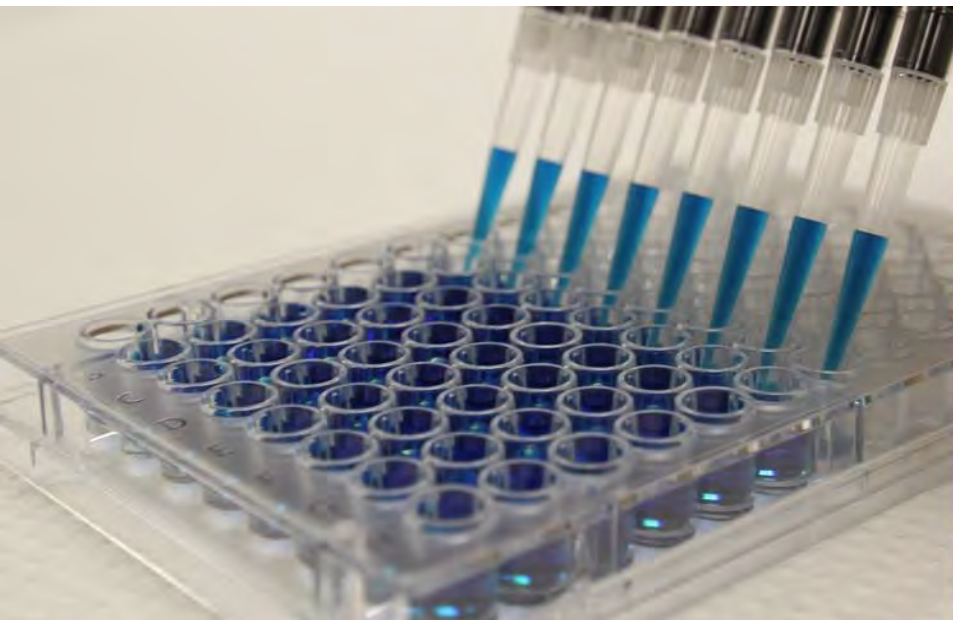




Linking Bioanalytical Methods to Biological Effects

Alvine C. Mehinto, Steven Bay, Keith A. Maruya
Southern California coastal Water Research Project Authority



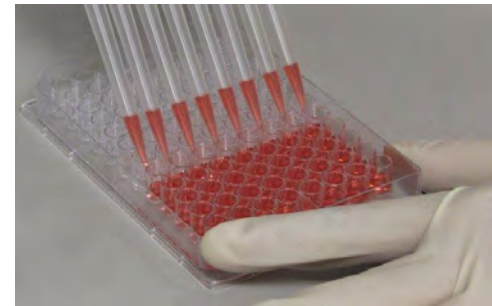
Effect-Based Monitoring Strategy

540

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A Tiered, Integrated Biological and Chemical Monitoring Framework for Contaminants of Emerging Concern in Aquatic Ecosystems

Keith A Maruya,*† Nathan G Dodder,† Alvine C Mehinto,† Nancy D Denslow,‡ Daniel Schlenk,§ Shane A Snyder,|| and Stephen B Weisberg†



RESEARCH

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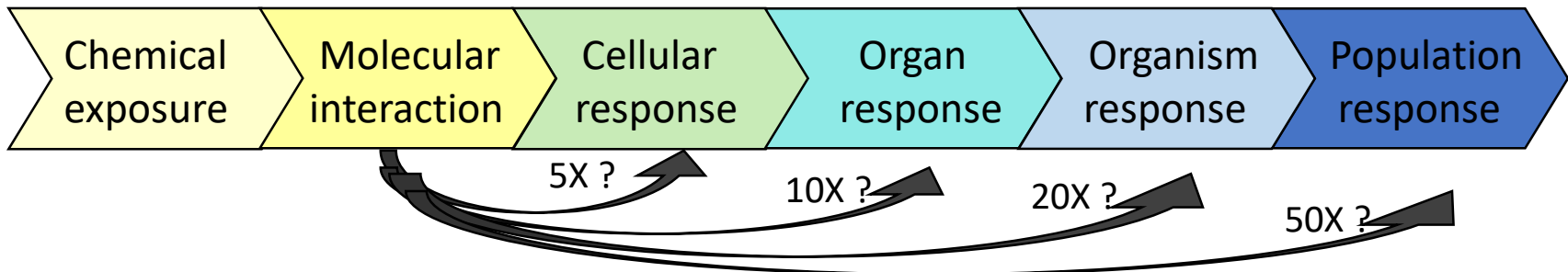
The European technical report on aquatic effect-based monitoring tools under the water framework directive

Ann-Sofie Wernersson¹, Mario Carere^{2*}, Chiara Maggi³, Petr Tusil⁴, Premysl Soldan⁴, Alice James⁵, Wilfried Sanchez⁵, Valeria Dulio⁵, Katja Broeg⁶, Georg Reifferscheid⁷, Sebastian Buchinger⁷, Hannie Maas⁸, Esther Van Der Grinten⁹,

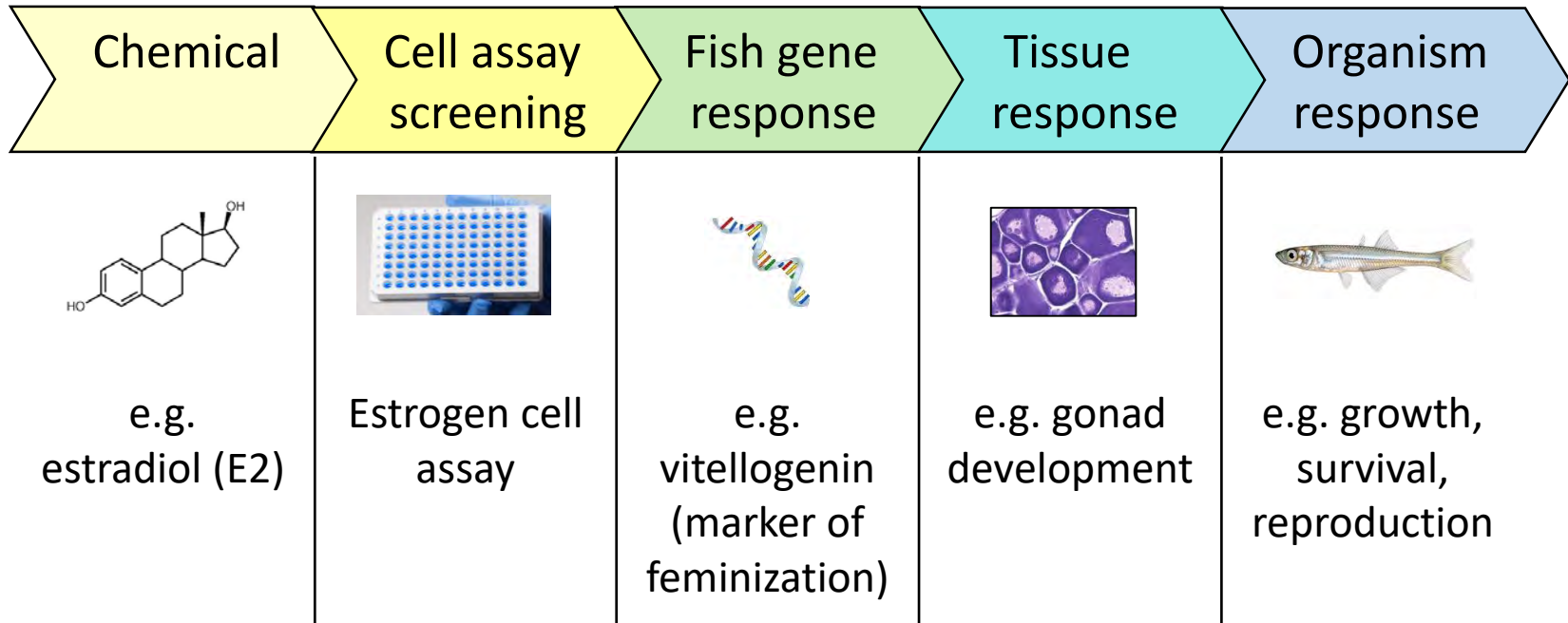
- Screening based on **MODE OF ACTION** to streamline assessment
- Approach uses *in vitro* cell assays to **PRIORITIZE** and **REFINE** chemistry and toxicity testing

Developing Effect Thresholds

- Effect thresholds needed to interpret cell assays results
- Requires **quantification** of the linkage between cell assay response and adverse outcome in test animals
- Approach is similar to Adverse Outcome Pathway



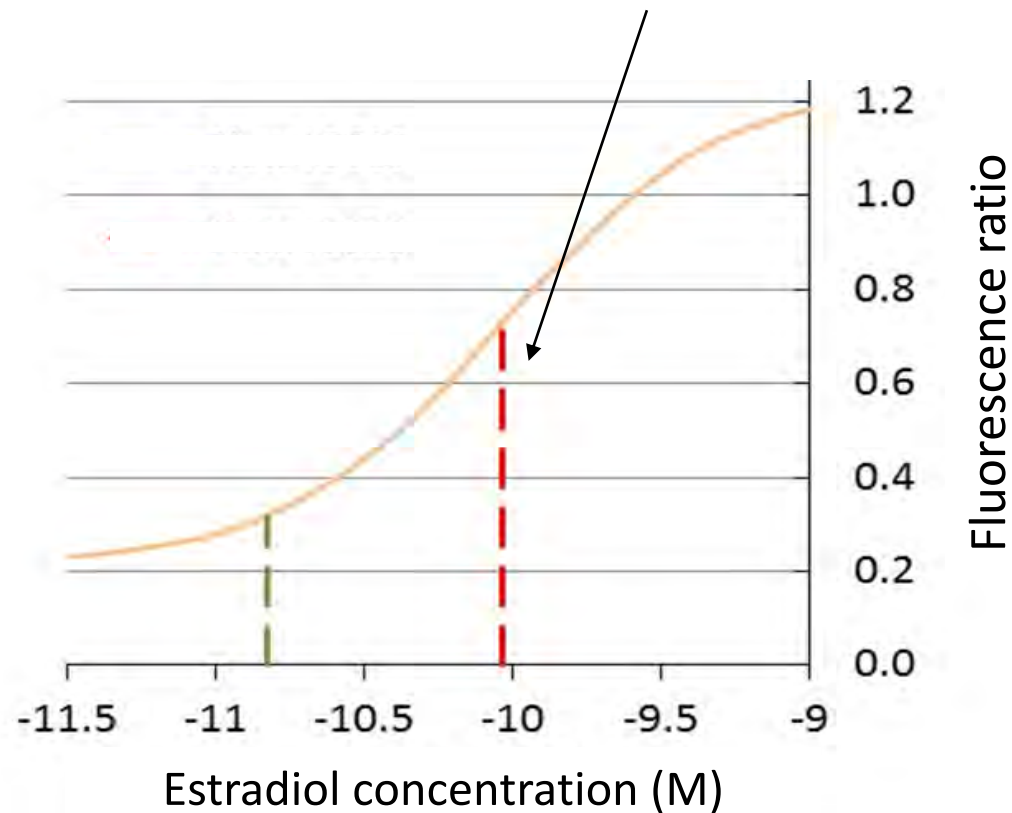
Case Study - relationship between estrogen bioscreen and fish health



Goal: Quantify the relationship between cell assay response and adverse effects in whole organisms

Cell Assay Response of Estradiol

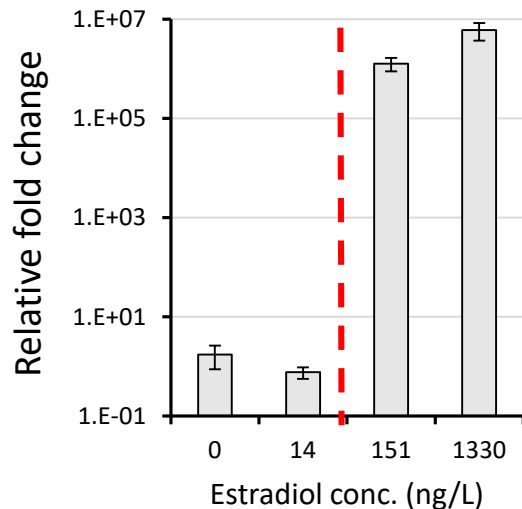
Cell assay threshold set at 50 % effect concentration; i.e. ~ **25 ng/L**



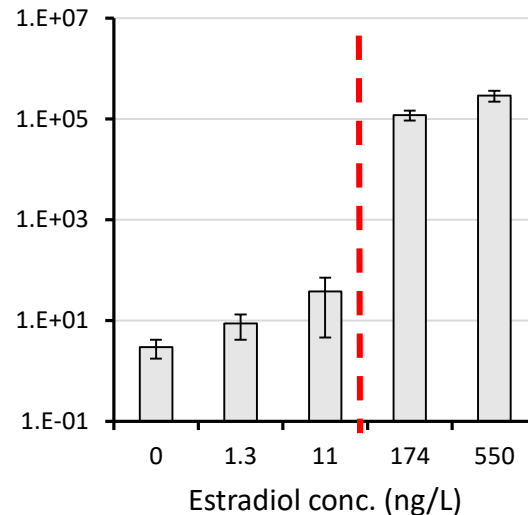
Link to Gene Expression Response

- Vitellogenin increase at concentrations \geq cell assay threshold
- Same patterns observed in different life stages and species

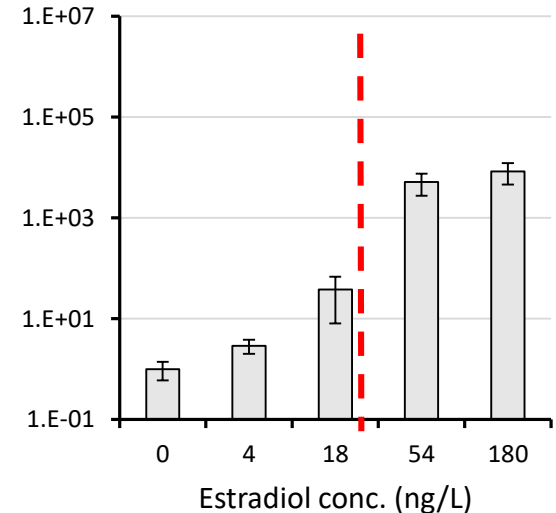
Silverside larvae



Juvenile silversides

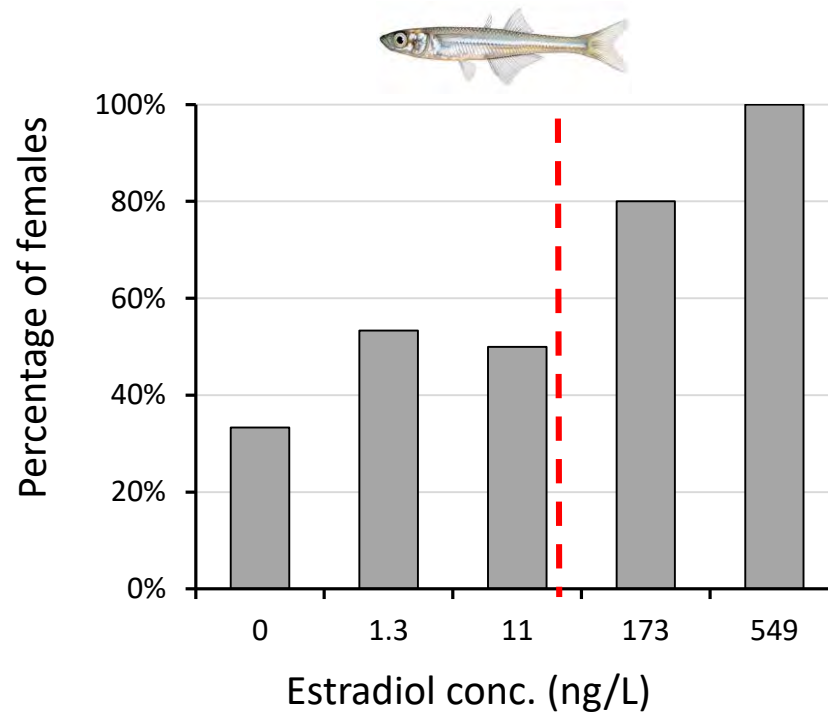


Adult fathead minnows



Link to Organ and Organism Response

- Major impact on gonad development of juvenile silversides, i.e. feminization



Establishing Cell Assay Thresholds is Possible

- Linkage demonstrated for different test species/life stages
- Fish health impacted at levels \geq cell assay threshold
- Potential to establish **thresholds protective of aquatic life**

Chemical	Cell assay screening	Fish gene response	Tissue response	Organism response
Estradiol	1 X (~ 25 ng/L) Estrogen receptor activation	$\leq 7 X$ (170 ng/L) Vitellogenin increase	$\leq 7 X$ (170 ng/L) Feminization of gonads	> 22 X (550 ng/L) Body weight; Survival

Research Needs

- Develop/optimize cell assays for other relevant modes of actions (e.g. neurotoxicity, immunotoxicity)
- Quantify relationship to higher order biological effects
 - for promising endpoints

Cell assay endpoint	Potential adverse effect	Chemicals screened
Estrogen receptor	Feminization, impaired reproduction	Estrogens, alkylphenols
Glucocorticoid receptor	Development, metabolic disorder	Anti-inflammatory steroids
Androgen receptor	Impaired reproduction	Fragrances, pesticides
Aryl hydrocarbon receptor	Cancer, embryonic malformations	Dioxin-like chemicals

Research Needs

- Conduct linkage studies in the laboratory and field
- Establish bioscreening effect thresholds
- Investigate the use of cell assays in a **weight of evidence approach**



Questions?

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**US Army Corps
of Engineers®**
Engineer Research and
Development Center



Mini-mobile unit (MMU) deployed at a field site impacted by stormwater runoff. The unit pulls water (effluent) directly from the stream (upper left) and circulates it through two exposure chambers before discharging back into the stream. The MMU is self-contained with battery-operated air and water pumps (upper right). Mature male fathead minnows were contained in two stainless steel chambers (n=10/chamber; 20 fish per site) (lower left) for 21 days.

Fathead Minnow Linkage Study



	Endpoint	LOEC	
Cell Assay Response	Estrogen receptor activation	≥ 0.5 ng E2/L	
Molecular Response	Increased vtg gene expression in males	≤ 18 ng E2/L	36 x
	Increased plasma vtg levels in males	≤ 54 ng E2/L	
	Disruption of steroid hormone pathway	≤ 180 ng E2/L	
Tissue Response	Reduced hepatosomatic index in females	≤ 180 ng E2/L	360 x
	Decreased # and index of males tubercles	≤ 180 ng E2/L	
	Reduced female maturity index	≤ 180 ng E2/L	
Organism Response	Weight loss in females	≤ 54 ng E2/L	360 x
	Decreased survival of females	≤ 180 ng E2/L	
	Reduced fecundity	≤ 180 ng E2/L	