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Contaminants

A Spatio-Temporal Exposure-Hazard Model for Assessing Biological Risk and Impact

Walker E, Leclerc M, Rey JF, Beaudouin R, Soubeyrand S, Messéan A. *Risk Anal.* 2017 Dec 11. doi: 10.1111/risa.12941. Article Link

Significance: This paper reports the outcomes of a new simulation model for spatio-temporal distribution of agricultural contaminants.

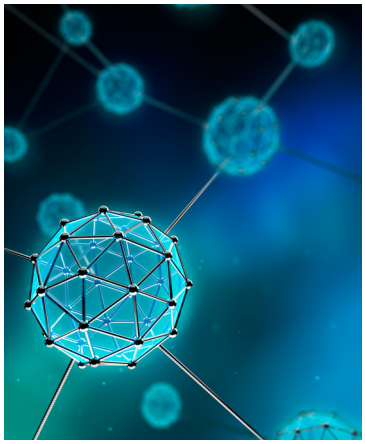
We developed a simulation model for quantifying the spatio-temporal distribution of contaminants (e.g., xenobiotics) and assessing the risk of exposed populations at the landscape level. The model is a spatio-temporal exposure-hazard model based on (i) tools of stochastic geometry (marked polygon and point processes) for structuring the landscape and describing the exposed individuals, (ii) a dispersal kernel describing the dissemination of contaminants from polygon sources, and (iii) an (eco)toxicological equation describing the toxicokinetics and dynamics of contaminants in affected individuals. The model was implemented in the briskaR package (biological risk assessment with R) of the R software. This article presents the model background, the use of the package in an illustrative example, namely, the effect of genetically modified maize pollen on nontarget Lepidoptera, and typical comparisons of landscape configurations that can be carried out with our model (different configurations lead to different mortality rates in the treated example). In real case studies, parameters and parametric functions encountered in the model will have to be precisely specified to obtain realistic measures of risk and impact and accurate comparisons of landscape configurations. Our modeling framework could be applied to study other risks related to agriculture, for instance, pathogen spread in crops or livestock, and could be adapted to cope with other hazards such as toxic emissions from industrial areas having health effects on surrounding populations. Moreover, the R package has the potential to help risk managers in running quantitative risk assessments and testing management strategies.

Nanomaterials

The Essential Elements of a Risk Governance Framework for Current and Future Nanotechnologies

Stone V, Führ M, Feindt PH, Bouwmeester H, Linkov I, Sabella S, et al. *Risk Anal.* 2017 Dec 14. doi: 10.1111/risa.12954. Article Link

Significance: This paper proposes components of a nanomaterial risk governance framework.



Societies worldwide are investing considerable resources into the safe development and use of nanomaterials. Although each of these protective efforts is crucial for governing the risks of nanomaterials, they are insufficient in isolation. What is missing is a more integrative governance approach that goes beyond legislation. Development of this approach must be evidence based and involve key stakeholders to ensure acceptance by end users. The challenge is to develop a framework that coordinates the variety of actors involved in nanotechnology and civil society to facilitate consideration of the complex issues that occur in this rapidly evolving research and development area. Here, we propose three sets of essential elements required to generate an effective risk governance framework for nanomaterials. (1) Advanced tools to facilitate risk-based decision making, including an assessment of the needs of users regarding risk assessment, mitigation, and transfer. (2) An integrated model of predicted human behavior and decision making concerning nanomaterial risks. (3) Legal and other (nano-specific and general) regulatory requirements to ensure compliance and to stimulate proactive approaches to safety. The implementation of such an approach should facilitate and motivate good practice for the various stakeholders to allow the safe and sustainable future development of nanotechnology.

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Adoption of In Vitro Systems and Zebrafish Embryos as Alternative Models for Reducing Rodent Use in Assessments of Immunological and Oxidative Stress Responses to Nanomaterials

Johnston HJ, Verdon R, Gillies S, Brown DM, Fernandes TF, Henry TB, et al. *Crit Rev Toxicol.* 2017 Dec 14:1–20. doi: 10.1080/10408444.2017.1404965. Article Link

Significance: This paper proposes a method for in vitro assessment of nanomaterial toxicity.

Assessing the safety of engineered nanomaterials (NMs) is paramount to the responsible and sustainable development of nanotechnology, which provides huge societal benefits. Currently, there is no evidence that engineered NMs cause detrimental health effects in humans. However, investigation of NM toxicity using in vivo, in vitro, in chemico, and in silico models has demonstrated that some NMs stimulate oxidative stress and inflammation, which may lead to adverse health effects. Accordingly, investigation of these responses currently dominates NM safety assessments. There is a need to reduce reliance on rodent testing in nanotoxicology for ethical, financial and legislative reasons, and due to evidence that rodent models do not always predict the human response. We advocate that in vitro models and zebrafish embryos should have greater prominence in screening for NM safety, to better align nanotoxicology with the 3Rs principles. Zebrafish are accepted for use by regulatory agencies in chemical safety assessments (e.g. developmental biology) and there is growing acceptance of their use in biomedical research, providing strong foundations for their use in nanotoxicology. We suggest that investigation of the response of phagocytic cells (e.g. neutrophils, macrophages) in vitro should also form a key part of NM safety assessments, due to their prominent role in the first line of defense. The development of a tiered testing strategy for NM hazard assessment that promotes the more widespread adoption of non-rodent, alternative models and focuses on investigation of inflammation and oxidative stress could make nanotoxicology testing more ethical, relevant, and cost and time efficient.

Nanomaterials in Food and Agriculture: An Overview on Their Safety Concerns and Regulatory Issues

Jain A, Ranjan S, Dasgupta N, Ramalingam C. *Crit Rev Food Sci Nutr.* 2018 Jan 22;58(2):297–317. Article Link

Significance: This article provides a state-of-the-science review of nanotoxicity and disease progression in the context of current nanomaterial use.

Nanotechnology has seen exponential growth in last decade due to its unique physicochemical properties; however, the risk associated with this emerging technology has withdrawn ample attention in the past decade. Nanotoxicity is majorly contributed to the small size and large surface area of nanomaterials, which allow easy dispersion and invasion of anatomical barriers in human body. Unique physio-chemical properties of nanoparticles make the investigation of their toxic consequences intricate and challenging. This makes it important to have an in-depth knowledge of different mechanisms involved in nanomaterials' action and toxicity. Nano-toxicity has various effects on human health and diseases as they can easily enter into the humans via different routes, mainly respiratory, dermal, and gastrointestinal routes. This also limits the use of nanomaterials as therapeutic and diagnostic tools. This review focuses on the nanomaterial-cell interactions leading to toxicological responses. Different mechanisms involved in nanoparticle-mediated toxicity with the main focus on oxidative stress, genotoxic, and carcinogenic potential has also been discussed. Different methods and techniques used for the characterization of nanomaterials in food and other biological matrices have also been discussed in detail. Nano-toxicity on different organs-with the major focus on the cardiac and respiratory system-have been discussed. Conclusively, the risk management of nanotoxicity is also summarized. This review provides a better understanding of the current scenario of the nanotoxicology, disease progression due to nanomaterials, and their use in the food industry and medical therapeutics. Briefly, the required rules, regulations, and the need of policy makers has been discussed critically.

Heavy Metals

Arsenic Exposure From Drinking Water and Urinary Metabolomics: Associations and Long-Term Reproducibility in Bangladesh Adults

Wu F, Chi L, Ru H, Parvez F, Slavkovich V, Eunus M, et al. *Environ Health Perspect.* 2018 Jan 12;126(1):017005. Article Link

Significance: This article identifies six metabolites significantly associated with either water arsenic or urinary arsenic after adjustment for multiple comparisons.

Background: Chronic exposure to inorganic arsenic from drinking water has been associated with a host of cancer and noncancer diseases. The application of metabolomics in epidemiologic studies may allow researchers to identify biomarkers associated with arsenic exposure and its health effects. *Objective:* Our goal was to evaluate the long-term reproducibility of urinary metabolites and associations between reproducible metabolites and arsenic exposure. *Methods:* We studied samples and data from 112 nonsmoking participants (58 men and 54 women) who were free of any major chronic

diseases and who were enrolled in the Health Effects of Arsenic Longitudinal Study (HEALS), a large prospective cohort study in Bangladesh. Using a global gas chromatography-mass spectrometry platform, we measured metabolites in their urine samples, which were collected at baseline and again 2 y apart, and estimated intraclass correlation coefficients (ICCs). Linear regression was used to assess the association between arsenic exposure at baseline and metabolite levels in baseline urine samples. *Results:* We identified 2,519 molecular features that were present in all 224 urine samples from the 112 participants, of which 301 had an ICC of ≥0.60. Of the 301 molecular features, water arsenic was significantly related to 31 molecular features and urinary arsenic was significantly related to 74 molecular features after adjusting for multiple comparisons. Six metabolites with a confirmed identity were identified from the 82 molecular features that were significantly associated with either water arsenic or urinary arsenic after adjustment for multiple comparisons. *Conclusions:* Our study identified urinary metabolites with long-term reproducibility that were associated with arsenic exposure. The data established the feasibility of using metabolomics in future larger studies.

An In Vitro Cytotoxic Approach to Assess the Toxicity of Heavy Metals and Their Binary Mixtures on Hippocampal HT-22 Cell Line

Karri V, Kumar V, Ramos D, Oliveira E, Schuhmacher M. *Toxicol Lett.* 2018 Jan 5;282:25–36. Article Link

Significance: By evaluating the in vitro cytotoxicity of a Pb, Cd, As, and MeHg mixture, the authors conclude that combined effects should be considered in risk assessment of heavy metal co-exposure.

Humans are exposed to a cocktail of heavy metal toxicants in the environment. Though heavy metals are deleterious, there is a paucity of information on the toxicity of mixtures. In this study, four common neurotoxicity heavy metals lead (Pb) cadmium (Cd), arsenic (As), and methylmercury (MeHg) were exposed individually and as mixtures to HT-22 cell line for 8 days. The study established that low dose exposures induced toxicity to the HT-22 cell line during 8 days. The results indicate potency dependent response, the toxicity of single metals on the HT-22 cells; MeHg > As > Cd > Pb. The cytotoxicity data of single metals were used to determine the mixtures interaction profile by using the dose additivity and effect additivity method. Metal mixtures showed higher toxicities compared to individual metals. Synergistic, antagonistic or additive effects of the toxicity were observed in different mixtures in low dose exposure. The interactive responses of mixtures depend on the co-exposure metal and their respective concentration. We concluded that the combined effects should be considered in the risk assessment of heavy metal co-exposure and potency. In future, comprehensive mechanistic based investigations needed for understanding the real interactive mixtures effects at molecular level.