Where Are We Heading in Nanotechnology Environmental Health and Safety and Materials Characterization?

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EDITORIAL

Where Are We Heading in Nanotechnology Environmental Health and Safety and Materials Characterization?

Every chemist, material scientist, physicist, engineer, and commercial enterprise involved in the synthesis and/or production of engineered nanomaterials (ENM) or nanoenabled products aspires to develop safe materials. Nanotechnology environmental health and safety (nanoEHS) is a research discipline that involves the study of the possible adverse health and biological effects that nanomaterials may have on humans and environmental organisms and ecosystems. Recent nanoEHS research has provided a body of experimental evidence indicating the possibility of hazardous outcomes as a result of the interactions of unique ENM physicochemical properties with similar scale processes occurring at a wide range of nano/bio interfaces, including at the biomolecular, cellular, subcellular, organ, systemic, whole organism, or ecosystem levels. This projected hazard and risk potential warrants rigorous attention to safety assessment, safe use, safe implementation, benign design, regulatory oversight, governance, and public awareness to address the possibility and prevention of nanotoxicity, now and at any time in the future.[1] Thus, we must understand the properties of the ENMs that are responsible for the toxicological response, so that we can re-engineer their physicochemical characteristics for risk prevention and safer ENM design.[2] However, in spite of widespread use, no human toxicological disease or major environmental impact has been reported for ENMs. Thus, while "nanotoxicology" is a thriving subdiscipline of nanoEHS, the use of the "root" word toxicology may elicit a feeling that nanomaterials are inherently toxic despite the fact that toxicity has not thus far been established in real life. As a community, we may want to rename this subdiscipline as "nanosafety" since the objective is to use toxicology information to guide the design of safer nanomaterials for use in medicine, biology, electronics, lighting systems, and other areas.

At *ACS Nano*, we publish articles and forward-looking Perspectives and reviews that determine and establish ENM physicochemical properties, structure–activity (SA) relationships, catalytic effects at the nano/bio interface, mechanistic injury responses, *in vitro* to *in vivo* prediction making, safer-by-design strategies, actionable screening and detection methods, hazard and risk ranking, fate and transport, ENM categorization, theory and modeling, societal implications, and regulatory/governance decisions.[3] Context is important in the immediate and long-range impact of this research, as we are interested in realistic nanoEHS exposure scenarios conducted with systematic variation of ENM physicochemical properties rather than investigations of a single or a limited number of materials in isolated *in vitro* studies that only address cytotoxicity at unrealistic doses. In order to make these data useful for researchers, government and regulatory agencies, and other interested parties, these studies, where possible, should include either appropriate positive and negative controls or benchmark materials to answer the important question, "as compared to what?" Dosimetry should be explained in terms of appropriate dose metrics relative to the type of materials, their mechanisms of injury, and exposure conditions, using *in vitro* to *in vivo* extrapolations where possible.

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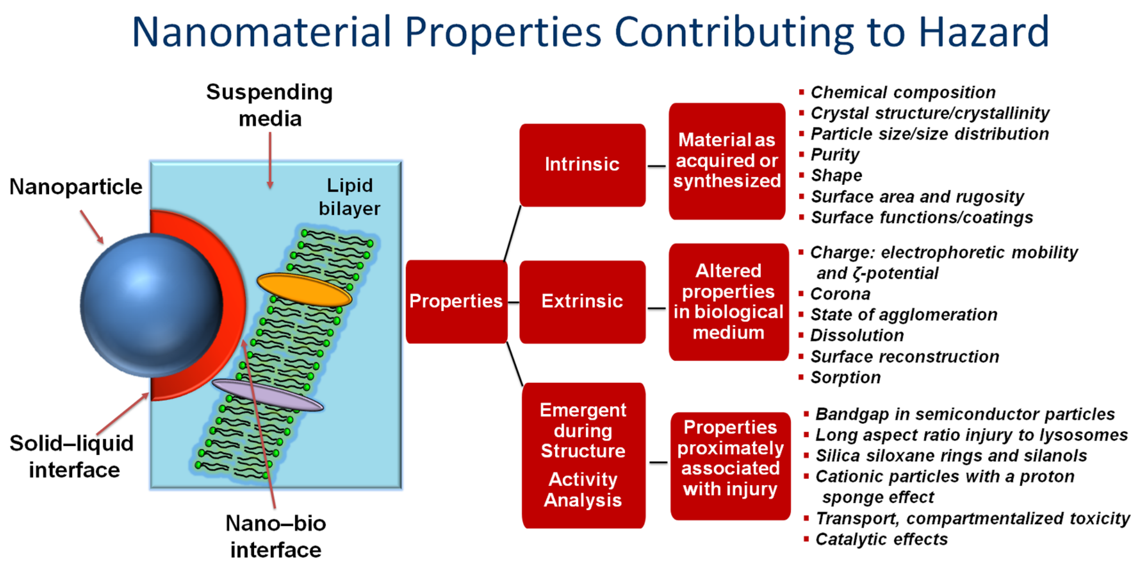

Figure 1. **(Left) Schematic representation of the interface between a nanoparticle and a lipid bilayer. (Right) Nanomaterial properties that play major roles at the nano–bio interface; these can be divided into intrinsic material properties, extrinsic properties modified through interactions with the suspending medium, and for hazardous materials, properties that, although dependent on the former categories, dynamically emerge at the nano–bio interface as the most proximate link to injury. The latter category often reveals structure–activity relationships that can be used quantitatively for modeling and safer design.**

Another important component of these studies includes appropriate physicochemical characterization of the nanomaterials. While there have been many discussions and suggestions of what constitutes a necessary set of physicochemical parameters that should be included in scientific communications,[4,5] our position at *ACS Nano* is that the characterization should be appropriate to the claims and conclusions of the study. A number of working groups have listed frequently used parameters that can facilitate the interpretation of nanoEHS data, such as (i) intrinsic material properties (properties of the as-synthesized or acquired materials), *e.g.*, particle size, size distribution, chemical composition, purity, crystallinity (where appropriate), shape or morphology, surface chemistry and charge (where appropriate), and surface area; (ii) external material properties (acquired during storage, handling or following ENMs suspension in experimental biological or environmental media), such as hydrodynamic diameter, the extent of ENM aggregation or agglomeration, surface reactivity (*e.g.*, the redox or membranolytic activity, where appropriate), charge or zeta-potential, and dissolution or persistence (where appropriate) (Figure 1). In addition, if properties such as agglomeration depend on the medium in which the ENMs are to be used, characterization should be performed in the relevant medium and not simply in water. However, there is a wide range of opinions, and we cannot be dogmatic since SA analyses of well-characterized material libraries used for exploring a series of nano/bio interfaces have elucidated nanoscale-specific properties that go beyond the traditional lists of intrinsic and extrinsic property characterization. For example, SA analyses of ENMs at a series of biophysicochemical boundaries has elucidated the role of (i) hydration-dependent density display of highly reactive silanols, leading to membrane damage by pyrolytic silica;[6] (ii) band and hydration energies playing roles in the generation of oxidative stress in bacteria and mammalian cells by metal oxide semiconductor materials;[7] (iii) complexation of structural cellular phosphate residues on the surface of rare earth oxide and up-conversion nanoparticles leading to lysosome damage;[8] and (iv) catalytically active, high aspect ratio multiwall and single-wall carbon nanotubes able to induce lysosomal injury depending on the stability of their surface coating in the acidic endosomal environment.[9] None of these SA relationships could have been predicted using the traditional list of intrinsic and extrinsic property evaluations. It is often this range (and need) of definition and dynamic interactions of ENMs that both challenges the elucidation of SA relationships and makes the field so interesting intellectually and so important commercially and from a regulatory standpoint.

Much remains to be learned about the relationships of nanoscale properties and functions to a wide field of biological outcomes. We look forward to guiding the development of this field through the publication of well-devised and executed studies on nanoEHS in order to continue to fill the large knowledge gaps that are required for the safe development and implementation of nanotechnology as one of the cornerstones of sustainability. We will also lay out in this and other fields the continually advancing needs of characterization to move these areas, and nanoscience and nanotechnology as a whole, forward.

Disclosure: Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

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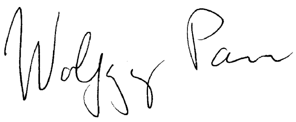

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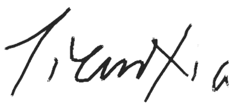

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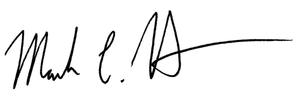

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