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A framework for incorporating the toxicity of pesticide mixtures into ecological risk assessments

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Incorporating the Toxicity of Pesticide Mixtures into Ecological Risk Assessments

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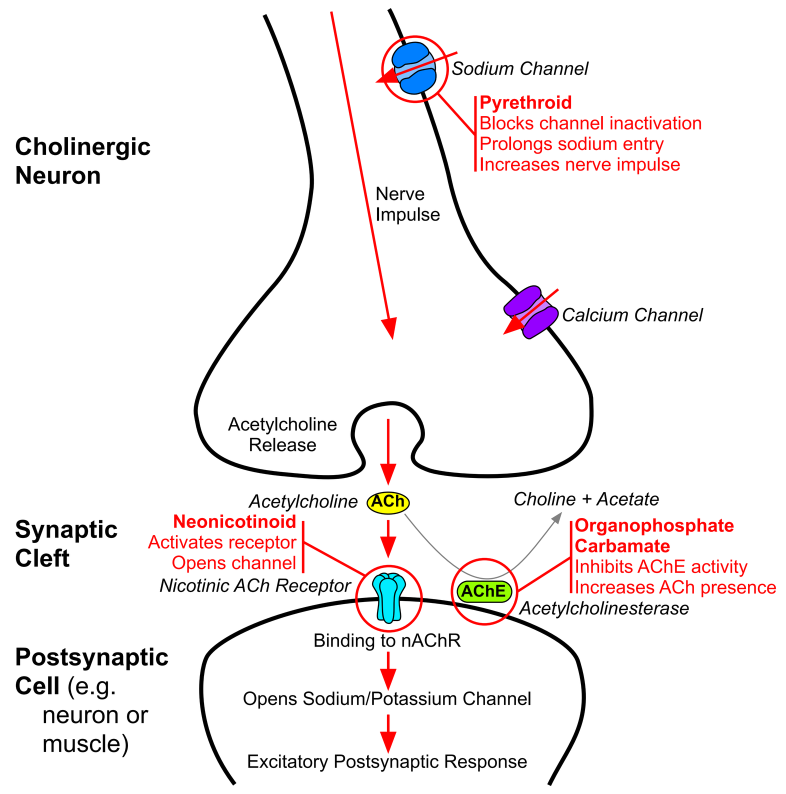
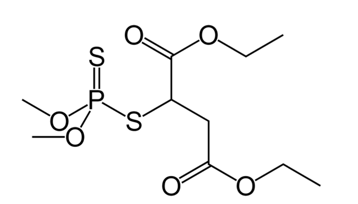
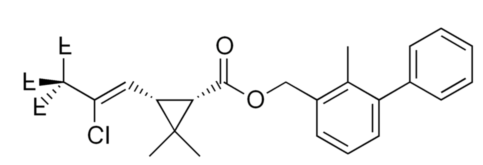
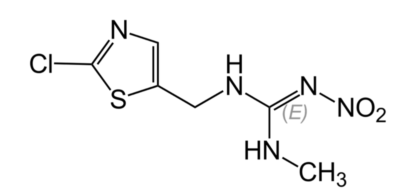
Pesticides are widely used throughout the United States and are frequently detected as complex mixtures in aquatic habitats. Therefore, pesticide mixture toxicity is an important component of risk assessments performed within different regulatory and policy contexts. Here we describe a process for assessing toxicity of three categories of pesticide mixtures; formulated products (one product containing multiple active ingredients), tank mixes (multiple pesticides applied simultaneously), and environmental mixtures (resulting from unrelated pesticide use over the landscape). Mixtures were assumed to be either dose-additive or response-additive, depending on the modes of action of the individual pesticide components. Toxicity estimates utilized two main pieces of information - exposure concentrations and taxa-specific toxicity values. Exposure concentrations were generated using either EPA's Pesticide Water Calculator (PWC), which incorporates chemical and application-specific parameters to calculate anticipated water concentrations over different durations, or utilized directly from routine monitoring studies. Standard measures of toxicity (typically the LC_{50}, or the concentration that is lethal to 50% of the test organisms) were used to represent taxa groups with different sensitivities to a given pesticide. Reflecting the three mixture categories, we predicted toxicity for formulated products containing organophosphates, co-applications reported in California's Pesticide Use Reporting System, and ambient water quality monitoring data from Washington. Results show that predicting mixture toxicity is possible with currently available information, and these predictions can be used in regulatory situations and ecological risk assessments. Importantly, failing to consider mixtures may underestimate pesticide risk, leading to erroneous risk conclusions and ineffective protections for aquatic species and habitats.



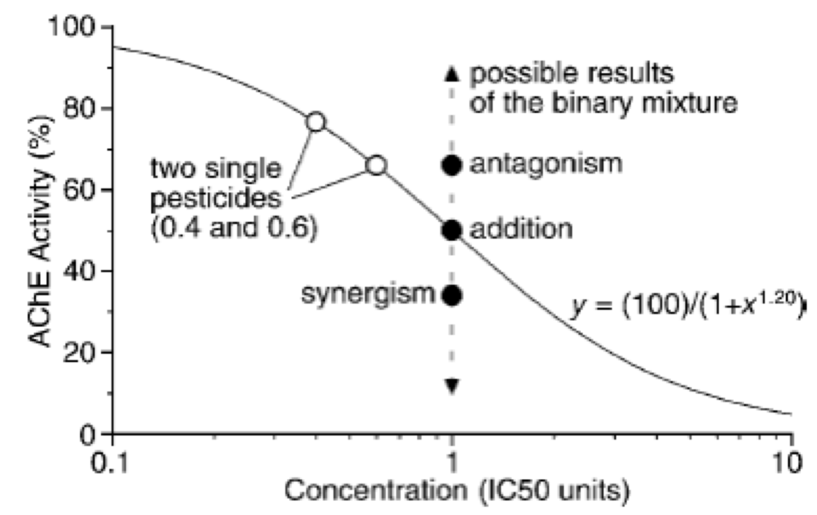
Disruption of normal neurological function can produce a suite of adverse effects including altered feeding and swimming behaviors that are critical for fish growth and survival.







Organophosphate/Carbamate	Pyrethroid	Neonicotinoid
chlorpyrifos	cypermethrin	**imidacloprid**
diazinon	**bifenthrin**	thiamethoxam
malathion	Gamma-cyhalothrin	clothianidin
ethoprop	permethrin	acetamiprid
methomyl	resmethrin	thiacloprid
carbaryl	tetramethrin	
carbofuran	esfenvalerate	



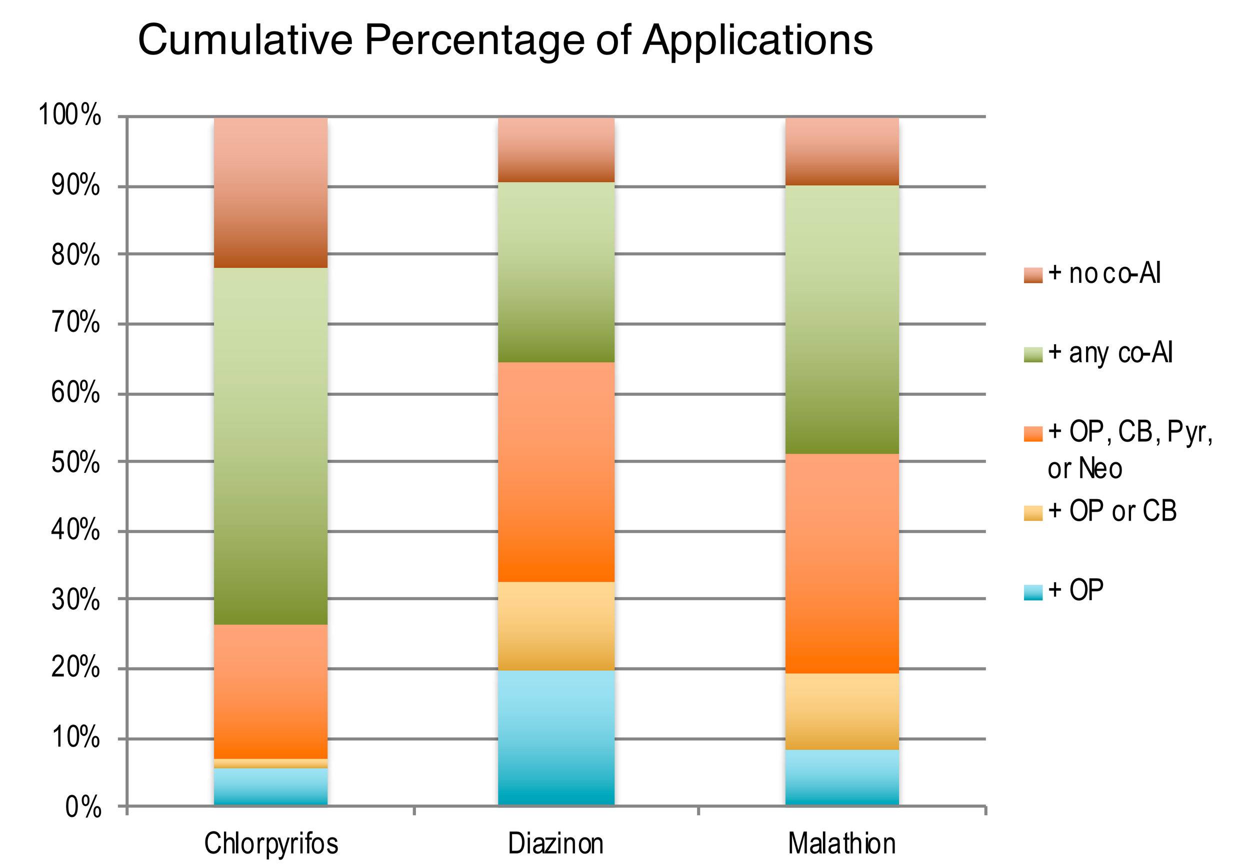
- Current methodologies for calculating mixture toxicity indicate that additivity is the appropriate initial assumption
- Concentration-addition models are appropriate for similar mode of action pesticides
- Response-addition models are used for dissimilar mode of action mixtures
- Taxa-specific toxicity values reflect differing levels of sensitivity and magnitudes of toxic effect

Daphnia sp.

Baetis sp.

Oncorhynchus sp.

- Existing tools and available information produce reliable and reasonable predictions of mixture toxicity.
- Primary data necessary for mixture predictions (i.e., exposure estimates and standard measures of toxicity) are widely available.
- Identified uncertainties regarding mixtures would benefit from additional data (i.e., estimating exposure concentrations across habitats, pesticide concentrations in marine environments).
- Pesticide risk assessments that do not incorporate mixtures may underestimate resulting toxicity.
- Examples show it is reasonable to conclude that exposure to pesticide mixtures poses a threat to many aquatic species.
- Risk assessments that do not include mixtures are likely to underestimate risk to aquatic species.



Recent pesticide use data from California (2008-2012) shows that organophosphates are frequently used with other neurotoxic pesticides.

Formulated Products

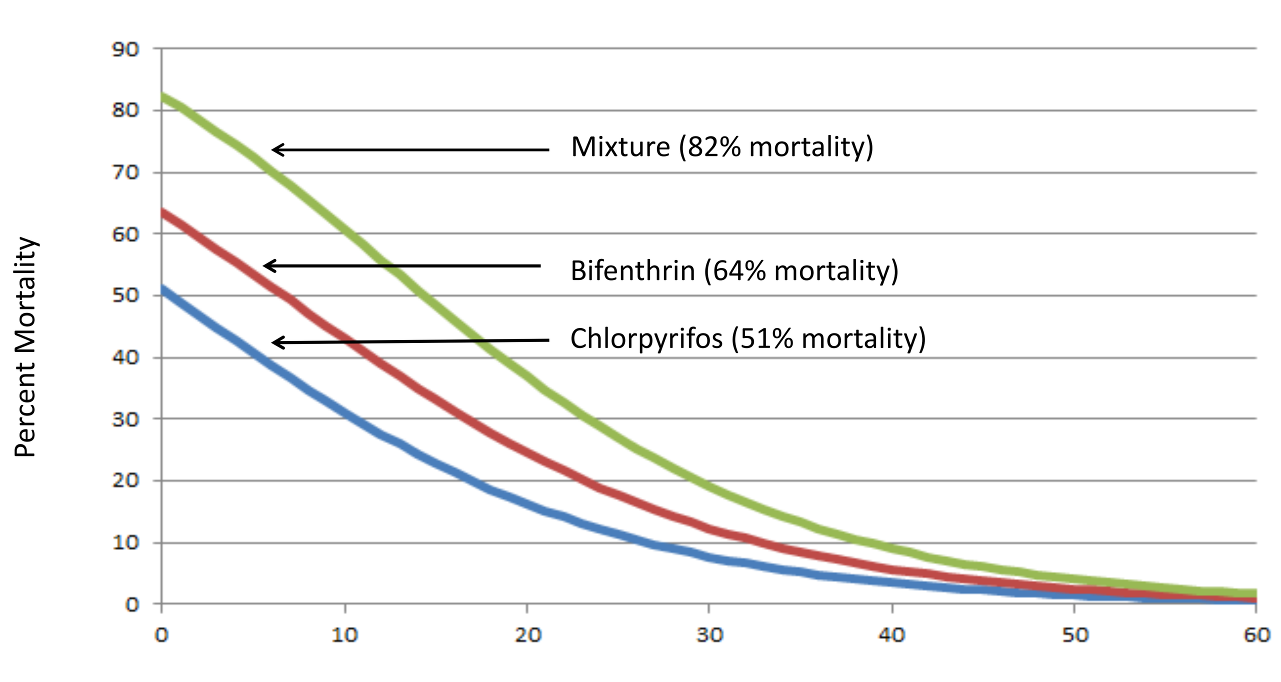
Formulated products are produced and sold as one product containing multiple active ingredients, with the exact types and amounts of active ingredients shown on product labels. Here, additive toxicity (assuming response-addition) was enhanced in freshwater fish exposed to a mixture of cyhalothrin and chlorpyrifos as compared to either chemical singly.

Process:
- ***Active ingredients identified on registered product labels***
- ***Taxa-specific LC_{50} values obtained from print and online sources (e.g. EPA reports)***
- ***Pesticide water calculator (PWC) predicted exposure concentrations in generic aquatic habitats***
- ***Dose-addition models (concentration-addition or response-addition) used to predict cumulative toxicity***

Image from: store.nzfarmsource.co.nz

Formulated Product					
	1-day exposure				
	EEC (ug/l)	Fish LC_{50}	Aquatic Invert LC_{50}	Fish Mortality	Invertebrate Mortality
chlorpyrifos	1.7994	1.8 ppb	0.06 ppb	54.42%	40.68%
cyhalothrin	0.0177	0.078 ppb	0.0014 ppb	16.73%	0.48%
cumulative mortality:				**62.05%**	**59.04%**

Formulated products containing multiple active ingredients can increase both the magnitude and duration of resulting toxicity.



Tank Mixes

Tank mixes occur when pesticide users apply multiple pesticides simultaneously at the use site. Many tank mixes are explicitly allowed on product labels, and their use is often encouraged to increase pesticide efficacy. California Department of Pesticide Regulation (CDPR) maintains the largest publically-available database of pesticide applications from which tank mixture application can be obtained.

Process:
- ***Active ingredients identified on registered product labels or from usage data (e.g., CDPR database)***
- ***Taxa-specific LC_{50} values obtained from print and online sources (e.g. EPA reports)***
- ***PWC (pesticide water calculator) predicted exposure concentrations in generic aquatic habitats***
- ***Dose-addition models (concentration-addition or response-addition) used to predict cumulative toxicity***

Example 1: Malathion and Naled applied to Strawberries

Generic Aquatic Habitat	Malathion EEC (ppb)	Naled EEC (ppb)
vernal pool, 1x1x0.1m	74	37
small pond, 10x10x1m	5.0	2.5
small lake, 100x100x2m	0.9	0.4

AgDrift estimates assuming ground application 2 lb malathion* + 1 lb naled/A, low boom, ASAE very fine-fine droplet distribution- 90th percentile, 25 ' buffer. *Labeled max rate for malathion in strawberries.

Analysis of CDPR data shows that naled was co-applied with malathion more than 1500 times in CA strawberries from 2008-2012. The majority of these co-applications occurred at the maximum labeled application rates (1 lb/acre and 2 lb/acre, respectively). No difference in application rate was observed for malathion when applied singly or with another pesticide.

Example 2: Malathion and Permethrin applied to Alfalfa

Generic Aquatic Habitat	Malathion EEC (ppb)	Permethrin EEC (ppb)
vernal pool, 1x1x0.1m	87	7.0
small pond, 10x10x1m	13	0.7
small lake, 100x100x2m	3.6	0.2

AgDrift estimates assuming aerial application 1.25* lb malathion + 0.1 lb permethrin/A, Tier 1 settings, fine-medium droplet distribution, 150' buffer. *Labeled max rate for malathion in alfalfa.

CDPR data also shows that permethrin was co-applied with malathion more than 1200 times in CA alfalfa crops from 2008-2012. The majority of these co-applications occurred at the maximum labeled application rates (0.1 lb/acre and 1.25 lb/acre, respectively). No difference in application rate was observed for these two chemicals when applied singly or together.

Environmental Mixtures

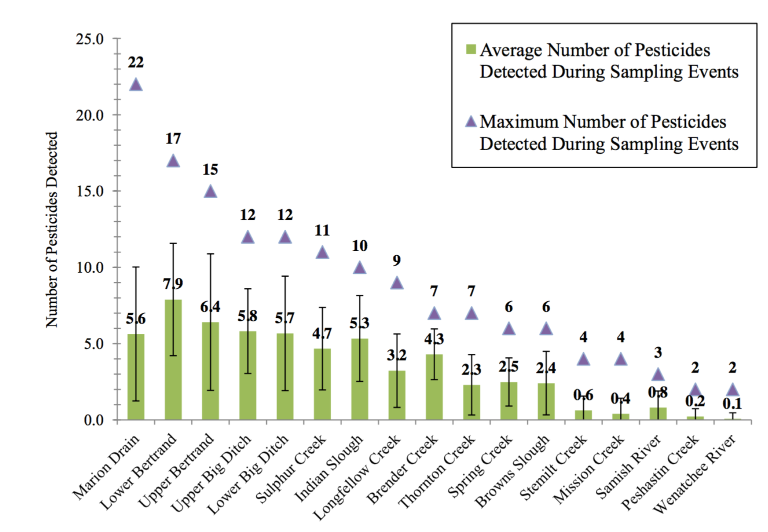


Figure 13: Average and Maximum Number of Pesticides Detected in 2013

Figure and photo from WA Dept of Agriculture, 2015

Environmental mixtures result from the unrelated use of multiple pesticides across the landscape, and are typically detected in ambient water quality monitoring. Pesticides that enter aquatic habitats following direct application, spray drift, and surface runoff from use sites can contaminate aquatic habitats, thereby posing a threat to the listed species occupying those habitats. In a typical year in the U.S., pesticides are applied at a rate of approximately five billion pounds of active ingredient per year. Ambient monitoring data shows that pesticide contamination in the nation's freshwater habitats is ubiquitous, and that pesticides usually occur in the environment as mixtures. For example, USGS NAWQA monitoring detected two or more pesticides in more than 90% of samples from urban, agricultural, and mixed-use streams nationwide.

Process:
- ***Active ingredients identified from ambient water quality monitoring***
- ***Taxa-specific LC_{50} values obtained from print and online sources (e.g. EPA reports)***
- ***Exposure concentrations measured in ambient monitoring***
- ***Dose-addition models (concentration-addition or response-addition) used to predict cumulative toxicity***

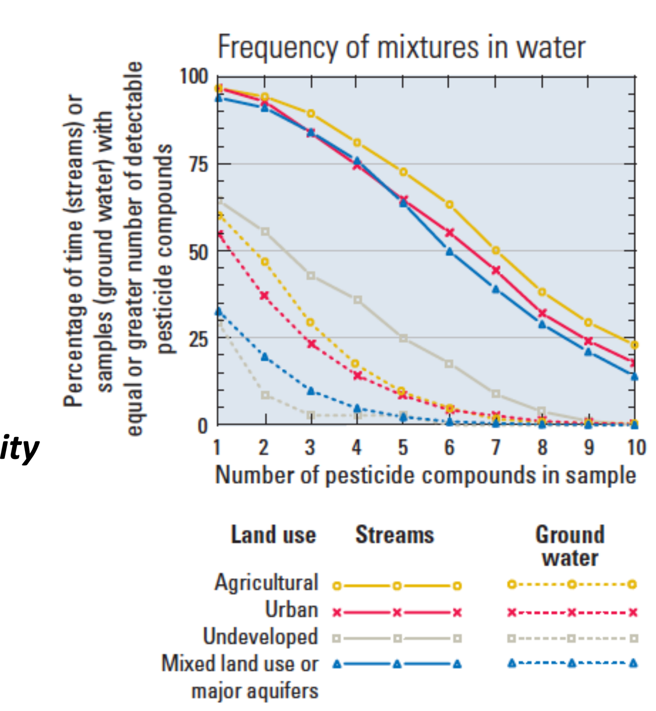


Figure from *RJ Gilliom, 2007, ES&T 3409-3414*

Photos from http://wwwapp.epa.ohio.gov/ and US EPA