

Abstract Title:

A Systems-based Approach to Predict Biological Responses of Aquatic Organisms to Complex Environmental Mixtures

A. Schroeder^{1,2}, G. Ankley¹, J. Berninger¹, E. Durhan¹, Z. Jorgenson³, K. Lee⁴, E. Perkins⁵, N. Garcia-Reyero⁶, E. Makynen¹, K. Stevens¹, D. Villeneuve¹

¹U.S. EPA Mid-Continent Ecology Division, Duluth, MN; ²University of Minnesota – Water Resources Center, St. Paul, MN; ³US Fish and Wildlife Service – Environmental Contaminants, Bloomington, MN; ⁴US Geological Survey – Minnesota Water Science Center, Mounds View, MN; ⁵US Army Engineer Research and Development Center, Vicksburg, MS, USA; ⁶Mississippi State University, Vicksburg, MS, USA.

Contaminants of emerging concern (CECs) such as new-generation pesticides, pharmaceuticals, household and personal care products, steroid hormones, and flame retardants enter the aquatic environment through multiple sources such as wastewater treatment plants and agricultural operations. CECs may have adverse effects on aquatic organisms, including fish. However, attempting to predict biological responses to environmental mixtures containing tens to hundreds of measured CECs can be an arduous task. In this presentation we describe a systems-based approach to develop chemical-gene interaction networks to help predict biological responses of fathead minnows to environmental mixtures of CECs. Caged fathead minnows were deployed for four days at multiple sites within five areas of concern (AOCs) in the Great Lakes. Ambient water samples also were collected from these sites by either grab or composite sampling. A suite of CECs including wastewater indicators (e.g., caffeine, cholesterol), human pharmaceuticals, and steroid hormones were analyzed. Of the 137 analytes measured, the number detected at any particular AOC ranged from 62 to 79. The Comparative Toxicogenomics Database and STITCH (<http://ctdbase.org> and <http://stitch.embl.de>, respectively) were used to identify known interactions between chemicals detected at our sites and the top 20 genes that the chemicals interact with. The criteria for selecting the top genes were based on the highest number of known interactions of a chemical with a particular gene from the published literature. Cytoscape was used to visualize chemical-gene interaction networks for each site. Analysis of the networks was then used to develop testable hypotheses concerning potential biological responses to the complex mixtures detected at the sites and prioritize the caged fish samples for subsequent transcriptomic analyses using microarrays, with the intent of comparing predicted responses with those observed in vivo. This approach illustrates a method for generating hypotheses for aquatic organism responses to complex environmental mixtures