UM environmental engineering faculty publishes paper on risk assessment

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Risk is composed of two parts: the probability of something going wrong and the subsequent consequences if it does. Although risks can never be predicted with certainty, they can be identified and analyzed to reduce the possibly catastrophic—and sometimes deadly—consequences of not taking a risk into account. The process of identifying and analyzing risks, called risk analysis or risk assessment, can be applied to all aspects of life, from start-ups and security issues to severe storms and public health.

Risk assessment is especially important in medicine and public health, where the characterization of potential adverse health effects from human exposures to environmental hazards and other chemicals is paramount to the safety of the general public. Health risk assessment is one of several tools that scientists, government agencies, and the public may use to make decisions about how to prevent and reduce exposures to harmful or toxic substances.

The relationship between the amount of chemical a person is exposed to and the response that a human population has to the chemical is characterized by a dose-response relationship—also called an exposure-response relationship. "Studying dose response, and developing dose-response models, is central to determining 'safe', 'hazardous' and—where relevant - 'beneficial' levels and dosages for drugs, pollutants, foods, and other substances to which humans or other organisms are exposed," explains James Englehardt, professor in the University of Miami College of Engineering Department of Civil, Architectural and Environmental Engineering. "These conclusions are often the basis for public policy."

Traditionally, dose-response models are developed using high-doses of a chemical on animals during short periods of time and measuring the animal's response. These data are later used to predict how a human would respond when exposed to the chemical in low-dosages during a longer period of time, which is more practical and applicable to the conditions humans face. "Long-term studies that expose subjects to a small amount of chemical during extended periods of time are difficult and expensive to carry out, making short terms studies with high dosages the feasible alternative," says Englehardt.

However, identifying the chemicals that pose a health risk during decades of exposure at extremely low doses is a challenge, often complicated even further by interactions with other chemicals and health-related issues that are sometimes hard or even impossible to identify. To address these issues, the U.S. National Research Council recommends assessing the risks of chemicals high throughput screening (HTS), a method for scientific experimentation that uses robotics, data processing software, liquid handling devices, and sensitive detectors to quickly conduct millions of chemical, genetic or pharmacological tests.

The problem with the current HTS data collection method is that it cannot measure responses at the extracellular, organ, and organism levels; it only works at the cellular level. As a result, HTS has been barely been used for chemical regulation. "In order to properly integrate HTS data into risk assessment and chemical regulation, there needs to be a unifying framework where all response levels are considered," says Englehardt.

Englehardt's recent work, in collaboration with Weihsueh Chiu, professor in College of Veterinary Medicine and Biomedical Sciences at Texas A&M University, received support from the National Science Foundation (NSF) and the National Institutes of Health (NIH) to publish a dose-response function for chronic chemical and other health stressors and mixtures, originally derived and submitted by Englehardt in 2007, that can provide the needed unifying framework for HTS analysis.

The basis behind Englehardt's newly published dose-response function is that the relationship between intra-cellular responses and multi-organ, multi-cellular governing processes is reflected in the overall dose-response function. This function predicts the fraction of the population to become ill at any particular exposure level or, equivalently, the probability that any randomly-selected individual will become ill at any particular dose.

"This approach to risk assessment is unique in that it can take advantage of both 'bottom-up' biologically-based modeling approaches, as well as 'top-down' statistical or artificial intelligence-based analyses," says Englehardt. "This new dose-response relationship will increase the efficiency of risk assessment by helping scientists, government agencies and the public make better and more accurate decisions on how to prevent and reduce exposures to harmful or toxic substances."

The research project, titled, "A general dose-response relationship for chronic chemical and other health stressors and mixtures based on an emergent illness severity model," was published in the prestigious *PLOS One* scientific journal.

More information: James D. Englehardt et al. A general dose-response relationship for chronic chemical and other health stressors and mixtures based on an emergent illness severity model, *PLOS ONE* (2019). DOI: 10.1371/journal.pone.0211780

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