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Editorial

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Untangling Species Sensitivity Paradox in Environmental Research

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Biologically, two species within a genus are more similar (e.g., morphologically and genetically) in many respects than two other species belonging to different genera. Despite the long history of ecotoxicology and efforts to understand interspecies variability in sensitivity to environmental contaminants, choosing representative species for screening potential toxicity of the environmental contaminants, be it the conventional toxicants such as the dioxins or the emerging contaminants such as the manufactured nanomaterials, has remained challenging. More challenges have, however, confronted the emerging nano-research community—a highly diverse community of researchers ranging from those with expertise involved in tailoring nanomaterial properties for desired applications to others engaged in identifying whether nanomaterial is a hazard and poses risk to environmental health and safety (EHS)—in discerning the mechanistic basis of toxicity, including both the intrinsic and extrinsic factors that could potentially modulate toxicity, of the manufactured nanomaterials on various biological organisms.

Typically, species sensitivity distribution is derived using the laboratory data, which most often had been based on acute toxicity endpoints involving several species. NOAEL (No-observed-adverse-effect-level), LOAEL (lowest-observed-adverse-effect-level), or LC_{50}/EC_{50} (lethal concentration that kills 50% of the test population/half maximal effective concentration) has limitations as these statistically significant end-effects may not always reflect biologically significant outcomes. For instance, 95% impairment of bacterial growth (say a particular strain) in the laboratory culture does not necessarily mean that the species will go extinct when similar concentration (that caused 95% effect) of the contaminant is present in the natural environment. Nature is admittedly complex to decipher and plethora of limiting factors that affect the growth and development of organisms in the environment are seldom applied in the laboratory test settings. Modifications of the existing test protocols, especially for toxicity assessment, should be encouraged and focus should be in developing test methods that could better simulate more realistic environment such that the data synthesized in the laboratory can precisely reflect the effects that would likely be observed in the field environment. Only then the derived NOAEL, LOAEL, and LC_{50}/EC_{50}values will begin to make sense as such data carry more realistic toxicity information then the ones emanating from unrealistic test environment. Various factors which modulate potential toxicity of the contaminant in the environment are, however, not typically integrated in the test for deriving the endpoints. Studies performed using innovative ideas and methodologies should be encouraged by the peer-review journals against those that embark on previously published protocol/literature, adhering to a fail-safe mechanism that facilitates publication.

Does intra/inter-test variability matter? As in other disciplines, intra- and inter-test variability is also commonplace in environmental biology research. Appropriate adjustments for intra- and inter-test variability should minimize the uncertainty in the response variable, such as the toxicity endpoint measured. Typically, increasing the number of replicates and/or sample size should increase statistical power and offer meaningful conclusion. In an emerging field of environmental nanoscience and technology, much of the literature published either fail to test the data for normal probability distribution or do not report it, thus affecting the judgment about the veracity of the data and the conclusions that follow. When several toxicity endpoints are measured for a given species, the collection of multiple end-effects can be at times inconvenient to determine species sensitivity. One potential solution to this historical problem would be to calculate the geometric mean employing multiple endpoint values (e.g., EC_{50} or LC_{50}) to derive an *Index of Toxicity* (IT), representative of each species and the types of nanomaterials used, for example; higher IT score denotes lower toxicity and vice-versa. Plotting these IT scores graphically should offer better understanding of the potency of toxicity of each test chemical (for example, differently coated AuNPs), including the sensitivity of the model species used (Figure 1).

Furthermore, modeling the data employing the Generalized Linear Model (GLIM), or the Generalized Estimating Equations (GEE) can enable us explain several factors which could collectively contribute to the response variable (e.g., observed toxicity) of the given chemical or the nanomaterial. Statistically considered robust, GLIM can offer very general model regardless of the types of variables (e.g., normally or log-normally distributed data, binary data, interval-censored survival data, etc.) that are often measured in environmental research and need to be considered in the model to understand the relationship sought. As an extension of GLIM, GEE accommodates correlated data (not considered by GLIM) and does not require data satisfy normality, hence considered appropriate for environmental data which would otherwise require data transformation to satisfy the basic assumptions; especially, with other linear models that are routinely used in environmental science such as ANOVA or regression models. GLIM or GEE method of data analysis has not been applied in environmental and/or nanotoxicology research, hence an adoption of simple yet robust statistical method as suggested here can be envisioned to take precedence in this area of research.

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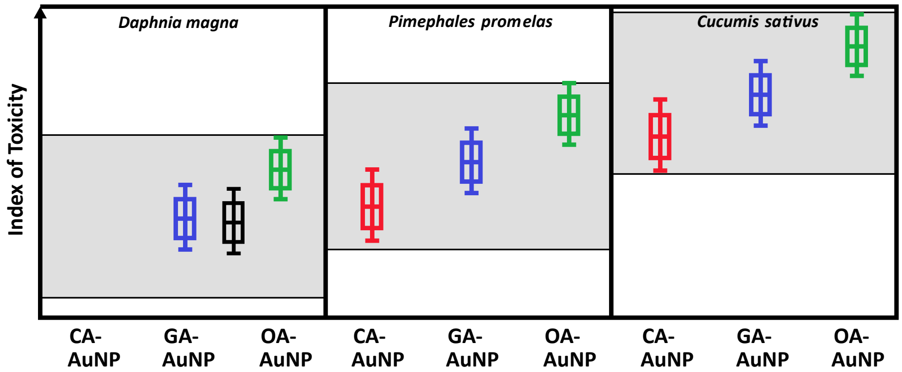

Figure 1: Index of Toxicity (IT) calculated taking geometric mean of the EC_{50}/LC_{50} values for different endpoints measured for each type of organically-coated gold nanoparticles (AuNP) against the three common species used in ecotoxicity. Lower IT score denotes higher toxicity and vice-versa. Hypothetical data showing *Daphnia magna* (water flea) as the most sensitive species while *Cucumis sativus* (cucumber) as the least sensitive species amongst the three ecological species tested for AuNP toxicity. Organic coating materials: CA, citric acid; GA, gum Arabic; and OA, oleic acid.

When automated high-content cellular analysis (HCCA) has emerged as a rapid screening tool, coupled with growing interest in minimizing animal use in research for ethical reasons, how long would species sensitivity paradigm sustain remains to be seen. Perhaps, inclusion of detail –Omics data analysis (e.g., proteomics, metabolomics, transcriptomics, genomics, etc.) and marrying environmental science, including emerging nanoscience, with already flourished biotechnology and information technology might be a promising path to explore more complex interactions that would occur at the bio-chemical interfaces and therefore improve the knowledge base of environmental biology, including that of the emerging nanoscience and technology as it pertains to the environment.

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