example comes from the systematic dissolution study performed with Ag-ENPs by Miao et al.[76] They (i) found Ag^+ release limited by the total surface area of Ag-ENPs in freshwater treatments with longer periods (days) required for Ag^+ to reach their maximum concentration in the medium, (ii) observed a decrease in total dissolved concentrations of Ag^+ ($[Ag^+]_T$), and (iii) observed the distribution of Ag-ENP at high nanoparticle concentrations (28 and 93 μM) remained unchanged over a 6 day period. The decrease in Ag^+ release may be (i) because of the slow formation of insoluble Ag complexes with various ligands in the media (e.g., with chloride),[136] (ii) due to adsorption of Ag^+ to the beaker walls, or (iii) because Ag-ENP solubility decreased as its specific surface area decreased with time.[137,138] The lower $[Ag^+]_T$ in the lower nanoparticle concentration treatments was unexpected, as theoretically the Ag-ENP solubility should be the same[137,138] unless, of course, their nanoparticle size was different from each other. Laban et al.[136] also observed that a higher percentage of Ag-ENPs were dissolved at lower nanoparticle concentrations. They found a more substantial difference in Ag-ENP concentration than that of $[Ag^+]_T$ between the different nanoparticle concentration treatments with a decrease in $[Ag^+]_T$ being less significant than a decrease of the nanoparticle concentration itself. Laban et al.[136] concluded that the different $[Ag^+]_T$ obtained in the different Ag-ENP concentration treatments could be explained by surface area limited release of Ag^+. Both the studies found that Ag-ENP dissolution and Ag^+ precipitation are a dynamic process in experimental systems.[76,136]

Surface complexation may be a mechanism by which Ag-ENPs are solubilized in the presence of glutathione. The time taken for $[Ag^+]_T$ to increase in the medium in the presence of glutathione (relative to a control with no glutathione) reflects Ag-ENP solubilization that can be limited by (i) the adsorption of glutathione to the Ag-ENP surface or (ii) by the dissociation of glutathione−Ag^+ complexes from the nanoparticle surface.[74−76] The second possibility is more likely given the rapidity of surface adsorption.[139] However, in the study of Li et al.,[91] the addition of glutathione did not inhibit the attachment of Ag-ENPs to the algal cell surface, suggesting that part of the Ag-ENPs had already entered the cells. But what happens in the natural environment? In experiments with Ag-ENPs and glutathione, the formation of glutathione−Ag^+ complexes in an aggregated form cause the decrease of Ag^+ in the media, especially when glutathione concentrations are high. The alternative possibility is that the glutathione−Ag^+ complexes are not stable, and their organic fragment(s) may be oxidized leading to the production of mononuclear or polynuclear Ag−S complexes with lower solubility.[139−141]

Below, we work through some examples from studies performed in marine (seawater) versus freshwater environments as it is widely accepted that the ionic strength of the medium plays a critical role in dissolution and aggregation behavior of ENPs.

Ag-ENP Seawater. Miao et al.[74] reported that silver ions from the oxidative dissolution (corrosion) of bare Ag-ENPs were toxic to the marine diatom *Thalassiosira weissflogii* (Bacillariophyta) rather than the ENPs themselves. Miao et al.[74] also found that most of the Ag-ENPs formed nontoxic aggregates (>0.22 μm) in seawater (salinity = 34, ionic strength = ∼0.72 mol kg^{-1}, pH 8.2). The rapid aggregation of the Ag-ENPs resulted in considerable Ag^+ release and the resulting observed toxicity. This indirect interaction led to severely suppressed cell growth, photosynthetic activity, and cellular chlorophyll production in the diatom. When the $[Ag^+]_F$ was greatly reduced by diafiltration or thiol complexation (glutathione or cysteine), no toxicity to *Thalassiosira weissflogii* was observed. Ag is one of the most toxic trace metals known to aquatic algae (freshwater, marine, and others) even at low concentrations.[142,143] The nature of Ag-ENPs (small size, very high surface area to volume ratio) may facilitate their corrosion in contrast to elemental Ag, one of the most corrosion resistant metals known. In order to elucidate whether polysaccharide-rich EPS could alter the direct and/or indirect toxicity of Ag-ENPs, Miao et al.[74] also grew the diatom *T. weissflogii* under nutrient (nitrogen as nitrate and phosphorus) limitation. This is known to cause algae to excrete more carbohydrate relative to cells growing in nutrient replete media. Both dissolved and particulate polysaccharide concentrations were higher in nutrient-limited cells, coinciding with a higher Ag^+ tolerance, suggesting that EPS is involved in Ag^+ detoxification.

Ag-ENP Freshwater. In studying the interaction between the carbonate-coated Ag-ENPs and the freshwater alga *C. reinhardtii*, Navarro et al.[53] found that Ag-ENPs were toxic by serving as a source of Ag^+. Similarly, Miao et al.[76] found Ag^+ ions were toxic to the freshwater alga *Ochromonas danica* (Chrysophyta). In both studies, the Ag^+ toxicity occurred in the range previously reported for freshwater algae (EC_{50} = 12−930 nM Ag).[142,143] The latter study found that despite their good dispersibility in freshwater, the Ag-ENPs (coated with the hydrophilic ligands polyacrylate sodium) continuously aggregated and dissolve rapidly. Miao et al.[76] was one of the first studies to show that Ag-ENPs could be taken in and accumulated within algal cells, where they were then able to exert their toxic effects. Nanoparticle internalization may be an alternative pathway through which algal growth can be impacted.

Zinc Oxide Nanoparticles (ZnO-ENPs). The luminescent properties of zinc oxide-engineered nanoparticles (ZnO-ENPs) have attracted considerable attention due to their potential application in ultraviolet light-emitting devices, including in thin films, nanowires, nanorods, or nanoparticles[144] and optoelectronic and electronic devices. They also can be used in the production of chemical sensors and solar cells[145] and sunscreens and cosmetics because of their property of blocking broad UV-A and UV-B rays.[146] This is a potentially important diffuse source of ENP contamination because of wash off from individuals into the environment.[32,147]

In a comparative toxicity study of nanoparticulate ZnO, bulk ZnO, and $ZnCl_2$ to the freshwater microalga *Pseudokirchneriella subcapitata* (Chlorophyta), Franklin et al.[52] found that the toxicity of ZnO-ENPs was partly related to their solubility. ZnO-ENPs toxicity to the marine diatom *Thalassiosira pseudonana* (Bacillariophyta) was explained to be a function of Zn^{2+} release.[75] This conclusion was based on comparable inhibitive effects from ZnO-ENPs with or without the ultrafiltration through a 3 kDa membrane and from media in which only Zn^{2+} was added (at an equivalent concentration). By comparison, the primary particle size of the dispersed ZnO-ENPs affected the overall toxicity to the marine alga *Dunaliella tertiolecta* (Chlorophyta).[57] Further, this study found nano ZnO was more toxic than its bulk counterpart. Considering the importance of dissolution in ZnO-ENPs toxicity, Zn^{2+} release kinetics has been examined under different conditions. It has been found to be influenced by their solubility and size distribution[94,148] and the pH and their aggregation state, that is, specific surface area.[75] Compared with deionized water, ZnO-ENPs dissolution rates were accelerated in seawater, whereas ZnO-ENPs concentration itself only had a very small effect on Zn^{2+} release.[75] Further, it was found that NOM compounds such as EPS could either enhance or reduce Zn^{2+} release, depending on their chemical composition and concentration.[75]

So challenges with comparing studies of ZnO-ENPs−algae interactions, aside from the nature of the aqueous media itself, is that in some cases the metal ENPs may be more toxic than either their ionic forms or their parent compounds,[50,57] but in other cases, the dissolved Zn ions are the most toxic agents,[52,75,133] while in other studies it is the free Zn^{2+} in the media.[52,149] This and other issues arising from the toxicity of ZnO-ENPs to ecological receptors (bacteria, algae and plants, aquatic and terrestrial invertebrates, and vertebrates) are discussed in the review by Ma et al.[147]

Titania Nanoparticles (TiO_2-ENPs). Photocatalysis of titania (TiO_2) nanoparticles is very important in the photodegradation and mineralization of toxic organic pollutants (e.g., treatment of wastewater and groundwater and the degradation of air pollutants).[85,150−152] TiO_2-ENPs, as ZnO-ENPs, are widely used in sunscreens and cosmetics because of their photoactivity.[15] TiO_2 nanoparticles with high morphological specificity have applications in solar energy conversion, photocatalysis, and photovoltaic devices.[153,154] Their annual production is projected to exceed 2.5 million tons by 2025.[9] Given this it is anticipated that TiO_2-ENPs will enter the environment during their production, utilization, and disposition.[32,155,156] While TiO_2-ENPs have not yet presented significant health risks for consumers, they do have known negative impacts on the aquatic environment.[157,158]

Toxicity of TiO_2-ENPs was found to be dependent on their specific surface area, that is, the smallest (25 nm) particles showed a clear concentration−effect relationship, while the larger (100 nm) particles were found to be less toxic to the freshwater algae *Desmodesmus subspicatus* (Chlorophyta).[51] In this early study, there were no measurements of aggregation size, which could also have had an influence on the inhibitory effects observed. Other algal studies found negligible to intermediate toxicity associated with TiO_2-ENPs.[113,114,149,159,160] The growth of *Pseudokirchneriella subcapitata* (a unicellular freshwater green alga; Chlorophyta) inhibited by nonadsorbed Cd^{2+}, was either alleviated or enhanced by different − size, structure - TiO_2-ENPs.[160] In contrast Yang et al.[113,114] found that polyacrylate-coated TiO_2-ENP could significantly diminish Cd^{2+} toxicity to the green alga *C. reinhardtii* by decreasing its ambient free ion concentration. At relatively high TiO_2 concentrations (100 mg L^{-1}), these particles were found to accumulate in cells.[114]

Other studies have shown that TiO_2 ENPs photon absorption leads to the creation of highly excited electron−hole pairs which act as strong oxidizing and reducing agents (redox agents) that target organic molecules. This can also lead to the generation of ROS that induce oxidative damage in bacteria, crustaceans, fish and mammal cells.[17,110,161−165] In rainbow trout, inflammatory injury and respiratory distress were also observed.[166,167] Numerous other toxicological studies have been performed to evaluate the environmental risks of TiO_2-ENPs.[11,157,158] Like other ENPs, the damaging effects of TiO_2-ENPs are magnified when present in a nanoparticle form, wherein there is a much higher surface area than standard size TiO_2-ENPs such that in an equivalent mass of material the reactivity is much greater.

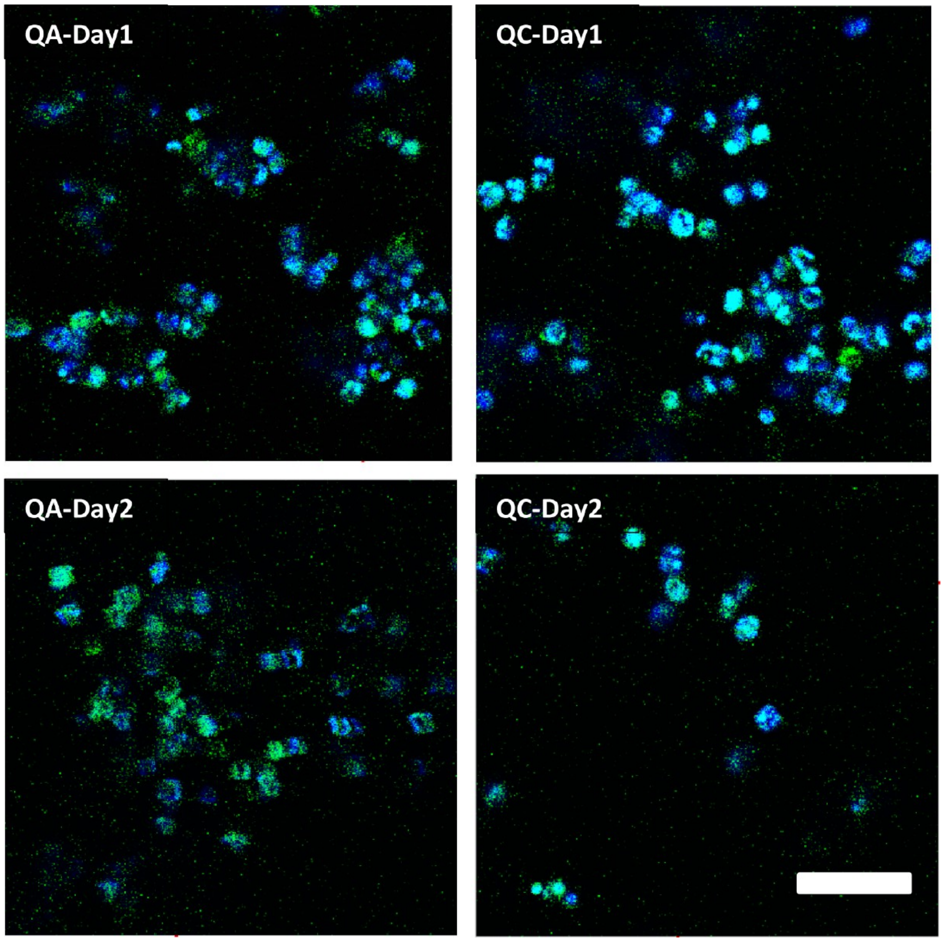

Figure 3. Interactions between QDs and *Thalassiosira pseudonana*.[73] The QDs (diameters ~20–25 nm) used in this study were composed of a CdSe core and ZnS shell with amine (QA) and carboxylate (QC) functional modifications. *Thalassiosira pseudonana* was cultured in the f/2 medium and grown at 19 ± 1 °C with 18.5 nM QA and 10.1 nM QC, respectively. The spatial distributions of QD (λ_{ex} = 488 nm/λ_{em} = 515 nm, pseudo image color green) and algae (λ_{ex} = 633 nm/λ_{em} = 650 nm, pseudo image color blue) were monitored with laser scanning confocal microscopy at during Day 1 and Day 2. Both QA and QC tended to aggregate in the culture matrix and associate with algal cells. After 48 h, QA showed more obvious association with algae than QC. (Scale bar = 25 μm).

Unlike other metallic ENPs, TiO_2-ENPs usually come in two allotropic forms: rutile and anatase. These have different surface properties, reactivities (rutile is lipophilic whereas anatase is hydrophilic), and consequently, toxicities.[23,103] In an investigation using algae, daphnid, rotifers, and plants as model organisms by Clément et al.,[103] anatase was found to be toxic in all tests (acute and chronic). Because of its lipophilicity, the rutile crystalline structure formed larger aggregates in the freshwater medium such that it had a lesser effect on the biological organisms. This highlights one of the challenges (see more below) when investigating ENPs using time course studies. Not only does their size and composition change, but the form will also play a critical role in deciphering ENP–organism interactions.

Quantum Dots (QDs). Quantum dots (QDs), also known as semiconductor crystals, are made up of a reactive core surrounded by a silica or ZnS shell to protect the core (e.g., CdS, CdSe, and CdTe) from oxidation and thus enhance their photostability.[14,90,168−172] They have promising potential applications in biological imaging, disease diagnostics, and therapeutics as a result of their photophysical properties including broad excitation spectrum, tunable emission wavelength, and quite stable fluorescence.[173−179] Quantum dots are small assemblies of semiconductor materials in the range between 2–10 nm.[180] They have been referred to as artificial atoms due to their unusual structures as they are considered to possess neither a solid structure nor a single molecular unit.[14] In terms of toxicology effects on organisms, the two major determinants are QDs physicochemical properties (e.g., size, functional groups, oxidative and photolytic stability) and environmental conditions (e.g., ionic strength, NOM).[56,173,181]

The ecotoxicity of quantum dots has only recently gained interest.[55] For instance, the toxicity of CdTe may be linked to the leaching of toxic heavy metals from the colloidal form and derived from the intrinsic properties of their size and surface chemistry.[182] In theory, they could transfer energy to nearby oxygen molecules and lead to the formation of ROS, which may lead to cell inflammation, damage, and death. In fact, Choi et al.[183] showed that QDs induce cell death by lipid peroxidation of human neuroblastoma cells. More recently, the ecotoxicological effects of CdTe QDs to freshwater mussel *Elliptio complanata* were reported showing that these ENPs cause oxidative stress in gills and damage DNA.[184]

Bare CdSe QDs, lacking the ZnS shell, undergo salinity-dependent degradation processes when examined at salinities typically found in coastal and open ocean environments (7.7 and 38.3, respectively).[185] Zhang et al.[68] found that regardless of the surface coating on QDs, immediate aggregation was

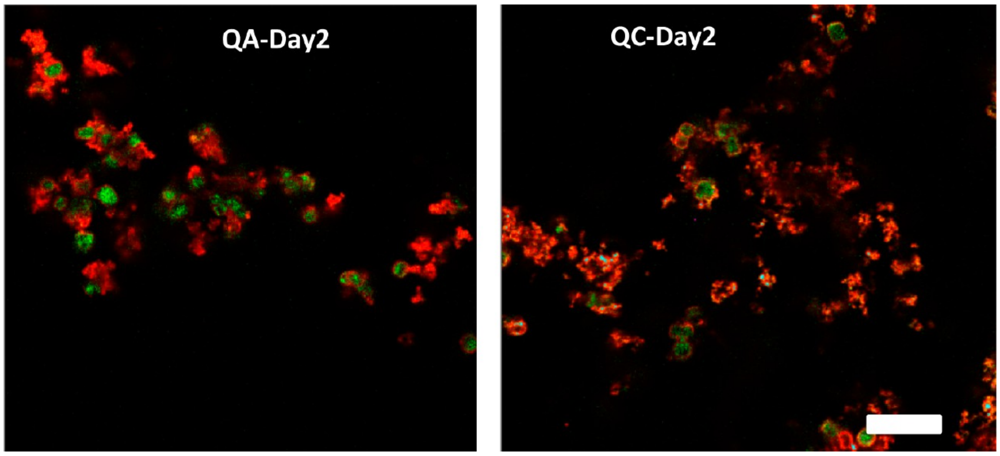

Figure 4. Distribution of QDs in the EPS matrixes of *Thalassiosira pseudonana*.[73] Fluorescence conjugated concanavalin A (25 μg mL^{-1}) was used to label the glucose and mannose residues of polysaccharide within EPS matrix. The fluorescent signal of QDs (λ_{ex} = 488 nm/λ_{em} = 515 nm, pseudo image color green) and concanavalin A (λ_{ex} = 561 nm/λ_{em} = 605 nm, pseudo image color red) were collected with laser scanning confocal microscopy. Amine-functionalized QDs (QA) with positive surface charged surfaces may facilitate assembly between QAs and the negatively charged EPS matrix. The negative surface charges on carboxyl-functionalized QDs (QC) may decrease the binding efficacy to EPS. (Scale bar = 25 μm).

detected in a high ionic strength environment (artificial seawater). When combined with EPS, this resulted in the formation of microgels from 1 to 2 μm and 2.5 to 6 μm for carboxyl-, non- and amine-functionalized QDs, respectively. In these experiments, EPS was acting as a strong assembly agent for the ENPs as a result of both hydrophobic and electrostatic interactions. The positively charged amine-functionalized QDs showed a stronger affinity for EPS than negatively charged carboxyl-functionalized QDs. In addition, Zhang et al.[68] showed that the amine-functionalized QDs demonstrated minimal degradation, while carboxyl- and non-functionalized QDs started to degrade after only four days of light exposure. This difference reflects the decreased stability of some coated QDs in the presence of EPS (and thereby greater degradation as reflected in the increased release of Cd into the dissolved fraction), while positively charged surfaces contribute to the relative stability of QDs (by strengthened cross-links in the gel networks).

This finding raised interesting insights into the chemistry of the QD-EPS interactions. Is enhanced degradation of QDs caused by a significant source of ROS associated with the EPS? Do the effects depend on the composition (ratio of proteins/carbohydrates) of the EPS? Given that proteins can be damaged and degraded by a large number of reactions involving ROS, did protein degradation in the EPS lead to oxidative damage of QDs? Or did the QDs themselves trigger the production of ROS? Zhang et al.[68] showed that the instability of QDs under light exposure could be successfully ameliorated by the addition of an antioxidant (N-acetyl cysteine), pointing to oxidative and photolytic stability of QDs as a determining factor in governing the fate of QDs in marine environments. The interactions between functionalized (amine and carboxyl) CdSe QDs and the marine diatom *T. pseudonana* were investigated by Zhang et al.[73] using laser scanning confocal microscopy (LSCM). Carboxyl-functionalized and amine-functionalized QDs behaved differently as shown in Figures 3 and 4. After five days in culture, carboxyl-coated QDs had mostly dissolved leaving only the *T. pseudonana,* while amine-functionalized QDs aggregated rather than dissolved. Aggregation/dissolution kinetics monitored by Cd^{2+} released into the <3 kDa fraction further confirmed the phenomenon. LSCM was used to quantify the amounts of attached QDs as well as provide 3-D visualization of the interactions between QDs and the surrounding environment, e.g., the presence of algae or EPS.

Given QDs are susceptible to photolysis and oxidation, it has been reported that they behave differently when experiments are performed with algae/EPS/NOM in the light versus dark. For example, gum arabic-coated QDs were found to be more toxic when irradiated with UV-B light.[186] UV reaching aquatic ecosystems is increasing due to ozone depletion, acidification, and climate change.[187] This UV can induce phototoxicity to many environmental contaminants, including polycyclic aromatic hydrocarbons, heavy metals, and sulfonamides, as well as QDs that become unstable over time when exposed to UV.[177,188,189] When QDs are irradiated by light, their luminescence is enhanced; this is so-called photoluminescence enhancement or photoactivation.[190] Following the photoluminescence enhancement, QDs may release Cd^{2+} ions from their CdS surface owing to slow photocorrosion induced by oxidative stress.[191] Hence, it is not surprising that different light intensities induce different levels of oxidative stress on ENPs.[192] Elevated UV light conditions can also affect the formation of microgels.[193] UV cleaves DOC polymers and yields shorter-chain polymers that are too large to permeate the bacterial membrane yet too short to assemble into microgels in the ocean.[193] Zhang et al.[68] recently showed the critical role light plays in the interactions between EPS and QDs by examining QDs-induced EPS assembly under two photic conditions: dark and simulated daylight exposure. In the dark, significant aggregation was observed between amine-functionalized QDs and EPS from the marine diatom *T. pseudonana*. Under light exposure, amine-functionalized QDs and EPS aggregated on the first day but to a lesser degree than those in the dark. Significant light-induced disaggregation of QDs-EPS was observed after 36 h incubation under light conditions.

■ CHALLENGES

Navarro et al.[50] suggested considering "ENPs as miniaturized toxic delivery systems through food webs, by releasing compounds or reacting against biological molecules at each trophic level without a remarkable loss of toxicity". If this is indeed the case, ENPs may have more long-term effects on ecosystems relative to other pollutants. In recent reviews, the focus has been placed on the difficulties of defining the specific consequences of ENPs on ecological systems.[24,26,28,34,54] The main issue is that there are now a remarkable number of different (eco)toxicology tests that may be applied to ENPs making it difficult to not only interpret results but to also generalize findings between studies. This remains a research priority.[11,20,24] Further complicating studies is that nanoparticles affect the toxicity of other pollutants such as heavy metals and polycyclic aromatic hydrocarbons.[67,113,114,194−196] We will not reiterate the challenges previously defined but rather define several we feel also require attention.

When making or purchasing ENPs, one of the first tests performed is the measurement of the size of the particles. One of the challenges is that during a time course experiment, the size (because of aggregation) of the particles may change in addition to the composition (because of dissolution). For example, Miao et al.[75] found that although the ZnO-ENPs had an average primary particle size of 20 nm, they tended to form, with time, larger aggregates even in deionized water (this effect was more pronounced in seawater). The instability of dispersed ZnO-ENPs in water and their tendency to aggregate were also observed in other studies.[52,108,111,197,198] This results in studies examining the effect of nano- and microscaled oxide particles rather than just nanomaterials.

Well known to those working in this arena is that the interactions of ENPs with organisms are dependent on their size, shape, chemical composition, charge, surface structure and area, solubility, and aggregation state. In each case, investigators must characterize both the physical and chemical nature of the ENPs themselves and that of the media. The presence of impurities or release of materials that could influence the toxic effects of ENPs also has to be considered, especially when using metallic ENPs, whose toxicity can be altered through the release of metal ions. This requires the quantification of soluble metal ions in the toxicity testing medium.

Given the complexity in evaluating effects of intrinsic properties of ENPs and the environmental factors (NOM and EPS) in aquatic systems (dissolution and stability of ENPs by physicochemical processes, aggregation/disaggregation, and indirect chemical reactions, e.g., redox reactions), understanding ENPs toxicity to marine organisms, especially algae is challenging. Even with the growing number of studies, the specific mechanisms of toxicity of ENPs remain largely unknown because of the diversity of ENPs and the complex environmental behaviors they experience once they enter into aquatic systems.[19] Identification of the pathways of ENPs entering the environment[22] and quantification of the fluxes through ecosystems are still required, particularly across a broad range of salinity gradients (and thus ionic strength). Without this information, we still have a long road ahead to determine the behavior, fate, and bioavailability of ENPs once they enter ecosystems.

Another important consideration for environmental studies is that ENPs are not just one class of potential pollutant.[1,16−28,34,50,54,78,112] Given that ENPs contain a wide range of different materials with different physical, chemical, and toxicological properties, they should *not be* considered a single homogeneous group. For example, the core materials of inorganic ENPs are metal oxides (e.g., Fe, Zn, Ti, Ce), and quantum dots have metal centers (e.g., CdSe). If the capping agent is also considered, then there are no less than two forms of potential pollutants in any one particle. Each of these components has a potential impact once it enters the aquatic environment.

Study of the ENPs fate and impact in the environment is becoming increasingly important due to the current and future discharges, their known toxicity, and the gaps in our knowledge leading to difficulties in risk assessment and management.[1,28,34,199] Very little is known about mechanisms of biological uptake and toxicity modes of action, about transport in and between environmental and biological compartments, and their chemical behavior in the environment. There is a paucity of information on background concentrations and physical−chemical form of ENPs in the environment. The development of accurate and robust methodologies for the measurement of ENP concentration and form under realistic conditions is required.

SUSTAINABLE NANOTECHNOLOGY?

The main characteristics and prospects of nanotechnology are well developed. But whether this emerging industry can develop in a sustainable "green" manner remains under debate.[200] The World Commission on Environment and Development report of 1987 defines "sustainable development" as that which meets the needs of the present without compromising the ability of future generations to meet their own needs.[201,202] However, for industrial ecology to work on a worldwide scale, we still need to identify the gaps in knowledge and understanding of nanotechnologies in order to advise governments, industry, international organizations, and other stakeholders. It is now generally accepted that the novel attributes of nanotechnology demand new approaches for risk−benefit assessment and risk management, but the development of the technology still far precedes the policy and regulatory processes. In recent years, emphasis has moved to the need for life cycle-based assessments, that is, following ENPs over their entire life cycle to better understanding of the potential environmental and human health consequences of not only the nanomaterials themselves but of the nanoenabled products, too.[31,32,203] The new ethos is to incorporate life cycle thinking for making informed decisions at the product design stage, combining life cycle and risk analysis, using sustainable manufacturing practices, and employing green chemistry alternatives as possible solutions. It is not within the scope of this perspective to go into greater detail, but the reader is referred to the many excellent sources.[21,24,26,200,203−207]

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Notes

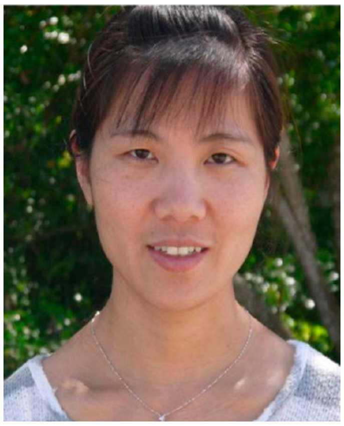
The authors declare no competing financial interest.

Biographies

Dr. Antonietta Quigg is a professor in the Departments of Marine Biology and Oceanography at Texas A&M University at Galveston and College Station, respectively. Antonietta Quigg obtained her Ph.D. degree in 2000 from Monash University (Melbourne, Australia). After postdoctoral training in the Environmental Biophysics & Molecular Ecology Program at the Institute of Marine and Coastal Sciences, Rutgers University (New Jersey, U.S.A.), she started her career at Texas A&M University in 2003. Her research is focused on using microalgae as model organisms to address questions related to water, climate, and energy. Both field- and laboratory-based experimental approaches are used to elucidate the importance of biotic and abiotic factors on influencing phytoplankton dynamics (evolution, physiology, ecology, and community composition). In recent years, her efforts have expanded to include understanding the fate and transport of the emergent pollutant, engineered nanoparticles, on aquatic systems (microbes and water).

Dr. Wei-Chun Chin obtained his bioengineering Ph.D. degree in 2000 from the University of Washington (Seattle), U.S.A. After postdoctoral training in the Department of Biomedical Engineering at Johns Hopkins University, Wei-Chun Chin started his career as an Assistant Professor at Florida State University. In 2005, he then moved to the University of California, Merced. His current research interests are (1) the study of the assembly kinetics of natural organic matter in aquatic environments, (2) the ecological impact of engineered nanomaterials, and (3) the applications and effects of nanomaterials on biological systems.

Dr. Chi-Shuo Chen received his Ph.D. degree in 2012 from the University of California, Merced, U.S.A. After graduating, Chi-Shuo Chen started his postdoctoral training in the same institute. His current research interests focus on (1) the assembly of natural organic matter in aquatic environmen, (2) the influences of microenvironments on cellular physiology and the potential applications in biomedical engineering, and (3) the development of optical methods with microfluidic systems for assessing cell physiology. His most recent works have centered on the impacts of climate change on natural organic matter.



Dr. Saijin Zhang is an assistant research scientist in the Department of Marine Science at Texas A&M University at Galveston. Saijin Zhang received her Ph.D. in Oceanography from Texas A&M University in 2010. Her research focuses on (1) biogeochemical cycling of radionuclides (I-129 and Th-234) and natural organic matter (e.g., humic acids and extracellular polymeric substances), (2) impacts of engineered nanoparticles on assembly of natural organic matter and on microorganisms (microalgae and bacteria, and (3) applications of trace metals in environmental chemistry and fish ecology.

Dr. Yuelu Jiang obtained her Ph.D. degree in 2009 from Hong Kong University of Science and Technology. Yuelu Jiang received her postdoctoral training in the Department of Marine Biology at Texas A&M University at Galveston. Her current research interests are (1) the effects of environmental stressors on microalgae species likely to cause cell death and physiological change, (2) identifying microalgae and growth conditions with the greatest potential for biofuels, and (3) effects of engineered particles on the physiology of marine microalgae and the transport of these material into cells.

Dr. Ai-Jun Miao obtained his Ph.D. degree from the Hong Kong University of Science and Technology in 2006. Ai-Jun Miao then worked at Texas A&M University at Galveston as a postdoctoral fellow for three years. After that, he moved back to China and is now an associate professor in the School of Environment at Nanjing University. His research interests lie mainly in the bioavailability and toxicity of trace metals and more recently of nanoparticles to aquatic organisms. The questions he is trying to answer are how pollutants in the environment may get into the aquatic organisms, how they are distributed in the organisms at the subcellular level, how they can be transformed or excreted out by the organisms, and how the organisms may response to the exposure.

Dr. Kathleen A. Schwehr received her Ph.D. in Chemical Oceanography from Texas A&M University in 2004. Currently, Kathleen A. Schwehr is an associate research scientist at the Laboratory for Oceanographic and Environmental Research in the Department of Marine Science at Texas A&M University at Galveston. Her interests involve biogeochemical cycling, speciation, binding, fate, and transport of radionuclides, trace elements, and engineered nanoparticles in aquatic and sediment environments and their interactions with microalgae, microbes, and natural organic matter, with some emphasis on biopolymeric colloids and gels.

Dr. Chen Xu is an assistant research scientist at Texas A&M University at Galveston. Chen Xu obtained her Ph.D. in 2011 from Texas A&M University, U.S.A. She received the Association of Former Students Distinguished Graduate Student Award for Excellence in Research for her doctoral research contributions. Her current research focus is on the study of biogeochemistry of natural organic matter in aquatic environments, in particular amphiphilic exopolymeric substances excreted by microorganisms (microalgae and bacteria) and humic substances, their composition at the molecular level, and the roles of biomolecules as colloidal carriers of radionuclides (e.g., ^{129}I, ^{234}Th, ^{239,240}Pu, etc.), as well as the application of radionuclides as tracers in aquatic environments.

Dr. Peter H. Santschi is a professor of oceanography and marine sciences at Texas A&M University. Peter H. Santschi received his Ph.D. in Chemistry from the University of Bern, Switzerland, and held senior positions at LDEO at Columbia University, New York, and EAWAG at ETH, Zurich, Switzerland. His research focuses on chemical oceanography, limnology, and hydrology. His work includes tracer applications using radioactive and stable isotopes, relationships between trace element and natural organic matter geochemistry, and the importance of exopolymeric substances for trace element binding and removal from natural waters. His most recent work is centered on relationships between actinide elements, Iodine-129, a number of trace and ultratrace elements, PCBs, dioxins, engineered nanoparticles, and natural organic matter compounds in the aquatic environment.

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