Exposure-response in environmental toxicology and risk assessment, from receptors to ecological landscapes

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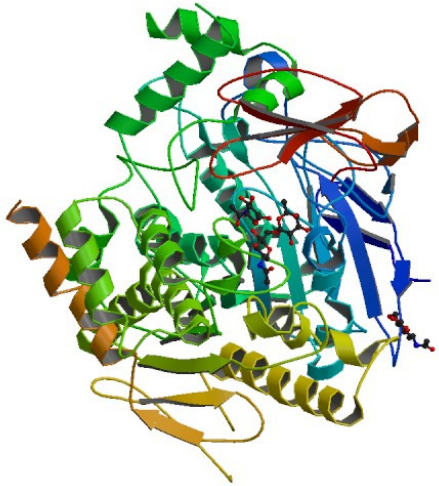
I have already published what I thought about NOECs. LOECs and ect…….

My thesis involved population biology and population genetics, not toxicology.

So I may have a different point of view….

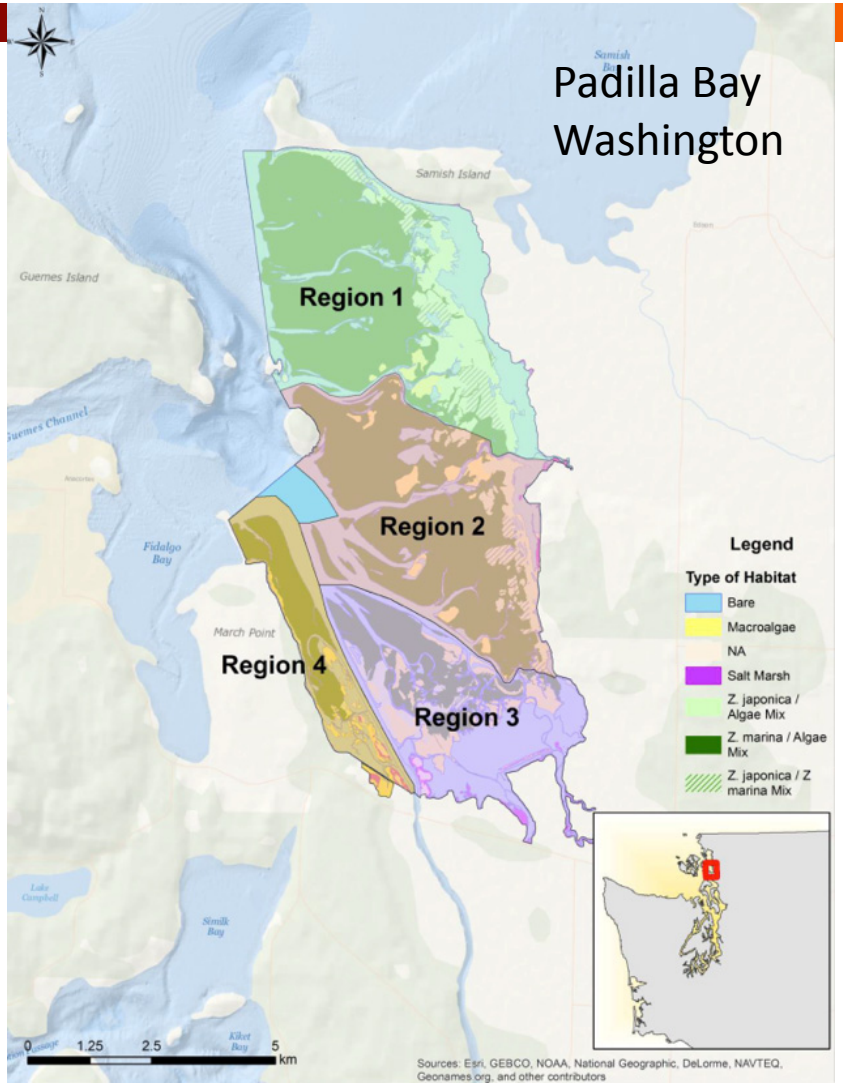
Research includes examining the ability of enzymes to degrade organophosphates, discovering microbes for the degradation of chemical warfare agents, testing chemicals in single species toxicity tests, evaluating ecological effects in multispecies toxicity tests (microcosms and mesocosms), being a collaborator in long term monitoring of receiving waters, and risk assessment at large physical scales with multiple stressors.

Dose-Response can be seen on a variety of scales



Acetylcholinesterase

Daphnia magna



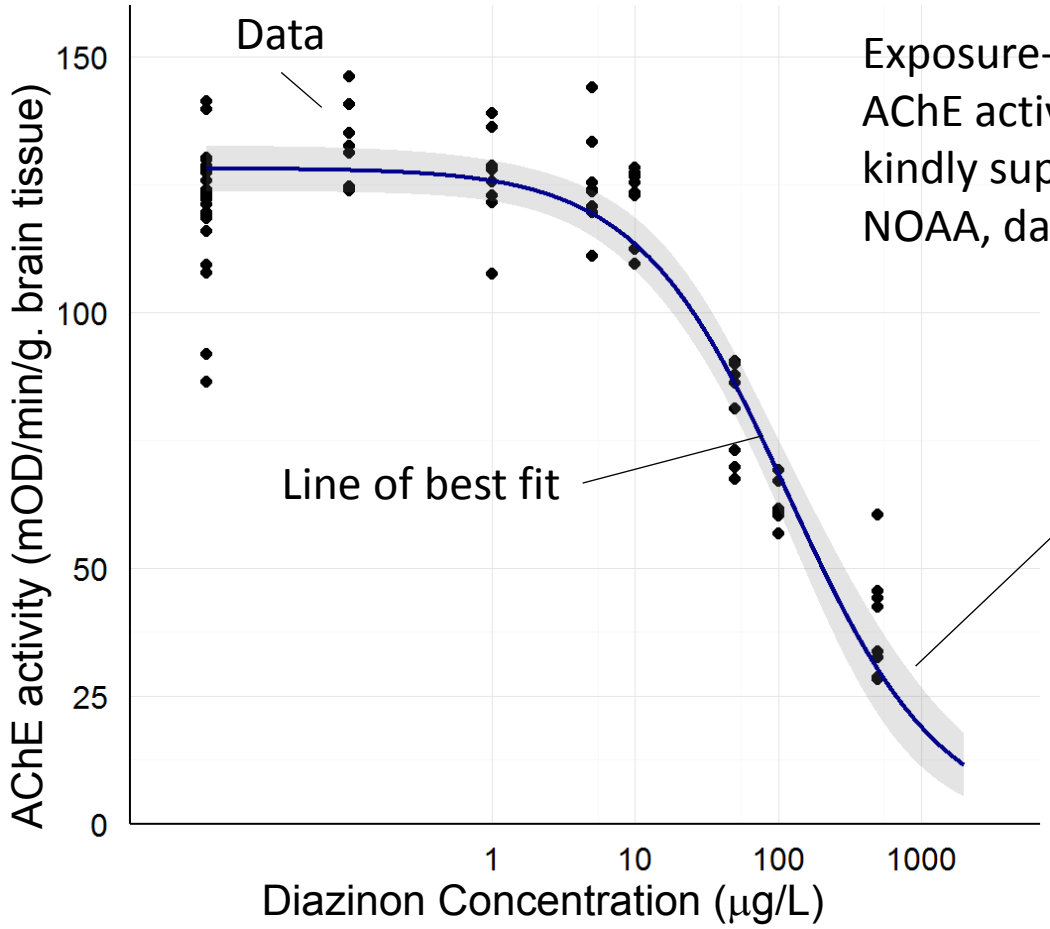
Exposure-response—the plan.

So I may have a different point of view……

First –remember that point estimates are not data as defined as an observation of nature.

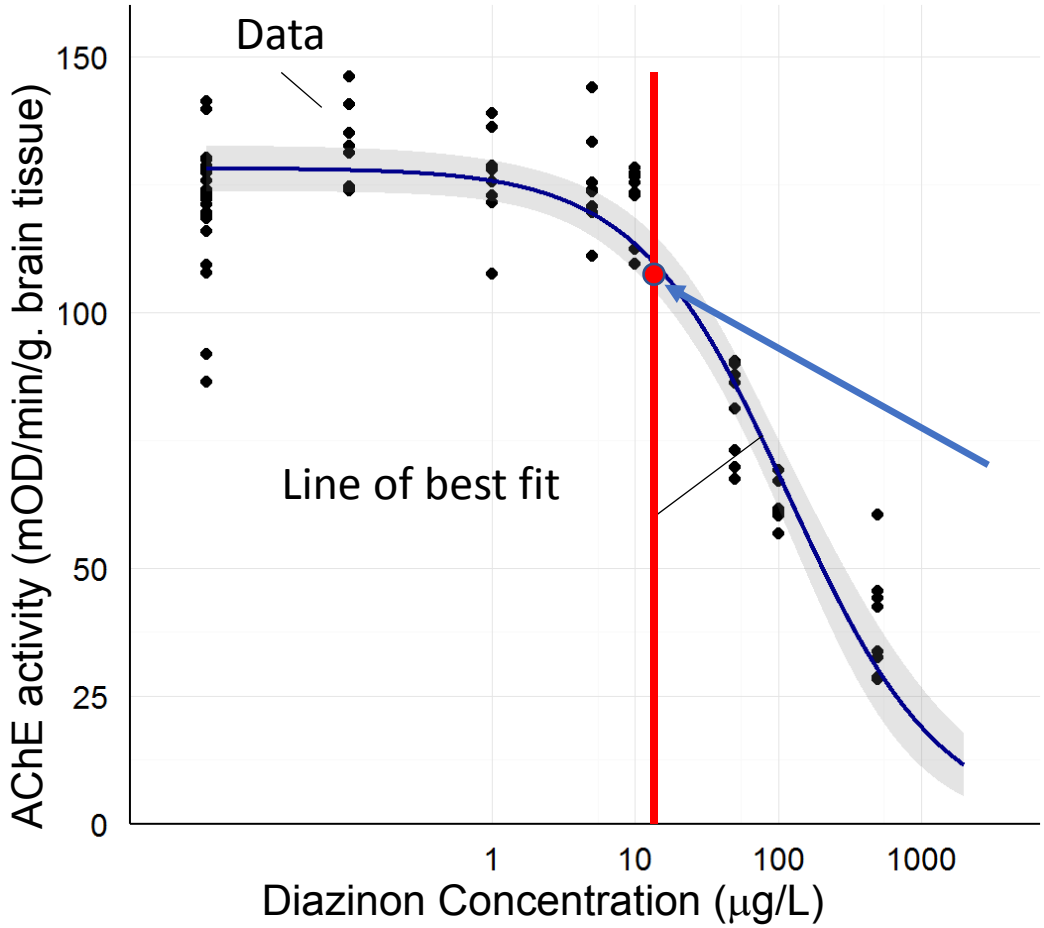
Single point estimates are a projection of the data and eliminates information.

Exposure-response for Diazinon and AChE activity for Coho Salmon



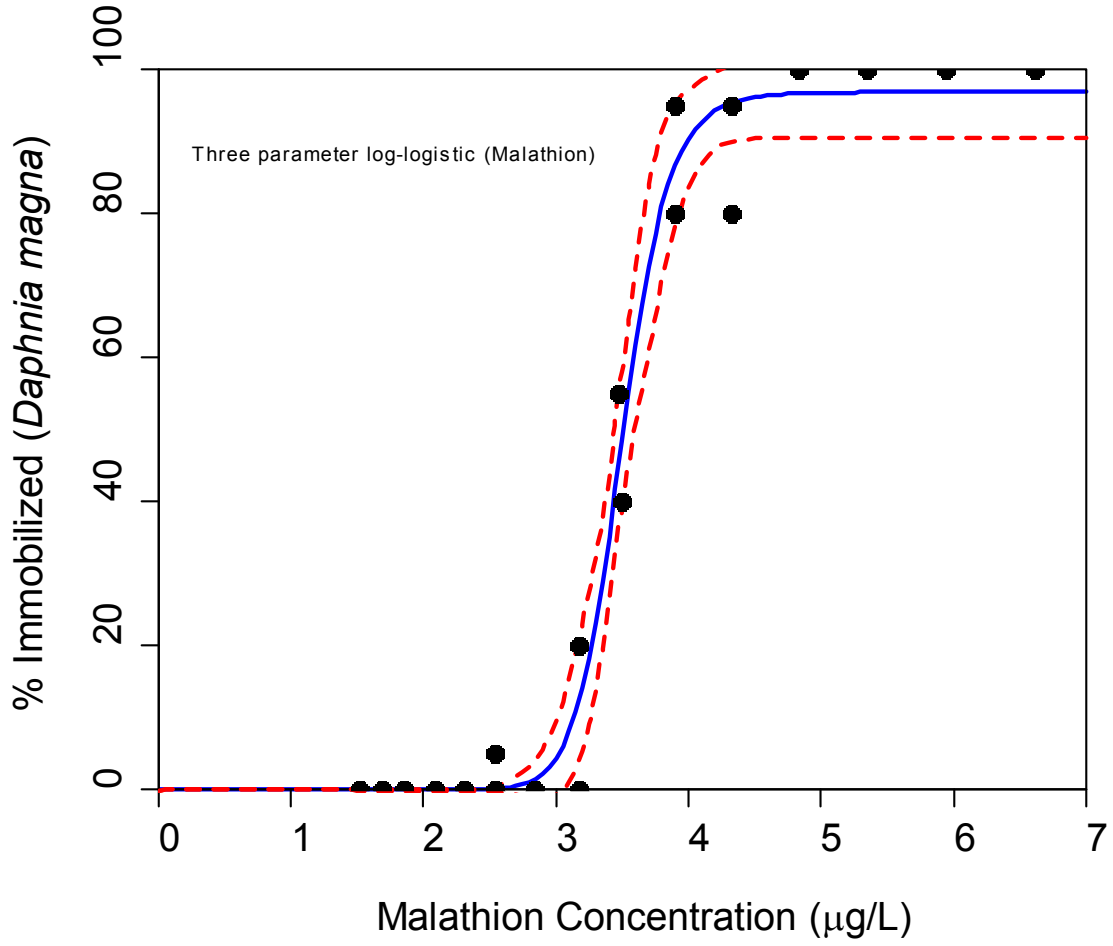
Exposure-response for Diazinon and AChE activity for Coho Salmon. Data are kindly supplied by Kathy Laetz and NOAA, data analysis by Meagan E. Harris.

Exposure-response for Diazinon and AChE activity for Coho Salmon



Results from the point estimate, an EC20 in this case. No confidence interval, no data, and not clear what that 20 percent means.

This is the projection that is commonly used.

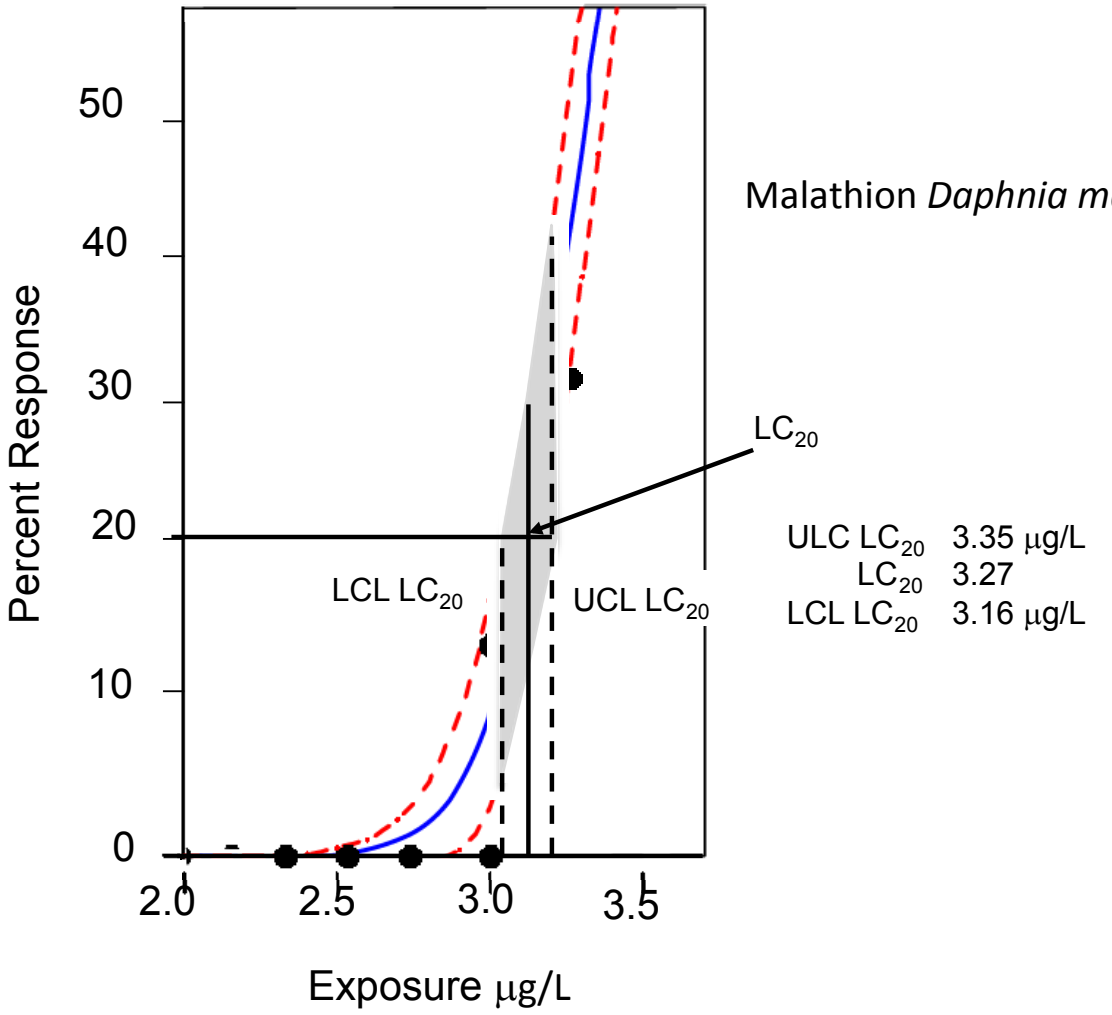


Notice that there is low replication of concentration—none is needed.

X axis is linear-not log. I prefer this projection to communicate variability.

Data are kindly supplied by G. LeBlanc (Rider and LeBlanc 2005) and analysis by Annie F. Gibbs (log-logistic model.)

How I think about exposure-response—a bounded distribution



So what is the EC20, it is a distribution set in part by the slope and the confidence interval.

So an ECx value is not a point.

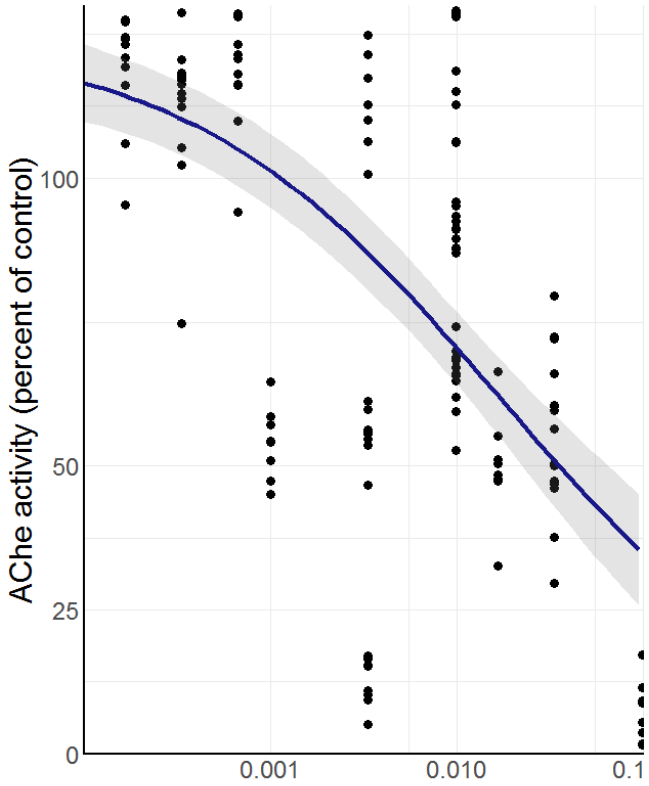
Some other thoughts about exposure-response curves

The type of regression model is not as important as having a wide range of exposures being assessed (Moore and Caux 1998).

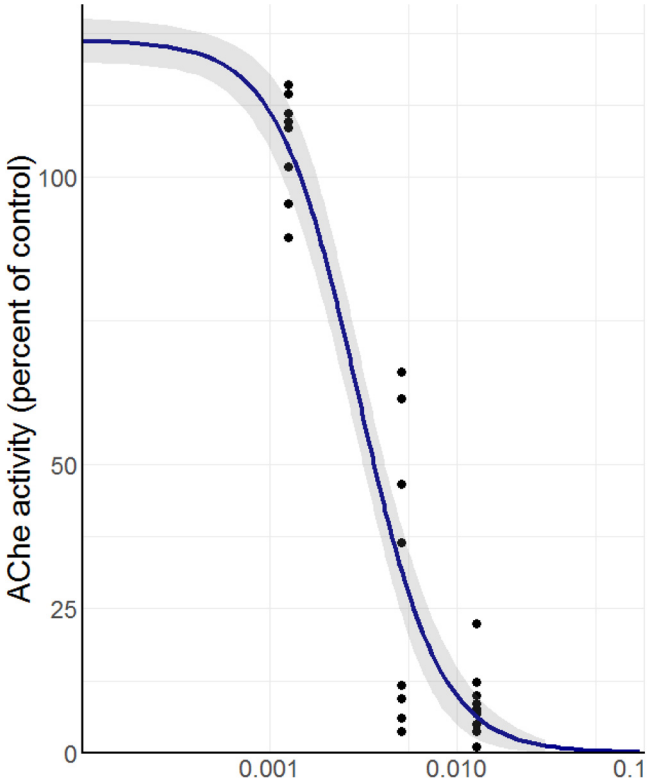
Replication is not as important as the number of concentrations being assessed.

Our choices are not determined by an understanding of mechanism in almost every case. In some instances models such as DEBTOX that start from first principles, might be applied.

Comparison of dose-response-molar basis—best for mixtures and SAR



Moles Malathion



Moles Malathion and Chlorpyrifos mixture

Data are kindly supplied by Kathy Laetz and NOAA, data analysis by Valerie Chu.

Lots of discussion regarding the use of hypothesis testing as an analysis tool. Just say no…

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Critical Review

DON'T BE FOOLED—A NO-OBSERVED-EFFECT CONCENTRATION IS NO SUBSTITUTE FOR A POOR CONCENTRATION–RESPONSE EXPERIMENT

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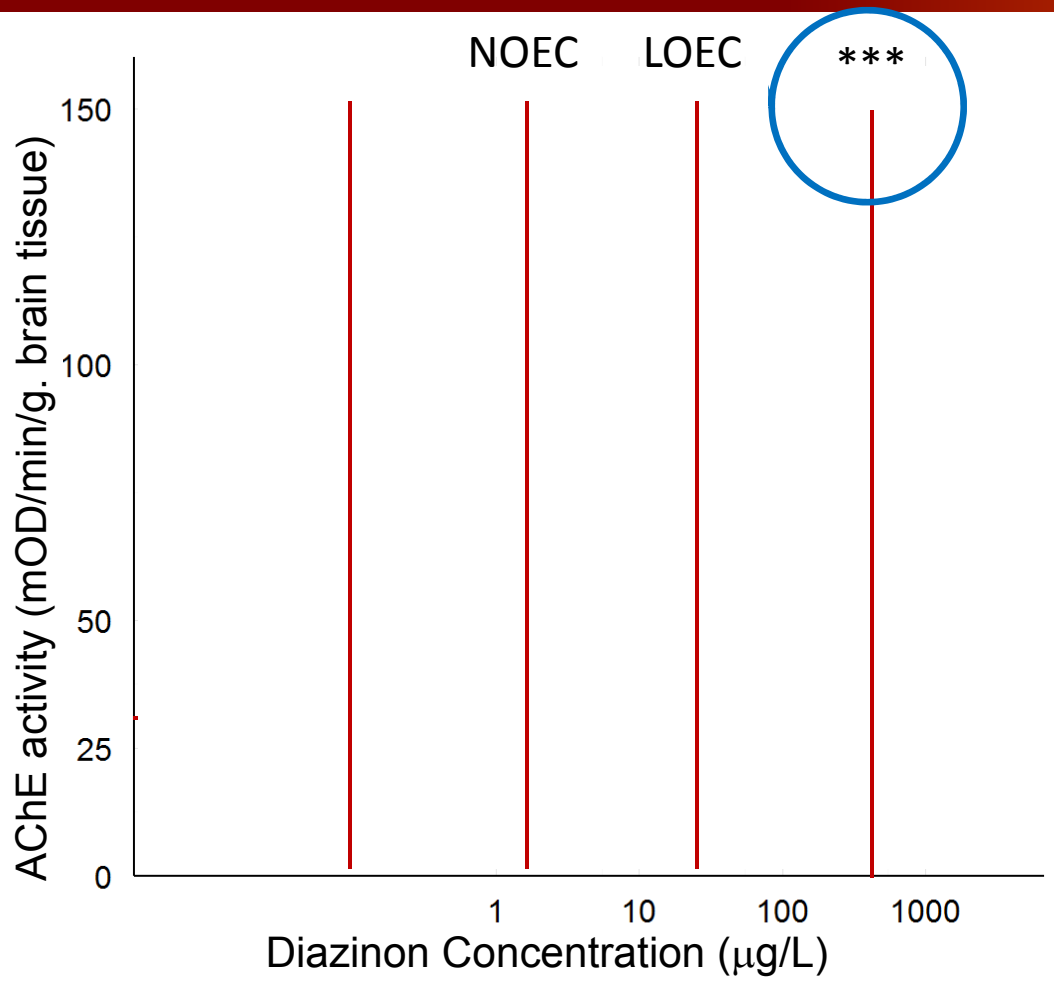
(Submitted 14 January 2016; Returned for Revision 7 March 2016; Accepted 13 April 2016)

"Renowned mathematician and science historian Jacob Bronowski once defined science as "the acceptance of what works and the rejection of what does not" and noted "that needs more courage than we might think." Such would also seem to be the case with no observed-effect concentrations (NOECs) and no-observed-effect levels in ecotoxicology."

Fox, D. R. and Landis, W. G. 2016, Don't be fooled—A no-observed-effect concentration is no substitute for a poor concentration–response experiment. *Environ Toxicol Chem*. 35:2141-2148

Here is the information usually reported.



LOEC/NOEC—does not measure response, uncertainty is not documented, slope is not reported, power is not usually documented, and the concentration is experimenter's choice.

*** <0.01—actually makes no sense statistically.

Controversy still exists—hence Fox and Landis 2016

Green (2016. Green et al 2015) does claim that hypothesis testing can be applied where regression models can not, in the evaluation of histopathology severity scores.

Actually regression models can be used to assess such datasets—as in Fox and Landis 2016.

Green JW. 2016. Issues with using only regression models for ecotoxicity studies. Integr Environ Assess Manag 12:198–199.

Green JW. 2015. In response: Challenges for statistical evaluation of ecotoxicological experiments—An industry perspective. Environ Toxicol Chem 34:2437–2439.

Let's generate an example dataset (Landis and Fox 2016)

Table 3. Artificial concentration–severity data generated by Model

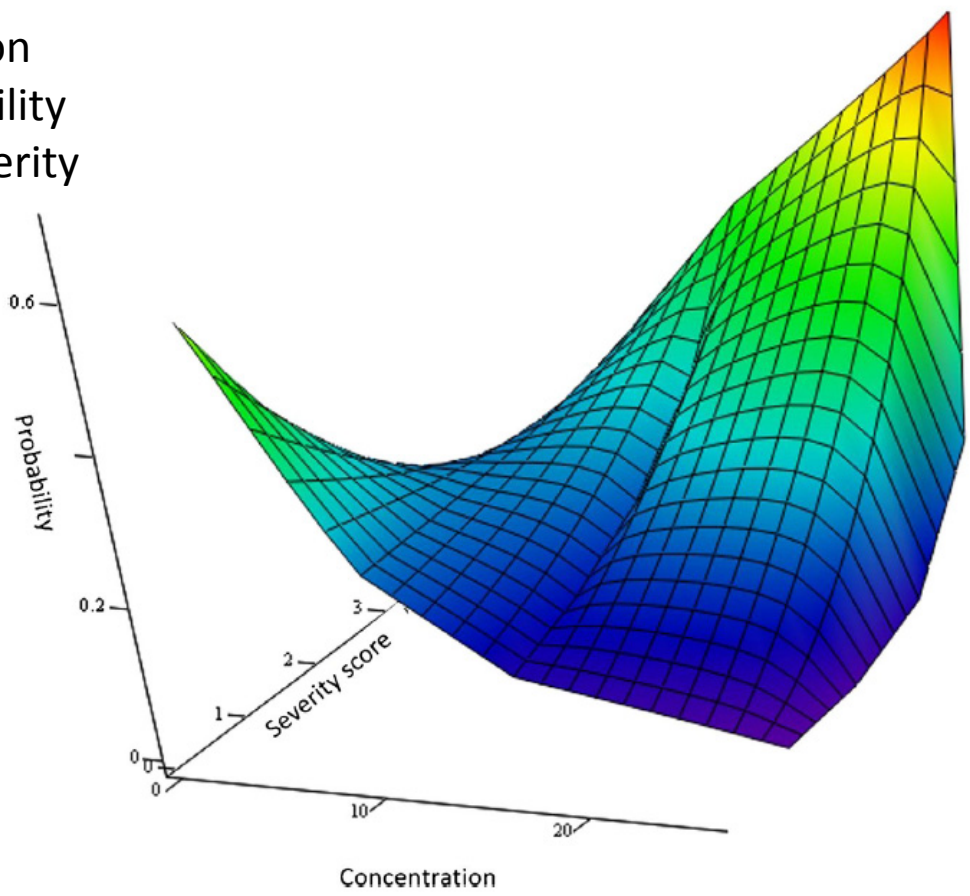
	Severity					
Concentration	1	2	3	4	5	*n*

•Numbers in each row generated using Equation (1) with sample size *n* and probabilities given in parentheses.

0.0	38 (0.500)	17 (0.300)	11 (0.150)	2 (0.050)	0 (0.000)	68
0.0625	29 (0.500)	18 (0.300)	6 (0.150)	1 (0.050)	0 (0.000)	54
3.5	24 (0.320)	18 (0.243)	14 (0.181)	9 (0.138)	7 (0.118)	72
6.25	12 (0.188)	7 (0.190)	8 (0.193)	10 (0.203)	12 (0.226)	49
13	12 (0.067)	10 (0.104)	12 (0.161)	26 (0.254)	26 (0.413)	86
26	1 (0.007)	2 (0.021)	4 (0.064)	13 (0.205)	42 (0.703)	62

Now plot the data in a probabilistic fashion

Low concentration high probability of a low severity score.



High concentration high probability of a high severity score.

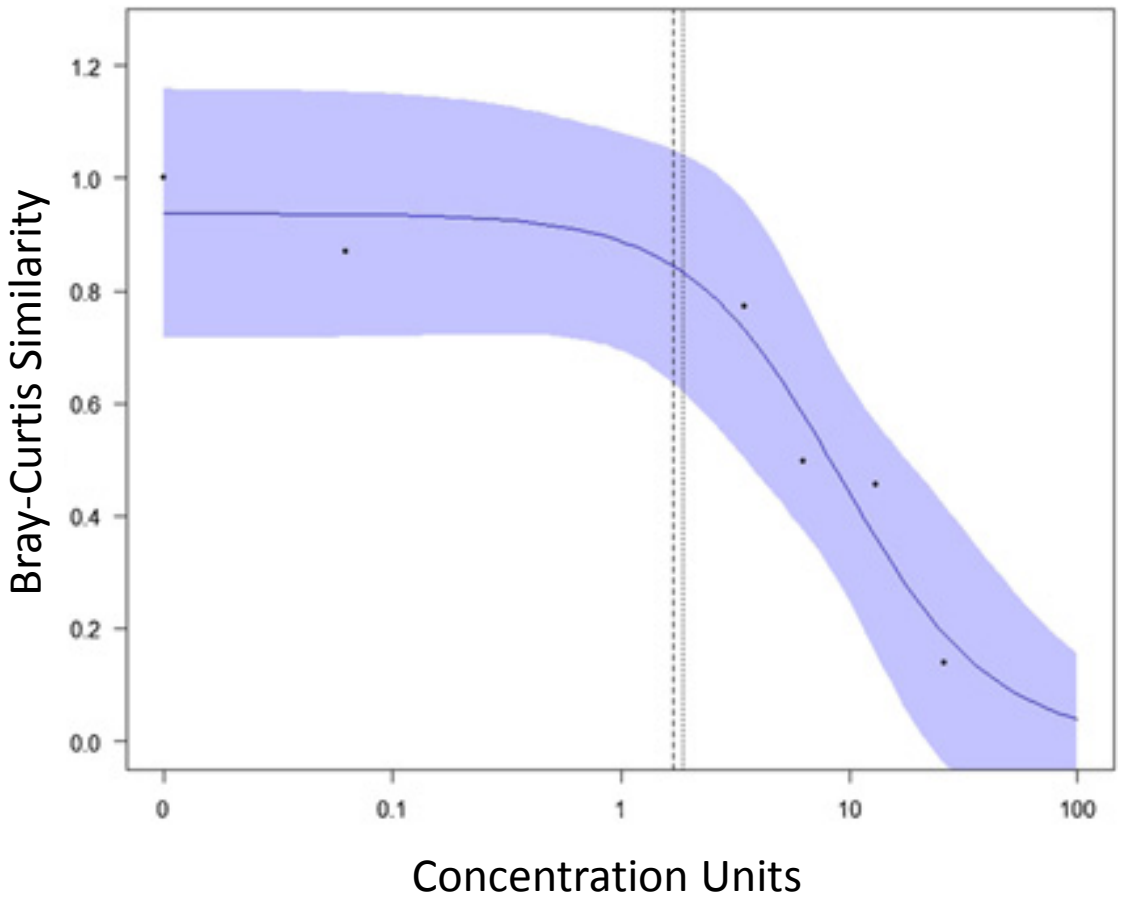
Calculate the Bray-Curtis similarity index-commonly used in ecology

Values of Bray-Curtis similarity index computed frequencies

Concentration	Bray-Curtis index relative to control
0	1.000
0.0625	0.869
3.5	0.771
6.25	0.496
13	0.455
26	0.138

Now a exposure-response curve with severity as the effect….(Fox and Landis 2016)

Values of Bray-Curtis similarity index computed frequencies

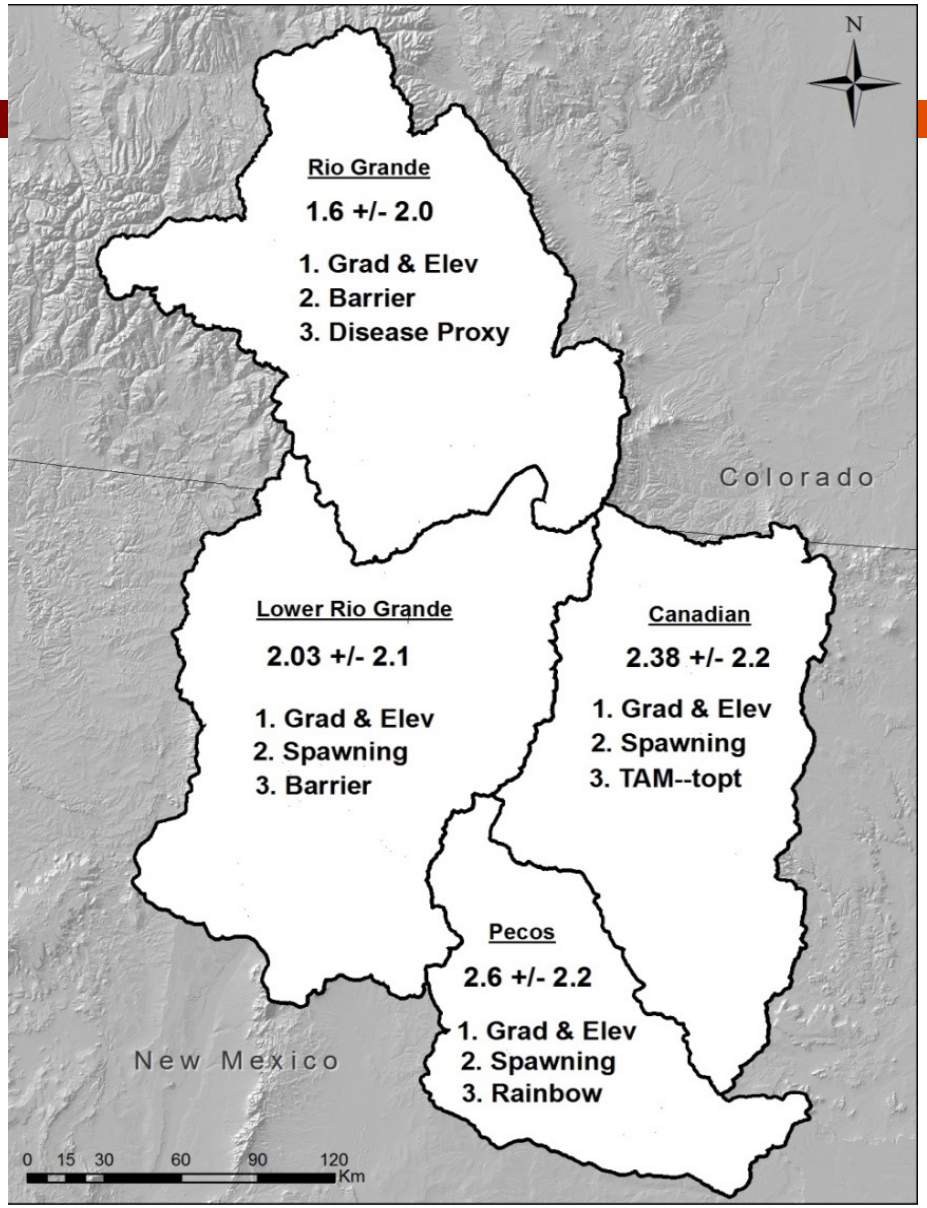


So why do I care so much about exposure-response and modeling?

Because I do ecological risk assessment for multiple endpoints incorporating multiple stressors over large landscapes.

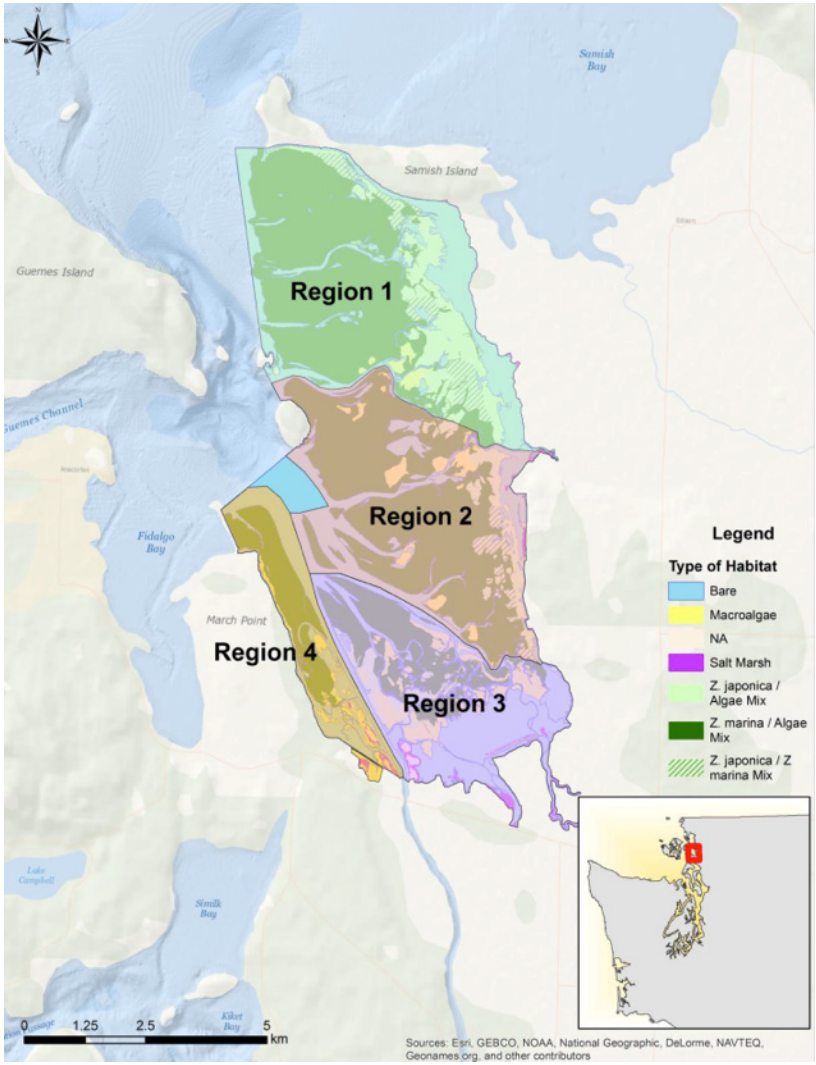
Whirling Disease to Cutthroat Trout

Ayre et al 2014



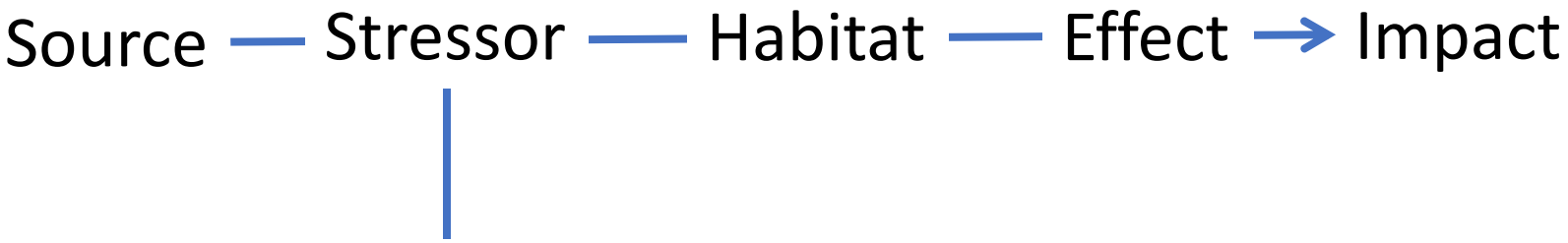
The World is lumpy—spatially explicit

Padilla Bay, Washington



Cause-effect diagrams

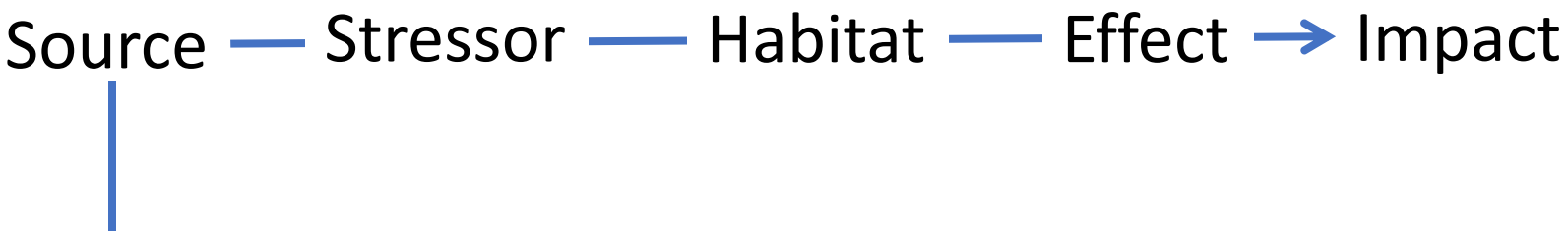
Start from each side and work inward-what do you care about and where…



Chemical or stressor specific (PAHs, PFAS, Flooding, increase in temperature).

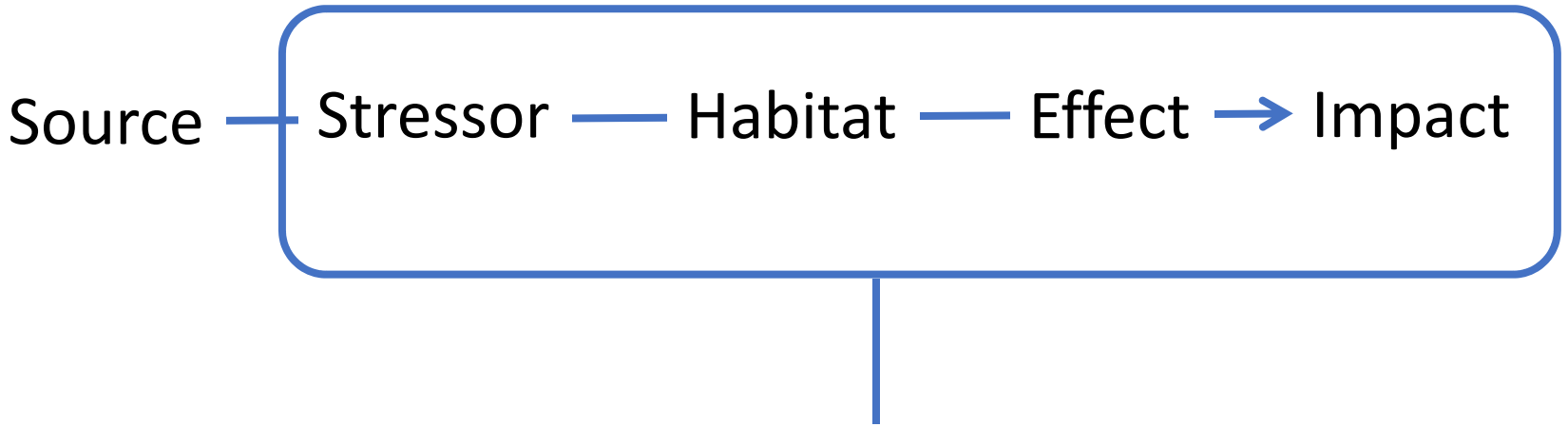
Conceptual Models are cause-effect diagrams

Start from each side and work inward-what do you care about and where…



Effluent, site or operation-the origins of the stressor. It can be the the smelter, the roadway, or a contaminated sediment.

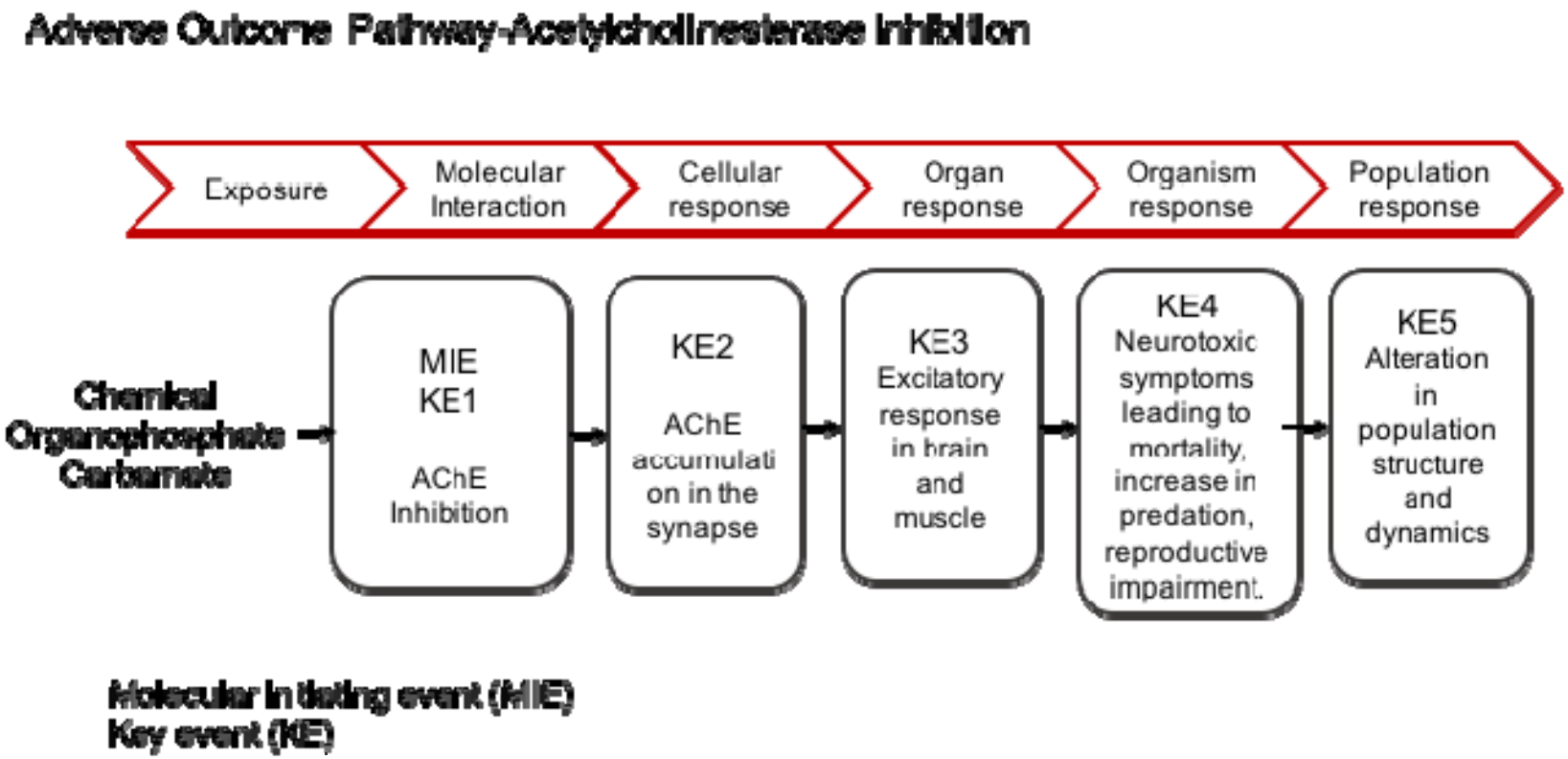
Cause-effect diagrams



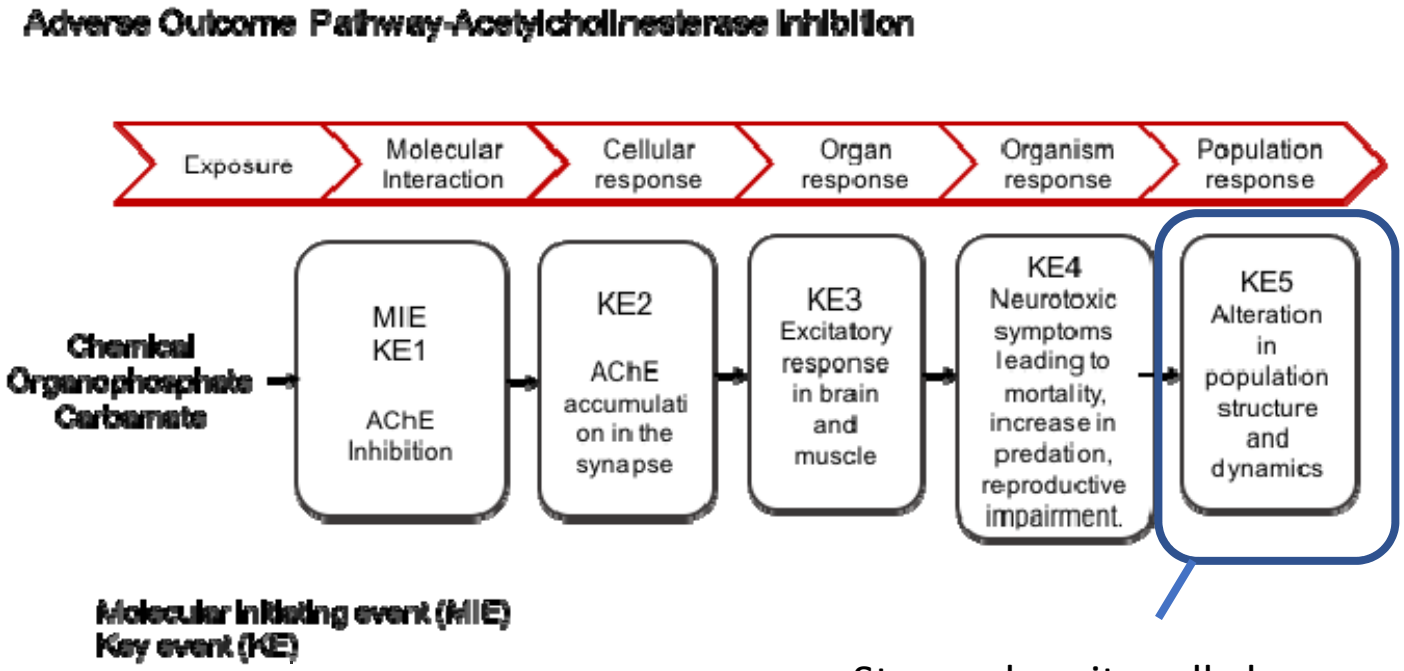
Now this should look familiar to toxicologists…….

Another name for a cause-effect pathway is an Adverse Outcome Pathway (Ankley et al 2010)

AOP (Russom et al 2014)



Scale is important but usually overlooked

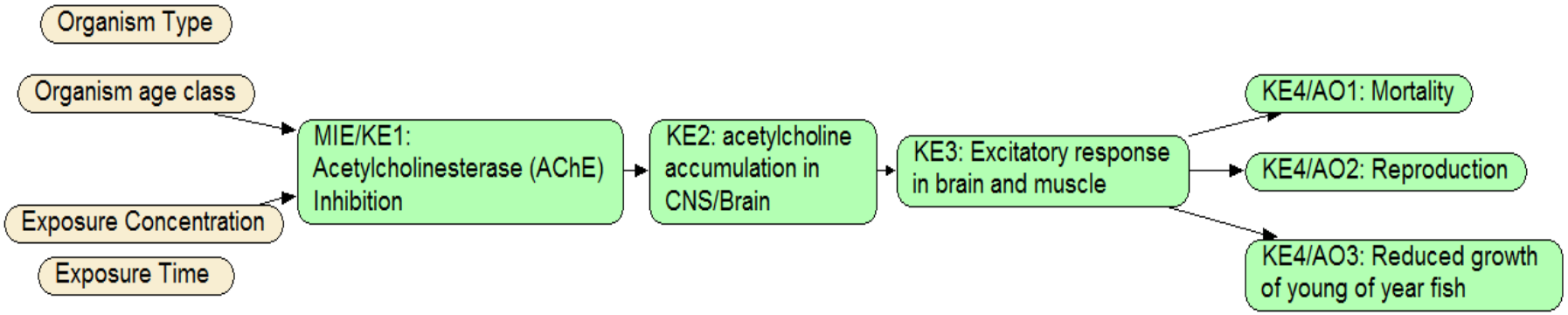


Stops when it really becomes ecological toxicology

All of this happens in a context and is an open system. Variability and probability are normal.

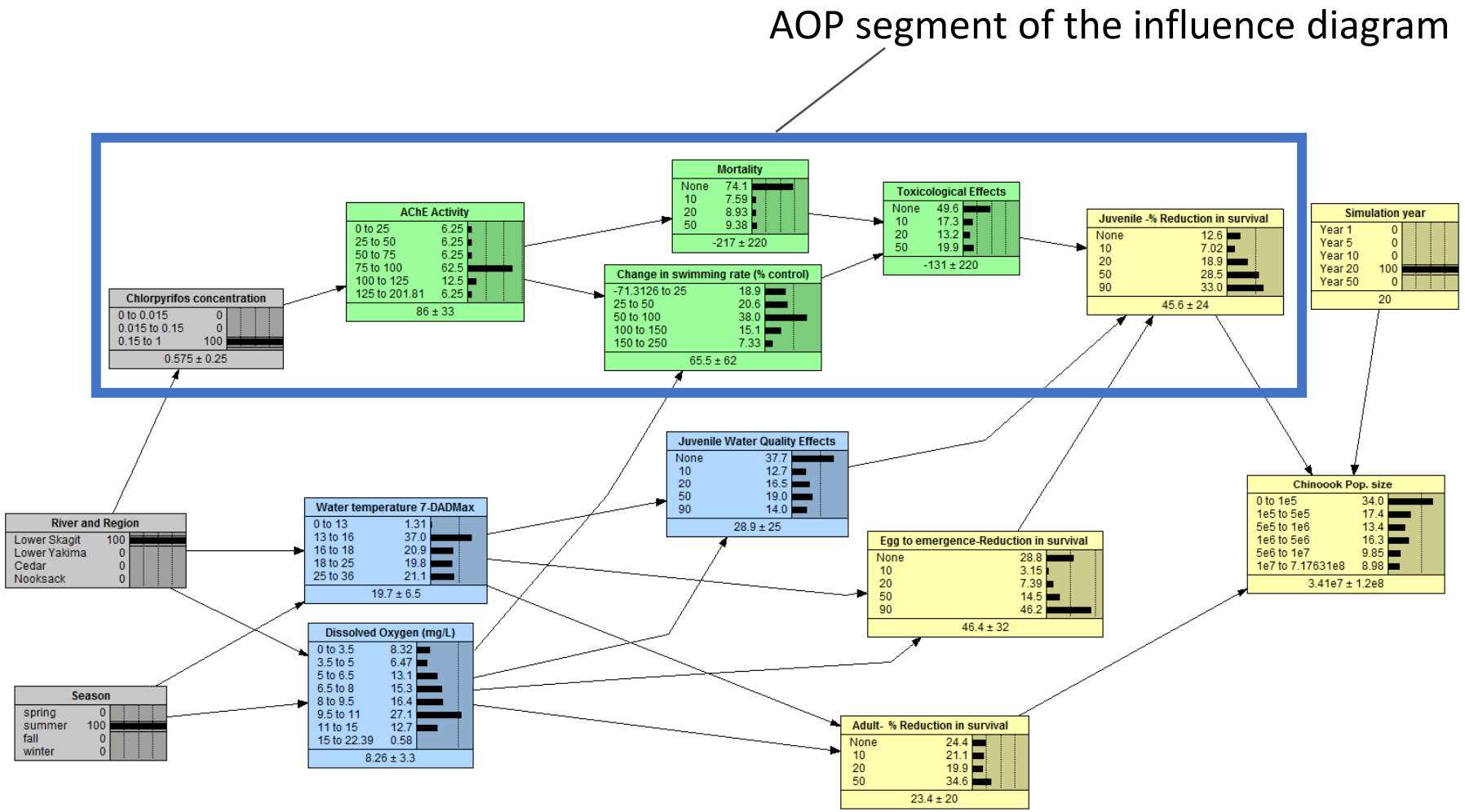
AOP turned into an influence diagram

Written using Netica.

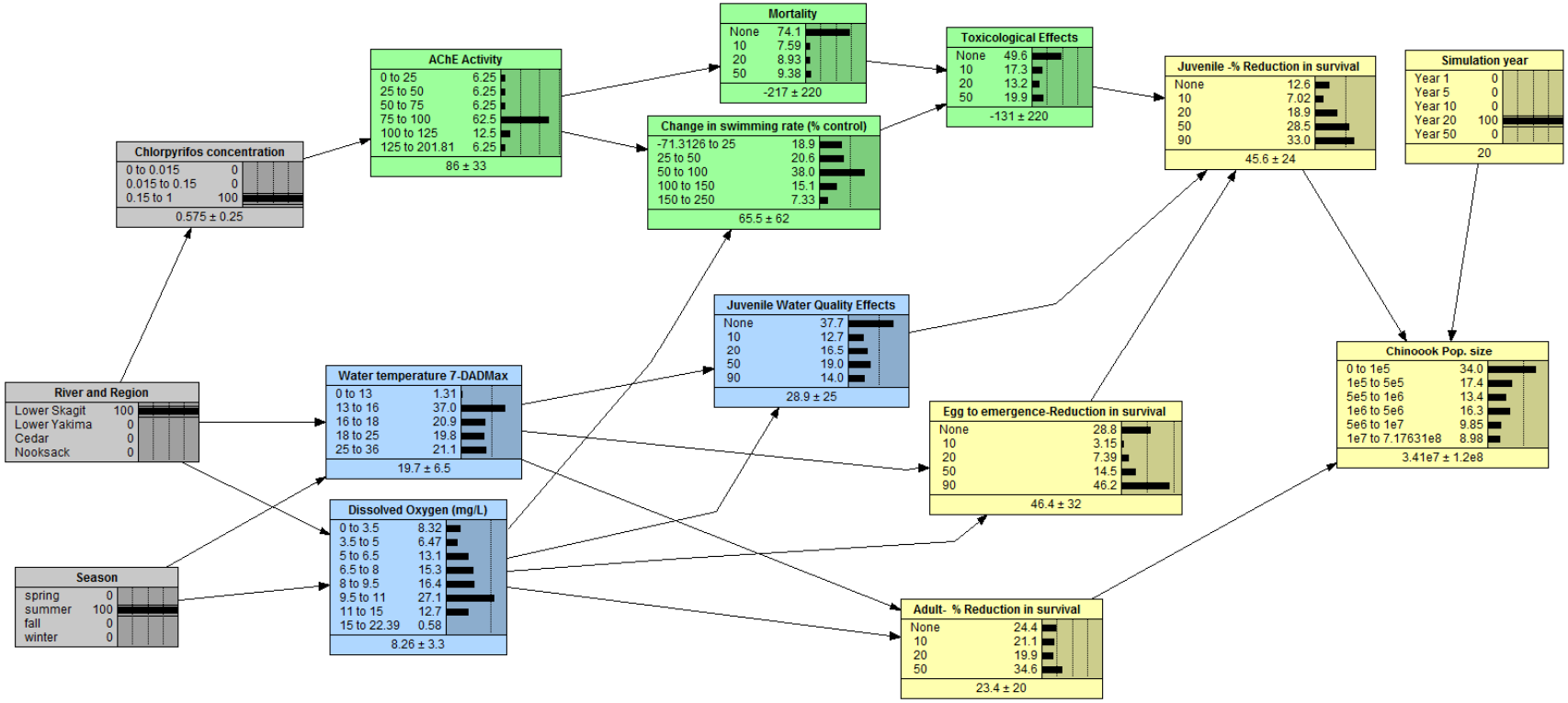


AOP is not sufficient to predict effects or risks to populations until scale, location, and environmental conditions are introduced.

AOP that now includes ecology…not magic.

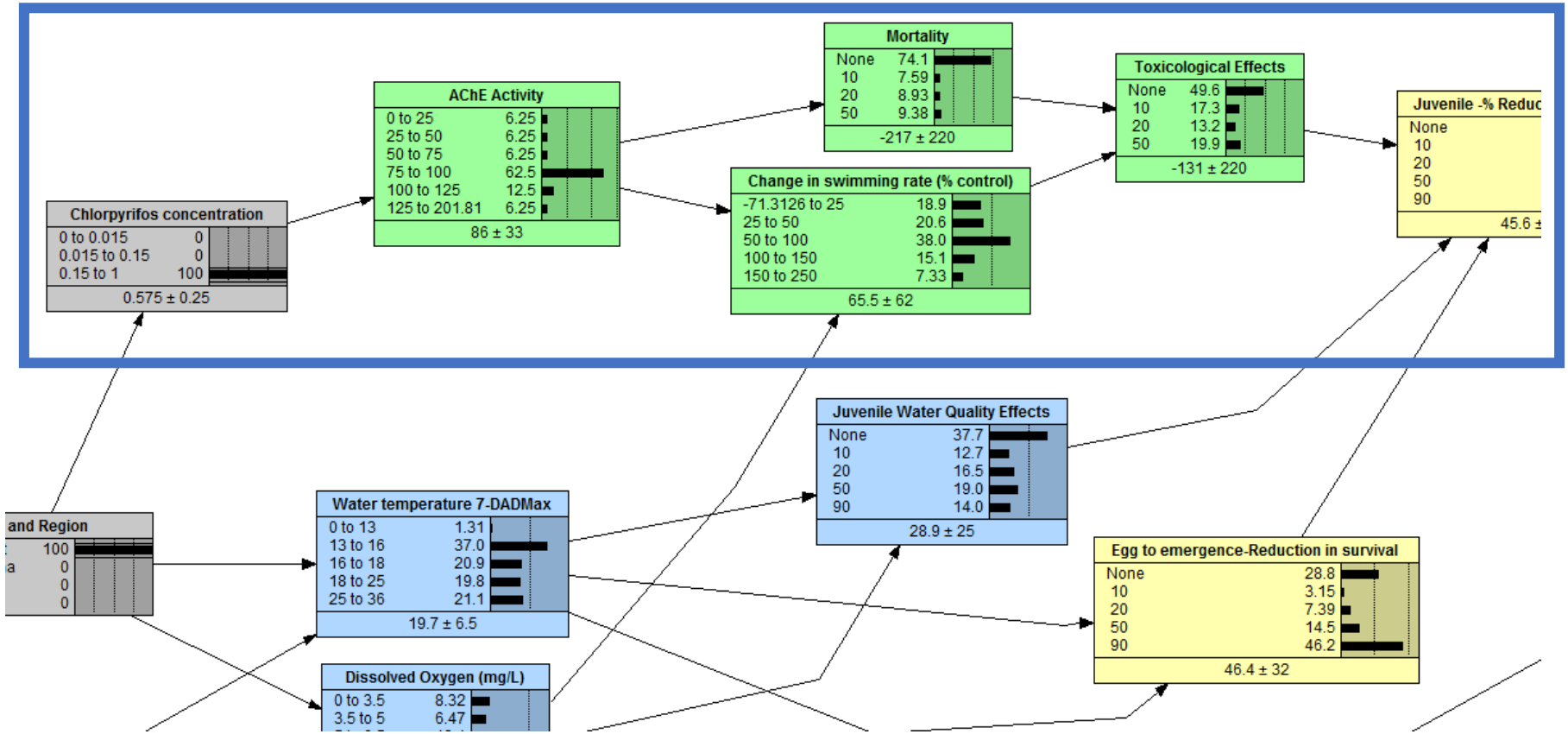


AOP is now part of our Bayesian network based model for estimating risk to Chinook Salmon in Northwest Rivers



AOP that now includes ecology…not magic.

AOP segment of the influence diagram-we use exposure-response curves to describe these relationships



Here are the ecological aspects of the cause-effect pathway

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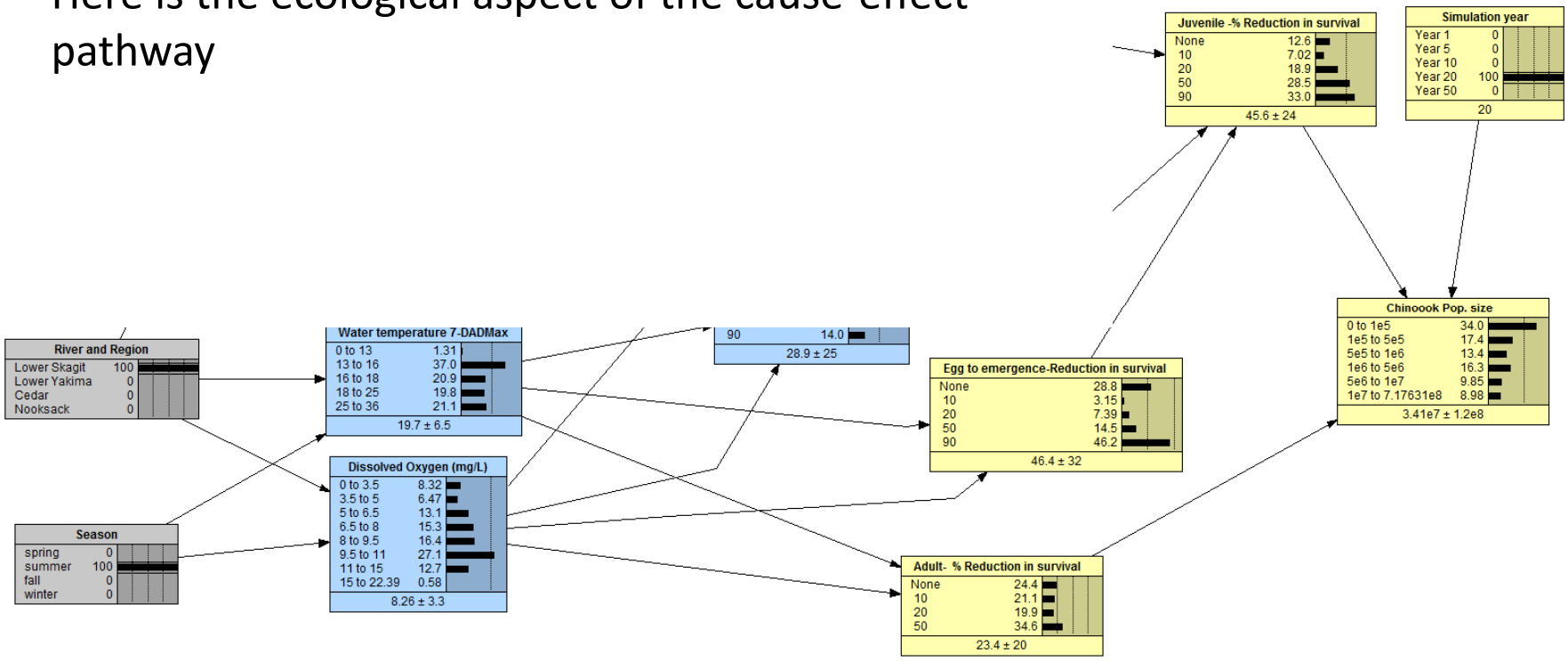
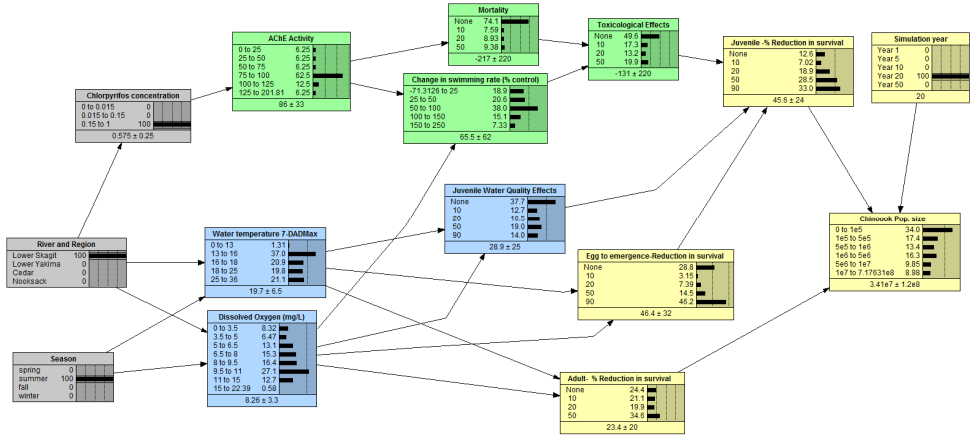


Exposure-response relationships in the risk assessment cause-effect pathway.

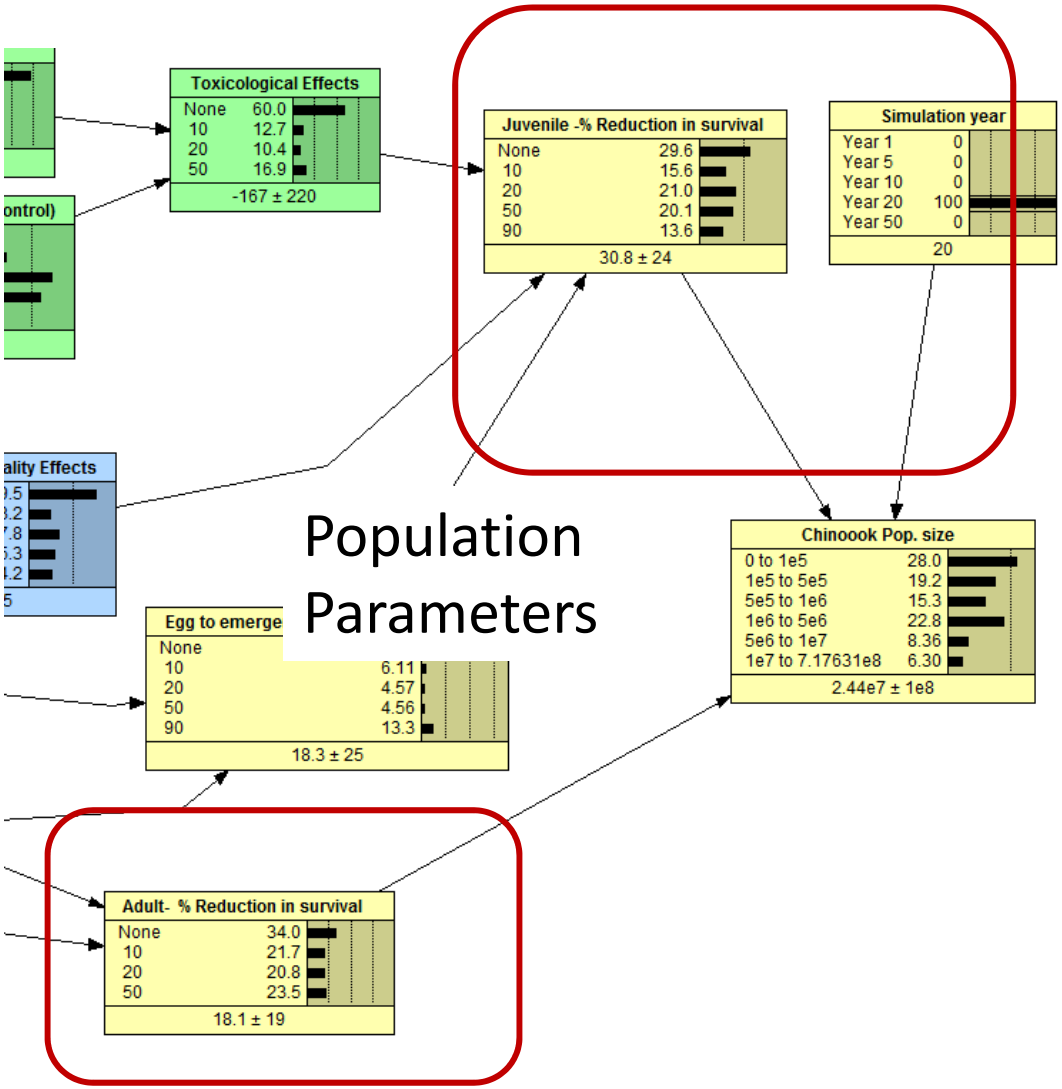
In both set of pathways exposure-response relationships are used to describe the interactions between the variables.

It makes little difference if it is an ecological interaction (water temperature or dissolved oxygen) or toxicity (Chlorpyrifos)



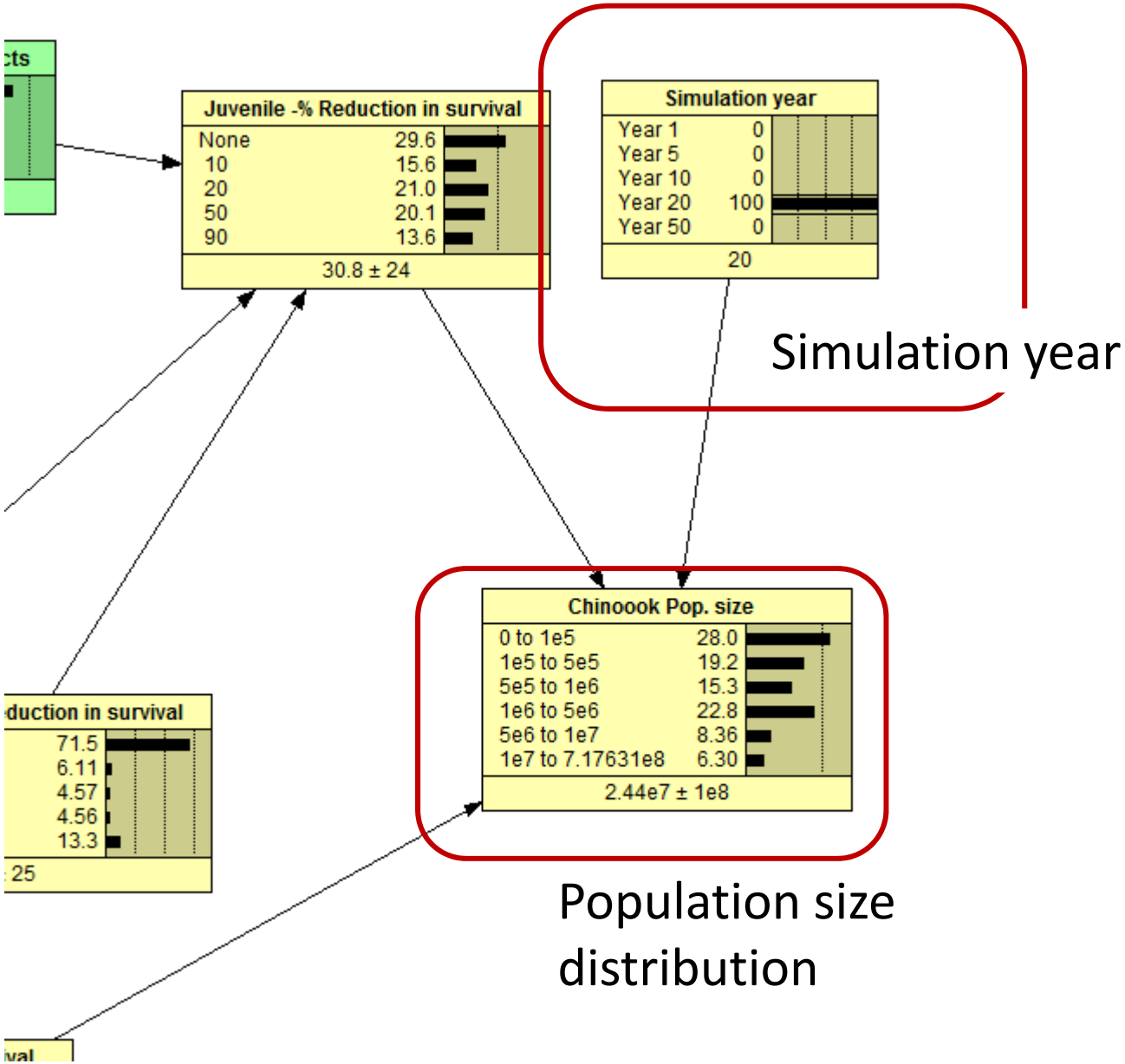
Still not an Ecological Risk Assessment—we need to build exposure-response from the individual to population.

Now we need an exposure-response relationship to go from survivorship to population dynamics.



Now for the Population part of the calculation….

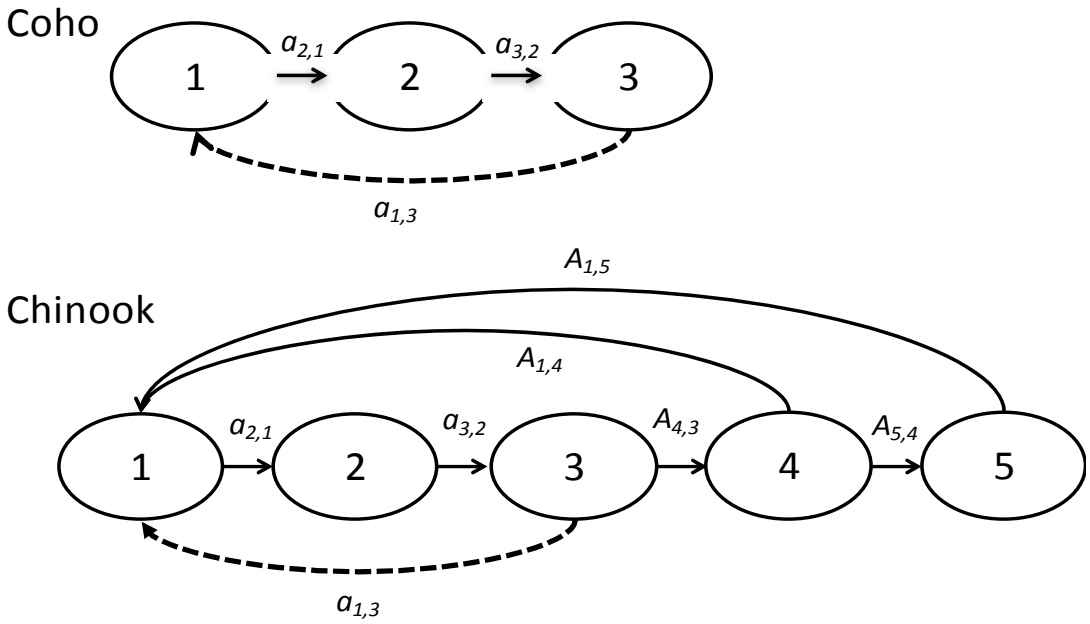
These nodes set up the input for the population simulations



Population modeling by Chelsea J. Mitchell and John D. Stark

RAMAS population modeling based on the models of Spromberg and Scholz (2011)

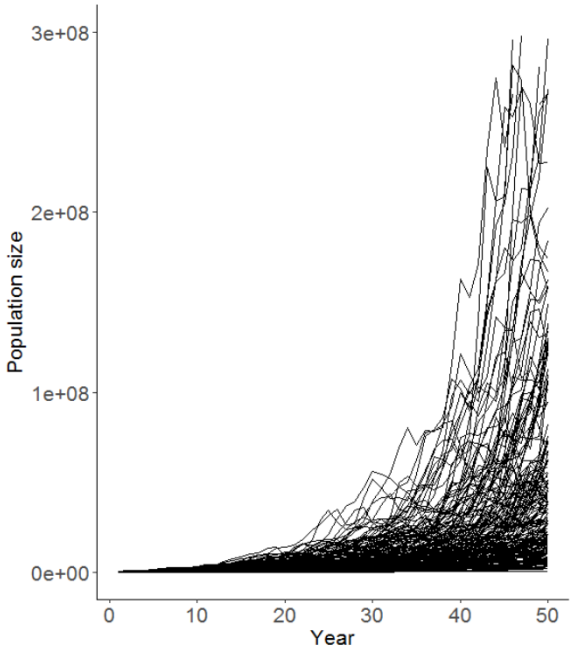
Population model based on Baldwin et al (2009) and Spromberg and Scholz (2011) to estimate changes in population and patches



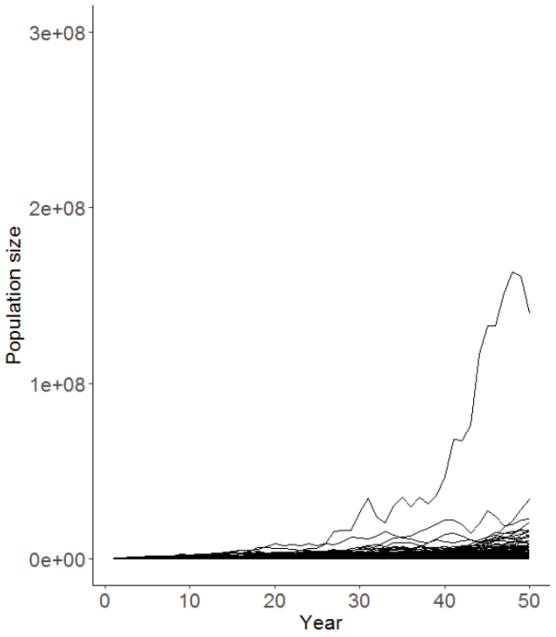
Baldwin et al 2009

RAMAS modeling and the model does predict exposure-response relationships-Chinook populations

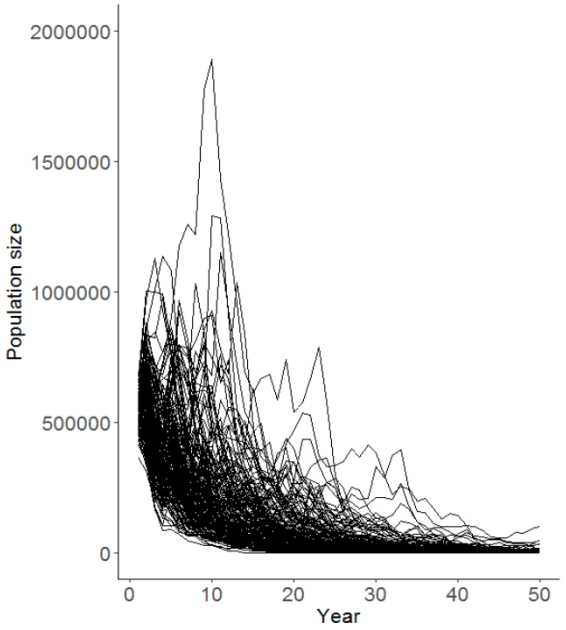
Baseline model



20 percent reduction

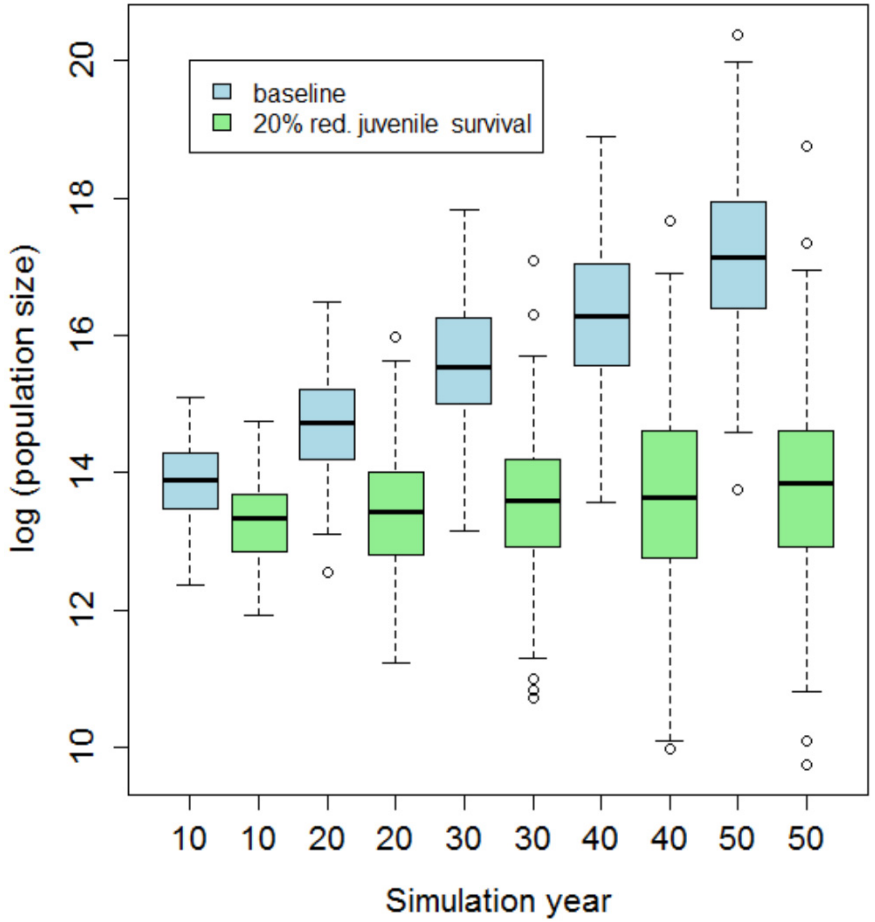


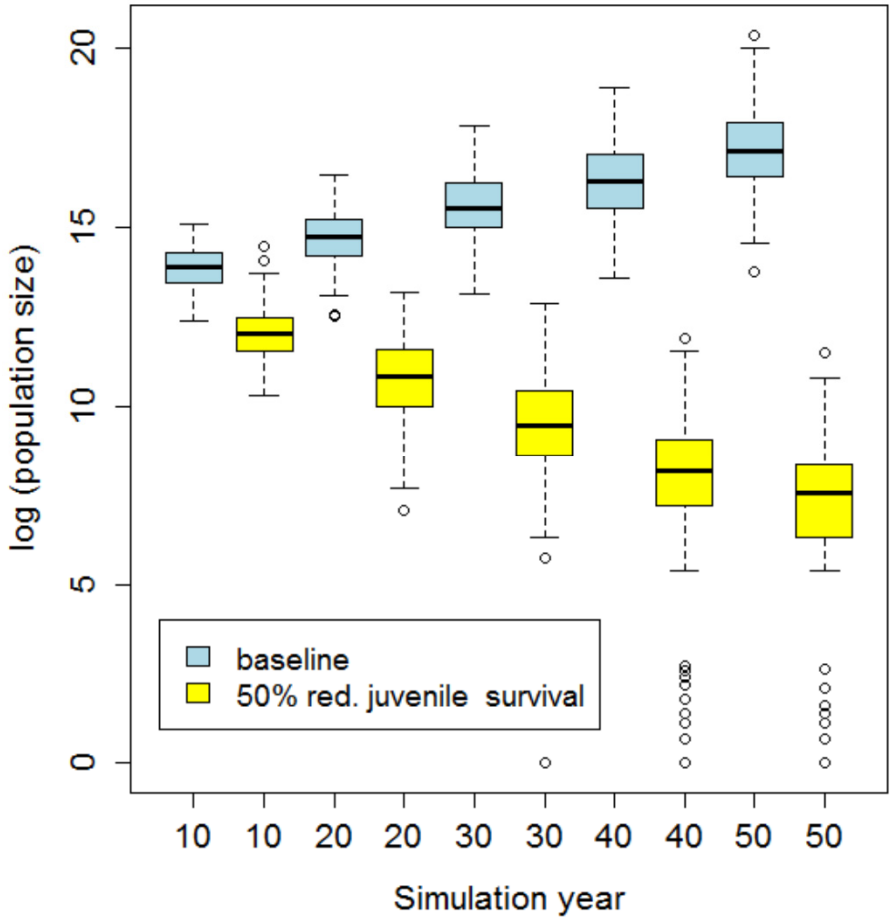
50 percent reduction



Note the change in the y axis for the final graph.

Populations and exposure-response-Chinook populations over time.





It is also possible to build exposure-response relationships using field datasets

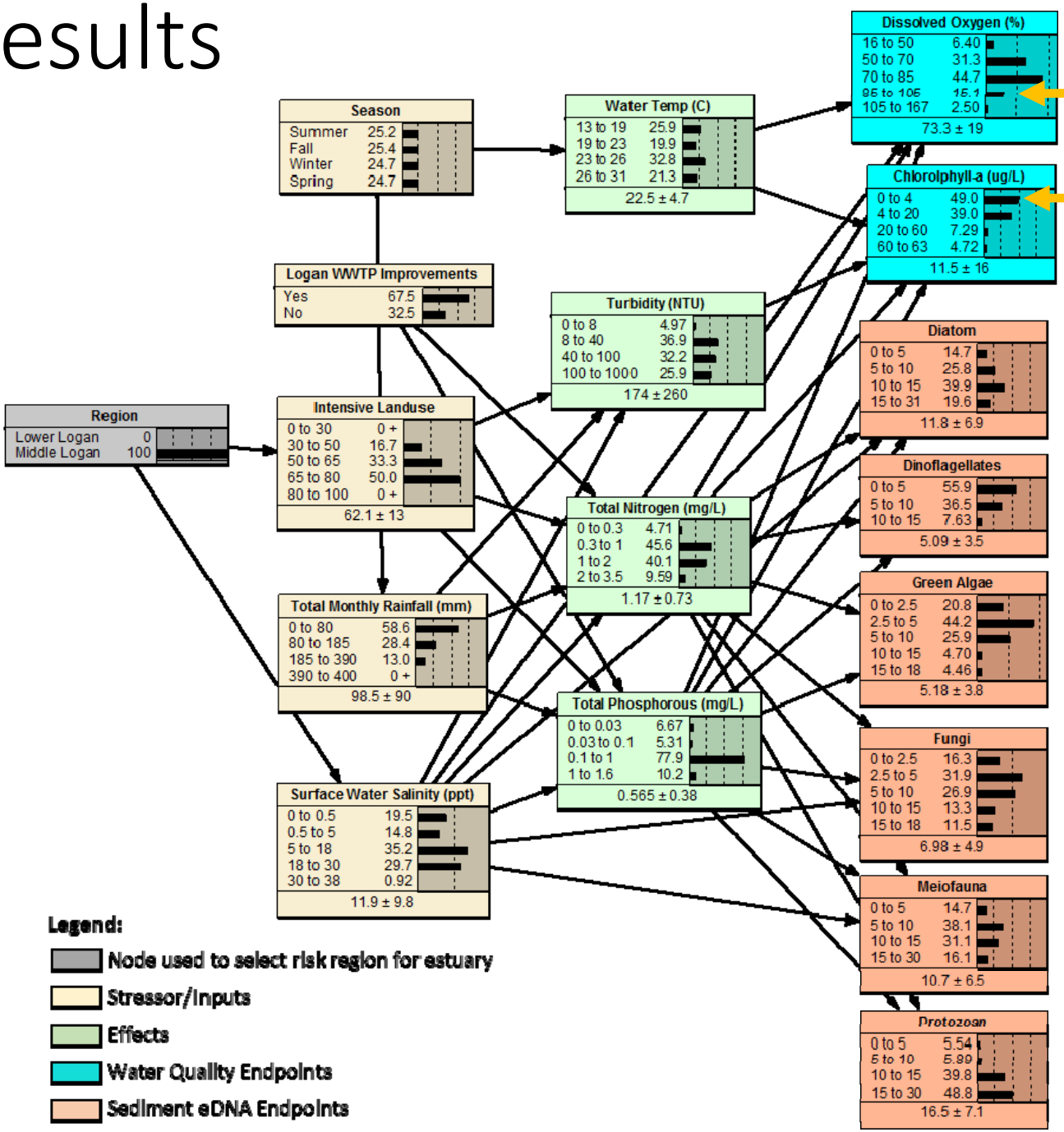
Using Bayesian networks Predicting Risk to Estuary Water Quality and Patterns of Benthic Environmental DNA in Queensland, Australia

Scarlett E. Graham, Wayne G. Landis, and Anthony A. Chariton

Extensive monitoring program for both inputs, water quality parameters and eDNA

- Nutrient and sediment loading from non-point sources
- Environmental DNA (eDNA) samples of the eukaryote benthic communities
- Dataset from 8,000 cases to derive relationships between input variables and the likelihood of meeting water quality standards.

Results



% probability of achieving water quality objective

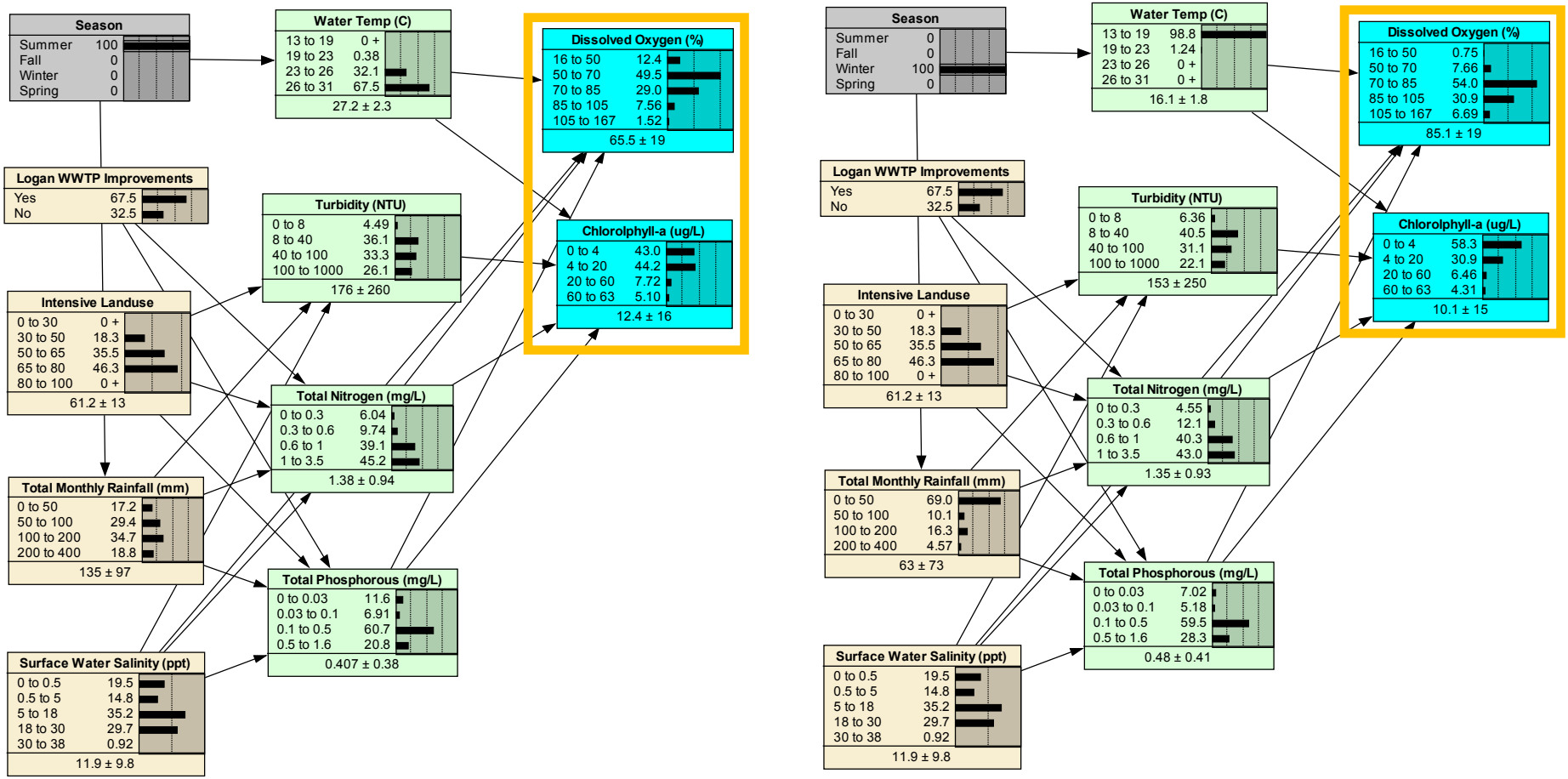
Results:

1. Given the inputs, predicts the most likely state for a variable.

2. Distribution communicates the uncertainty around that prediction.

Interactive Capability

Summer Predictions versus Winter Predictions



Finally…….

Exposure-response modeling can be done with the datasets that have been examined—and they provide a wealth of information.

Exposure-response modeling allows the incorporation of toxicity information from the AOP with ecological response data sets to predict ecological impacts.

We can also used environmental datasets to model exposure-response sufficiently to make predictions.