Assessing the Effects of Chemical Mixtures using a Bayesian Network- Relative Risk Model (BN-RRM) Integrating Adverse Outcome Pathways (AOPs)

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Introduction

There are long-standing uncertainties about toxicity of chemical mixtures to populations. Laboratory toxicity tests have confirmed synergistic and antagonistic effects to individuals, but not to populations. We will conduct a regional scale ecological risk assessment by evaluating the effects chemical mixtures to populations with a new Bayesian Network- Relative Risk Model (BN-RRM) incorporating an Adverse Outcome Pathway (AOP) (Figure 7). We started applying this new BN-RRM framework in a case study with organophosphate pesticide (OP) mixtures (diazinon, chlorpyrifos, and malathion). Acetylcholinesterase inhibition (AChE) was chosen the molecular initiating event and the Puget Sound Chinook salmon (Onchorhyncus tshawytscha) and Coho salmon (Onchorhyncus kisutch) Evolutionary Significant Units (ESU) were chosen as population endpoints.

Background

Malathion and chlorpyrifos (Figure 1 and 2) make up of 50% of OP pesticides detected in urban streams in the Pacific Northwest[1]. Urban streams are where Coho and Chinook salmon inhabit and spawn and the streams typically contain two or more OPs [1]. Because mixtures are normally encountered in urban streams, toxicity testing of OP mixtures (Figure 3) is comparable to environmentally realistic exposures.[2-4]

Organophosphate pesticides such as chlorpyrifos and malathion act synergistically to Chinook salmon. The presence of an organophosphate compound such as chlorpyrifos inhibits the enzyme carbamate esterases (Cae) which results in the potentiation of malathion, a metabolite of malathion, leading to synergism.[5,6]

What is Next?

- We expect to see a greater contribution of toxicological effects with the mixtures
- We will add suitable habitat nodes from Geographic Information Systems (GIS) and other data sets. Adults pick suitable habitats to spawn based on discharge, substrate, streambank condition, riparian vegetation as well as cover & refuge[78]
- Climate change will also be added as a stressor

See also:

- Landis et al. (2017) Incorporating Spatially Explicit Metapopulation Models as the Adverse Outcome Pathway Endpoint of a Bayesian Network- Relative Risk Model.

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Sensitivity Analysis for Single Organophosphate Pesticides

In our model, toxicological effects did not have much of an effect on salmon populations (Figure 5). This is not surprising because our model only accounted for single chemicals. Toxicological effects were more sensitive depending on the watershed. Total toxicological effects are more important in the Cedar and Lower Skagit watersheds for all years. Water temperature (Figure 5) is more important in the Nooksack and Lower Yakima watersheds.

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Isoboles are contours that can connect two chemicals of equal effect into one response surface (Figure 4). If the isoboles are linear, then the mixture indicates concentration addition. Isoboles which curve towards the origin indicate synergistic mixtures; while ones that curve away from the origin are antagonistic[5,6]. The next steps will be to create an isobologram and fit mixture rays to a model.

NOTE: Probabilities of population estimations from the organophosphate pesticide mixtures have NOT been compiled yet. However, results from single pesticide exposures have been compiled.

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