Use of Toxicity Models in ALC to Address Different Levels of Effect as a Function of Exposure Time-Series

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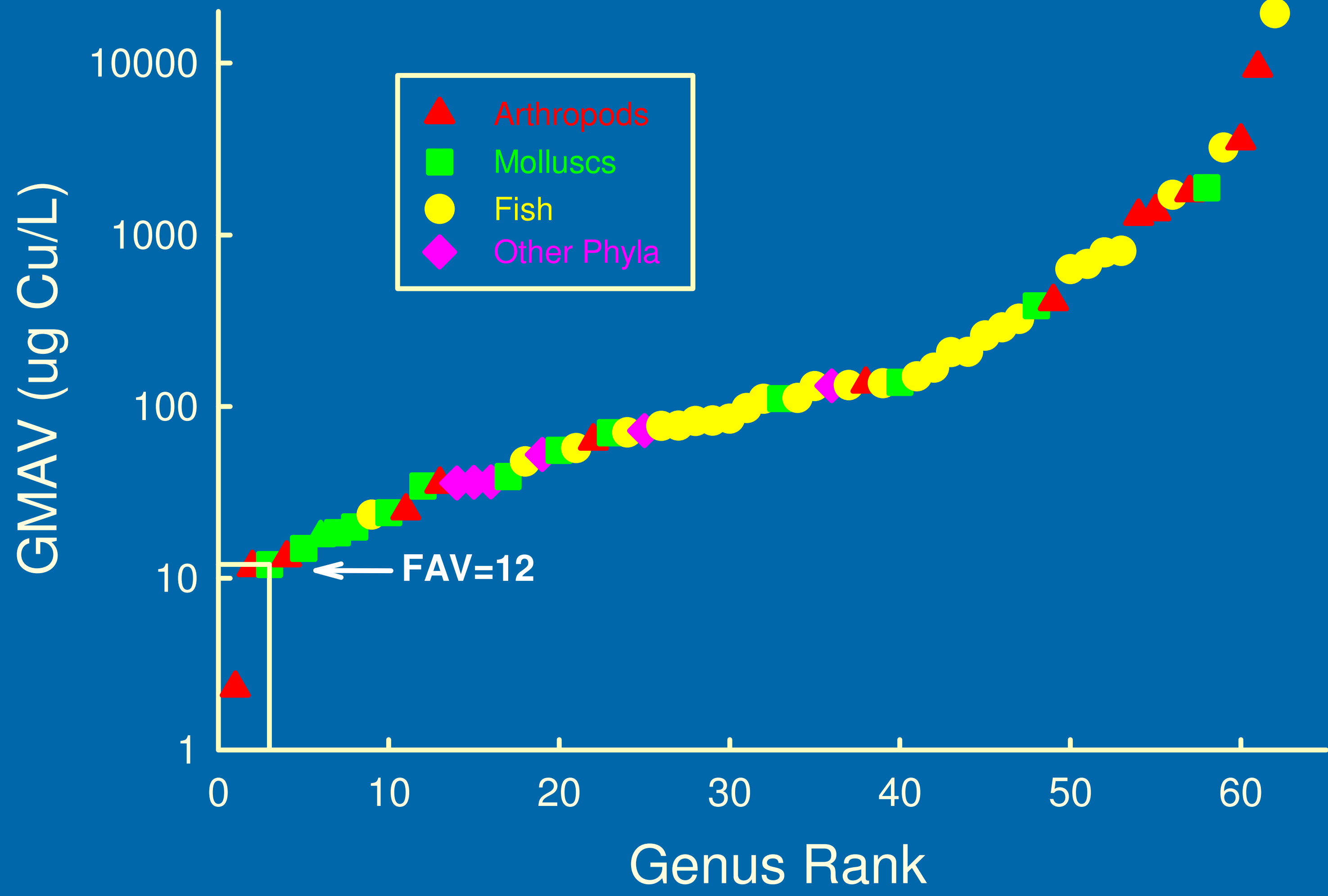
Mid-Continent Ecology Division, Duluth, MN

Meeting on Revising U.S.EPA's Guidelines for Deriving Aquatic Life Criteria

September 14-16, 2015
Arlington, VA

Species Sensitivity Distribution



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Often an important/effective tool for risk assessments, but effects characterizations can be ill-defined due to:

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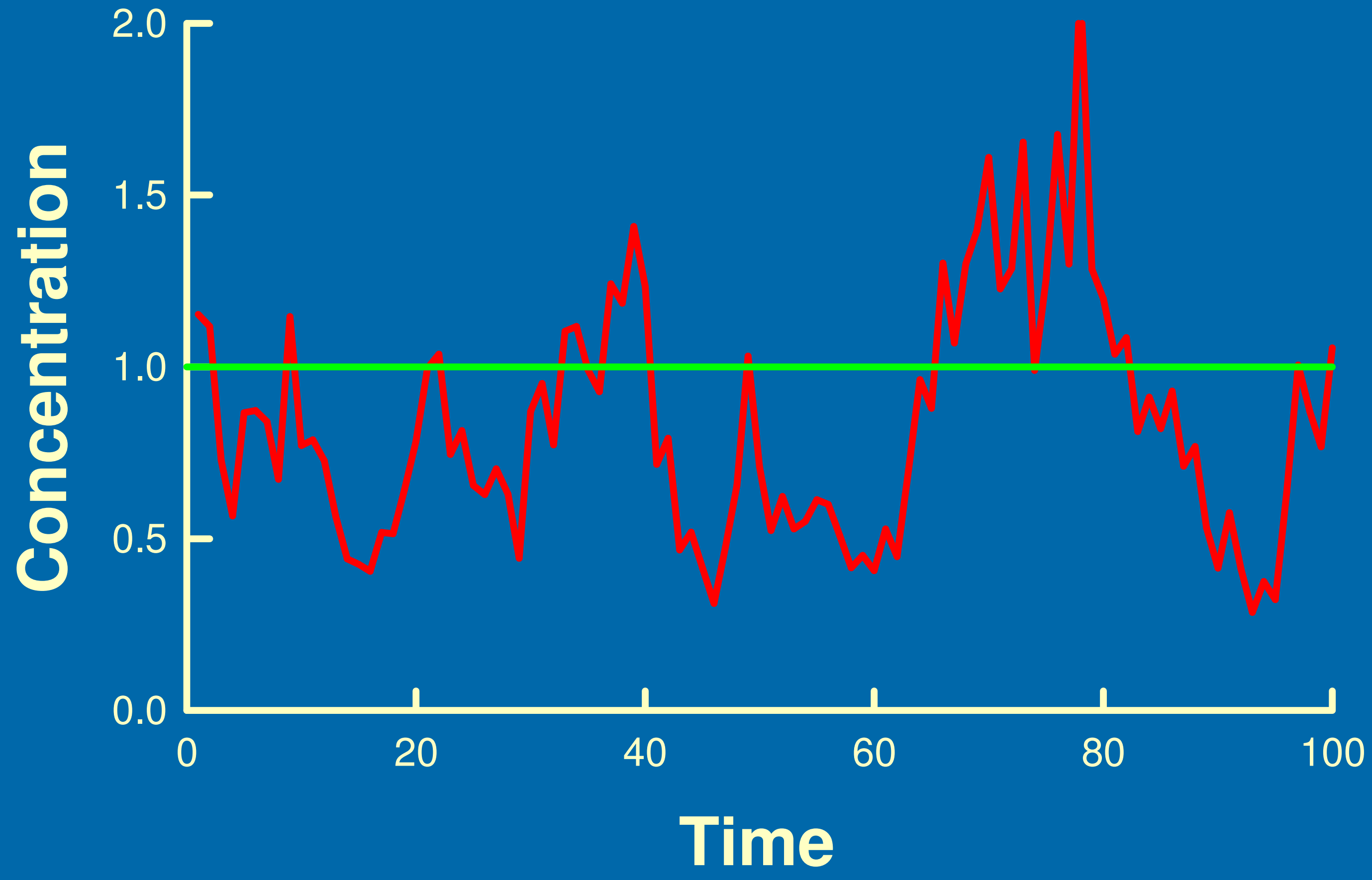
(4) Basis for percentile choice – how does this relate to ecosystem risk?

Limited Risk Characterization for Assessment Benchmarks



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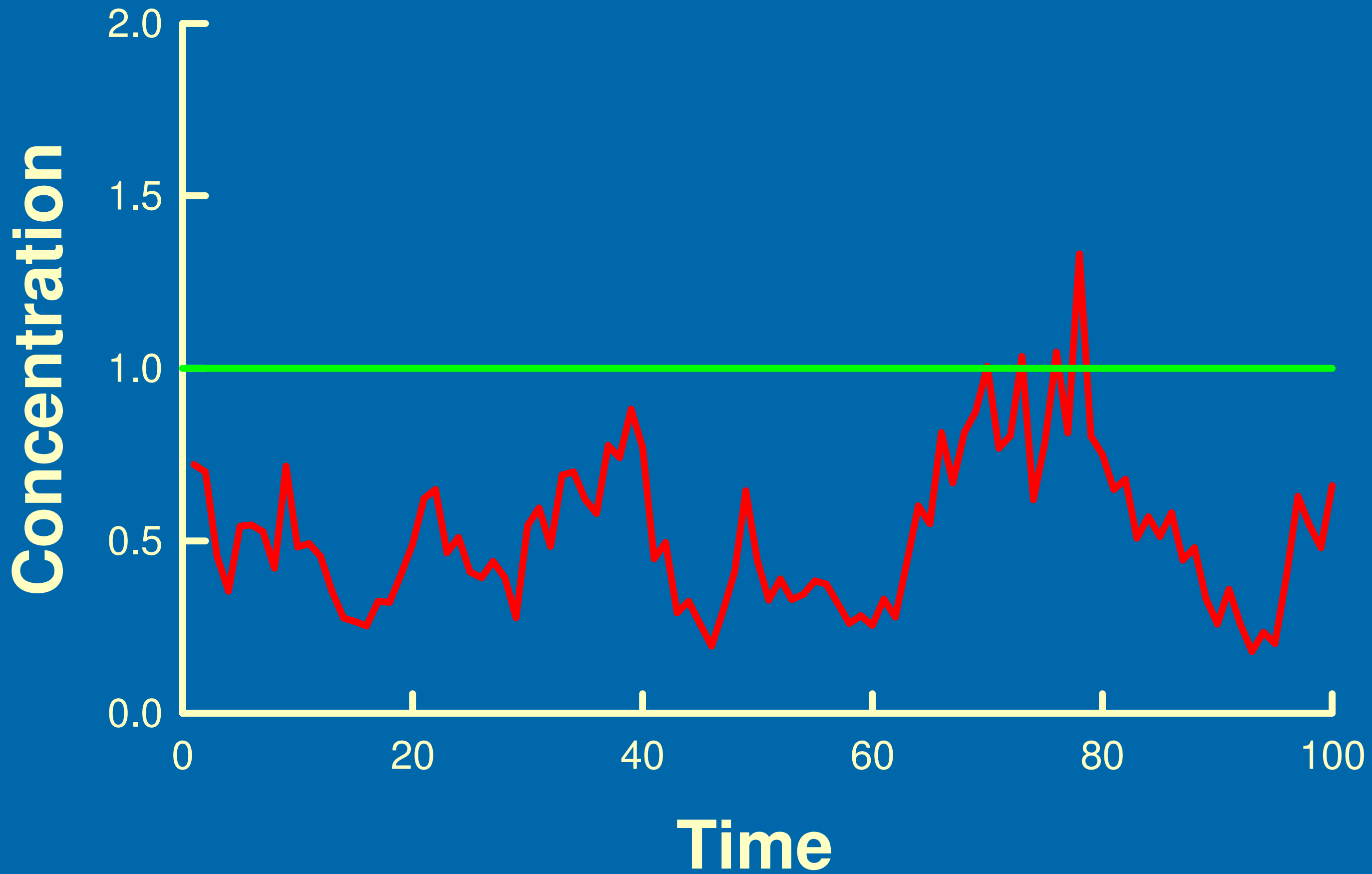

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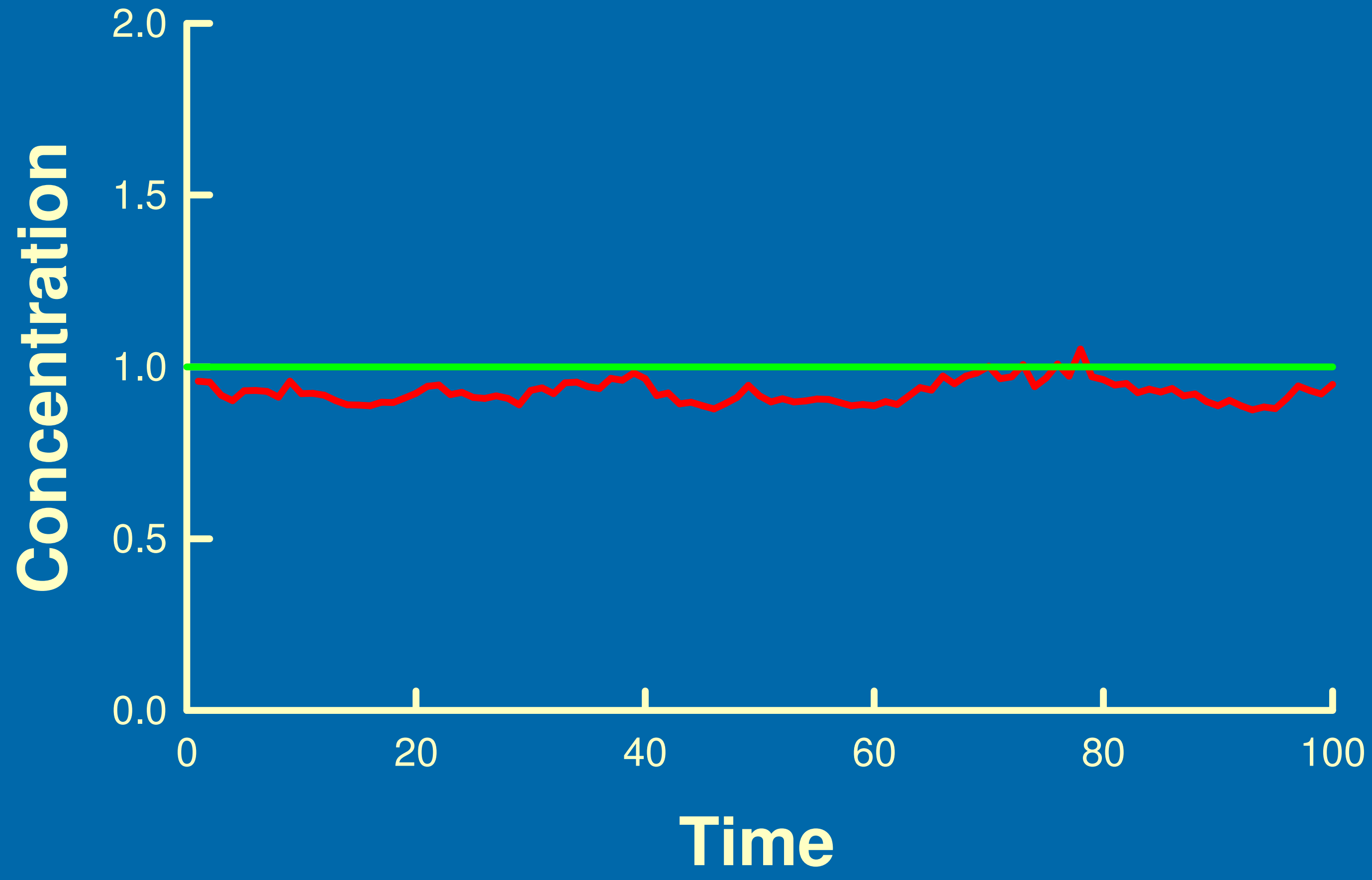

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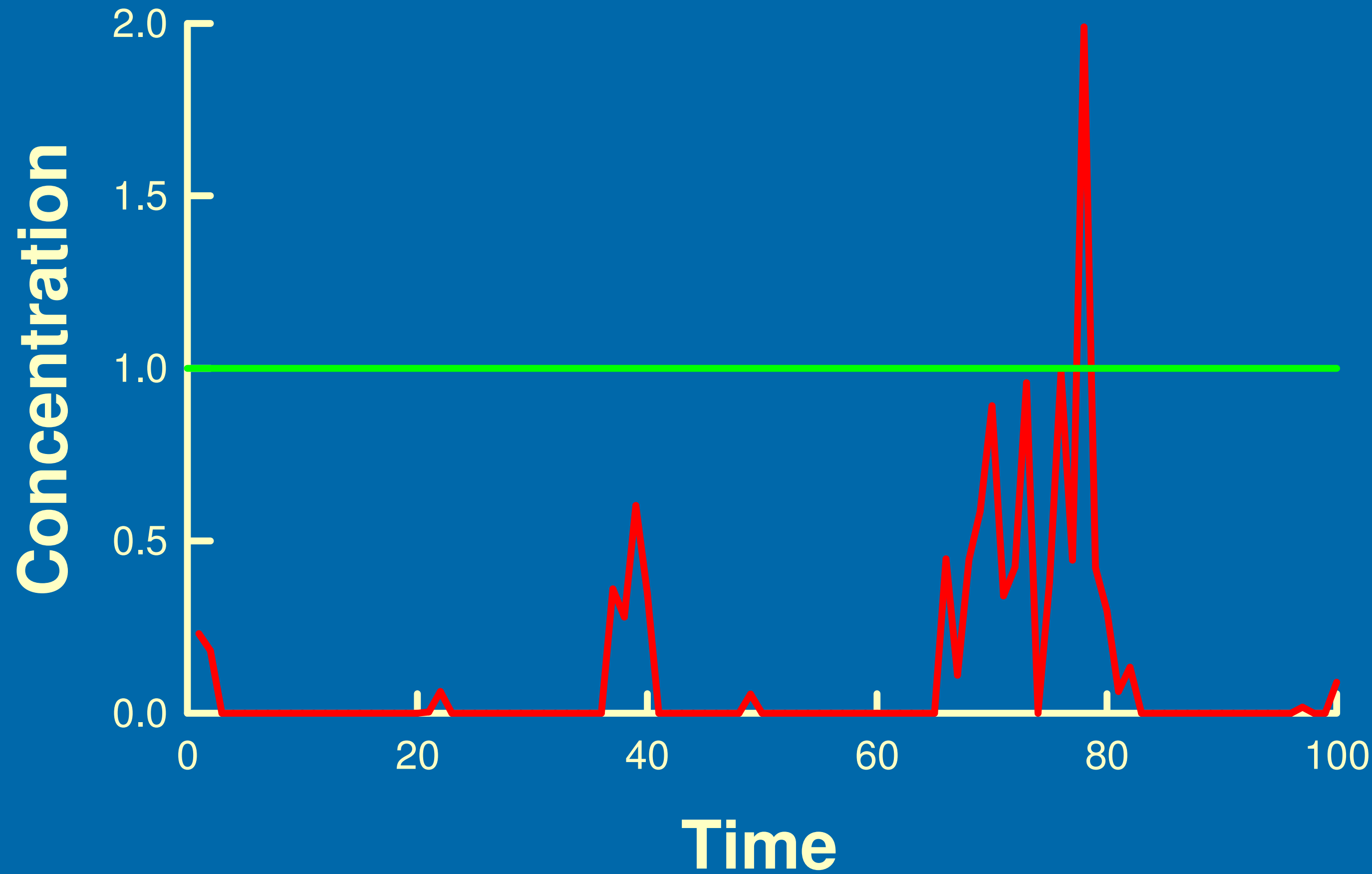

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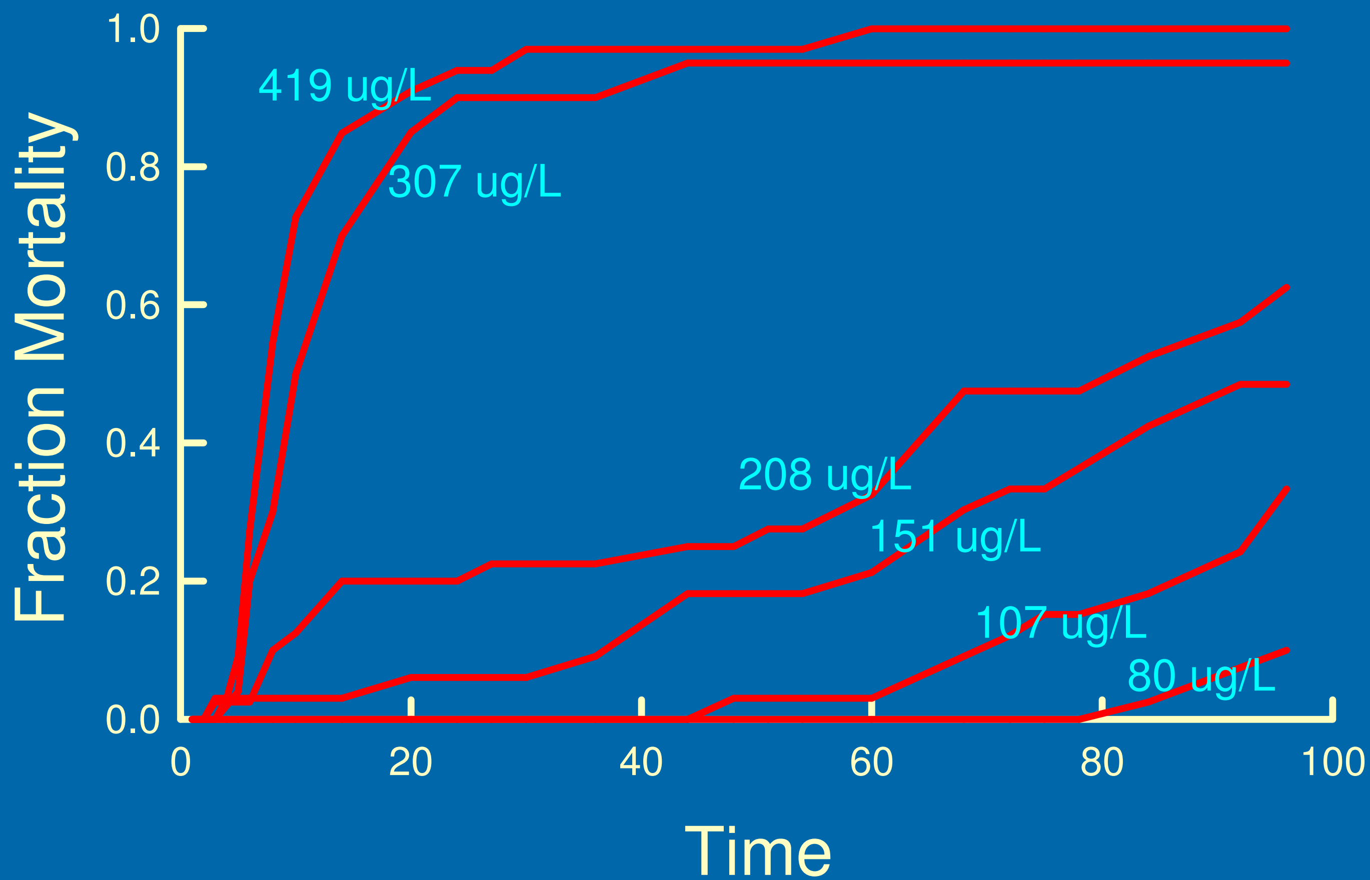
Limited Use of Information from Toxicity Tests



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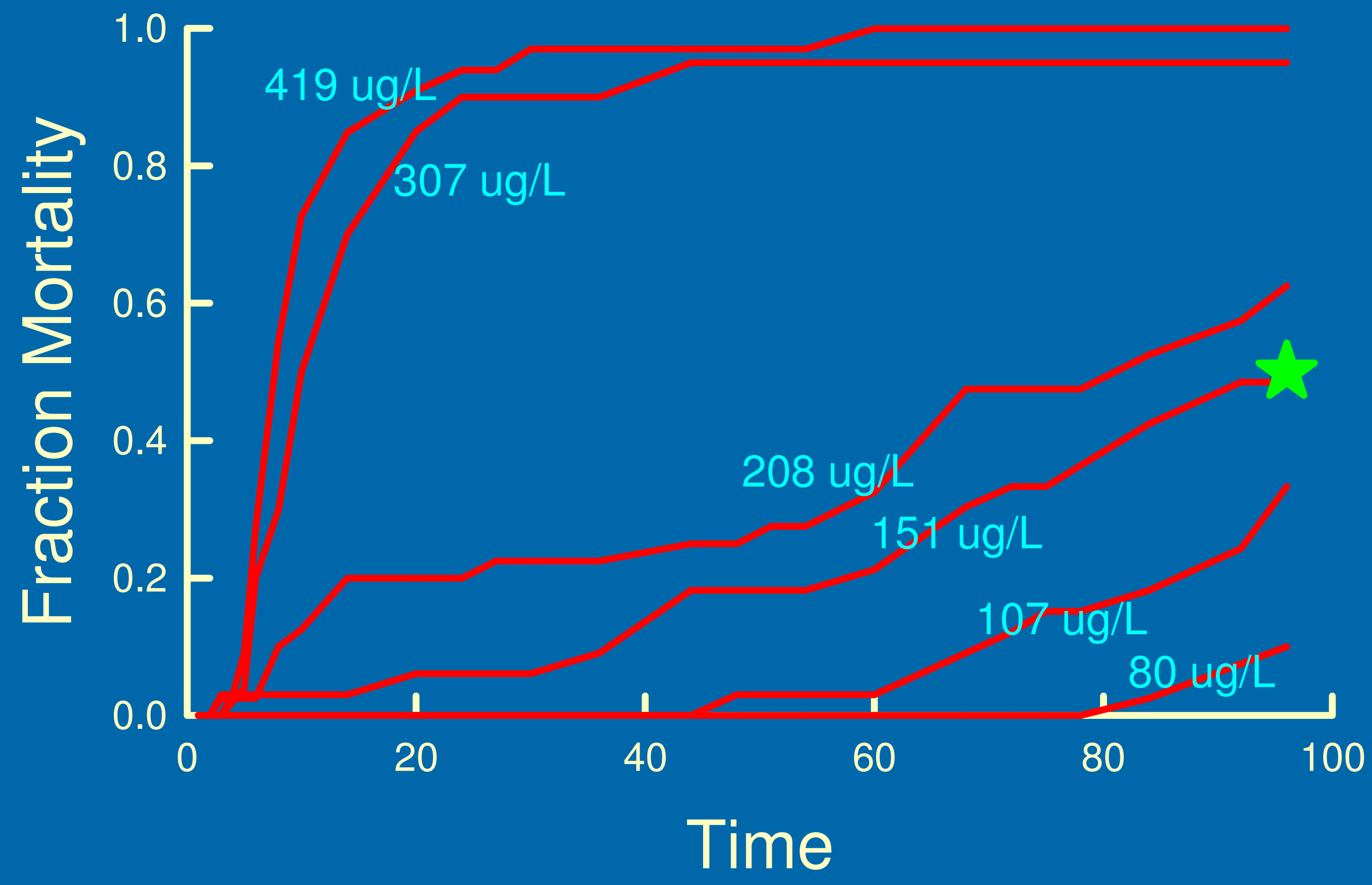

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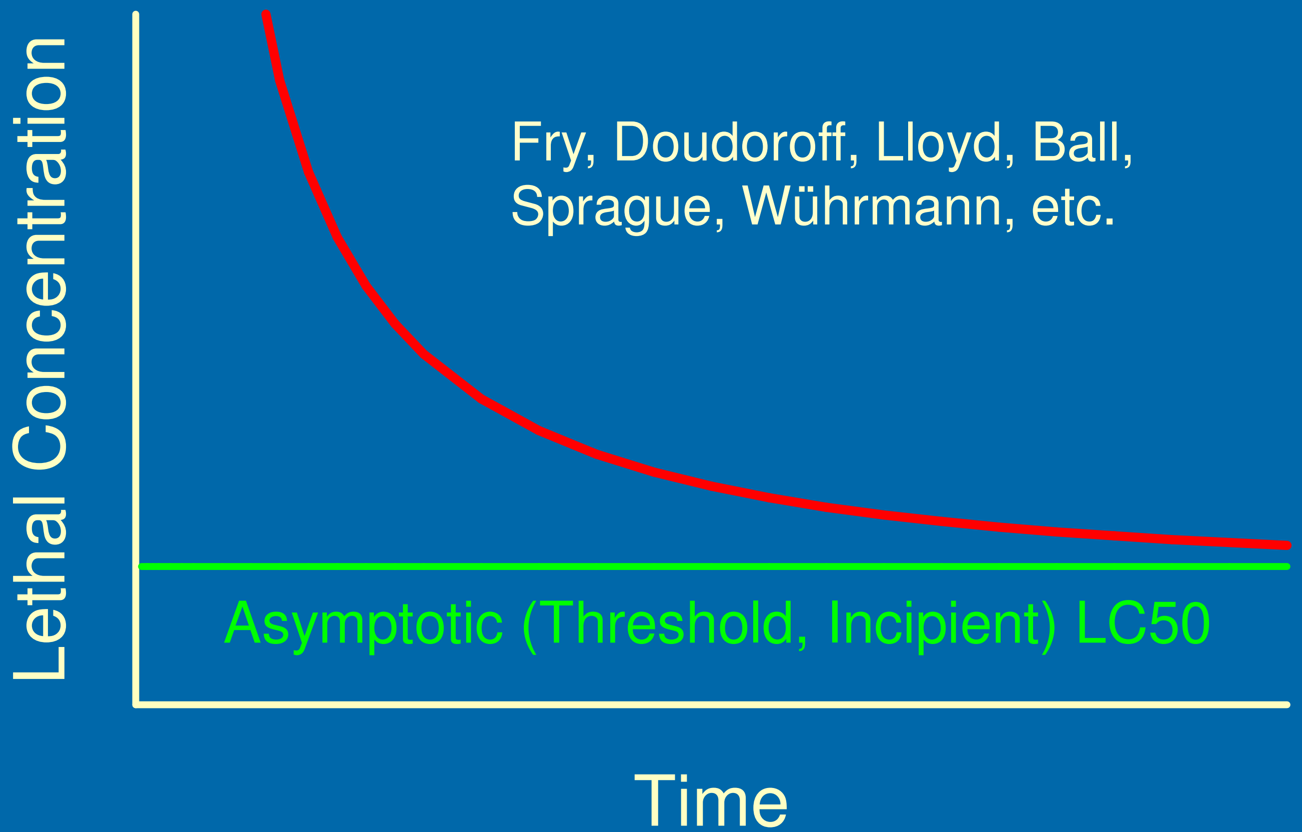
Methods to Describe Time and Concentration Dependence?



Methods to Describe Time and Concentration Dependence?

Deterministic toxicokinetics/toxicodynamics models:
Chen and Selleck (1969), Zitko (1979), Mancini (1983), Neely (1984), Chew and Hamilton (1985), McCarty and Mackay (1993), Connolly (1987), Breck (1989), Hickie et al (1995), Ankley et al (1995), Lee et al (2002), Landrum et al (2004)

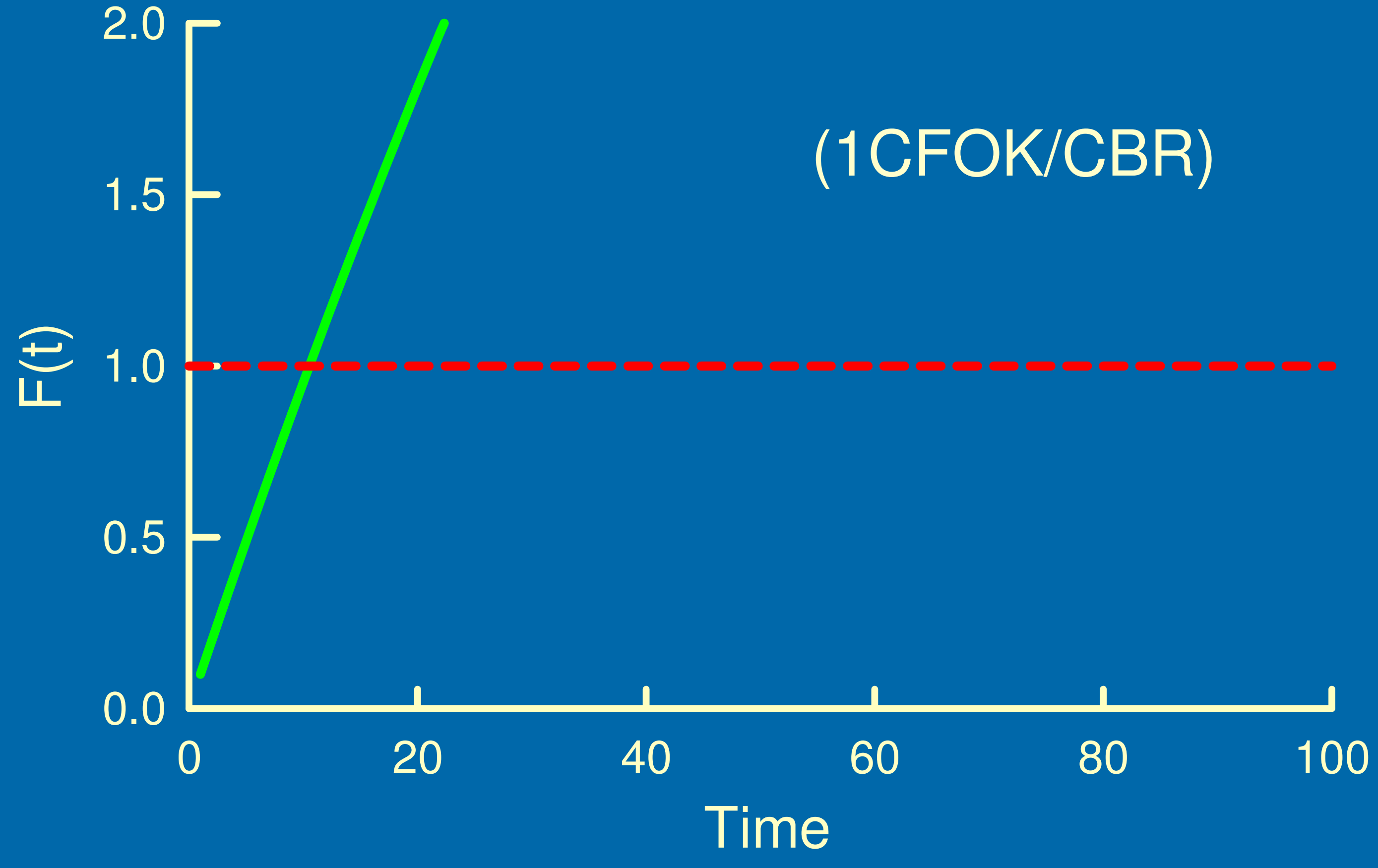
Stochastic models-distributional time-to-death, hazard rate:
Dixon and Newman (1991), Newman (1995), Crane et al (2002)
Kooijman and Bedaux (1996a,1996b), Ashauer et al (2006,2007)

Unified model – *Jager, Albert, Preuss & Ashauer (2011)*

Numerous studies of pulsed exposures, model use

Deterministic Model for Lethality

One-Compartment, First-Order Kinetics
Critical Body Residue Model



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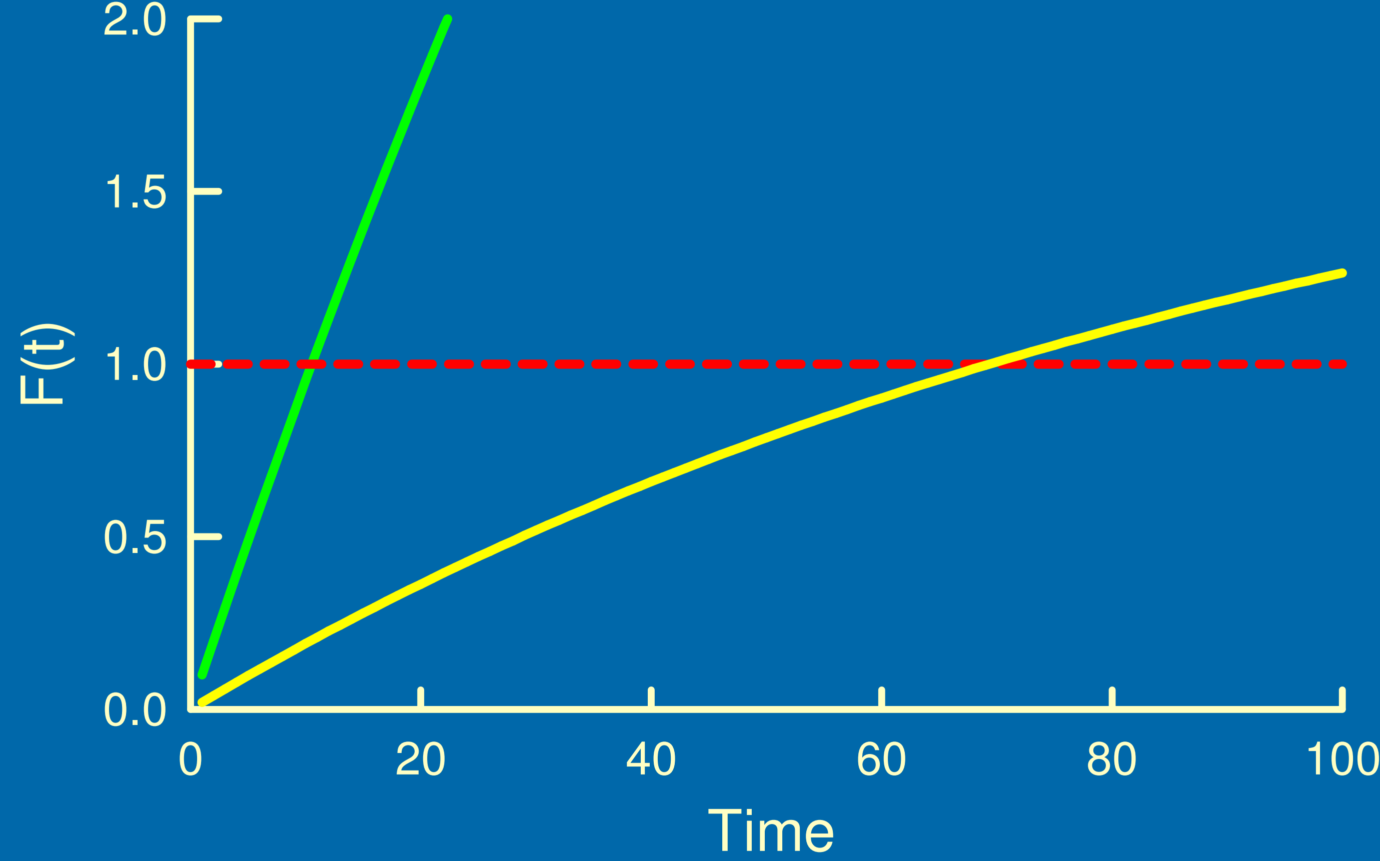

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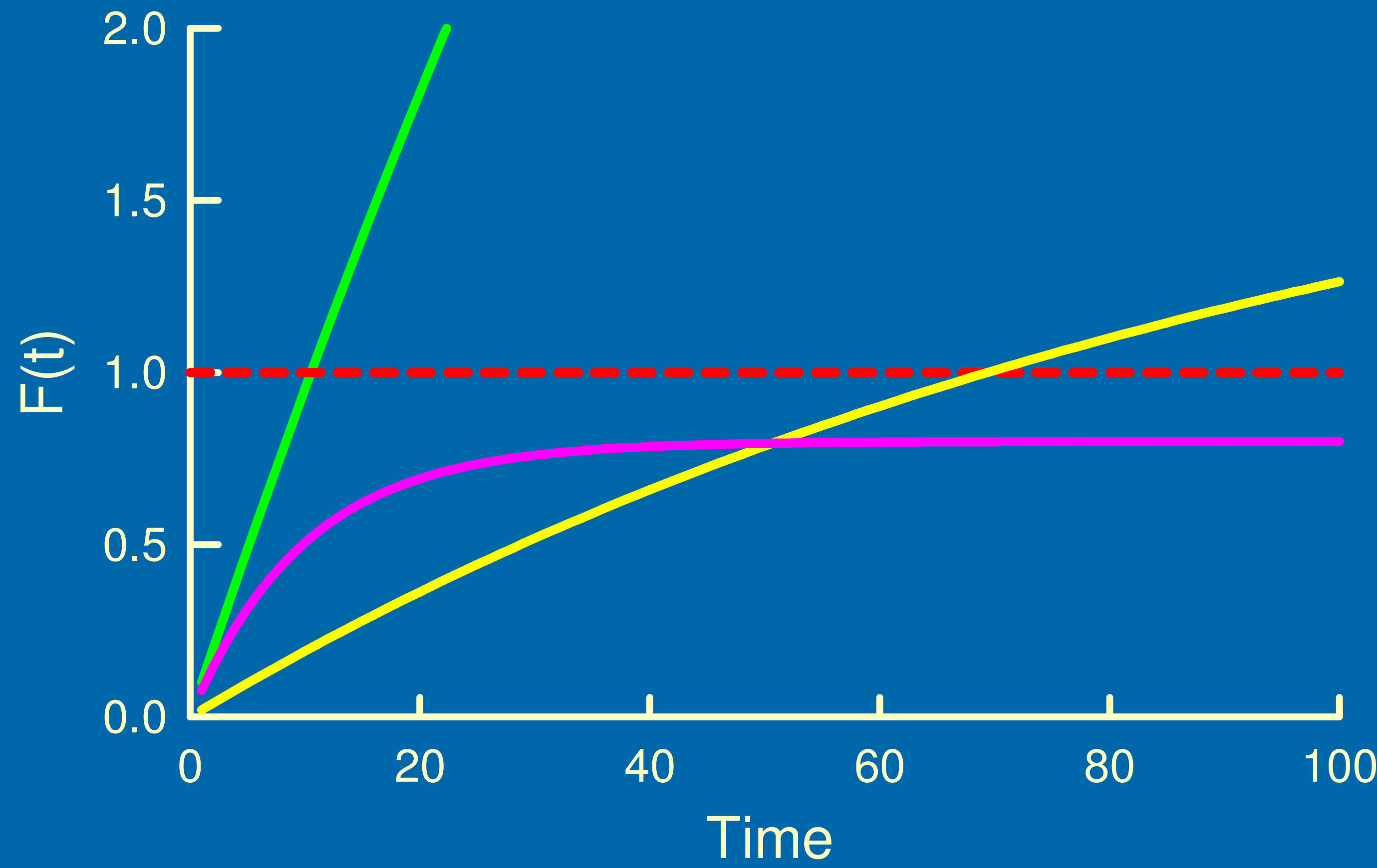

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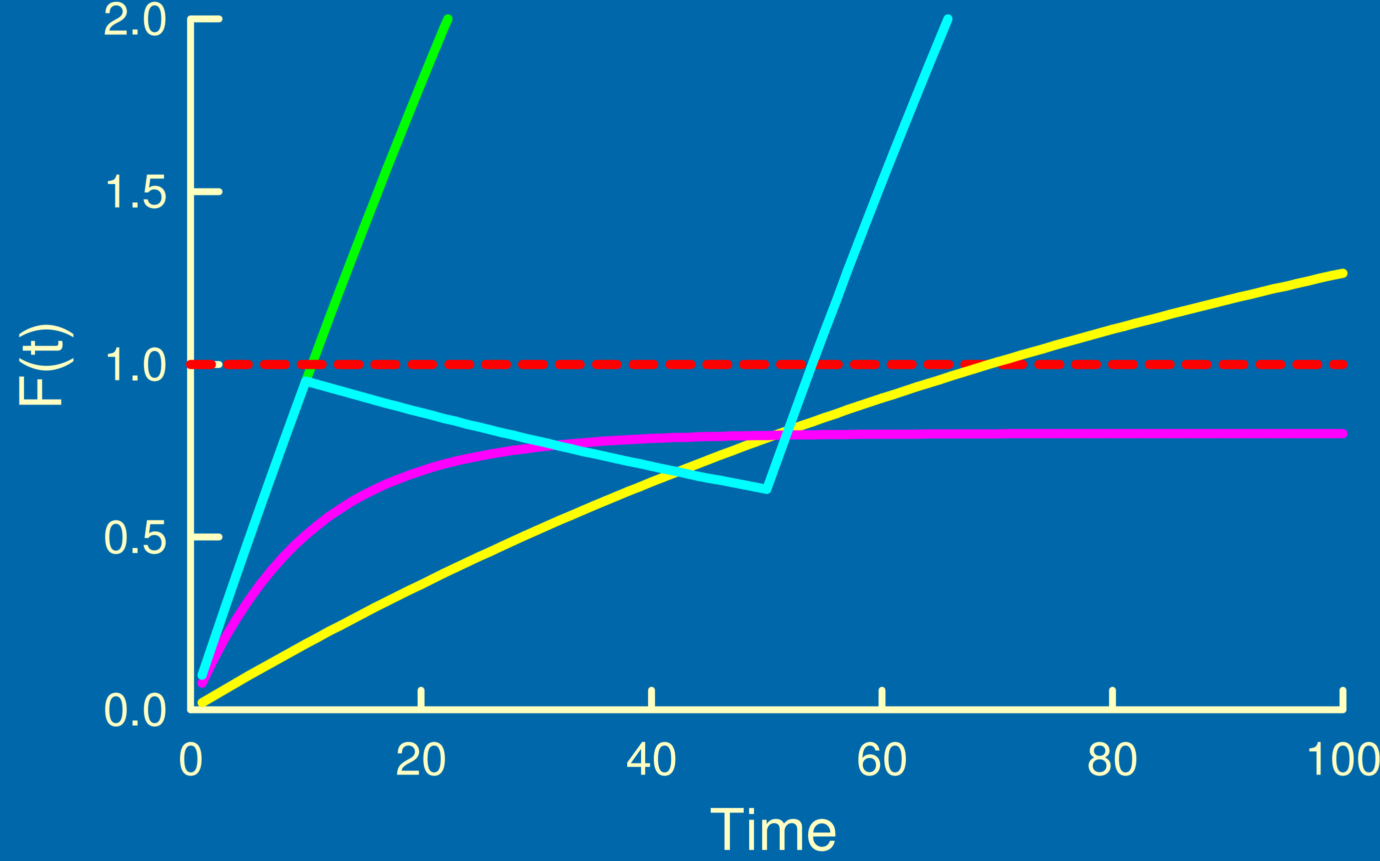


Deterministic Model for Lethality

One-Compartment, First-Order Kinetics
Critical Body Residue Model

Toxicokinetics:

$$\frac{dA(t)}{dt} = k_U \cdot C(t) - k_E \cdot A(t)$$

Toxicodynamics:

$$A(t) \overset{?}{>} LA$$

(Note: Parameters differ for individual organisms)

Deterministic Model for Lethality

One-Compartment, First-Order Kinetics
Critical Body Residue Model

For $A(t_0)=0$ and constant exposure concentration C:

$$A(t)=\frac{k_U}{k_E}\cdot C\cdot\left(1-e^{-k_E\cdot t}\right)=BCF_{ss}\cdot C\cdot\left(1-e^{-k_E\cdot t}\right)$$

$$LC=\frac{LA}{BCF\cdot\left(1-e^{-k_E\cdot t_D}\right)}=\frac{LC_\infty}{\left(1-e^{-k_E\cdot t_D}\right)}$$

Deterministic Model for Lethality

One-Compartment, First-Order Kinetics
Critical Body Residue Model

For $A(t_0)=0$ and a general exposure time series $C(t)$:

$$A(t)=\frac{k_U}{k_E}\cdot\int_{x=t_0}^{x=t}\left(C(x)\cdot k_E\cdot e^{-k_E\cdot(t-x)}\right)dx=BCF\cdot\bar{C}(t)$$

$$\overline{LC}(t)=\frac{LA}{BCF}=LC_\infty$$

Deterministic Model for Lethality

One-Compartment, First-Order Kinetics
Critical Body Residue Model

Variation among individual organisms is addressed by a distribution for the model parameters LC_{∞} , k_e

Model can be extended/modified for:

- Damage/repair processes
- Multi-compartment kinetics
- Multiple mechanisms
- Delayed mortality

Stochastic Model for Lethality (part of DEBtox)

Toxicokinetics:

$$\frac{dA(t)}{dt} = k_U \cdot C(t) - k_E \cdot A(t)$$

Toxicodynamics:

$$h(t) = max\left(0, d \cdot \left(A(t) - A_0\right)\right)$$

(Note: Parameters are same for individual organisms)

Model Parameterization

Number of deaths within each time interval for each treatment									
Treatment	Time Interval								Survivors
	1	2	3	4	5	6	7	8	
1									10
2							3	4	3
3					1	2	7		
4				5	5				
5		2	3	4	1				

Parameters estimated by maximum likelihood analysis:

$$L(\boldsymbol{N} \mid \Theta) = \prod_{j=1}^{J} \left(\prod_{i=1}^{I+1} P_{i,j}{}^{N_{i,j}} \right)$$

Example:
Copper Acute Toxicity to Fathead Minnows

Copper Toxicity to Fathead Minnows

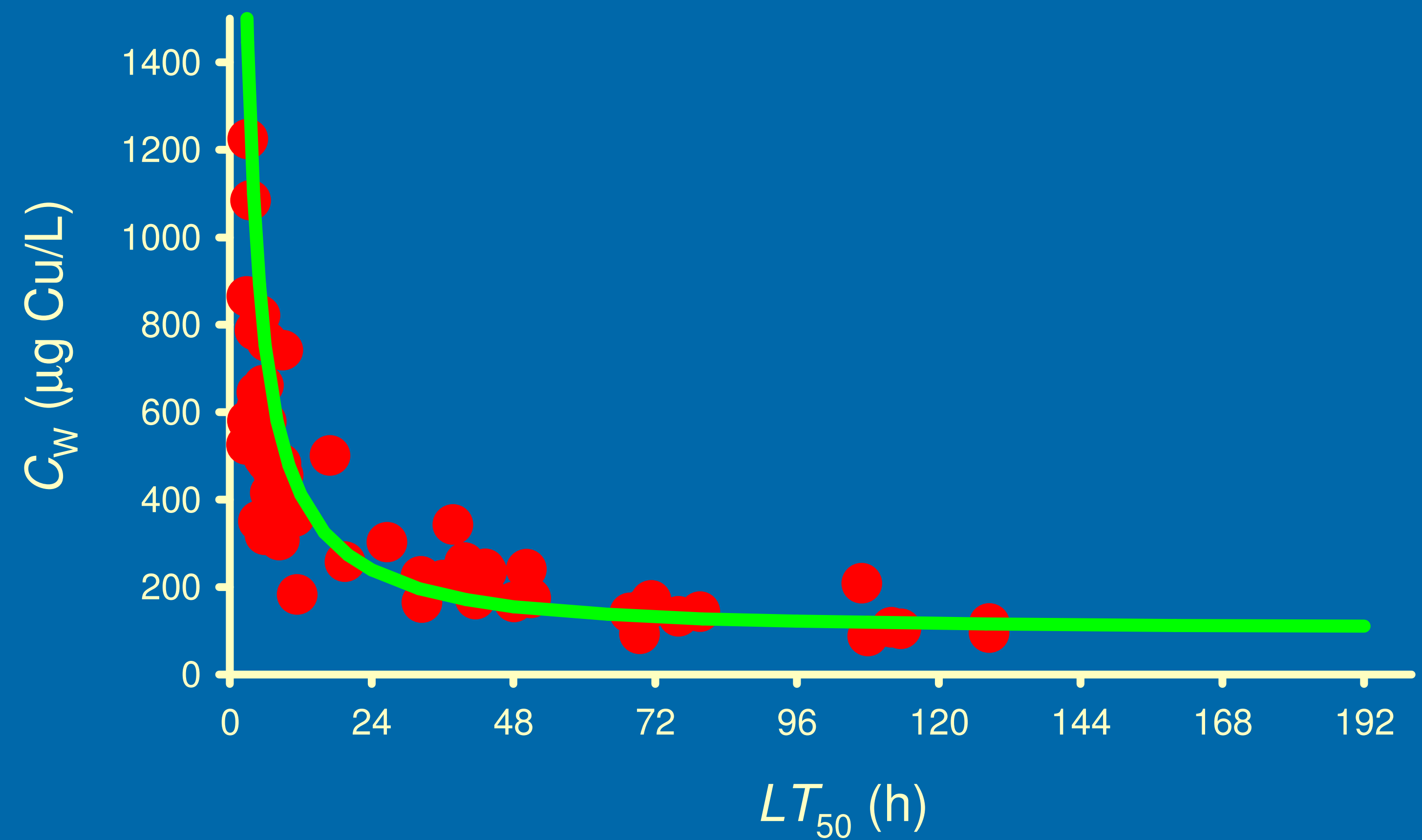
(Lindberg and Yurk; 1982, 1983)

31 constant-exposure toxicity tests on lethality of copper to juvenile fathead minnows; durations ranging from 2.5 h to 192 h; observations of delayed mortality for exposure durations of 24 h or less.

6 pulsed-exposure toxicity tests; pulse durations from 2.5 to 12 h; pulse intervals from 8 to 24 h.

Copper Toxicity to Fathead Minnows

LT50s for Constant Exposures



Copper Toxicity to Fathead Minnows

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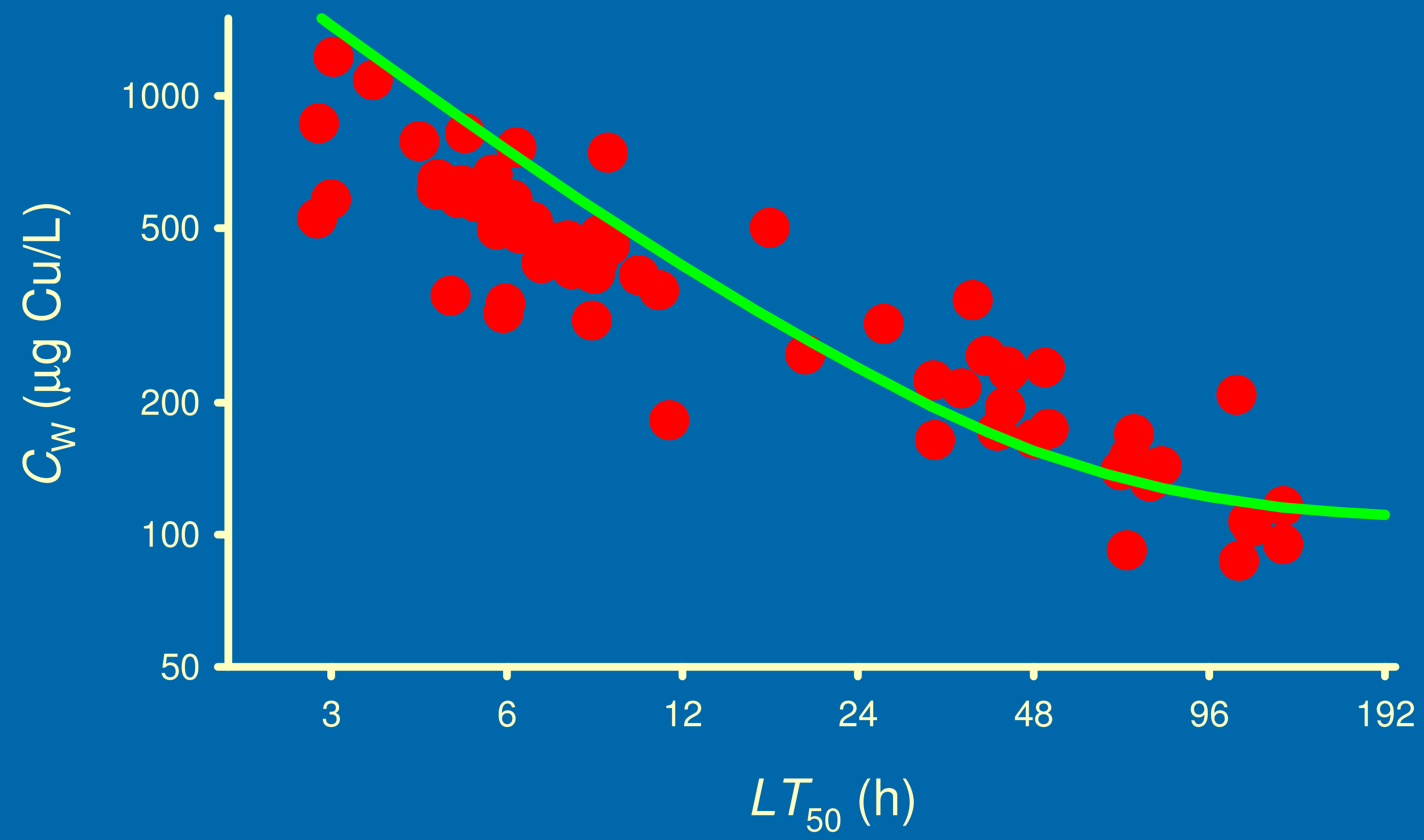

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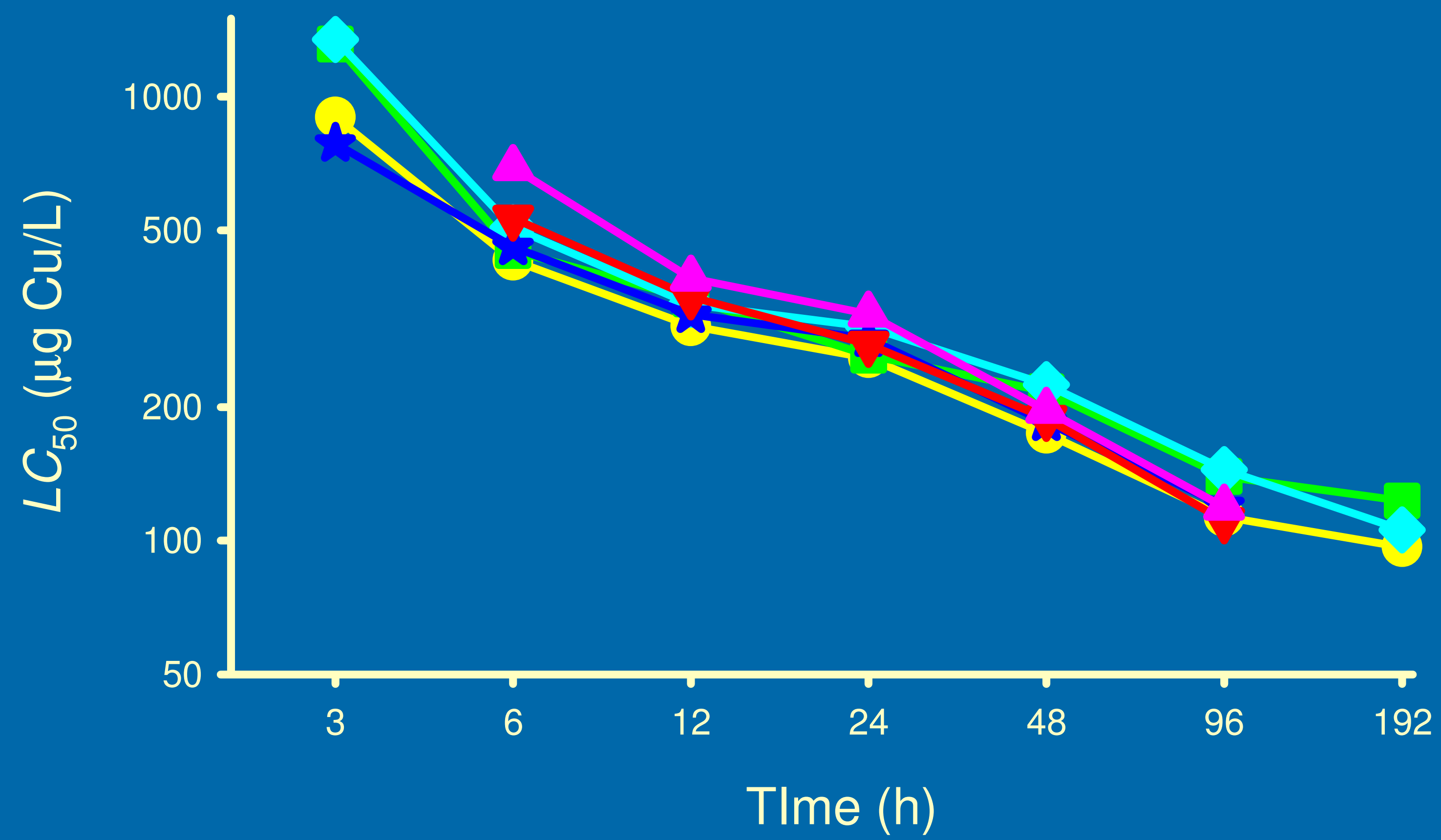

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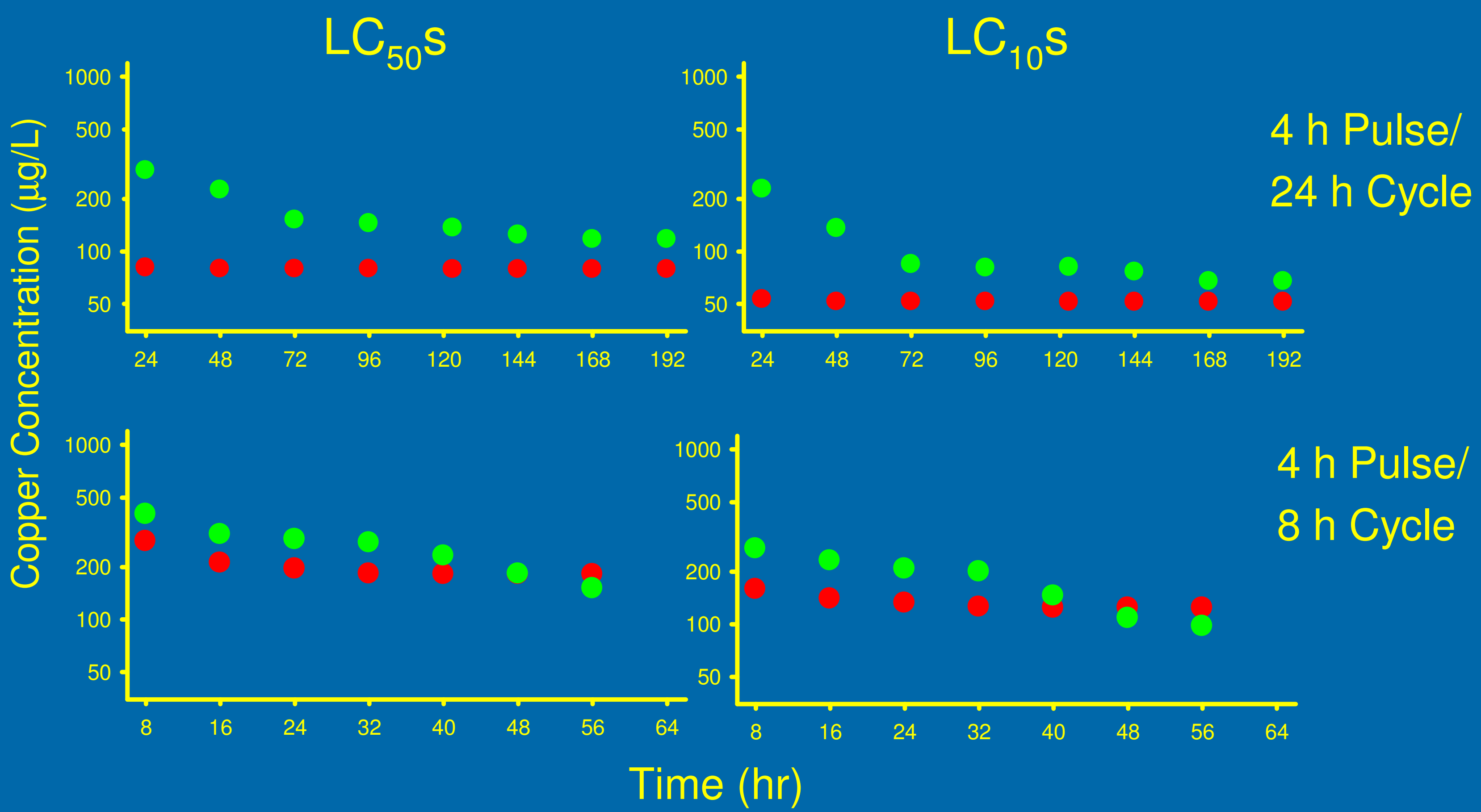
Copper Toxicity to Fathead Minnows

LC50s and LC10s for Pulsed Exposures



Copper Toxicity to Fathead Minnows

Model Characteristics

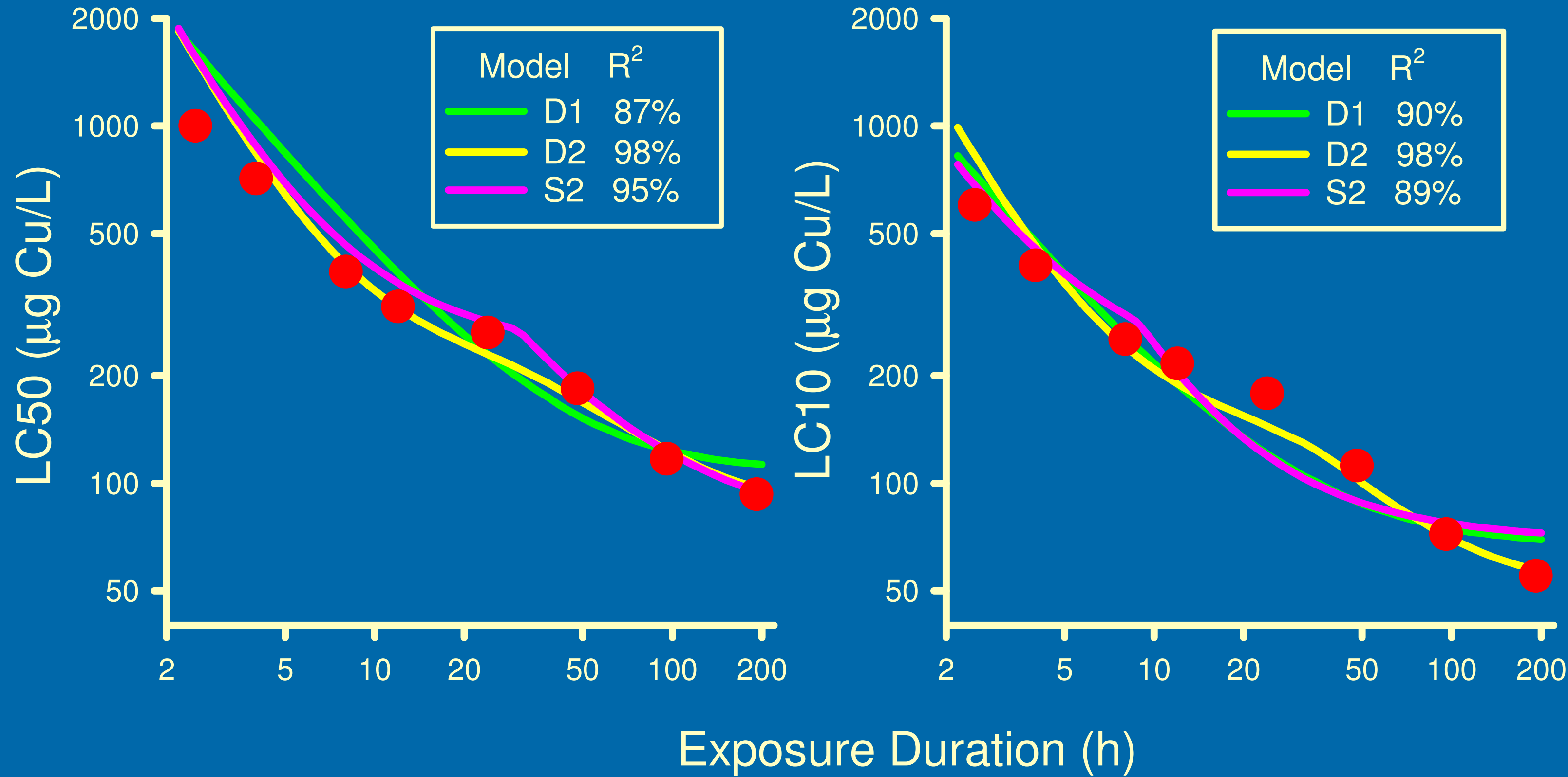
D1 – Deterministic, one mechanism,
first-order kinetics

D2 – Deterministic, two mechanisms,
first-order kinetics, delay-adjusted

S2 – Stochastic, two mechanisms

Copper Toxicity to Fathead Minnows

Model Fit to Constant Exposures



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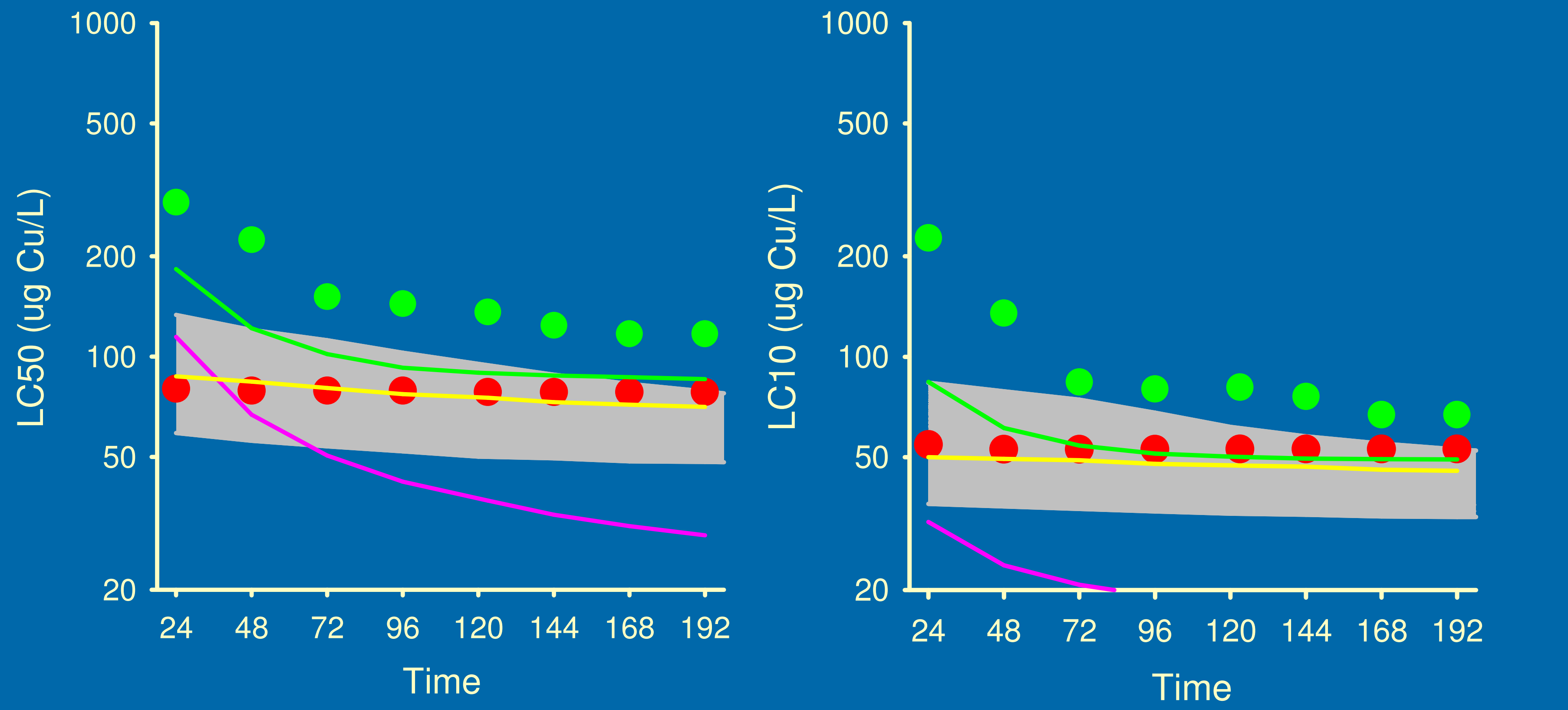
Copper Toxicity to Fathead Minnows

Model Fit to 4h/24h Pulsed Exposures



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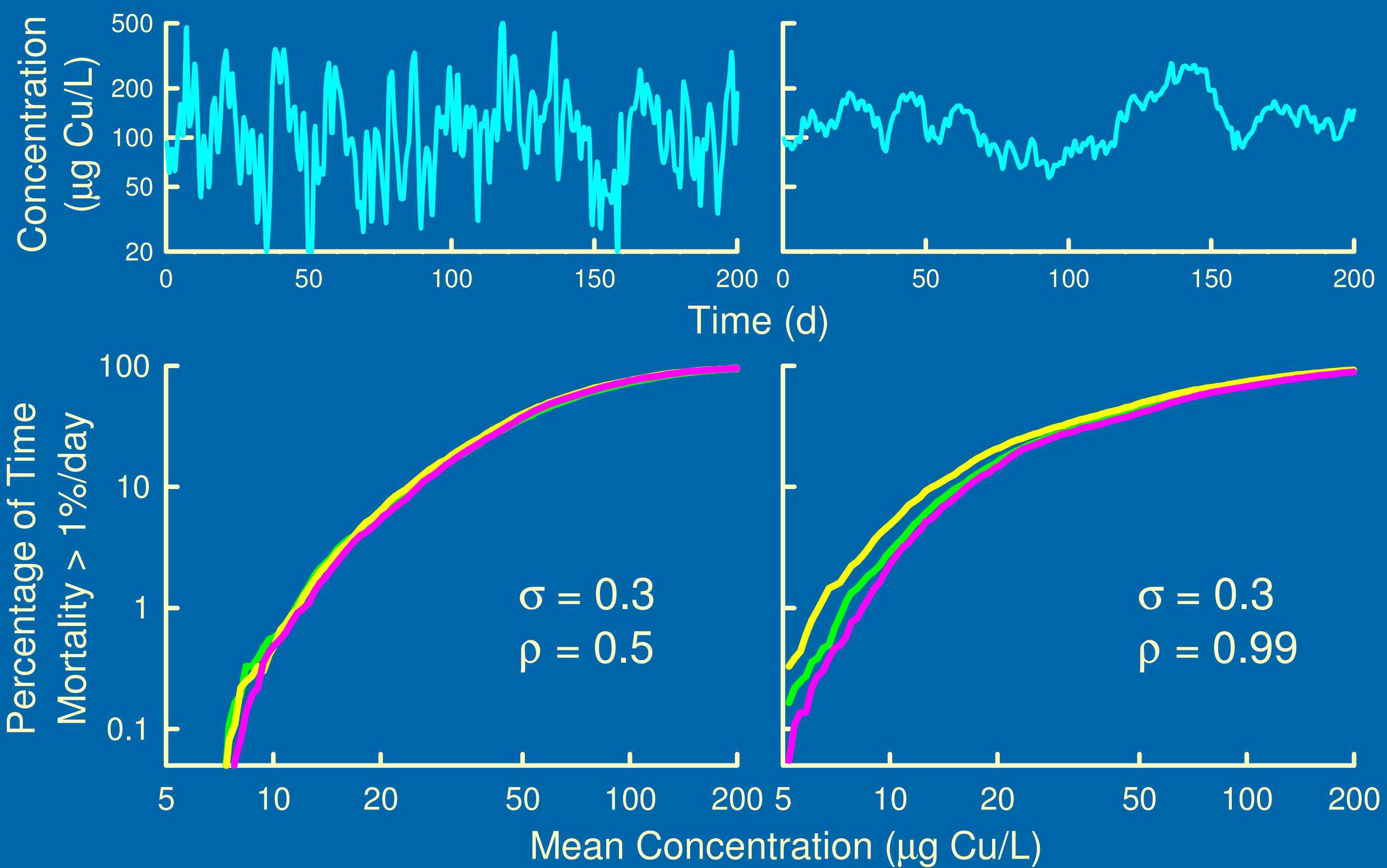
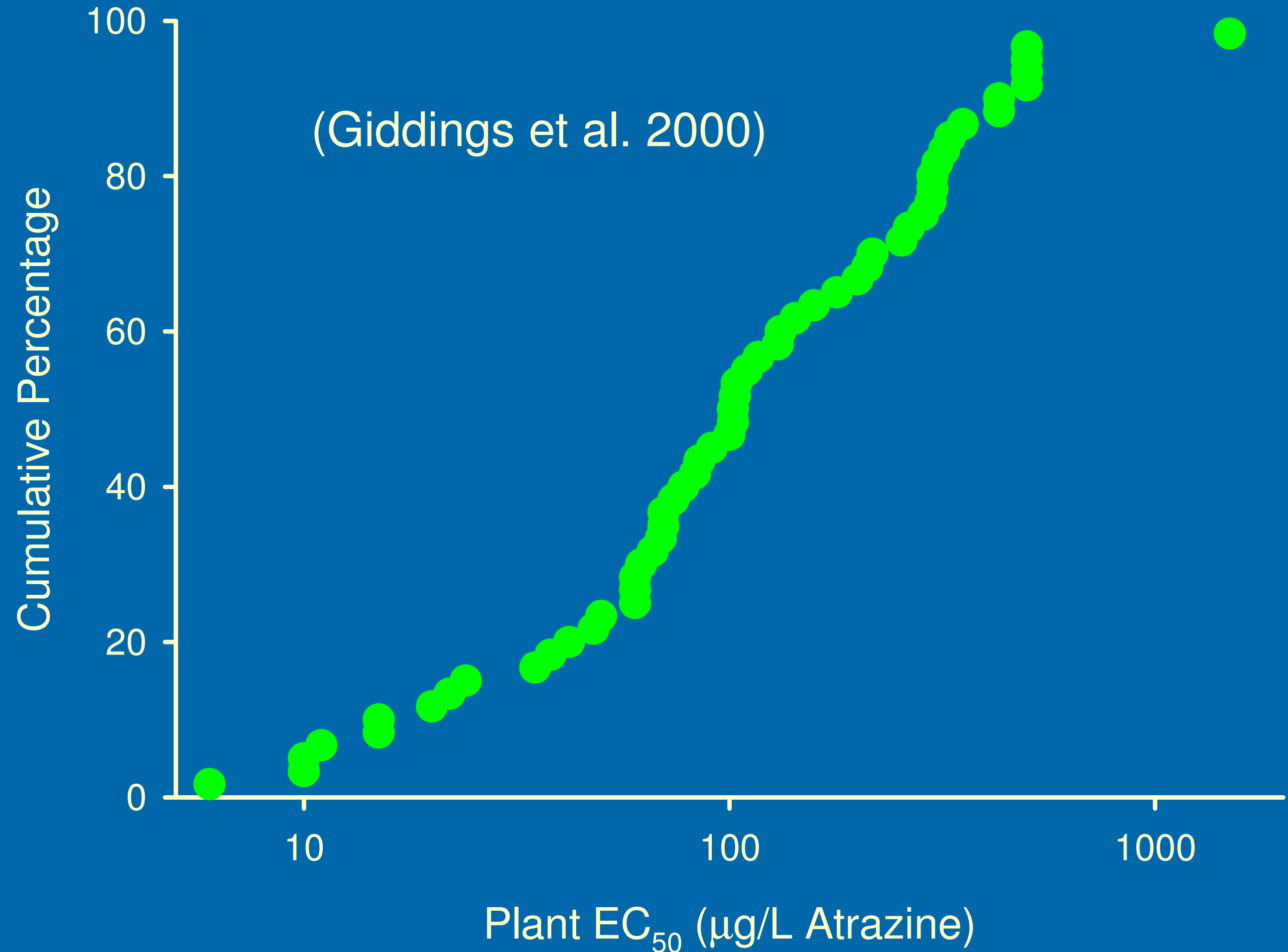
Copper Toxicity to Fathead Minnows

Risk Characterizations



Example:
Atrazine Effects on
Aquatic Plant Growth

Species Sensitivity Distribution



Specific Growth Rate (SGR)

SGR Definition:

$$SGR = \frac{1}{P(t)} \cdot \frac{dP(t)}{d(t)}$$

Constant SGR:

$$P(t) = P(0) \cdot e^{SGR \cdot t}$$

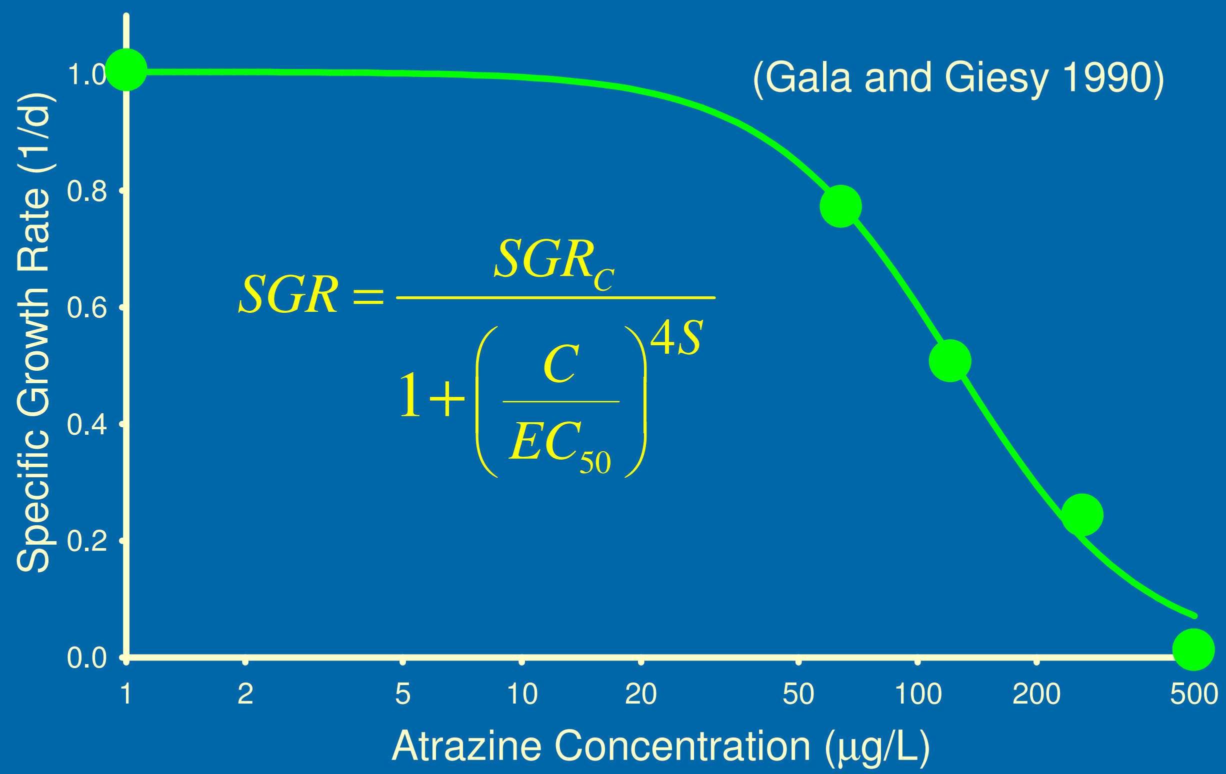
Time-variable SGR:

$$P(t) = P(0) \cdot e^{\int_0^t SGR(t) \cdot dt}$$

(Note: for atrazine, SGR responses quickly to changes in concentration – time lags are not addressed here)

Toxicity Relationships

Plant toxicity tests reanalyzed to provide relationships of specific growth rate to atrazine concentration.



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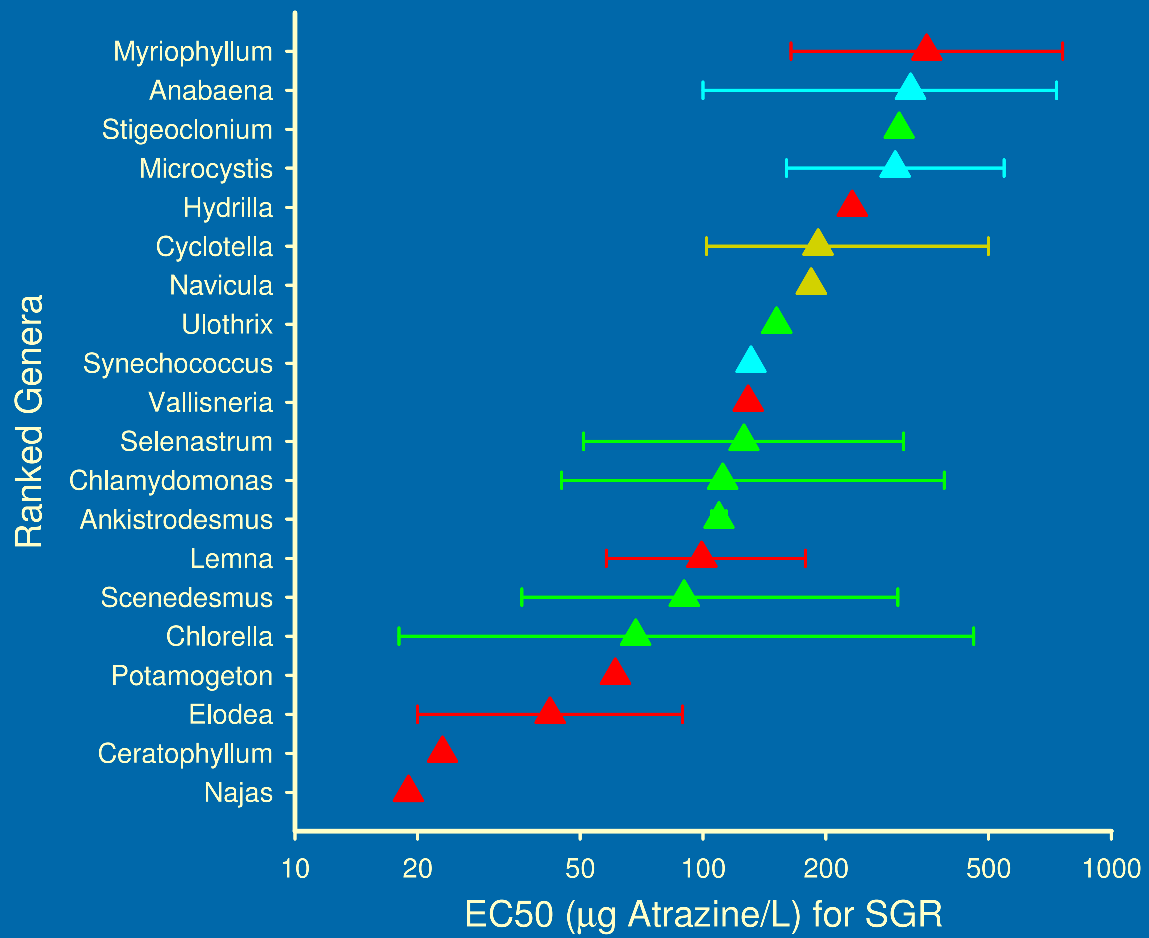

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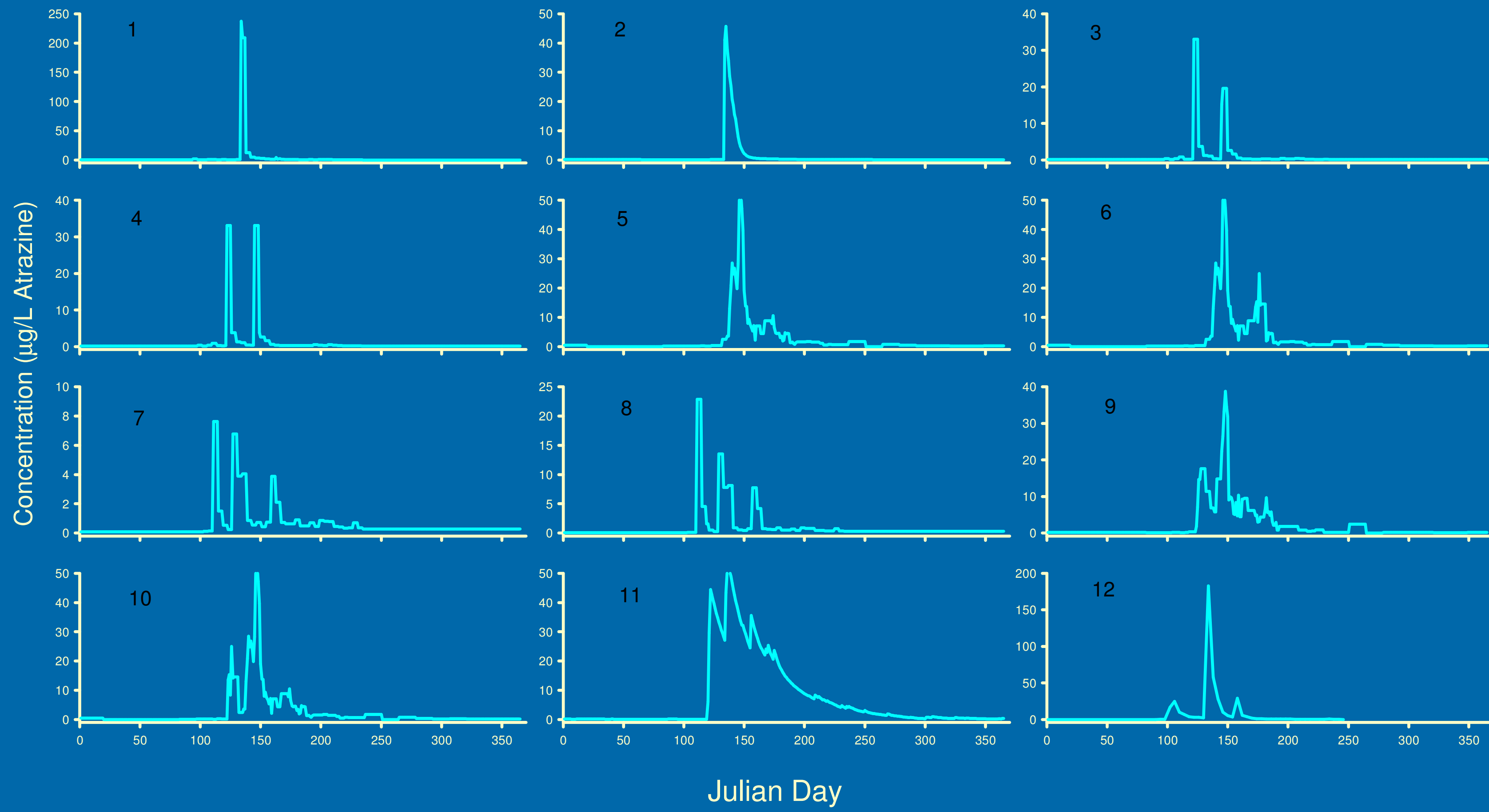
Exposures in Natural Systems



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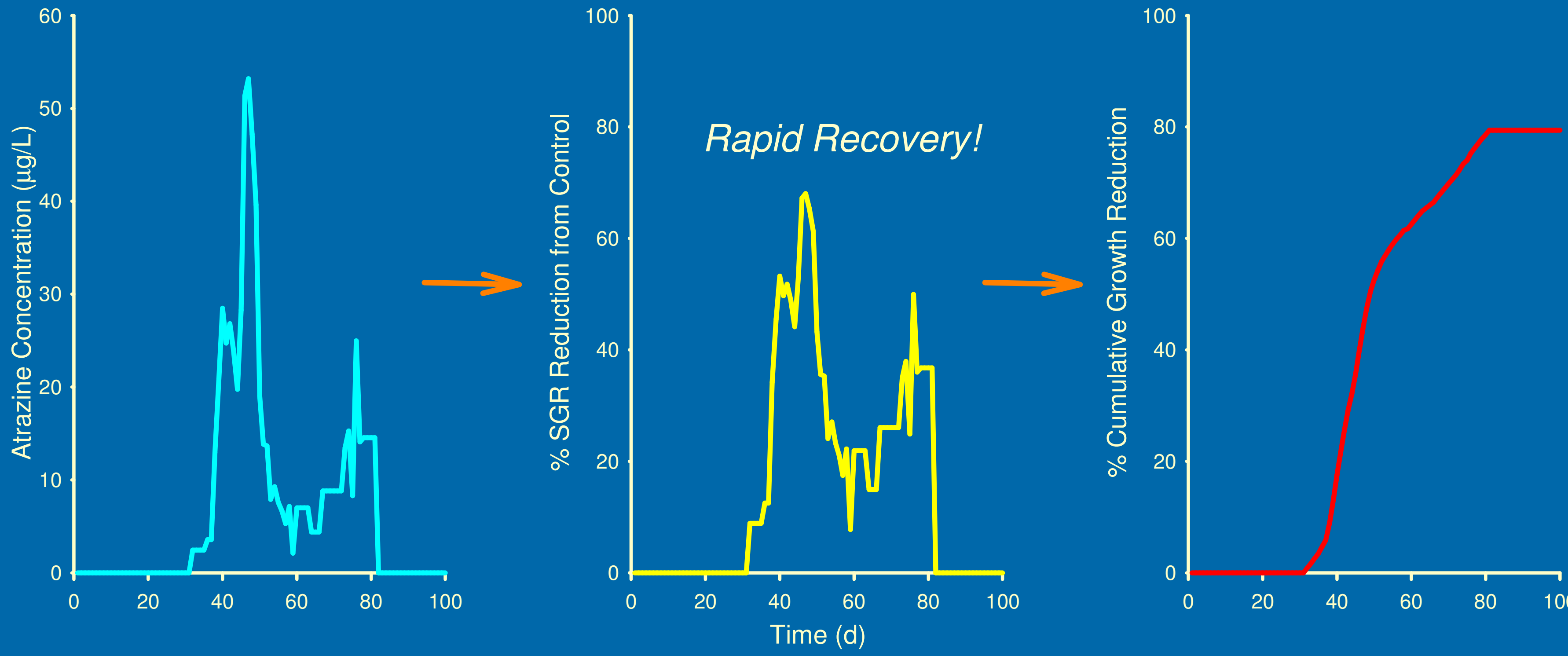
Cumulative Effects



(Note: Cumulative growth reduction does not address other factors regulating growth, so should be interpreted as a relative effects index, not an absolute prediction. More on this in next talk!)

Questions?