UC Center for Environmental Implications of Nanotechnology

NSF Cooperative Agreement DBI-0830117

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The University of California Center for Environmental Implications of Nanotechnology (UC CEIN) was established in September 2008 with a long-term vision of developing a multidisciplinary and quantitative framework for assessing the potential environmental impact, hazard and exposure to ENMs, in both their primary as well as commercial nano-enabled formulations. The Center also provides feedback and guidance for the safer implementation of nanotechnology, including risk reduction and safer design strategies. The multidisciplinary approach of the Center involves materials science, environmental chemistry and engineering, toxicology, ecology, social science, computer science and modeling, statistics, public health and policy formulation. Collectively, these fields of expertise are necessary to address the complexity of the ENM physicochemical properties involved in hazard generation, establishment of structure-activity relationships (SARs), and use of exposure assessment to evaluate ecosystems impact. The UC CEIN's vision is to generate predictive tools for environmental hazard and exposure assessment as well as to develop strategies to ensure the safe implementation of nanotechnology to the benefit of society, the environment and the economy. These tools and knowledge are disseminated through vibrant and impactful educational and outreach programs.

The Center makes use of well-characterized compositional and combinatorial ENM libraries to study their fate and transport in parallel with the materials' bioavailability and potential to engage toxicological pathways in organisms and environmental life forms. Where possible, this exploration involves high throughput screening (HTS) to develop structure-activity relationships (SARs) that can be used to predict the impact of primary ENMs' on organisms in freshwater, seawater, and terrestrial environments. *In silico* data transformation and decision-making tools are involved in data processing to provide hazard ranking, exposure modeling, risk profiling, and construction of nano-SARs. These research activities are combined with educational programs that inform the public, students, federal and state agencies, as well as industrial stakeholders of the impact of CEIN's research on the safe implementation of nanotechnology in the environment. Collectively, these activities contribute to evidence-based nanotechnology environmental health and safety (nano EHS) for society.

The research of the UC CEIN is carried out by 44 distinct but interactive research projects across seven interdisciplinary research themes:

- Theme 1: Compositional and Combinatorial ENM Libraries for Property-Activity Analysis
- Theme 2: Molecular, Cellular, and Organism High-Throughput Screening for Hazard Assessment
- Theme 3: Fate, Transport, Exposure, and Life Cycle Assessment
- Theme 4: Terrestrial Ecosystems Impact and Hazard Assessment
- Theme 5: Marine and Freshwater Ecosystems Impact and Toxicology
- Theme 6: Environmental Decision Analysis for ENMs
- Theme 7: Societal Implications, Risk Perception, and Outreach Activities

Through the pursuit of interdisciplinary, predictive and high throughput approaches, the UC CEIN has made, and will continue to make, a transformative impact on nano EHS assessment. The cornerstone of this impact is our ability to use an interdisciplinary approach for acquisition and synthesis of ENM libraries, which are assessed by high throughput and facilitative test strategies that inform about nanomaterial hazard and potential impact across a broad range of nano/bio interfaces, from cells to ecosystems. Coupled with our computational analysis tools and fate and transport modeling, this allows environmental impact analysis of broad material categories, including the use of this information for safety assessment, safer design and regulatory decision-making. The paradigm shift in nano EHS assessment in UC CEIN is reflected in the major research progress over the first five years, including the following highlights:

- The synthesis and characterization of ENM libraries in Theme 1 have enabled the UC CEIN to assemble materials that highlight the contributions of chemical composition, electronic structure, surface reactivity, material dissolution, charge, size, shape, and surface area on biological outcomes in cells, bacteria, algae, terrestrial plants, phytoplankton, daphnia, copepods, zebrafish, mussels and sea urchins. We have also been able to demonstrate the importance of metal oxide conduction band energy, aspect ratio, and surface chemistry in determining the materials' toxicological potential, allowing us to develop SARs for some of the high production materials in this category.
- Work in Theme 2 has demonstrated that toxicological profiling of library materials through HTS and SAR analysis (in collaboration with Theme 6) can be used for prediction making about their toxicological impact *in vivo*, including in zebrafish and other environmental organisms. We have demonstrated that this predictive toxicological approach can speed up hazard ranking and environmental decision-making of a large numbers of ENMs. These efforts assist the logistical planning and execution of animal studies in Theme 5.
- A collaboration between Themes 1, 2, 3, 4, 5 and 6 has also shown that at least one high-volume commercial nanomaterial, ZnO, can be "more safely designed" through iron-doping and has also sparked similar efforts to implement safer design strategies for CNTs, cationic nanomaterials, and nano-Ag.
- Theme 3 has provided answers on bioavailability, persistence, mobility, and reactivity for a wide range of ENMs in real environmental matrices and relevant light conditions. We have found that bioavailability and photoactivation is higher in freshwater systems than marine or groundwater systems. Additionally, there is a higher potential for environmental damage from rapidly dissolving ENMs (ZnO, Fe) and bioprocessing of ENMs can lead to increased bioavailability.
- Theme 4 has addressed key questions regarding the potential for ENMs to impact terrestrial ecosystems, and has revealed how those impacts occur. Among the key findings: a broad range of ENMs are toxic to bacteria under dark conditions (as in soils); ENMs inhibits bacterial growth by associating with and damaging bacterial membranes; ENMs that are attached to or taken up in bacteria are trophically-transferred to protozoan predators, which bioaccumulate the materials; ENMs alter soil microbial community diversity including functionally (e.g. N and C cycling) important taxa, and effects are exacerbated under drought conditions; plants bioaccumulate and process specific ENMs; ENMs can genetically alter hydroponic plants; and ENMs negatively impact important crop plants and soil microbial processes relevant to soil fertility.
- Theme 5 demonstrated that individuals, populations, and communities of aquatic organisms, specifically those that provide a suite of ecosystems services, can be used to screen for toxicological effects of ENMs, and that specific mechanisms of toxicity can be uncovered through high content screening (HCS) for cellular, organelle, or tissue-related injury pathways. HCS and microcosm studies provided data for dynamic energy budget modeling to predict ENM impacts in individual organisms, communities, mesocosms and natural ecosystems.
- The data collection and environmental decision analysis tools in Theme 6 have resulted in one of the most comprehensive nano EHS databases in the country, as well as modeling tools for identifying and ranking ENMs of potential environmental concern. This includes the development of a mechanistic transport model of agglomerated ENMs that is highly predictive of the environmental distribution of the study materials in a variety of media. Theme 6 has also developed novel algorithms and computational tools for HTS data (Theme 2) to quantify toxicological outcomes and provide hazard ranking. These include feature extraction, clustering and quantitative SAR tools that are being used for prediction making about the relationship between fundamental properties of metal, metal oxide, and surface-modified ENMs and toxicological outcomes.

- The activities in Theme 7 have demonstrated the importance of surveying critical stakeholders about their perceptions and beliefs, conducting research to understand the factors that contribute to those perceptions and beliefs, and acting upon the insights generated from those studies. We now have a better understanding of how to engage the public in a way that builds trust for both academic researchers and for nanotechnology, as well as the priorities of critical stakeholders when it comes to both the regulation and deployment of nanotechnology. Theme 7 has also made important strides in developing outreach materials based on our research products for use across our stakeholder groups.

A major goal of the UC CEIN is to educate the next generation of nano-scale scientists, engineers, and policy makers to anticipate and mitigate potential future environmental hazards associated with nanotechnology. Our *educational programs* are developed to broaden the knowledge base of the environmental implications through academic coursework, research, and training courses for industrial practitioners, public outreach, and a journalist/scientist communication program. Through the activities of our education team (Theme 8), we have had a profound impact on the quality and quantity of educational materials available both nationally and internationally in the area of Environmental Nanotechnology, including the development of a publicly available online course in Nanotoxicology (a 13-lecture online series that is packaged with readings and evaluation quizzes). The Center has also greatly enhanced the professional development opportunities for graduate students and postdoctoral researchers within our Center, as we build a cohesive and interdisciplinary environment for science and education. Since inception, we have offered 3 professional development workshops for our students, and are often able to include students and postdocs from outside institutions to take part in these activities. We regularly engaged the public in settings like museums and libraries to inform them of our work. We have made concerted efforts to involve minority institutions, including the recruitment of minority faculty and students. Additionally, we are proud to have two minority serving institutions (with UCSB soon to become a third minority serving institution) as core partners in our Center ,and are working to incorporate strategies for promoting diversity and inclusion and underrepresented minorities into all of our educational activities.

Select Publications 2012

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[1]For additional information about the Center, its projects, and a full list of publications, please visit http://www.cein.ucla.edu.

[2]The UC CEIN is headquartered at UC Los Angeles in partnership with UC Santa Barbara, UC Davis, UC Riverside, Columbia University, University of Texas El Paso, University of New Mexico/Sandia National Laboratory, Northwestern University, Nanyang Technological University (Singapore), the Molecular Foundry at Lawrence Berkeley National Laboratory, Lawrence Livermore National Laboratory , the University of Bremen (Germany), University of British Colombia (Canada), Cardiff University (Wales), University College Dublin (Ireland), and the Universitat Rovira i Virgili (Spain).