

Survival time models quantitatively predict lethal effects of pulsed and different duration exposures to oil spill PAHs

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www.crrc.unh.edu



Rationale

Most toxicity data are derived from conventional concentration-effect test designs that produce an effect metric (e.g., 96hLC50), at a set exposure time.

- ✦ Only gross prediction if mortality data not collected during the exposure.
- ✦ Mortality occurring after exposure stops is not included in predictions.

Conventional approach is suboptimal for predicting all mortality for exposures differing in duration from conventional tests.

These shortcomings are weighty impediments to accurately predicting effects from spilled oil exposures that vary in both duration and concentration through time, and that require prediction of all mortality resulting from exposure.

These shortcomings can be avoided by noting mortality through time including post-exposure mortality, and applying survival time modeling



Goal in Classic Toxicology

Accurate/precise estimation of poison or drug potency under controlled conditions

Goal in Ecotoxicology

Reliable prediction of lethal consequences of an environmental exposure

- to individuals under all reasonable exposure scenarios
- to populations as a consequence of death of members of the population
- to ecological communities as a consequence of population changes

Classic toxicology methods emerged in 1920-1930's

Adopted by ecotoxicologists in 1950-1960's

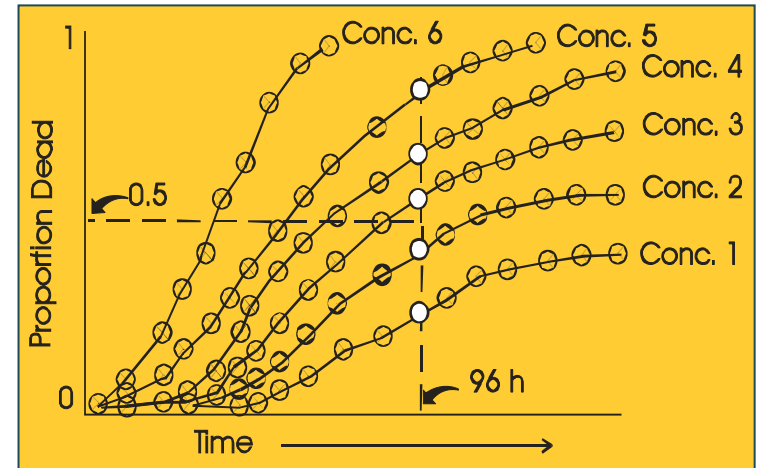
Now used to produce most of the available lethality metrics for risk assessment



Is there a better way?

Dose/concentration treatments optimal for one duration

Ignores information emerging before and after the specific duration for which the LC50 is estimated.



Other widely applied methods that avoid these shortcomings:

population ecology

demography

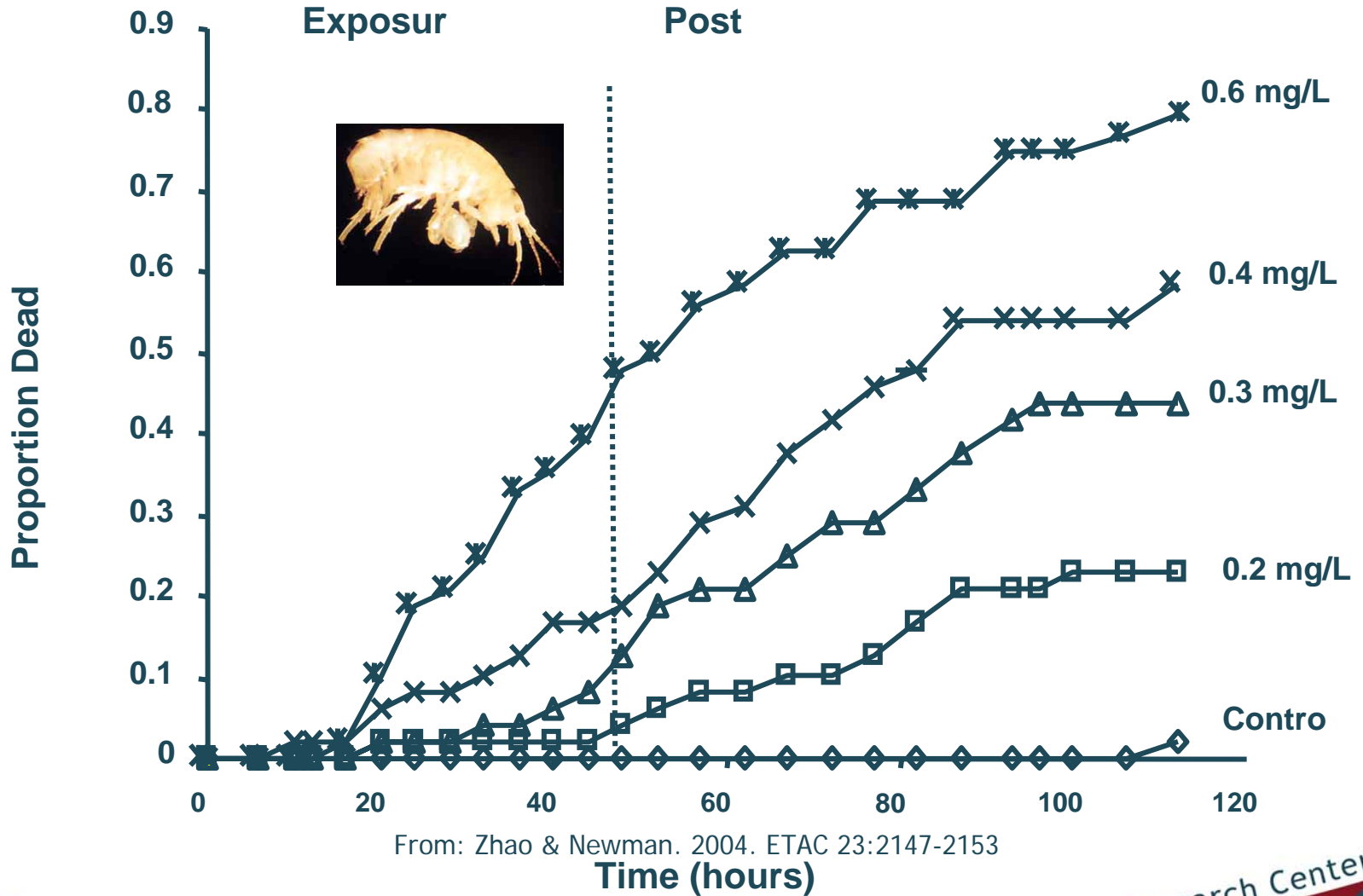
epidemiology

engineering

clinical sciences



Potential for Post-exposure Mortality



From: Zhao & Newman. 2004. ETAC 23:2147-2153

Time (hours)



Time-to-Death (Survival) Analysis As An Alternative

Generally same test design but monitor time-to-death of individuals

Survivors are treated as censored in modeling

Fit data to best of several candidate models via MLE

$$\textit{Survival Time} = e^a e^{b(\ln \textit{Concentration})} e^\varepsilon$$

Why isn't this done? Tradition established before computers.

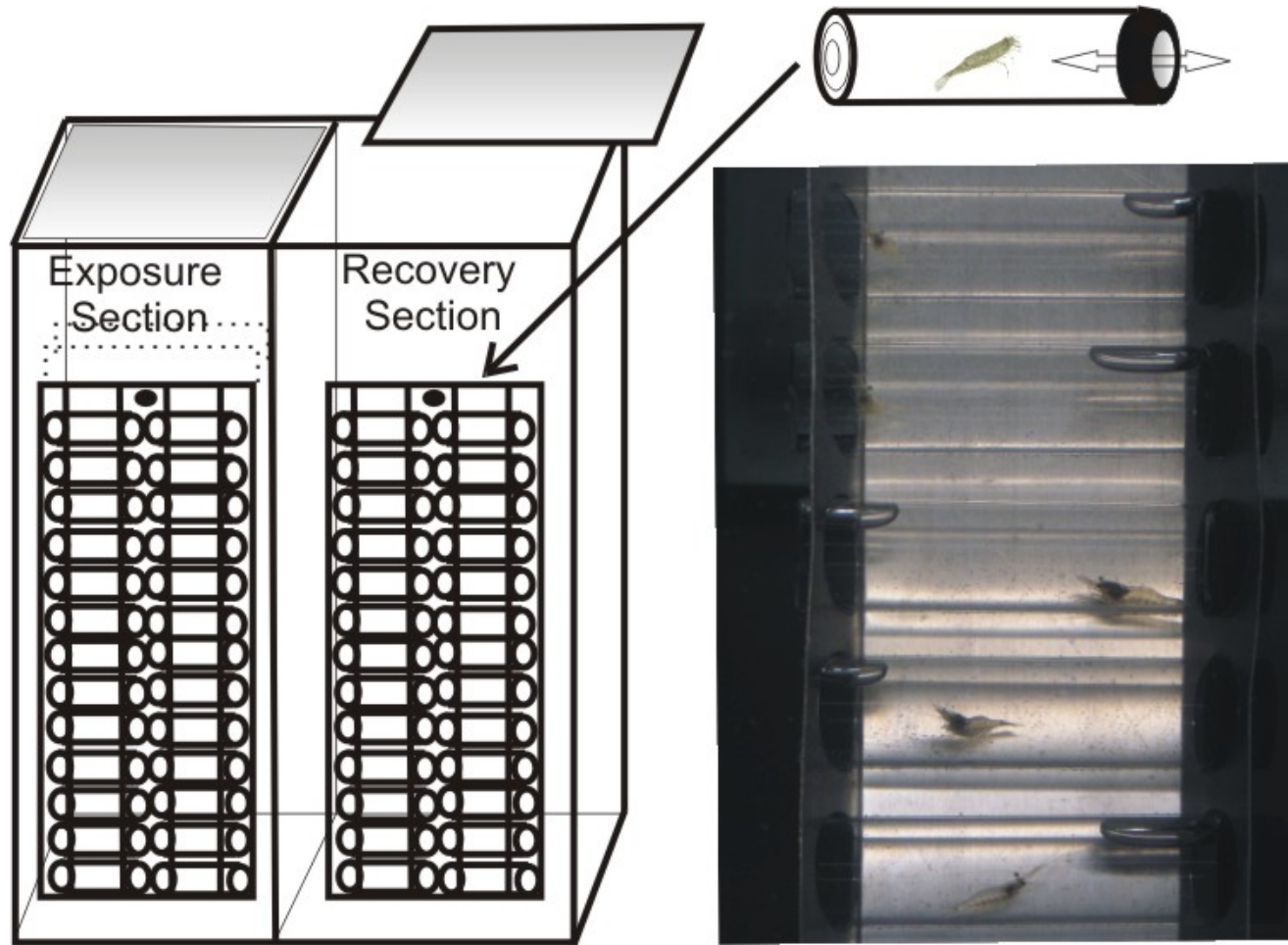


Objectives

- Produce predictive survival time models for grass shrimp exposed to six representative PAH in weathered oil WAF. Models will include pulse and post-pulse mortality at realistic ranges of exposure duration and concentration.
- Produce predictive survival time models that incorporate molecular qualities (e.g., log Kow) of the six PAH. Such a model will potentially allow prediction by interpolation to other untested PAH.
- Produce predictive survival time models for grass shrimp exposed to a mixture of the PAH.



Exposure System - 1



Exposure System - 2

30 Liter chamber

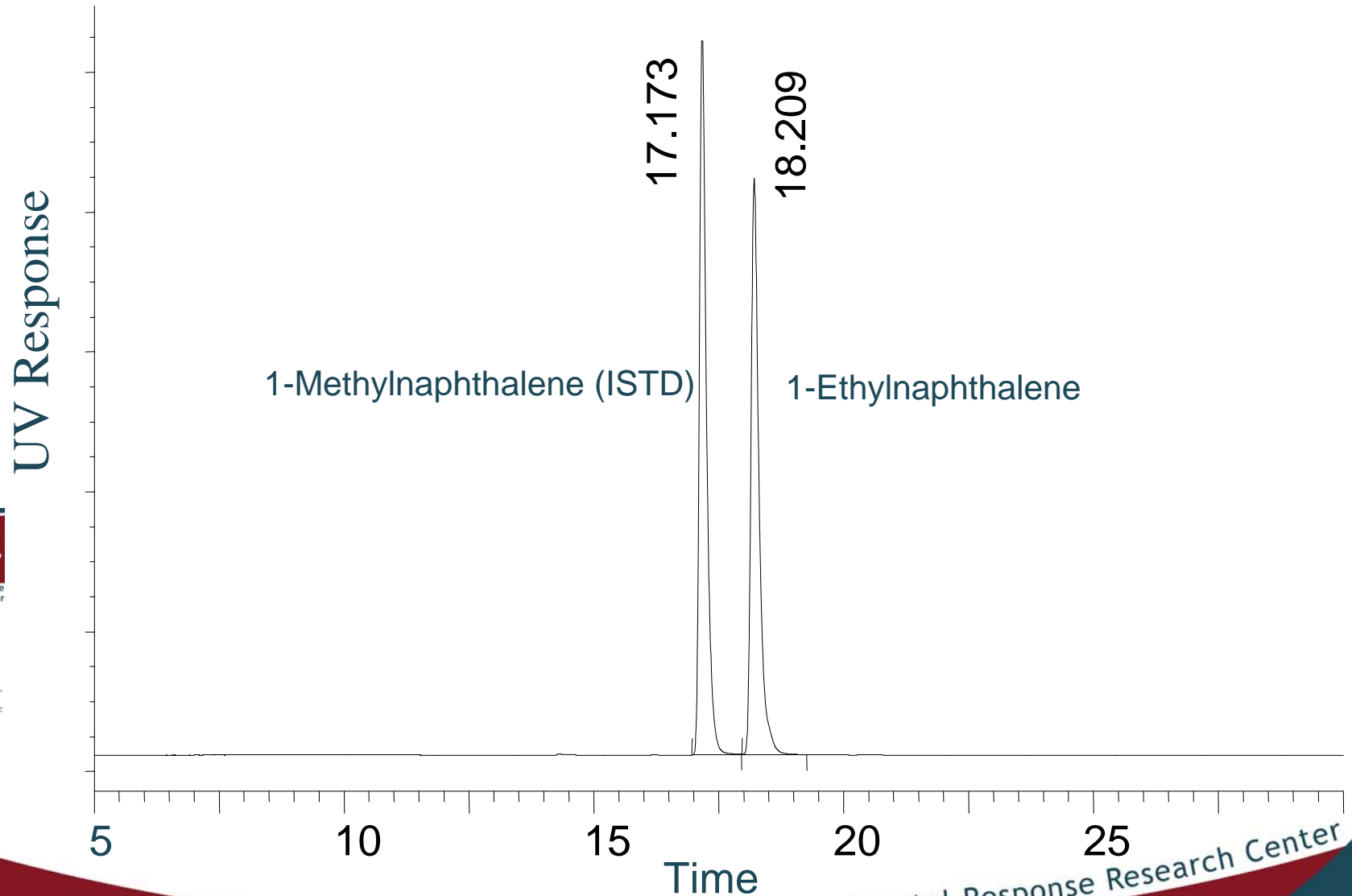


PAH Generator Column

>350 Liters every 12 hours

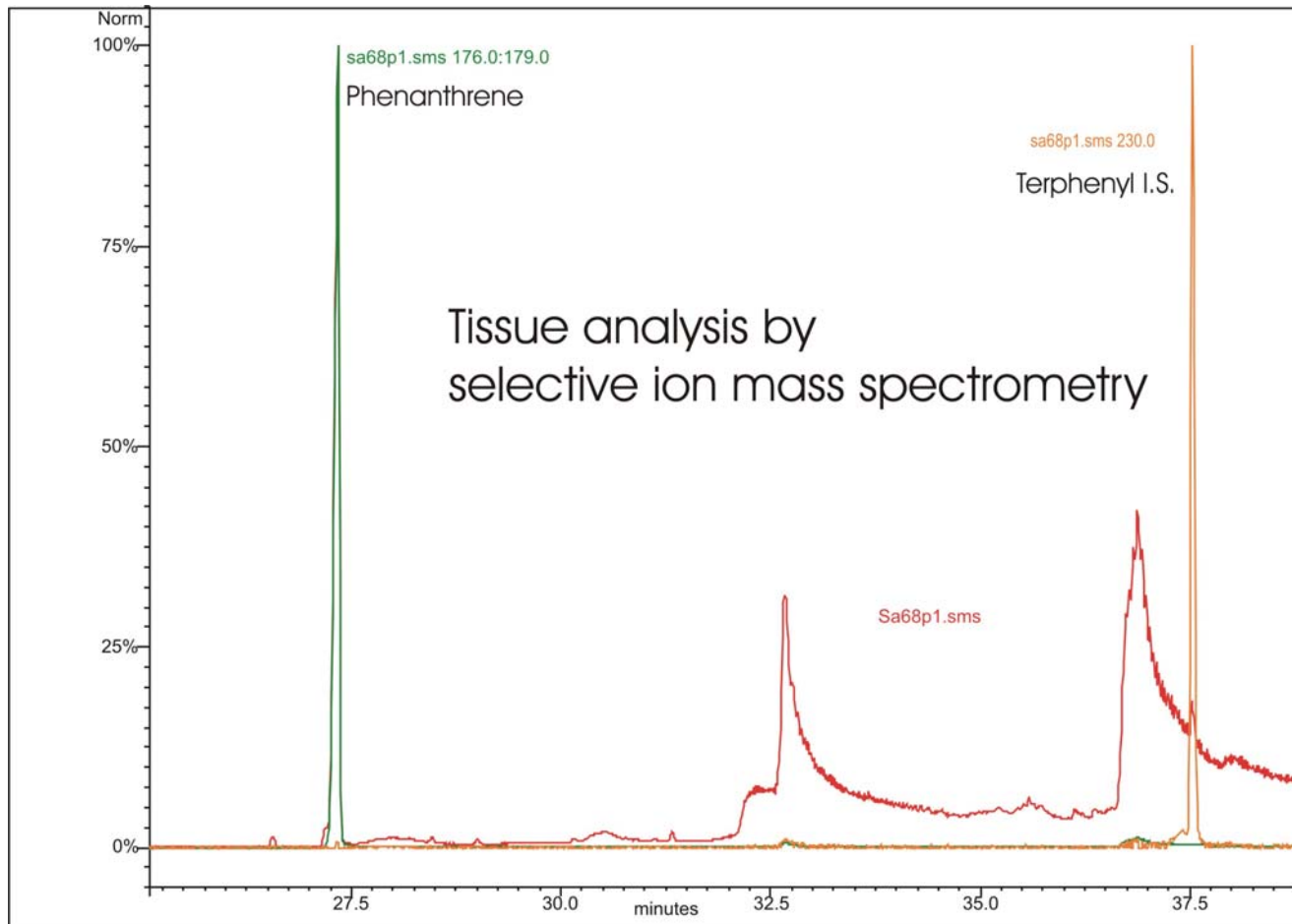


Water Analysis by HPLC

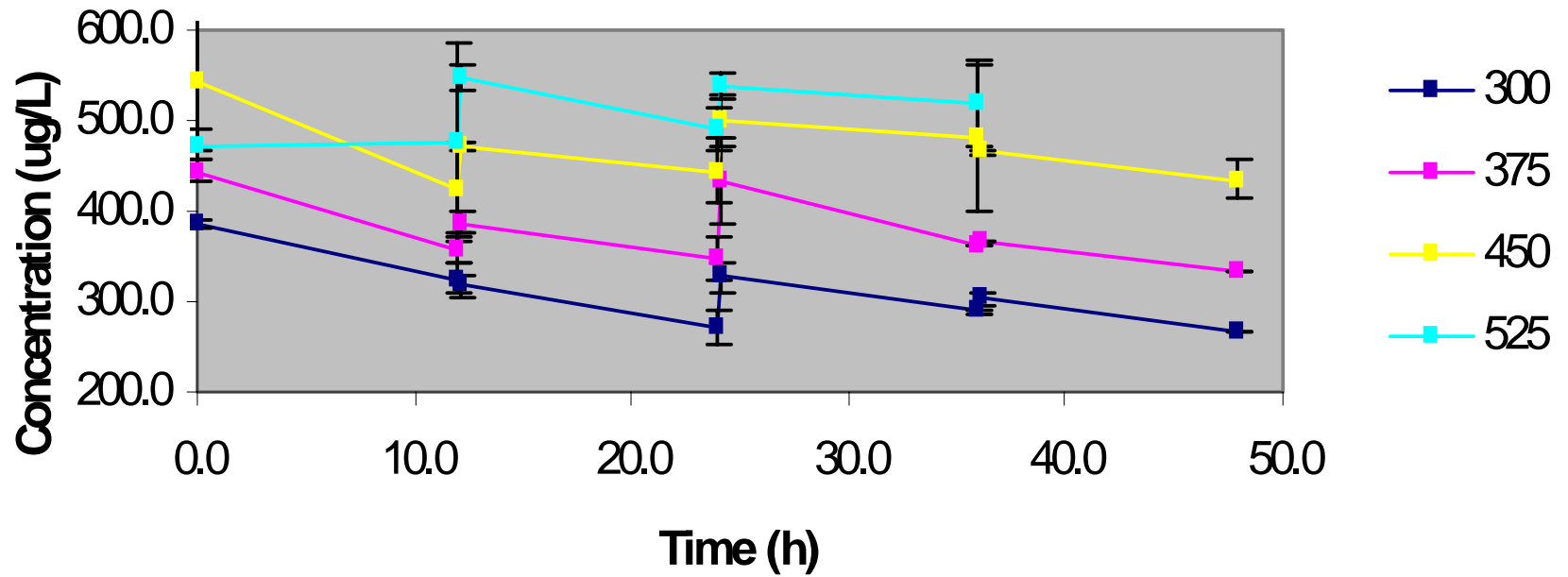


Tissue Analysis by MS/SIMS

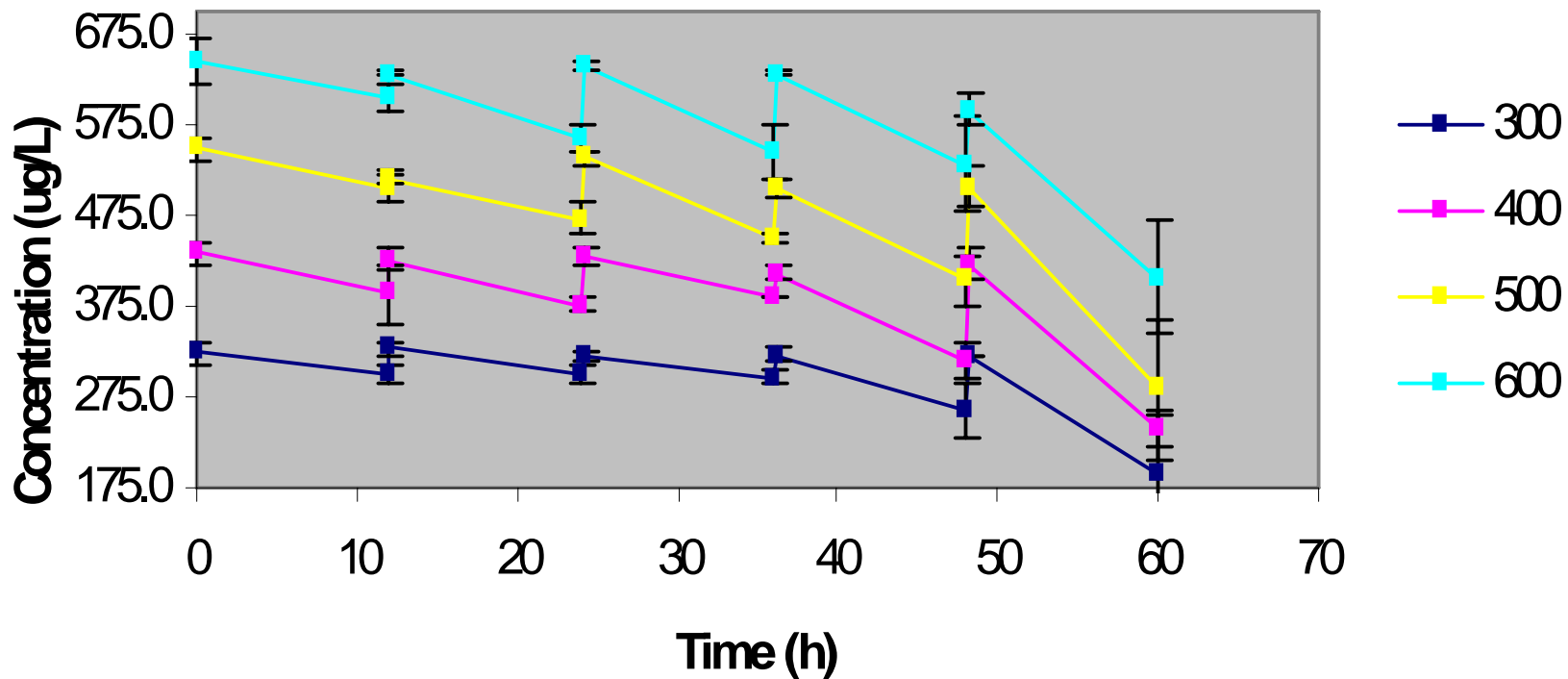
Measure PAH in individual shrimp



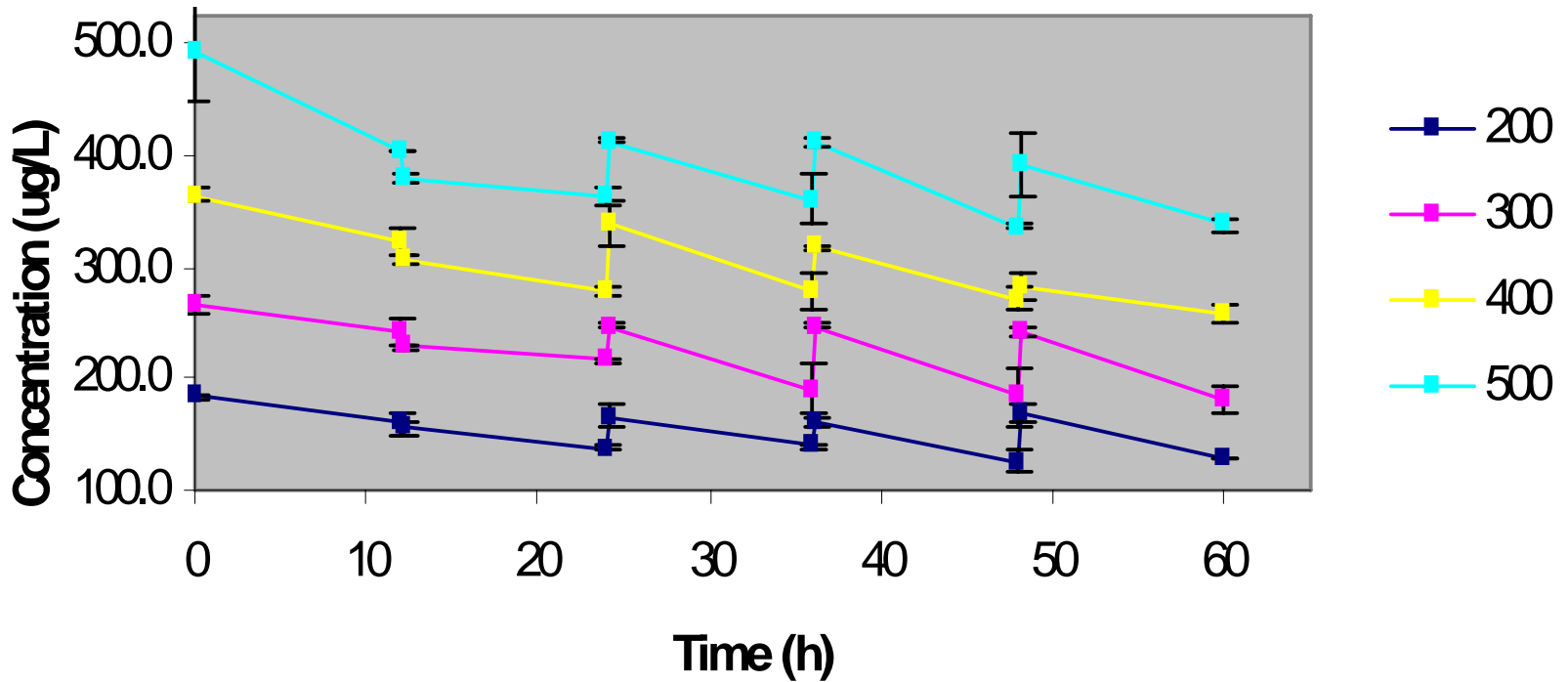
Water Concentrations for Ethyl-naphthalene



Water Concentrations for Dimethylnaphthalene

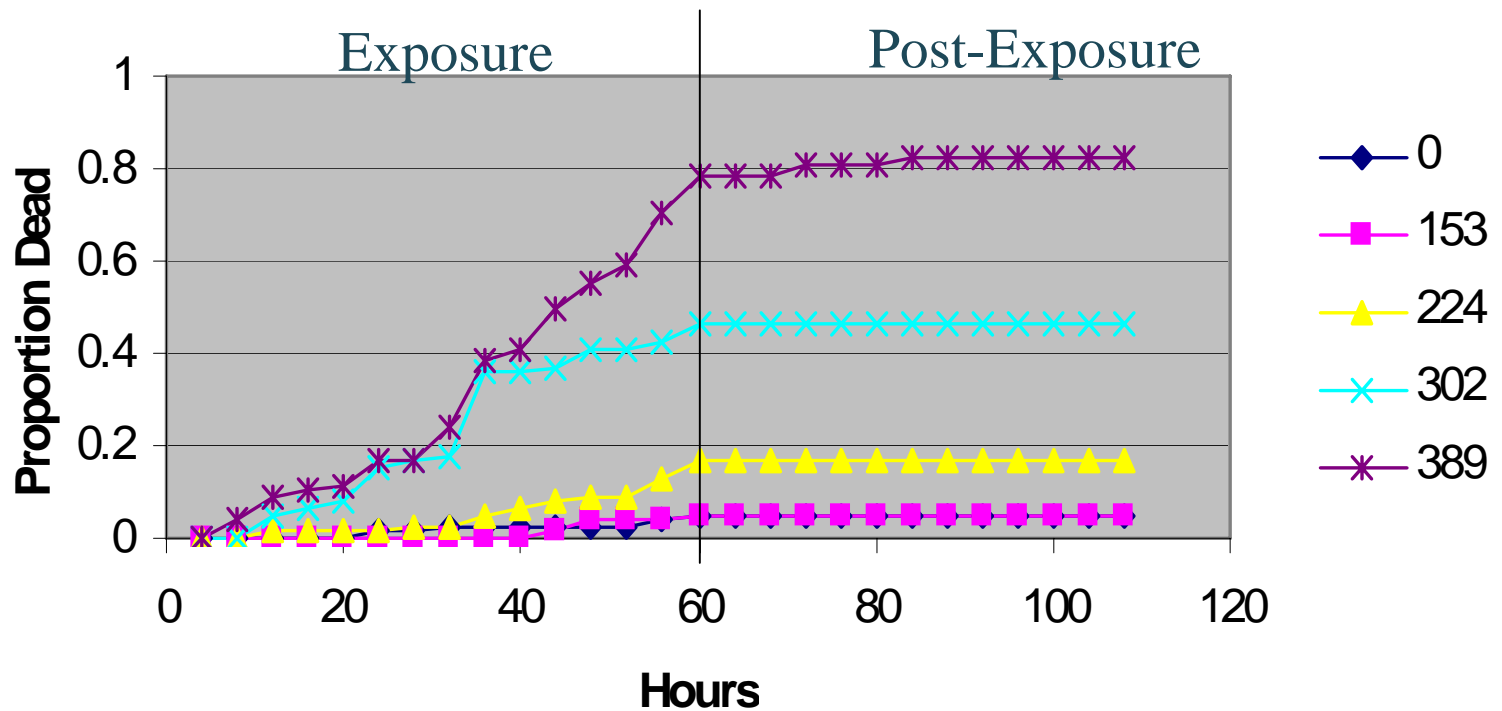


Water Concentrations for Phenanthrene

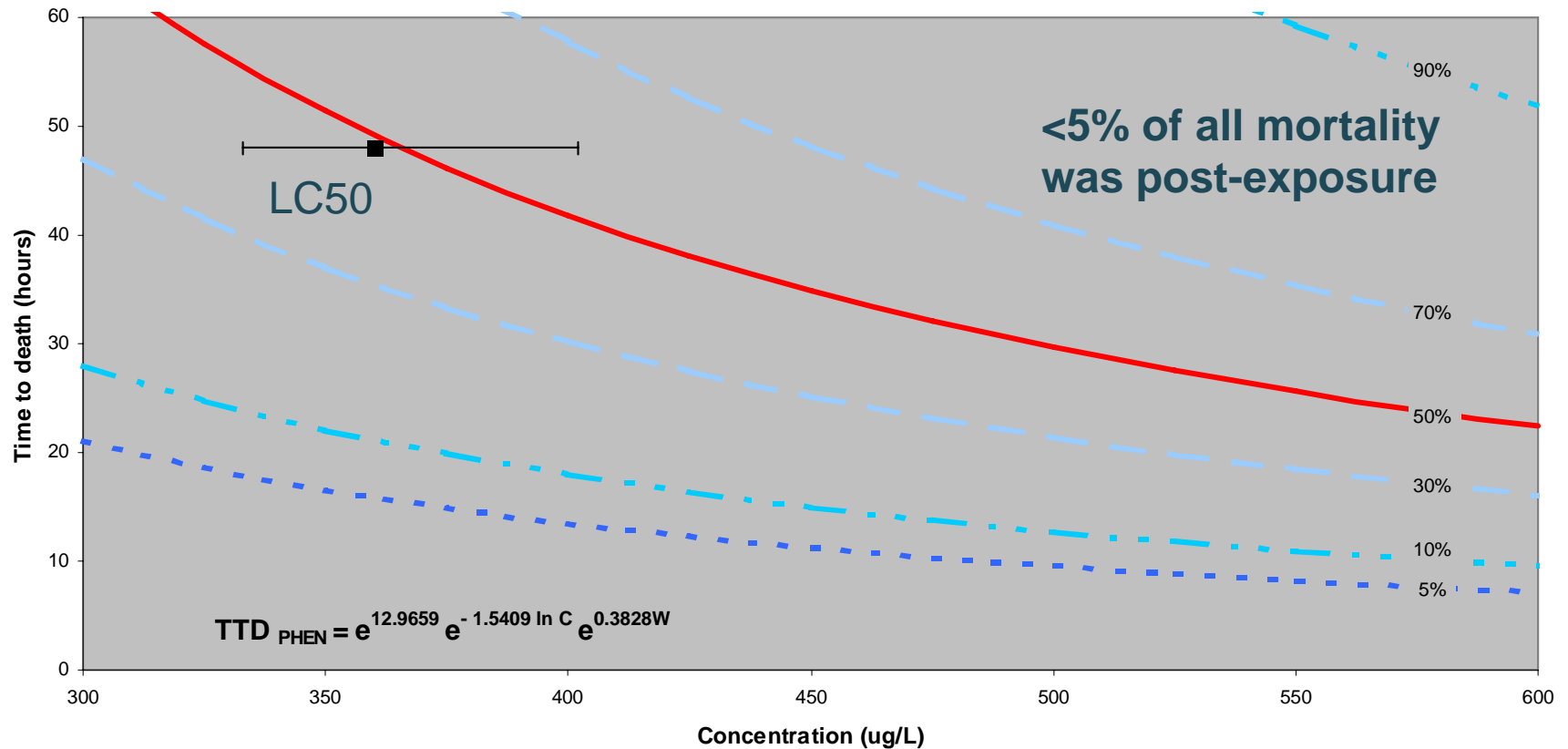


Survival Raw Data

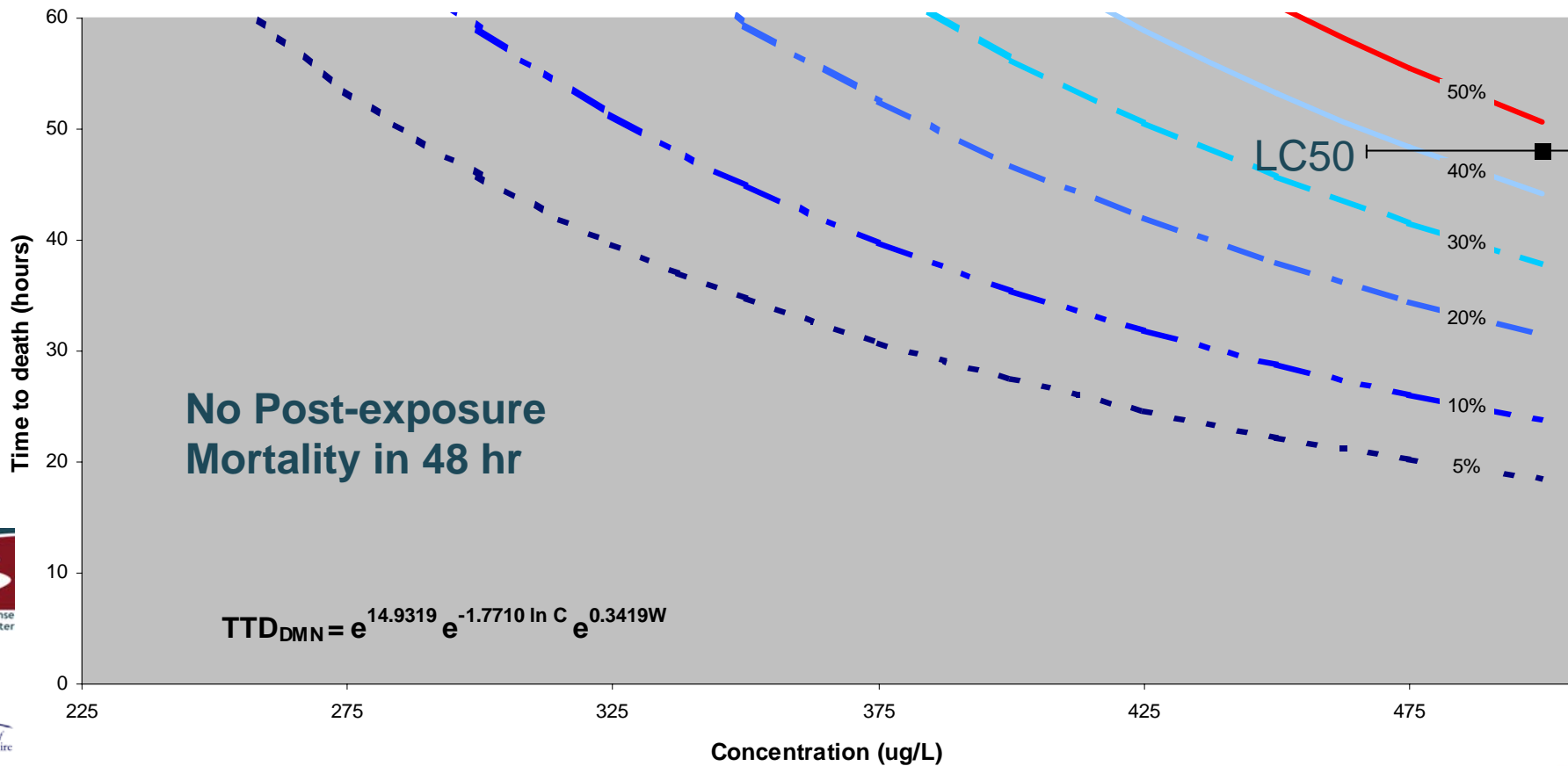
Phenanthrene



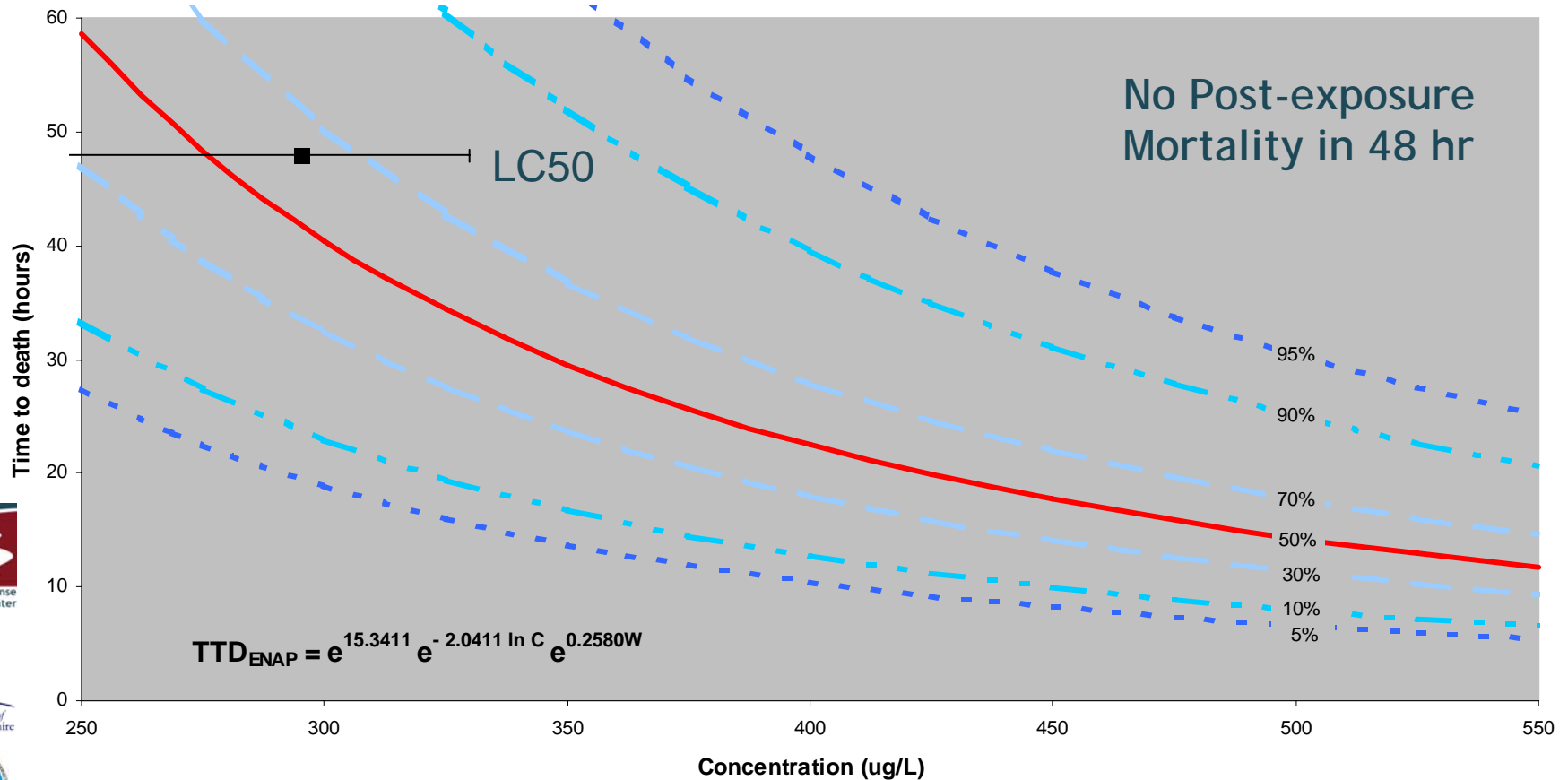
Survival Profiles for Phenanthrene



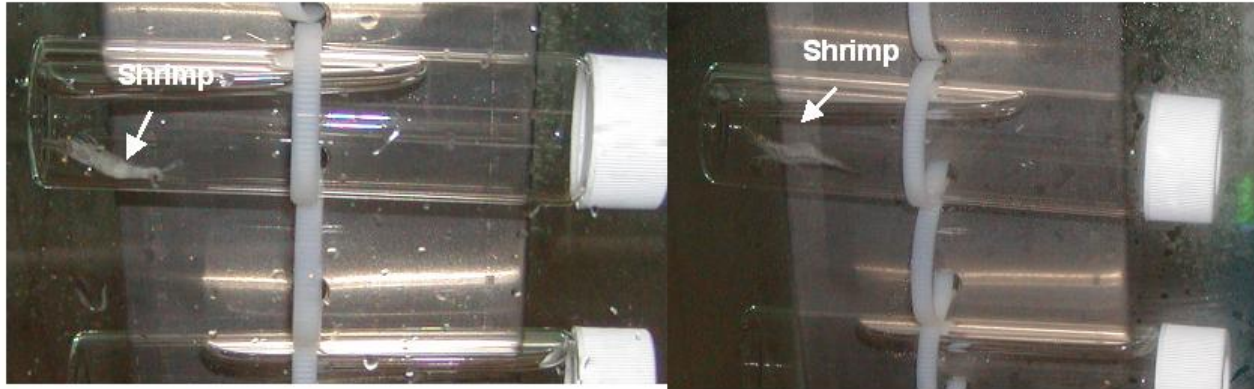
Survival Profiles for Dimethylnaphthalene



Survival Profiles for 1-ethylnaphthalene

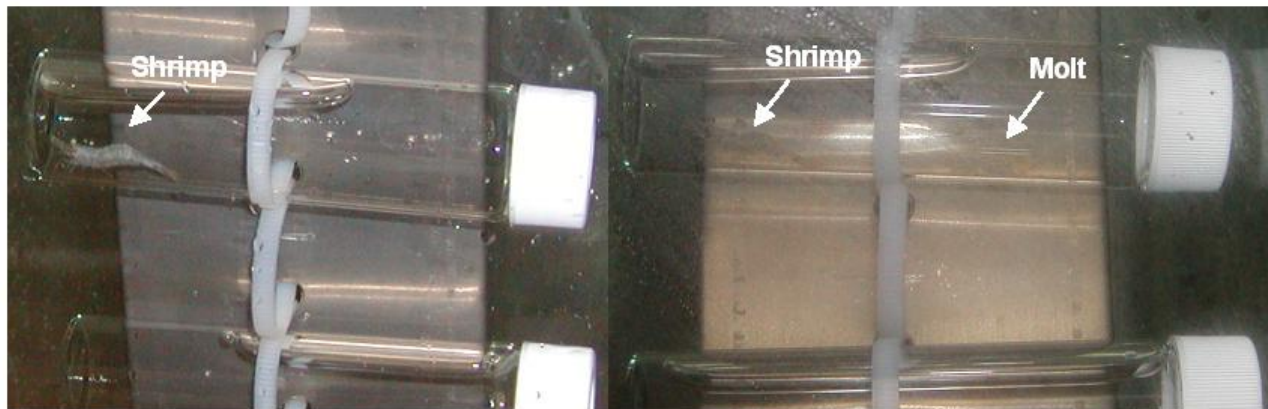


1-ethylnaphthalene Exposure Recovery



**48 hours of 375 ppb ENAP exposure
Shrimp inverted, opaque, immobile**

**56 hours (8 hours post exposure)
Upright, some mobility in tube**



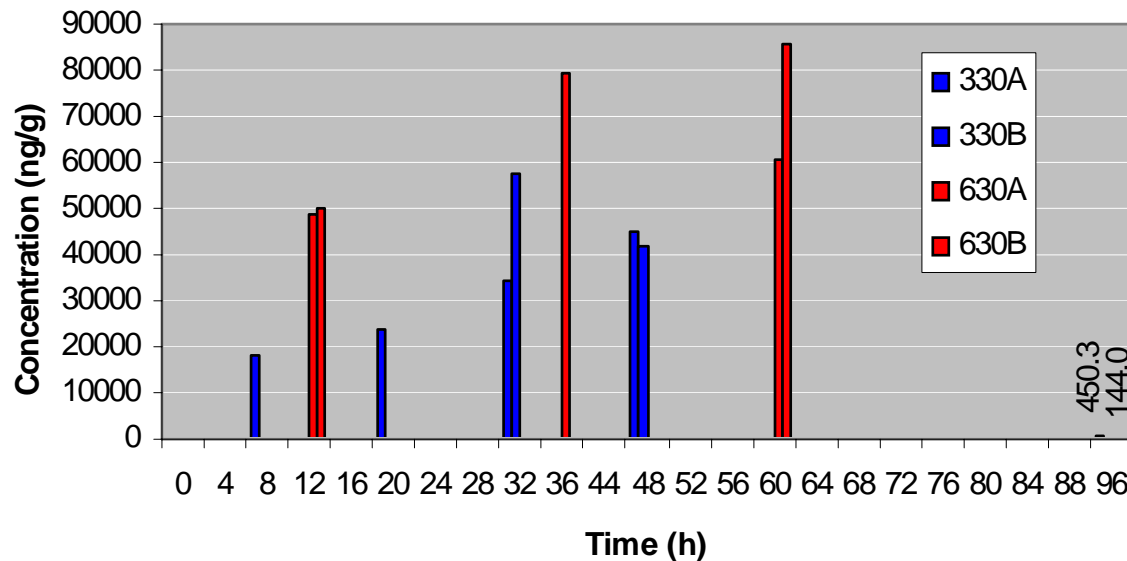
**60 hours (12 hours post exposure)
Still opaque but full mobility**

**72 hours (24 hours post exposure)
Shrimp has shed, appears completely normal**



Shrimp Tissue Concentrations

Dimethylnaphthalene



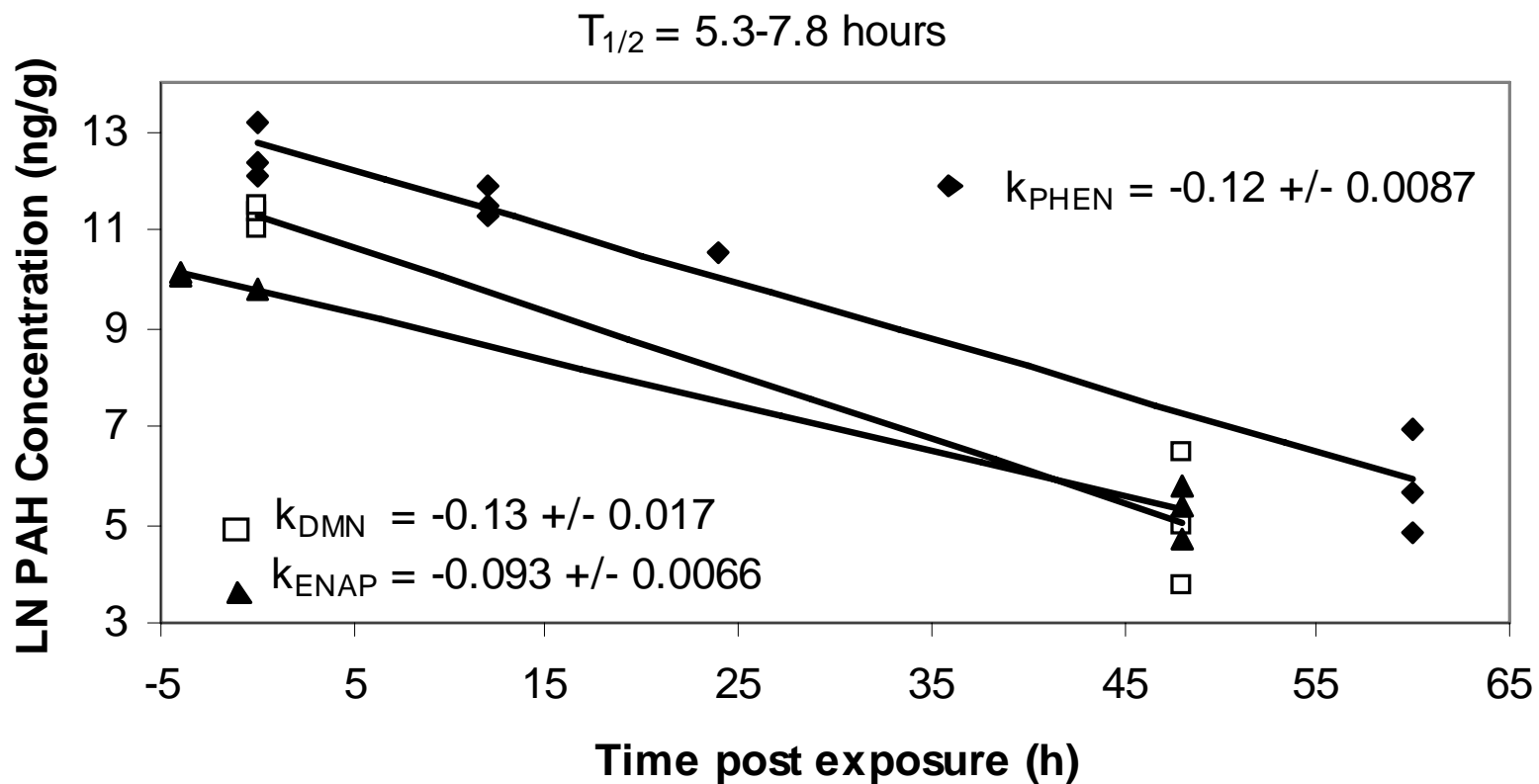
Ethyl naphthalene (MW 156.23) = 18-98 ug/g

Phenanthrene (MW 178.23) = 30-300 ug/g



Shrimp Tissue Concentrations

Rapid Elimination



Results from Year 1

- Compounds tested are narcotics
 - Very narrow window of toxicity
 - Rapid recovery, little or no latent mortality
- Implications
 - Small changes in concentration or duration of the toxicant can affect populations when near the effects “window”



Results from Year 1

- Tissue concentrations are variable
 - Body burdens appear dose dependant
 - Rapid elimination of PAH supports lack of latent mortality
 - Preliminary data indicate body burden ranges for compounds may support critical body burden based on PAH molar concentration
- Tissue Concentration implications for monitoring
 - Not good predictor of TTD for acute exposures
 - Body burden ranges may indicate if shrimp were exposed to toxic concentrations



Applying Survival Analysis to Predict Oil Spill Toxicity

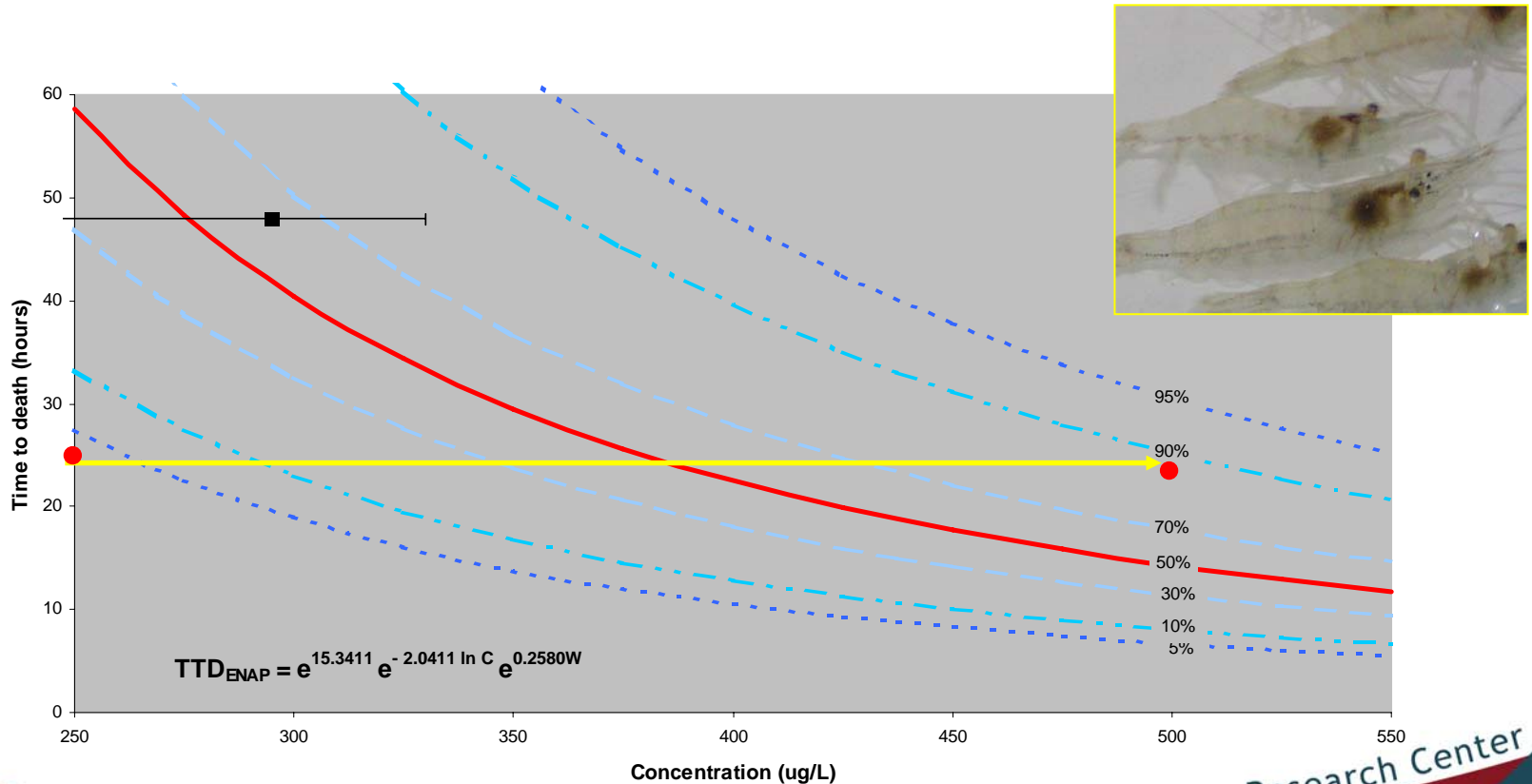
- Factors affecting acute PAH exposure
 - Tides
 - Cyclic variation in PAH concentration
 - Dispersants
 - Increasing PAH solubility 1-5X
 - (Couillard et al. 2005, Environ. Tox. Chem. 24:6, 1496-1504)
 - Salinity (“salting out effect”)
 - 20-40% decrease in PAH solubility in saltwater
 - Fate models can be coupled with survival analysis to predict population level effects



Applying Survival Analysis to Predict Oil Spill Toxicity

Application of oil dispersants: What would be the result of a 2X increase in PAH concentration for 24h?

An increase of ENAP from 250ug/L to 500 ug/L for 24h would increase mortality in the grass shrimp population from <5% to 90%



2006 Year 2 Experiments

- Test three additional compounds: naphthalene, dibenzothiophene, fluorene
 - Scoping experiments for 3 compounds completed
 - Naphthalene, 1st survival experiment completed
- Toxicity of mixture (six compounds)
 - Are single compound effects additive?
- Develop survival model based on mixture results
- Develop QSAR for 6 compounds tested
 - Can we extend results to other PAH?

