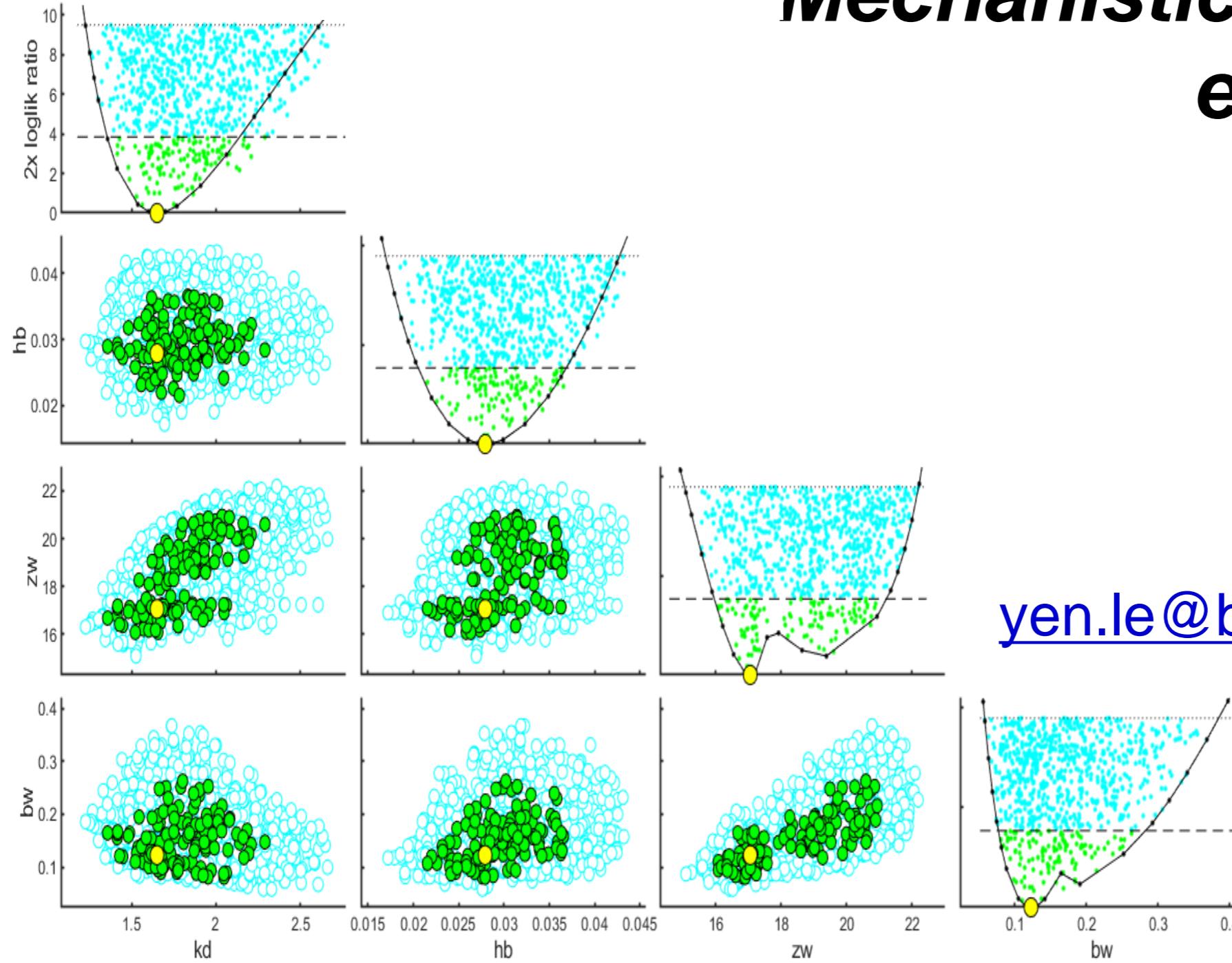


Mechanistic modelling in ecotoxicology

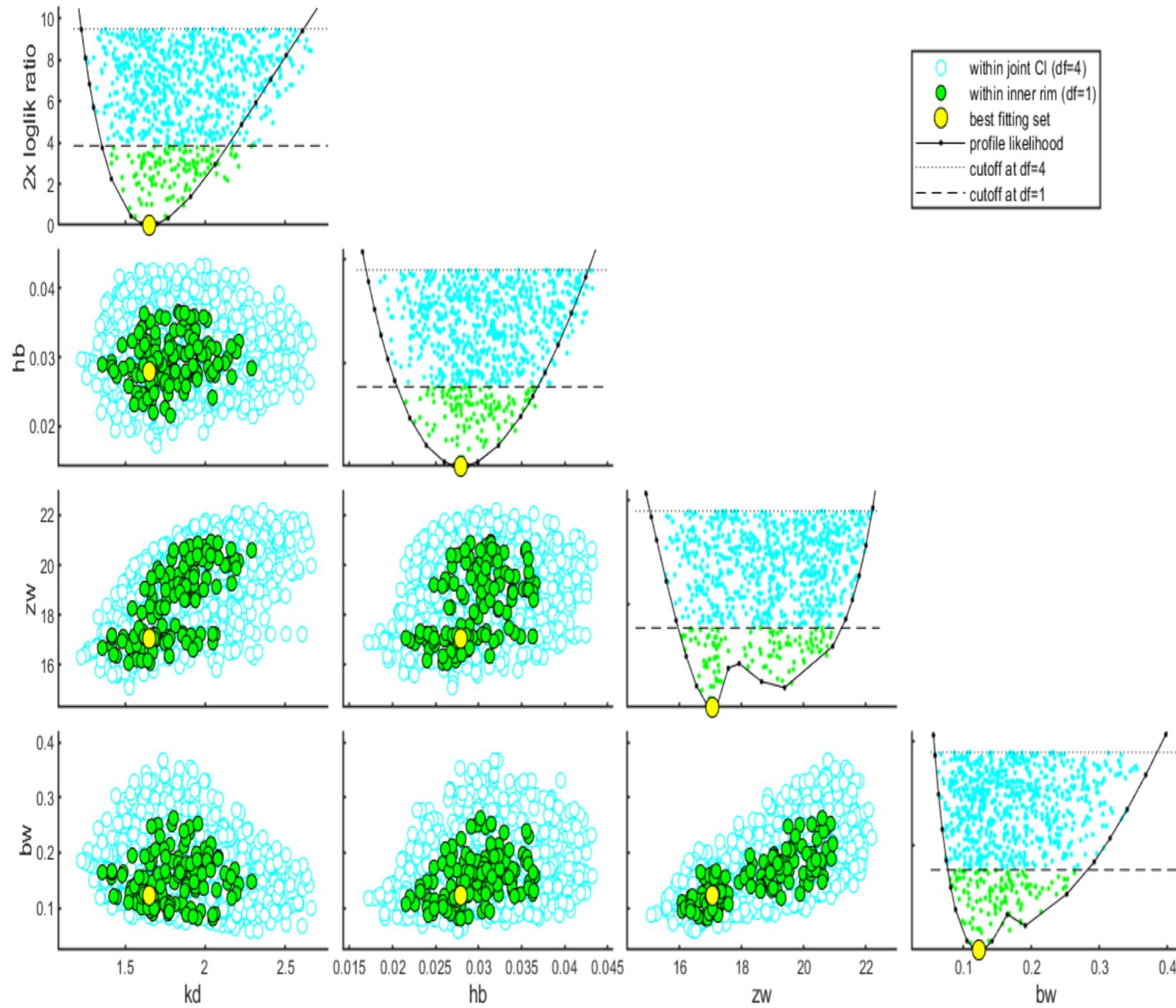


08.12.2022

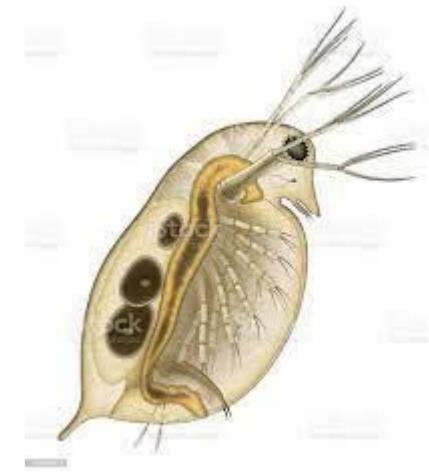
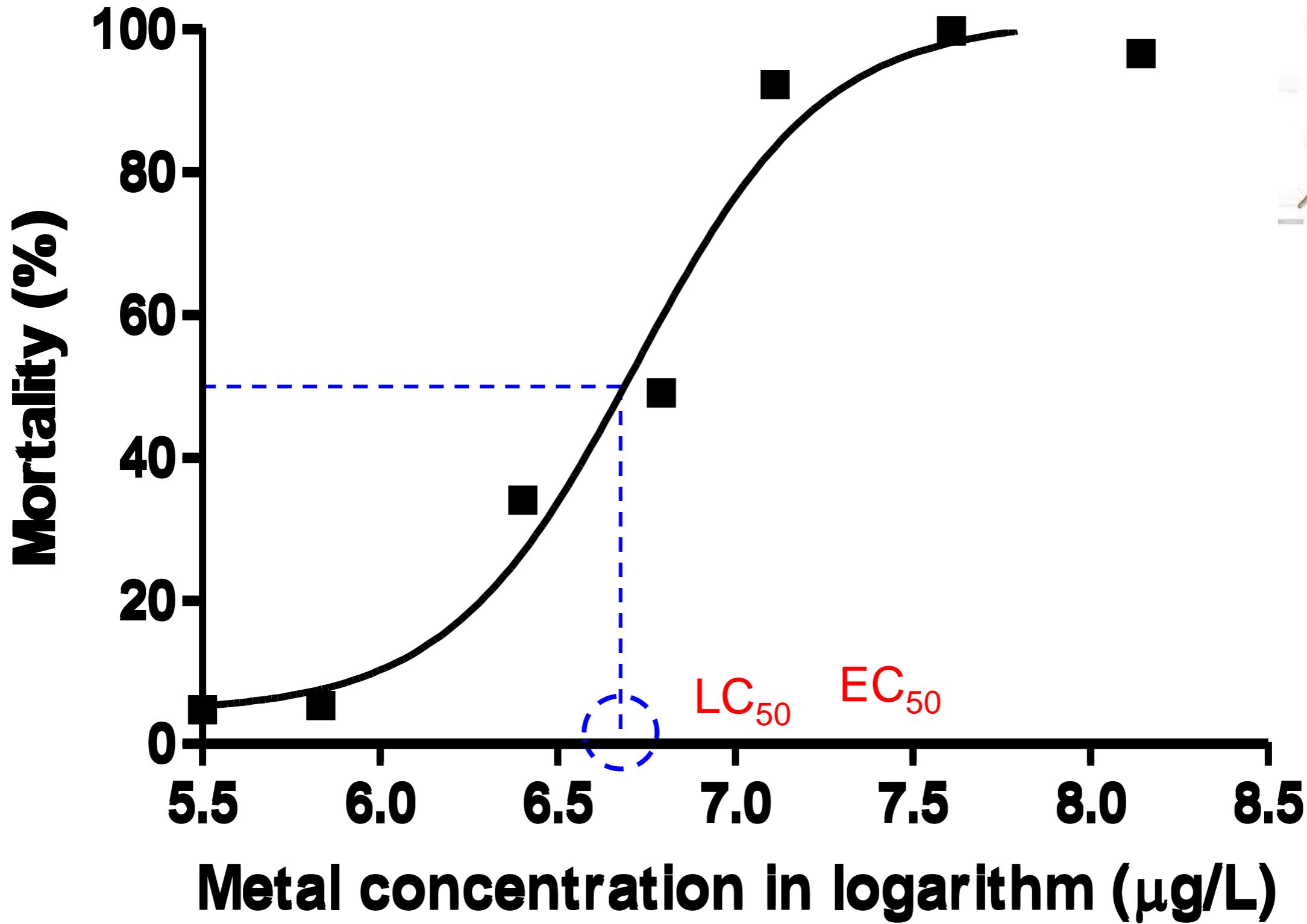
T.T. Yen Le
Aquatic Ecology
yen.le@uni-due.de
yen.le@biologie-uni-due.org

S05 T03 B19

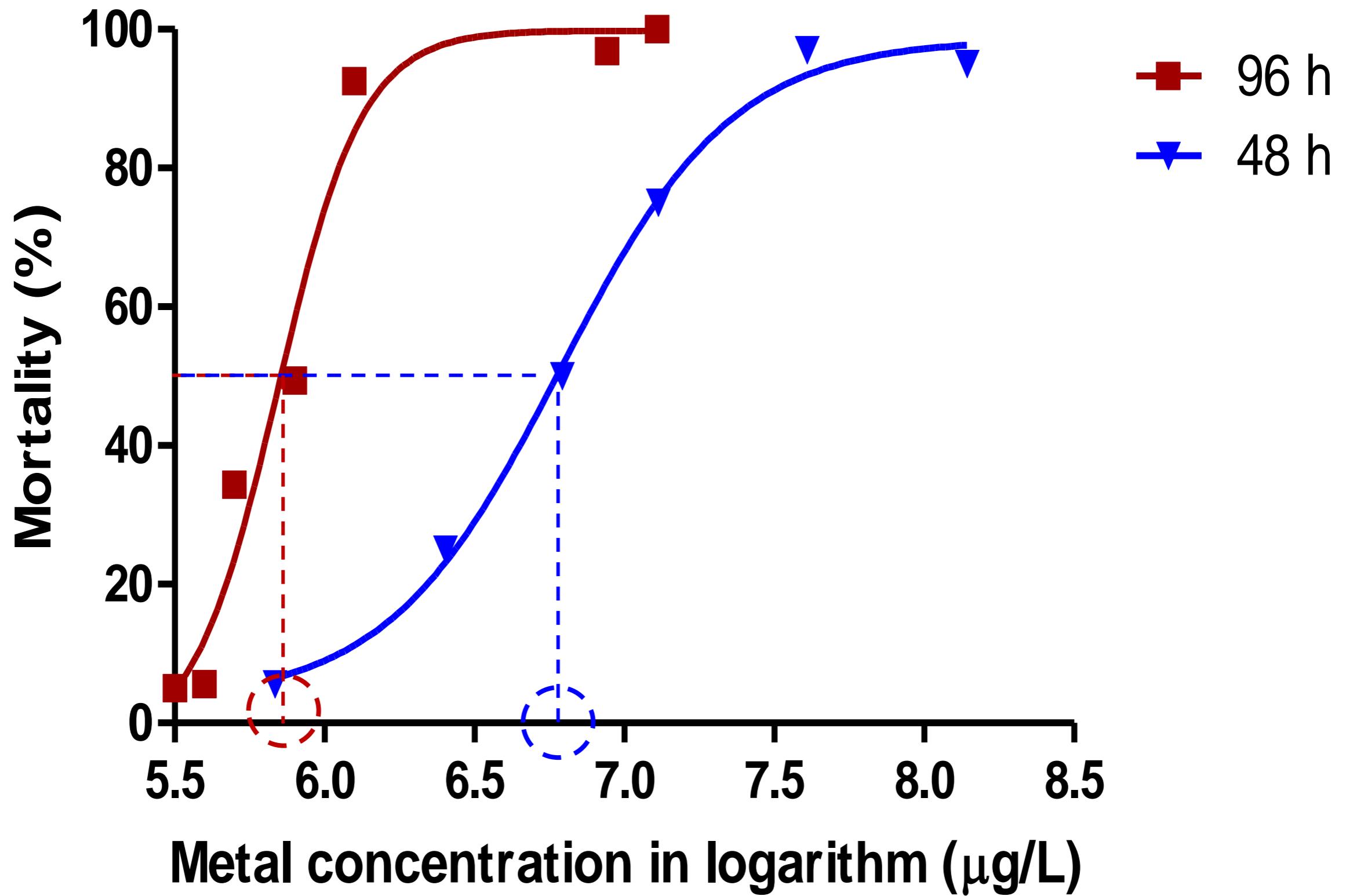
Why do we need mechanistic modelling in ecotoxicology?



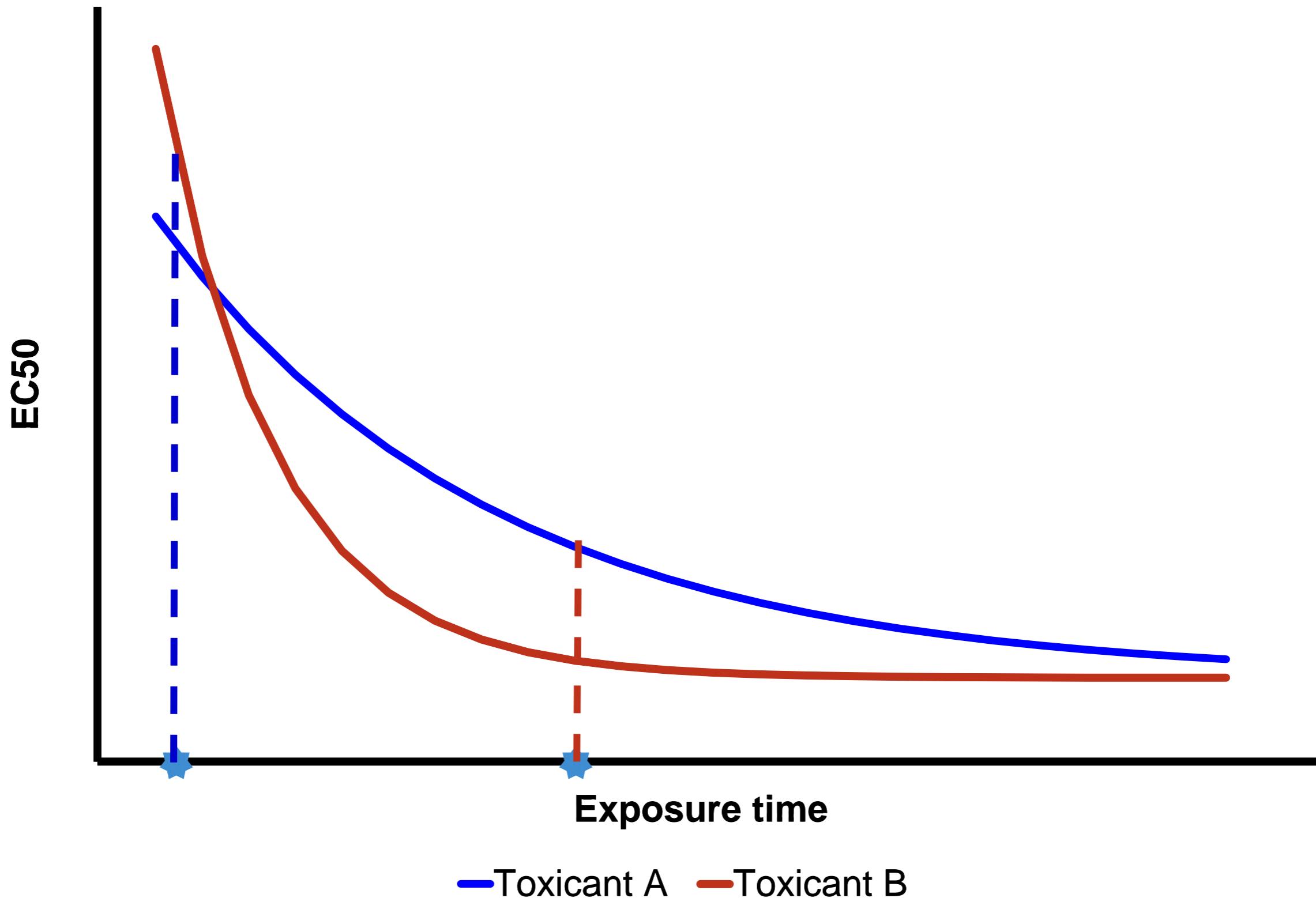
Benchmark dose in Ecotoxicology



EC_{50} depending on exposure duration



Limited significance in comparative toxicity



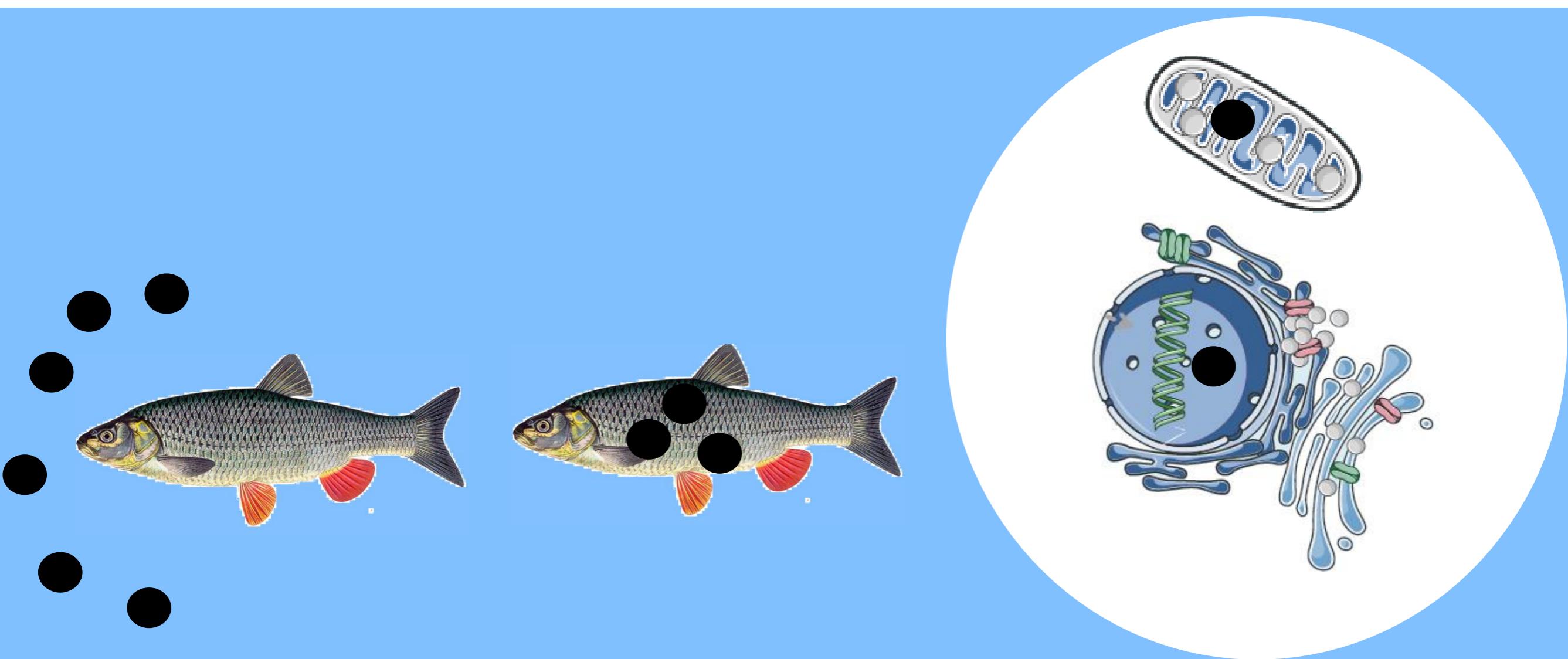
Mechanistic modelling at the individual level

Toxicokinetics

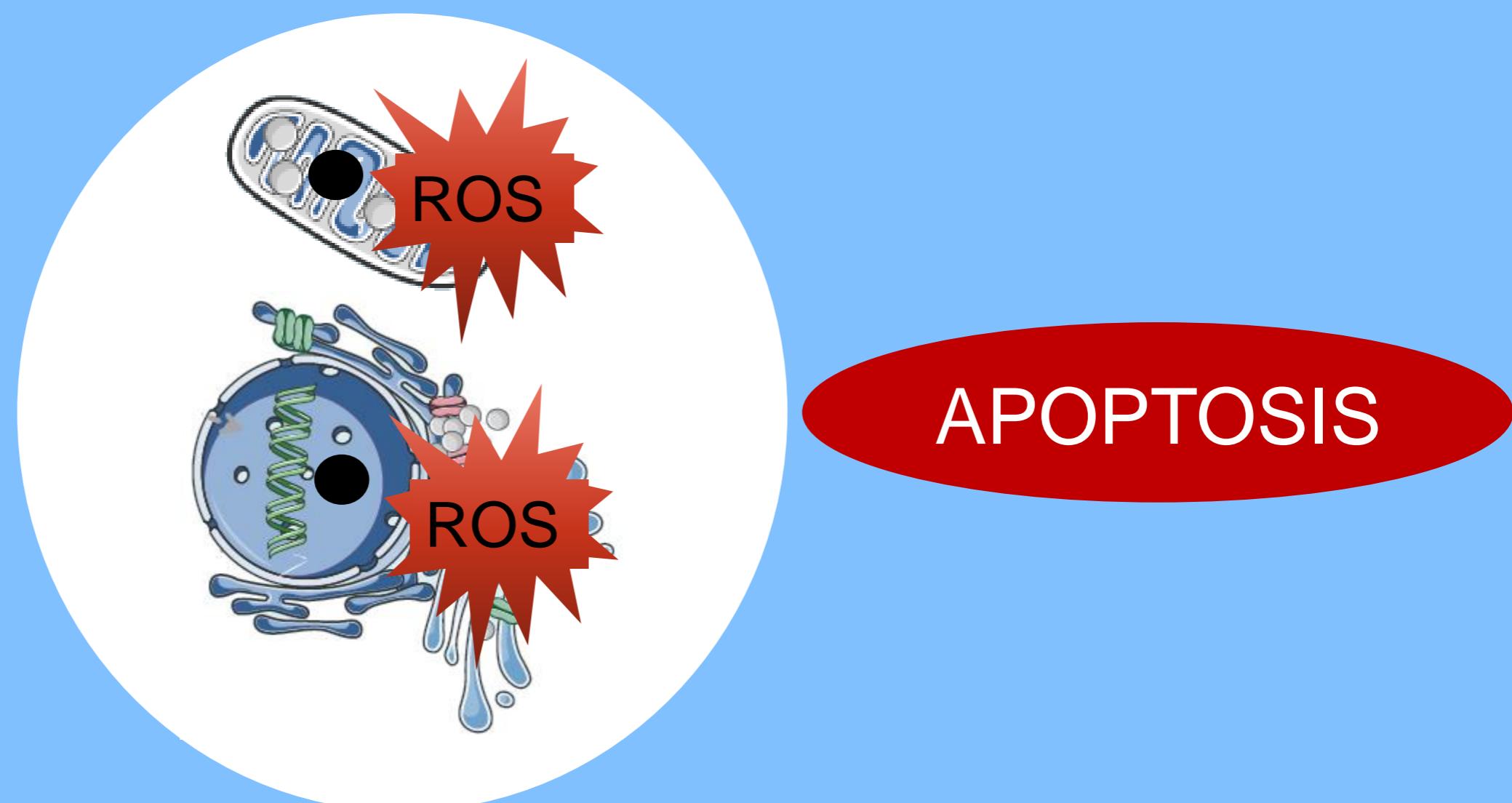
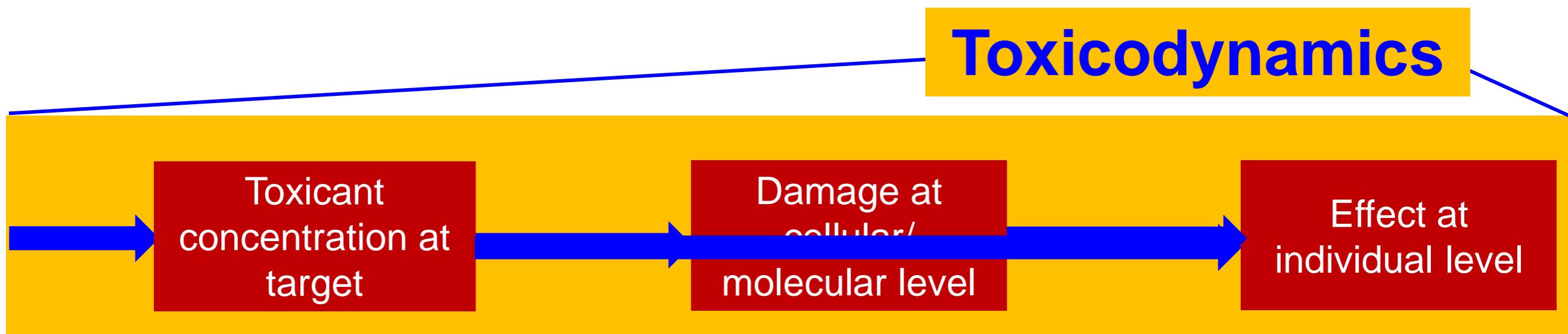
Toxicant concentration in medium

Toxicant concentration in body

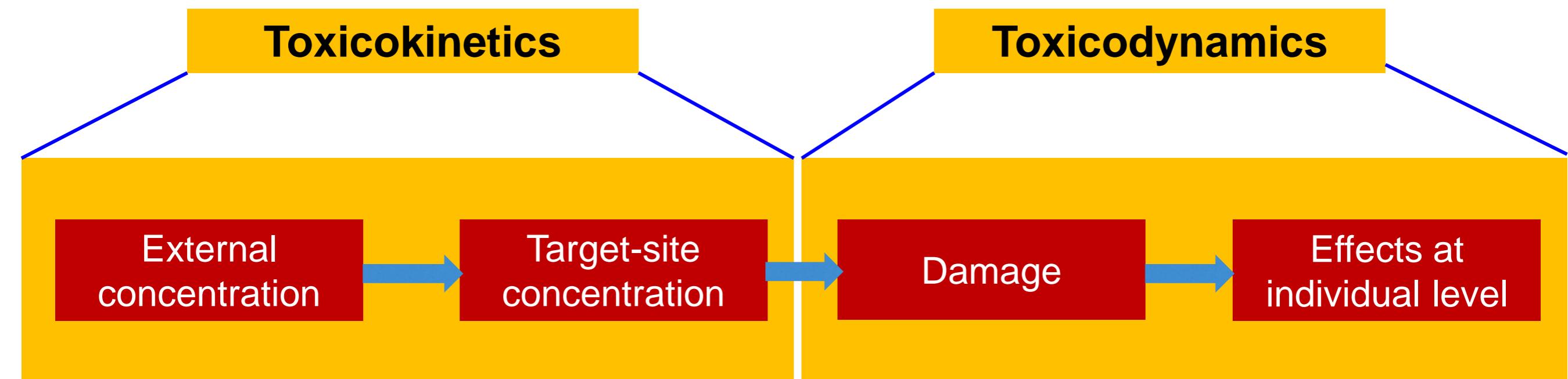
Toxicant concentration at target



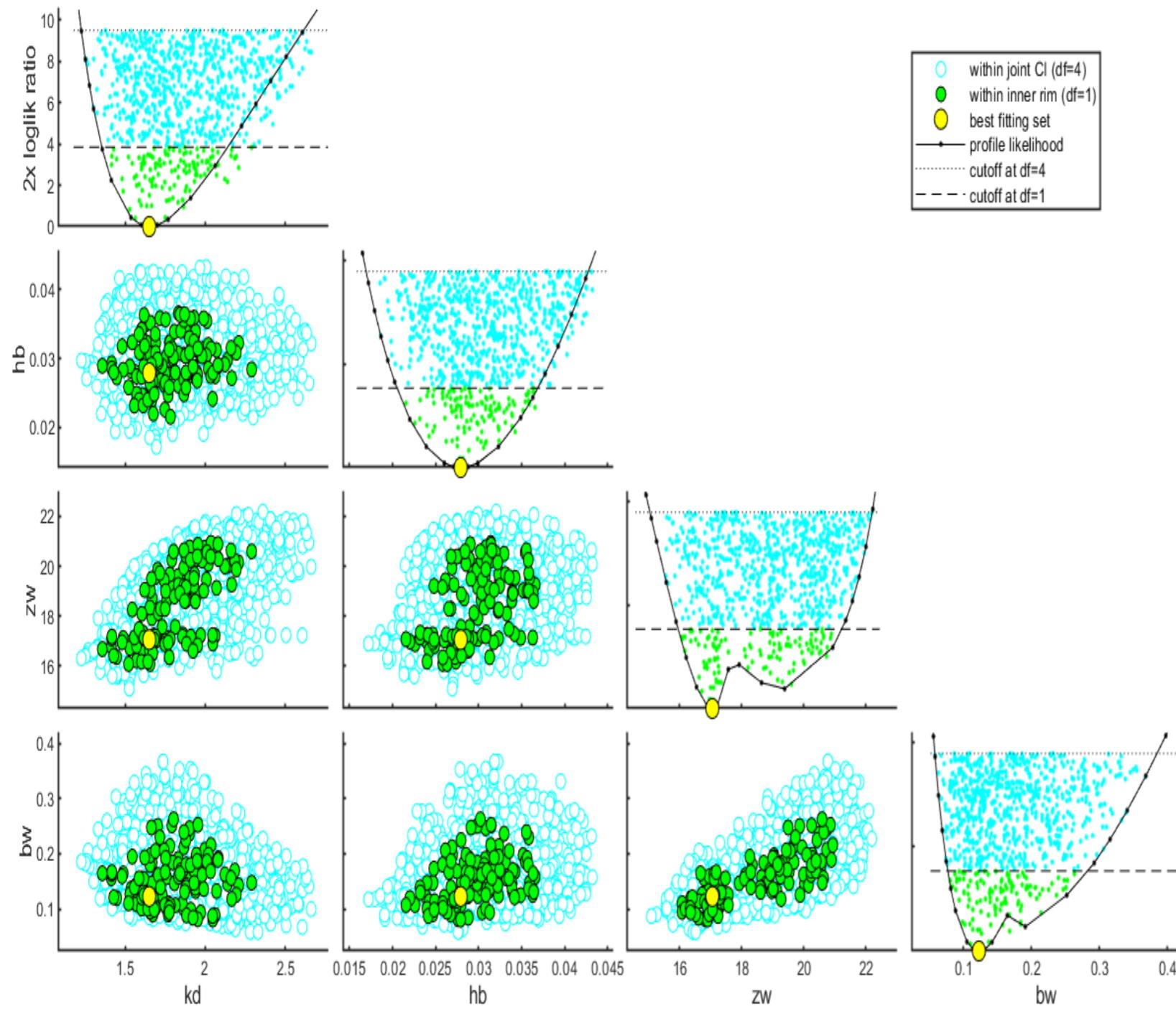
Mechanistic modelling at the individual level



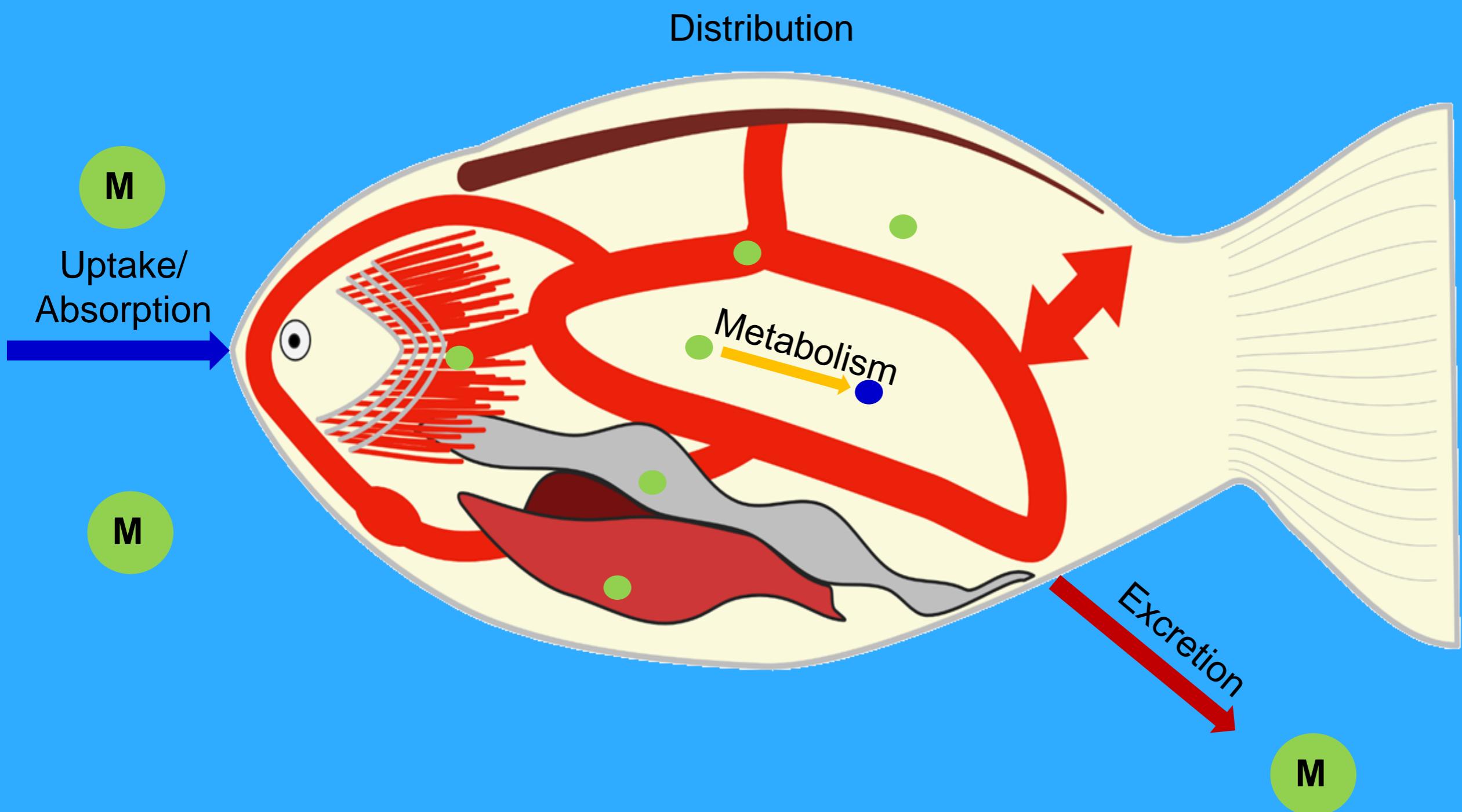
Mechanistic modelling at the individual level

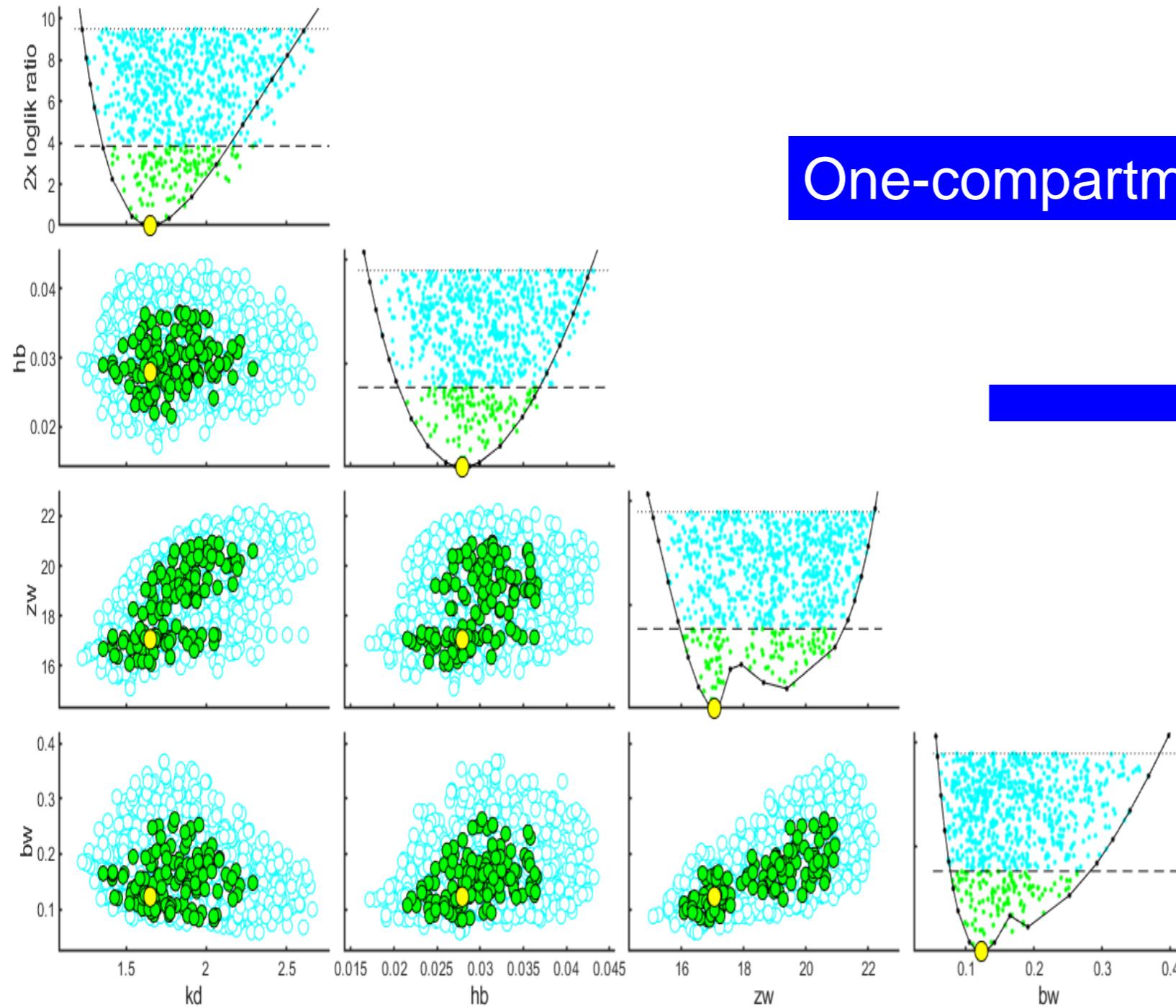


Toxicokinetic modelling

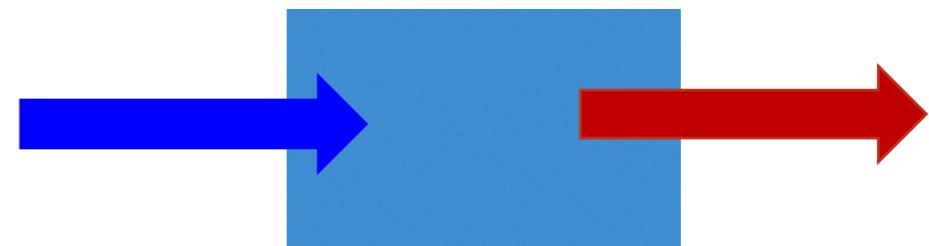


Toxicokinetics: ADME

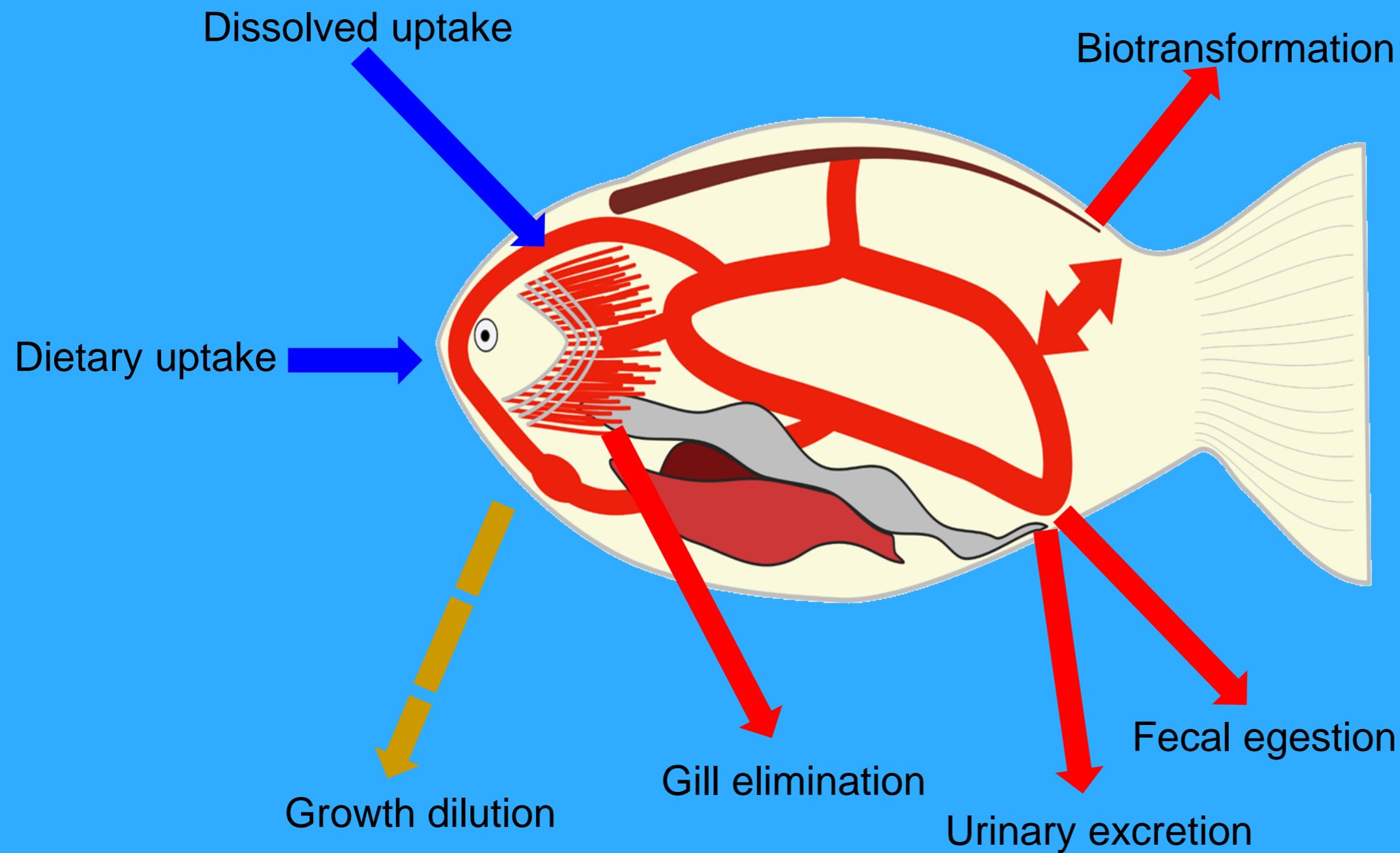




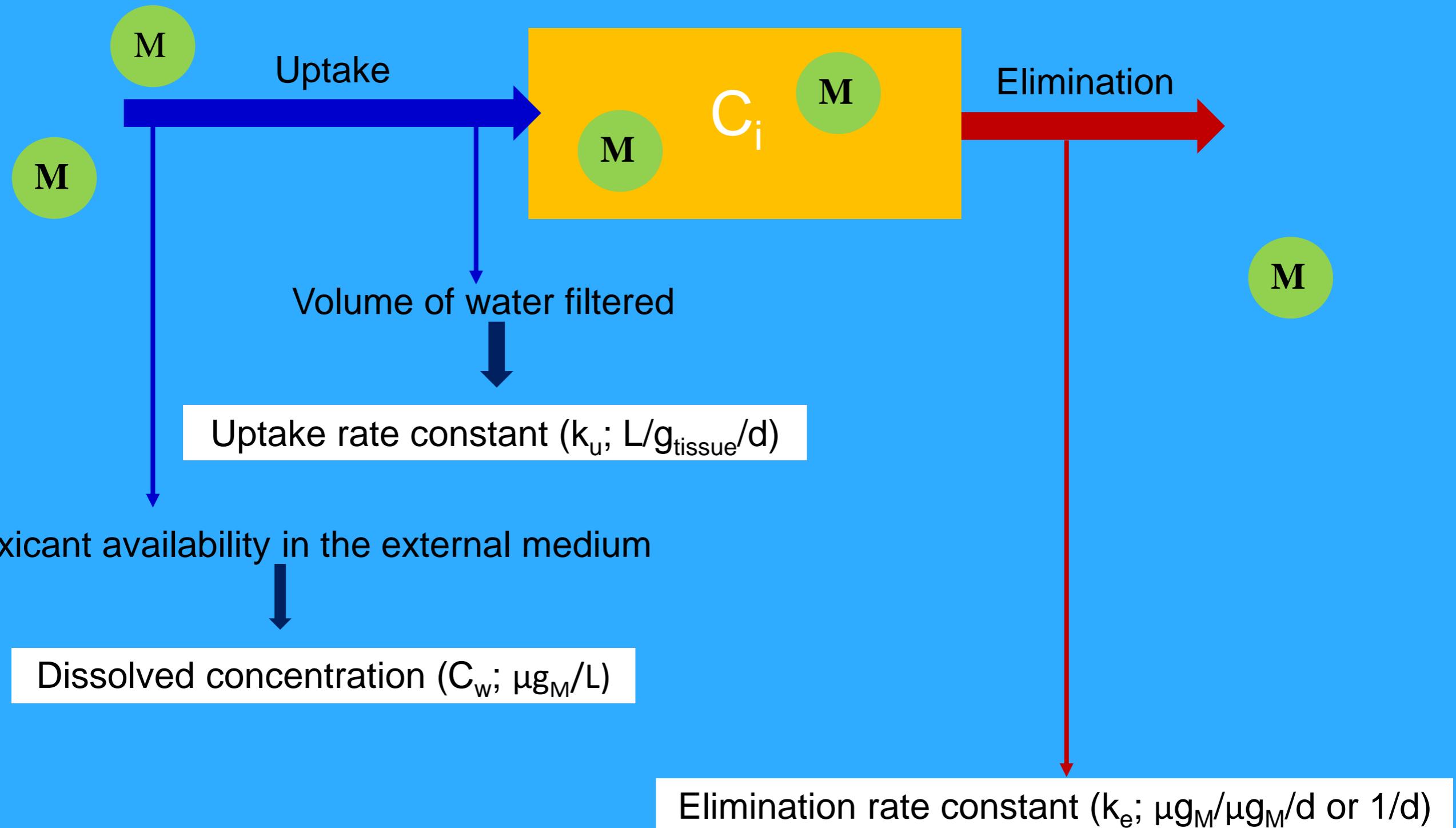
One-compartment toxicokinetic model



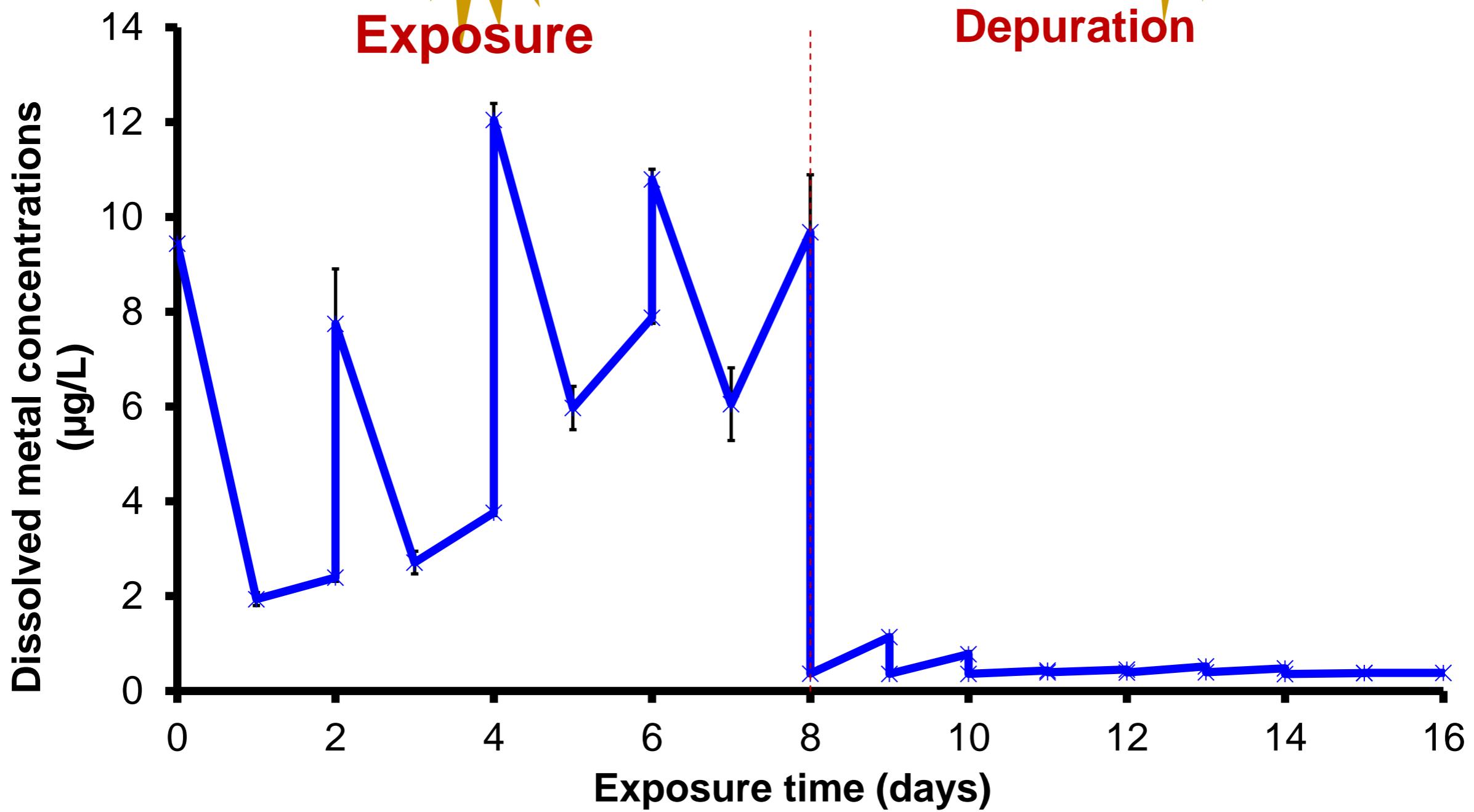
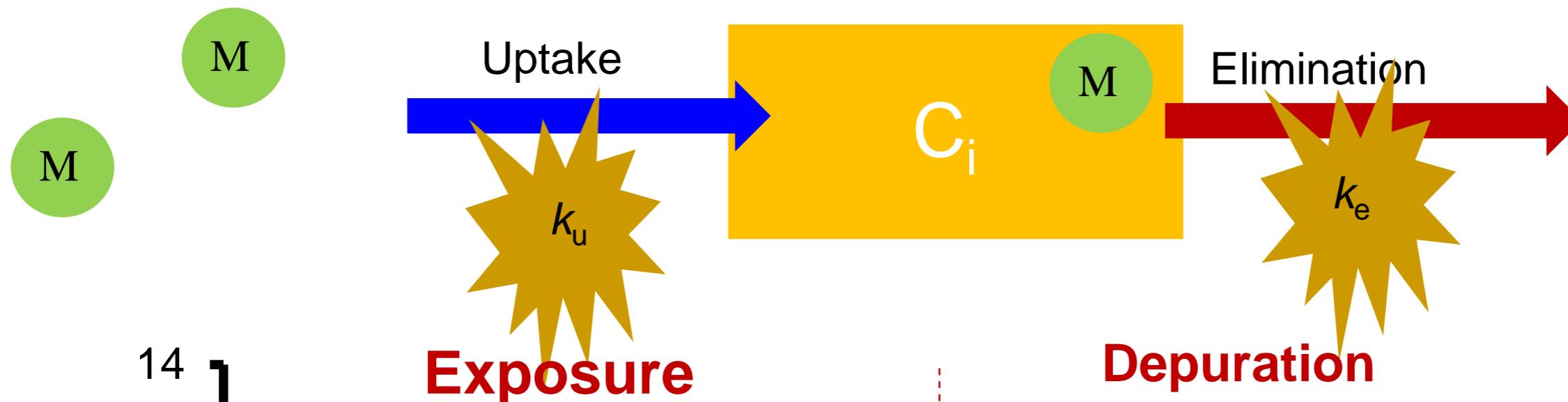
One-compartment toxicokinetic model



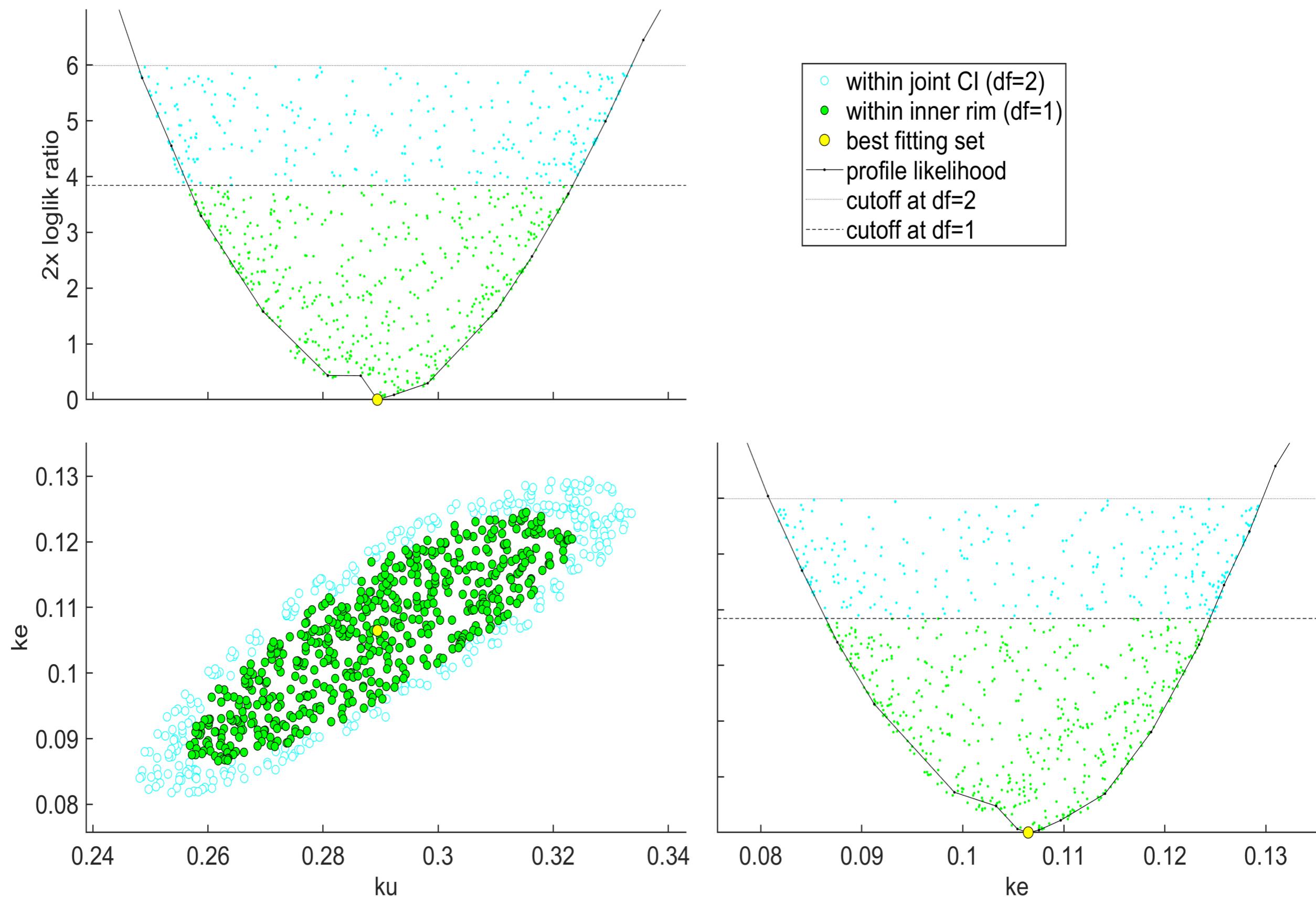
One-compartment toxicokinetic model



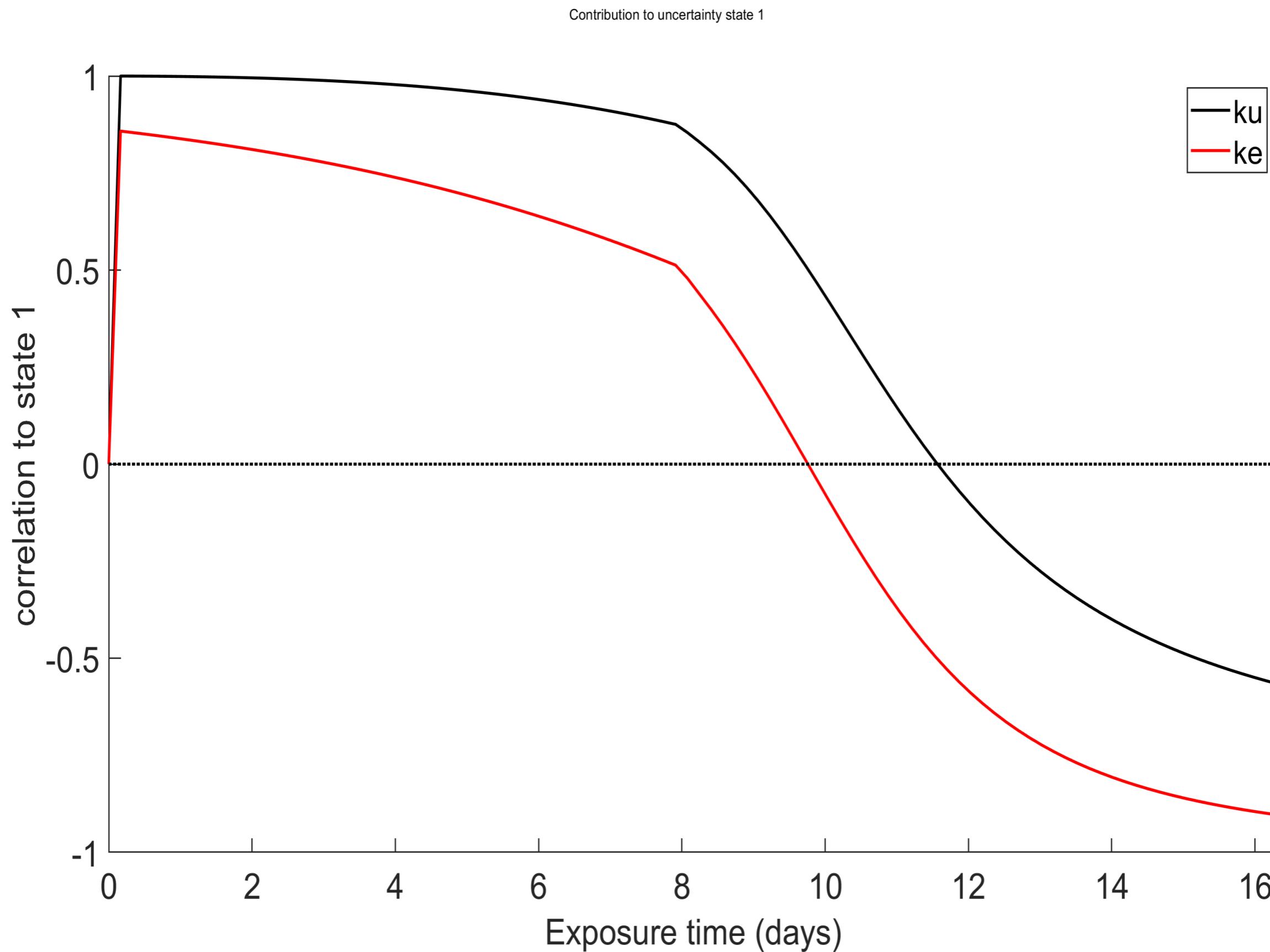
One-compartment toxicokinetic model



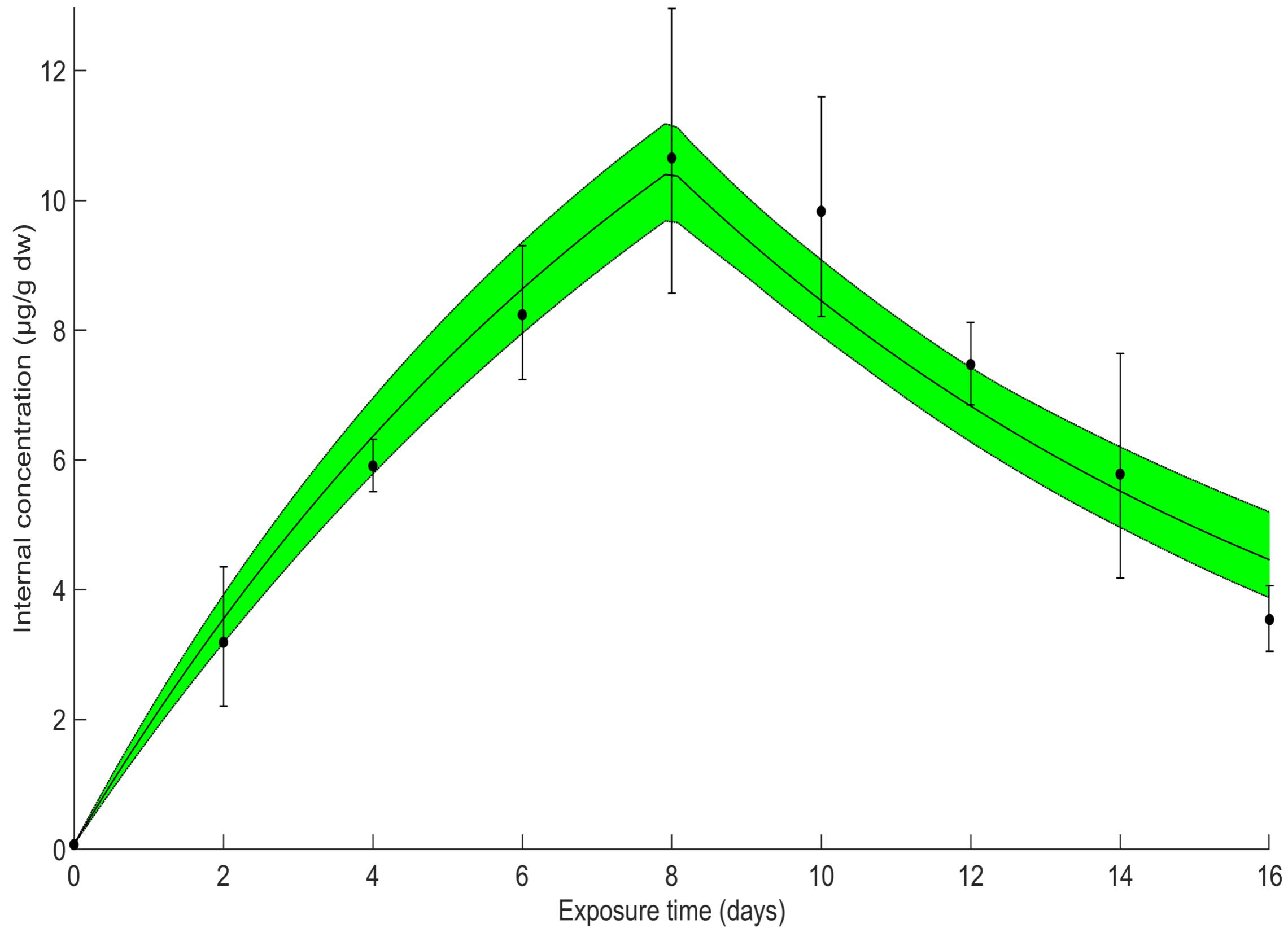
One-compartment kinetic model: calibration



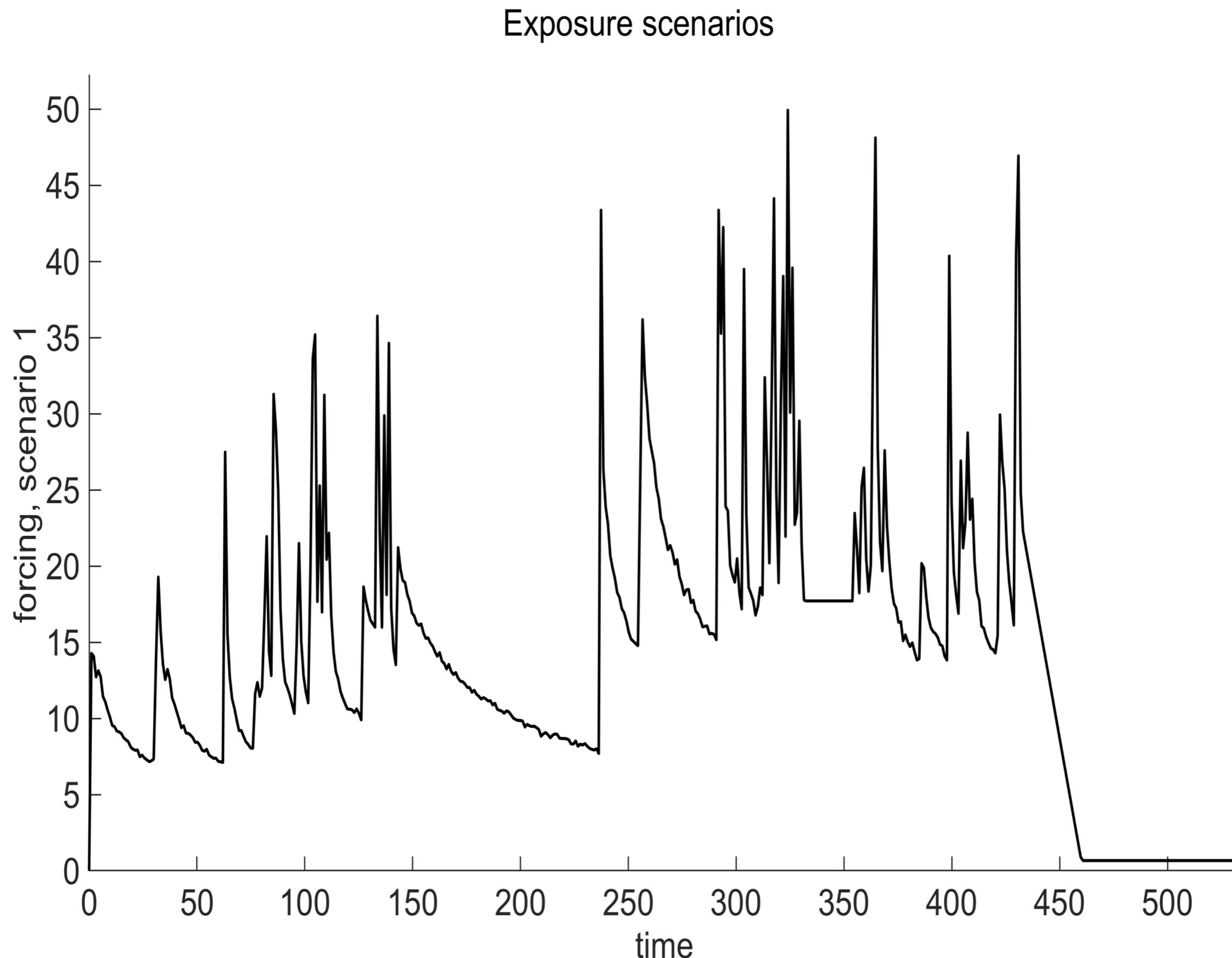
One-compartment kinetic model: sensitivity analysis



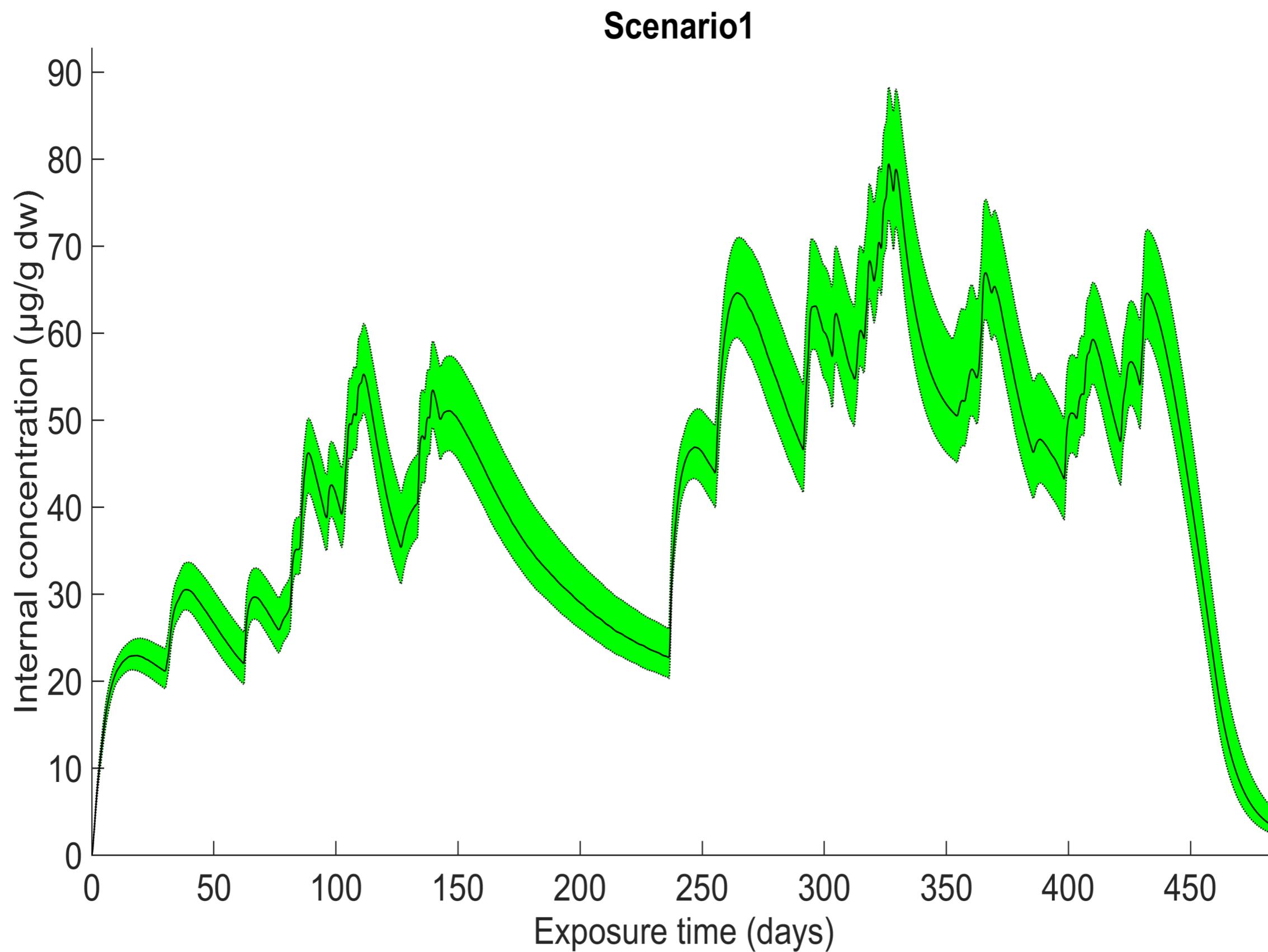
One-compartment kinetic model: calibration



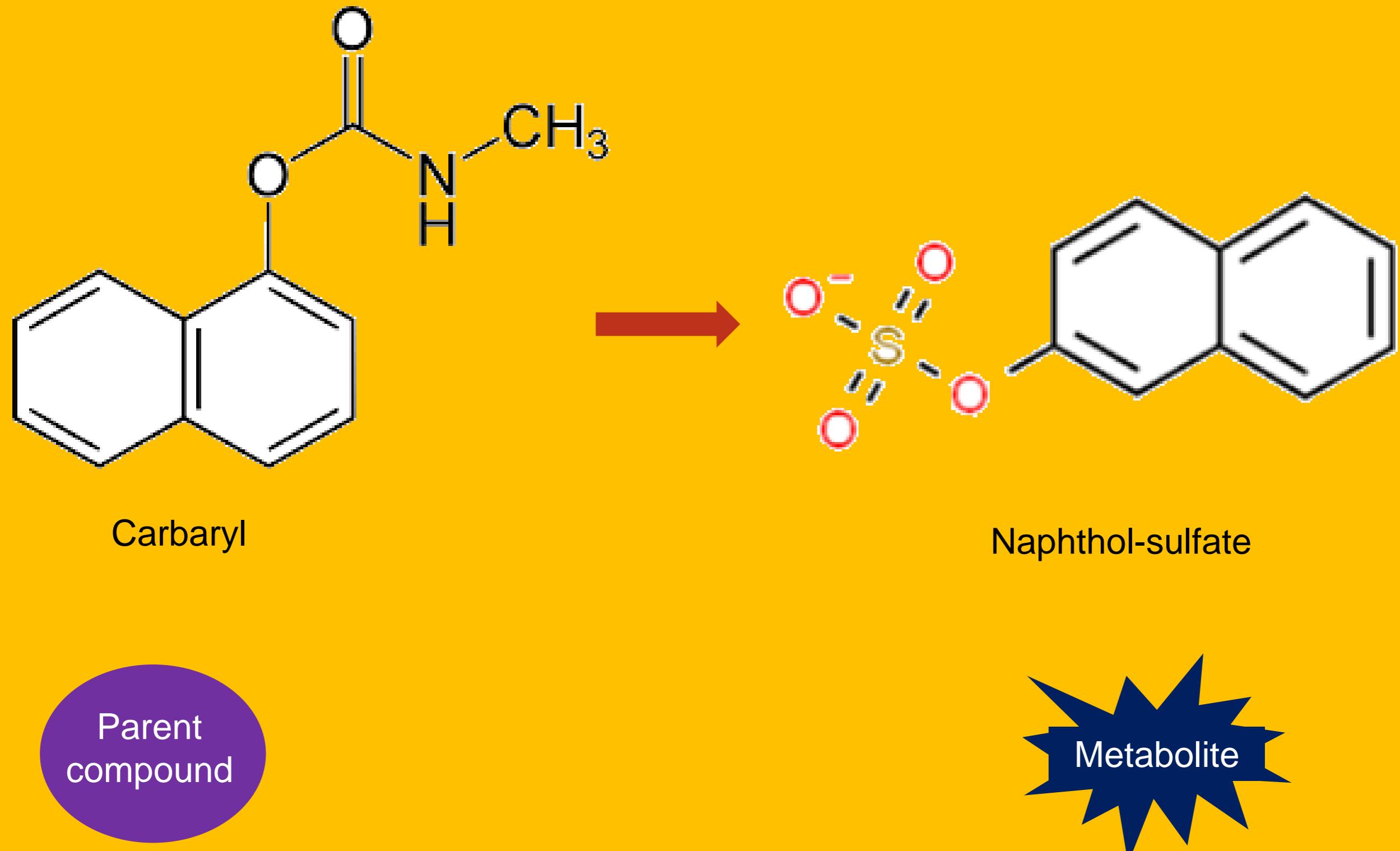
One-compartment kinetic model: validation



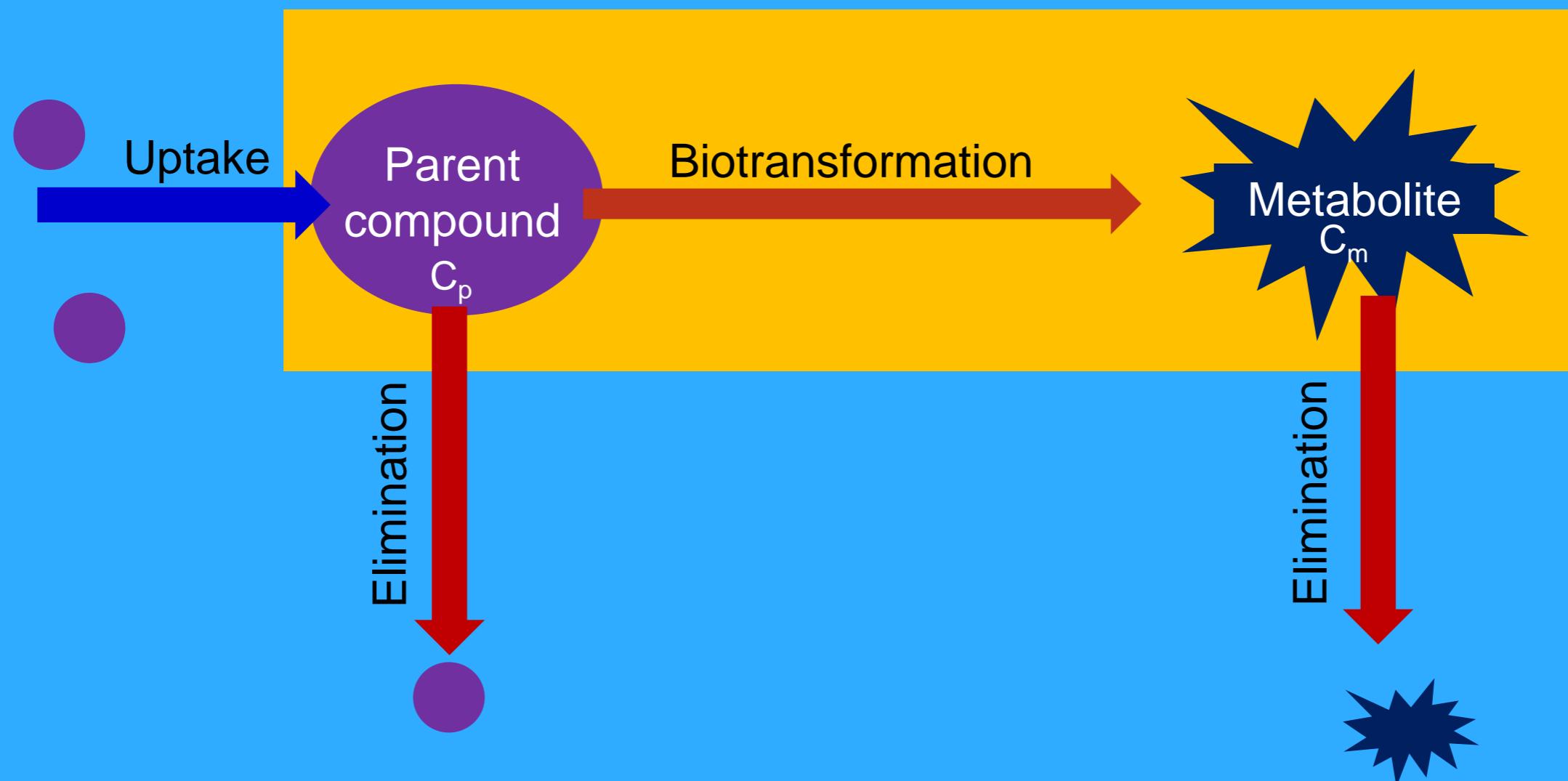
One-compartment kinetic model: validation

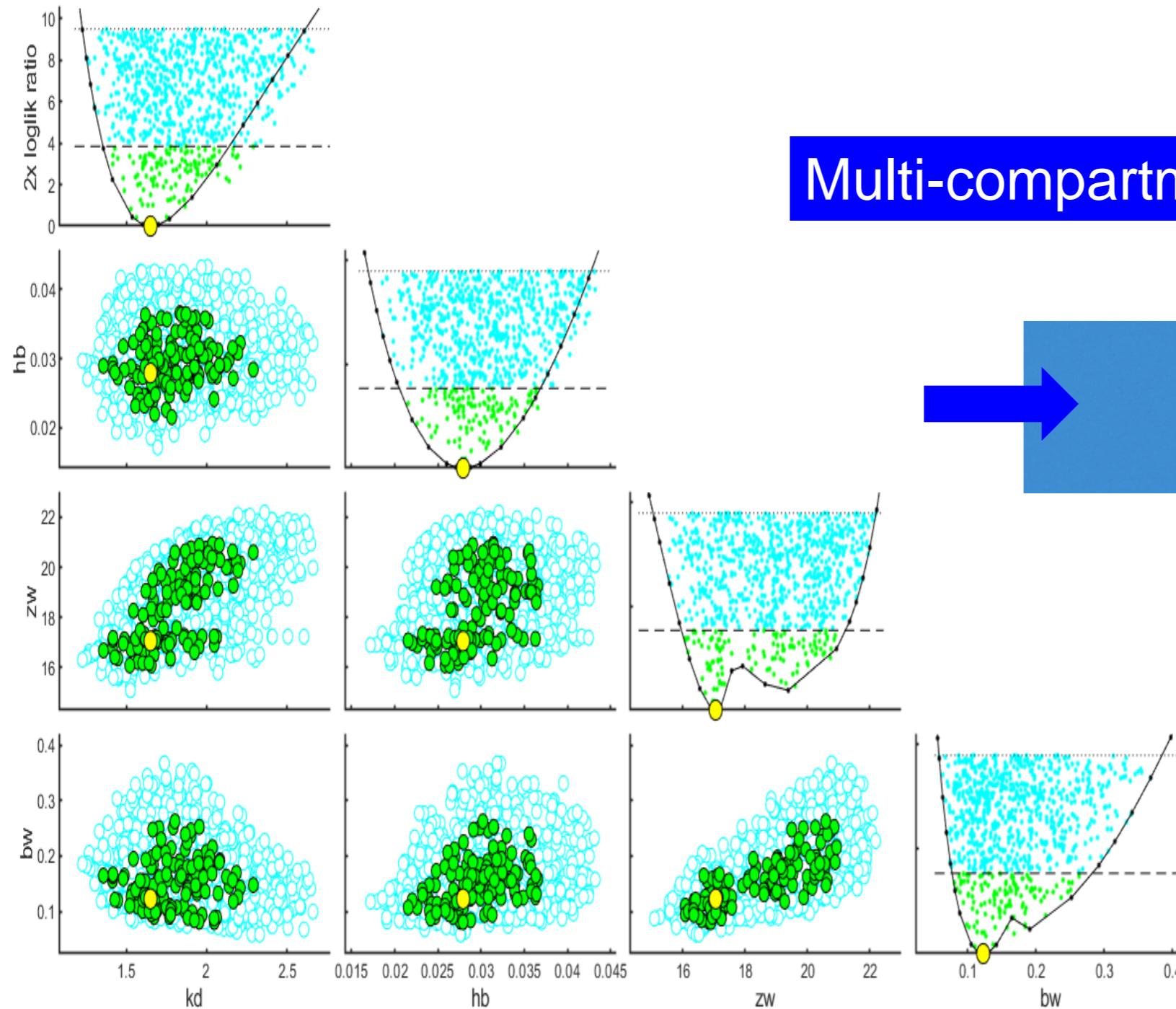


One-compartment TK models with biotransformation

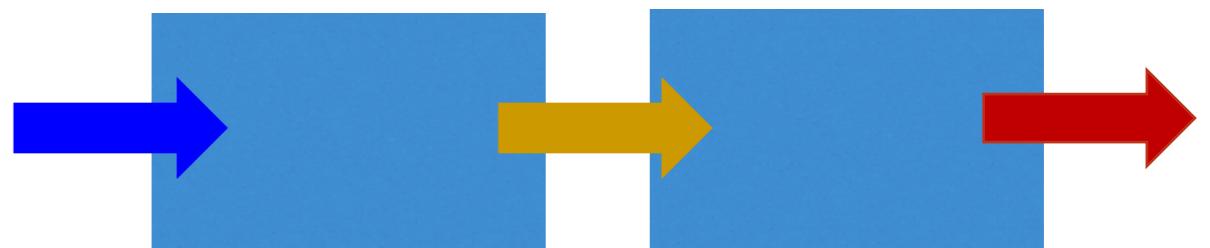


One-compartment TK models with biotransformation

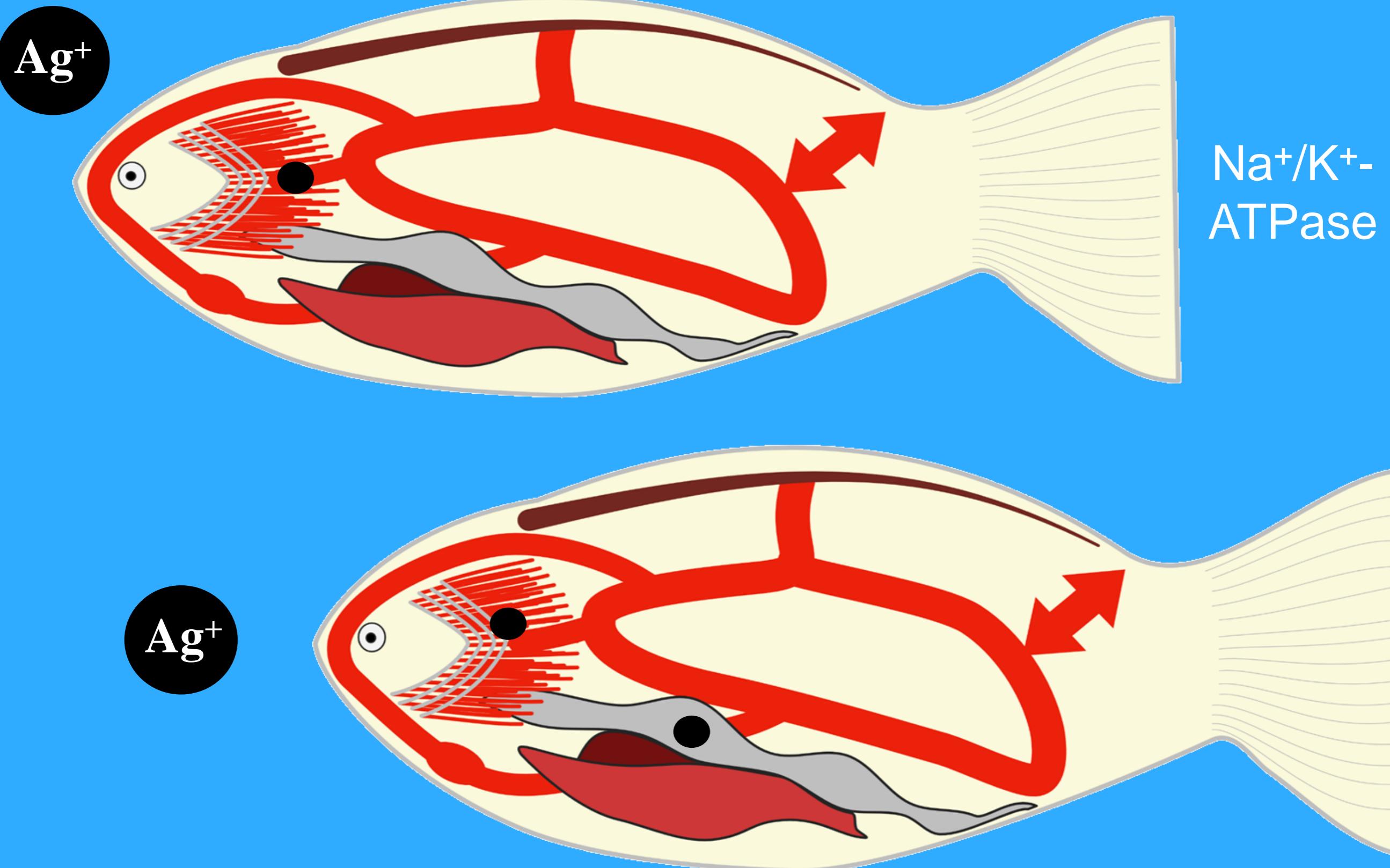




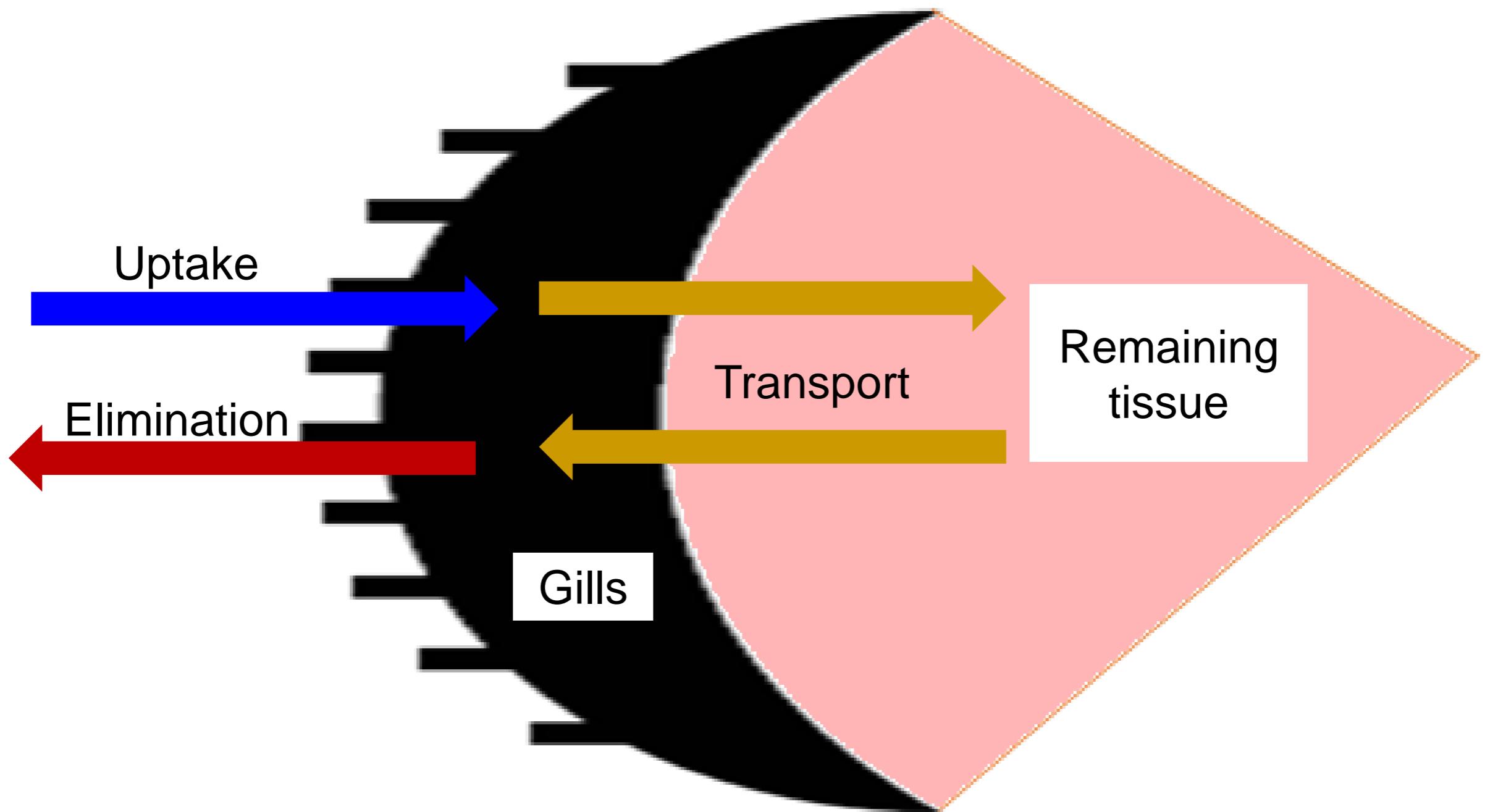
Multi-compartment toxicokinetic model



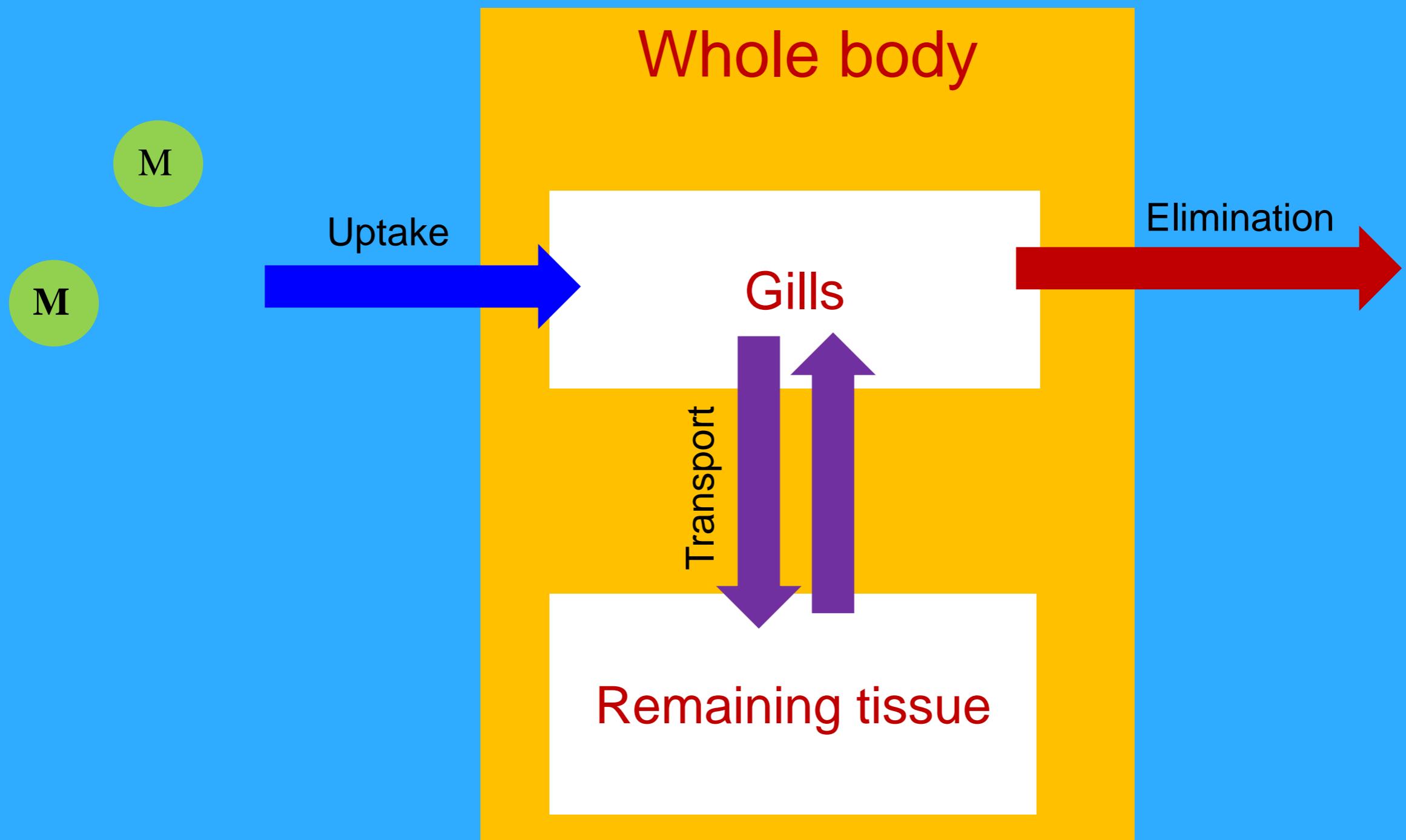
Tissue-specific significance of accumulation



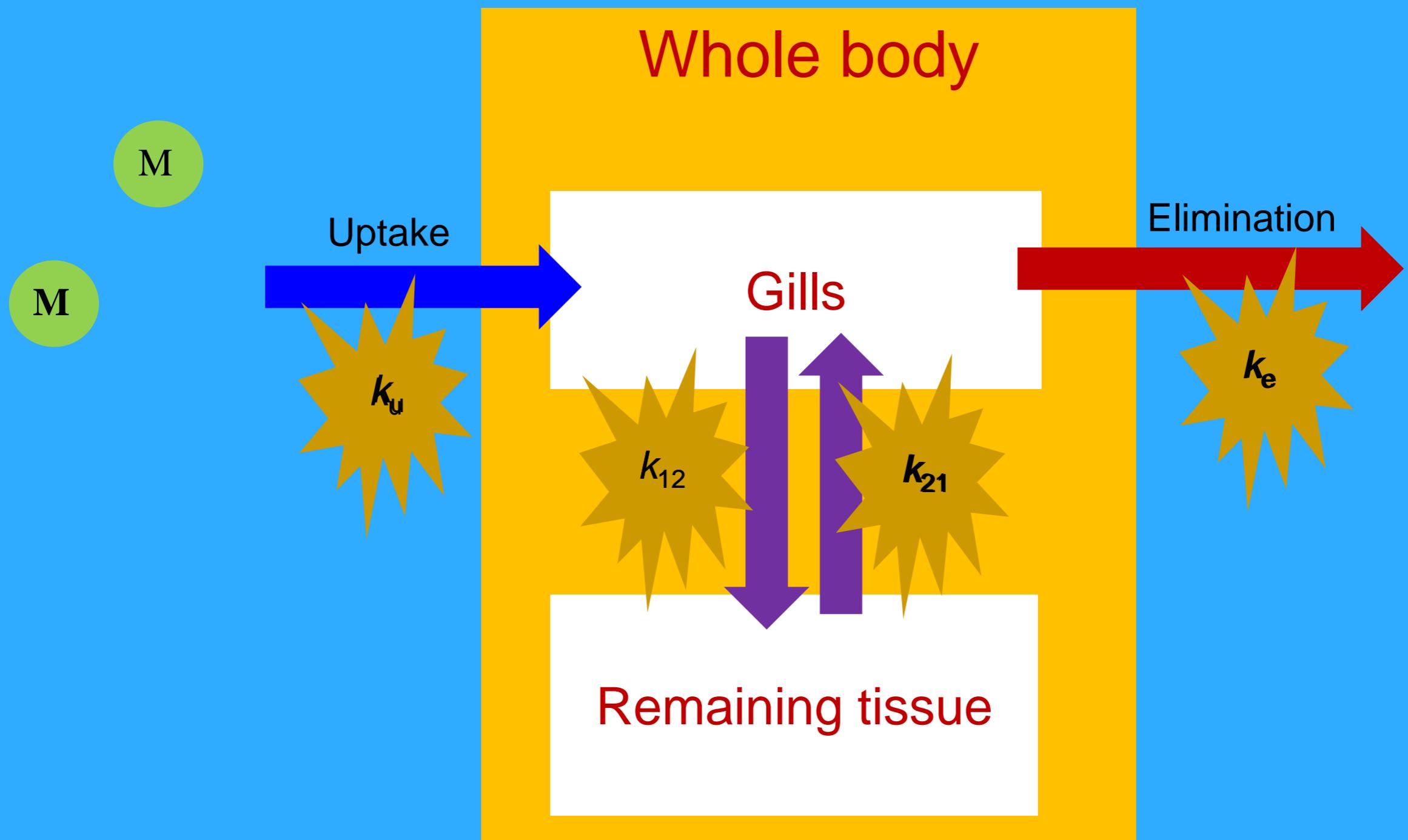
Multi-compartment toxicokinetic model



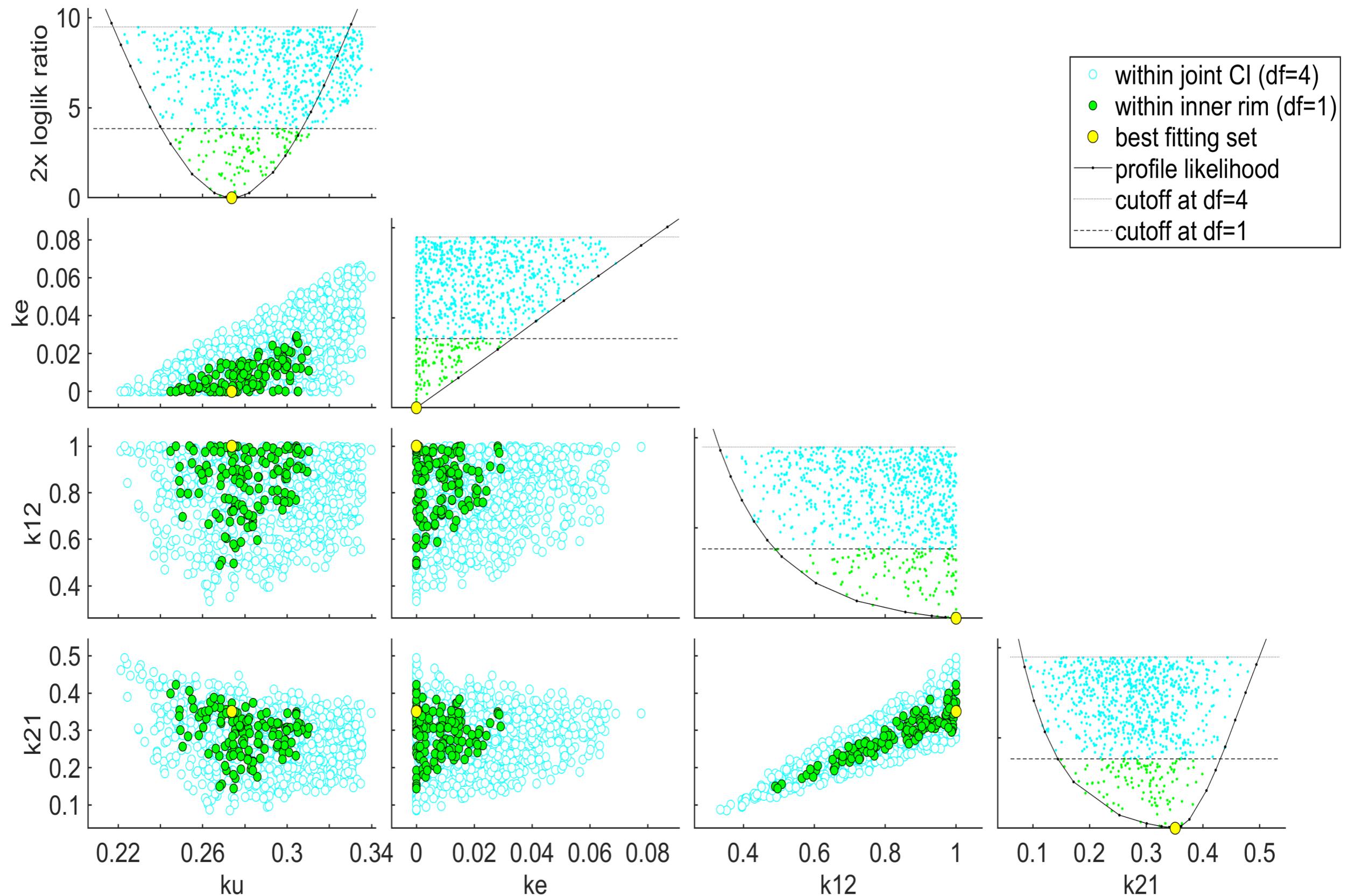
Two-compartment toxicokinetic model



Two-compartment toxicokinetic model

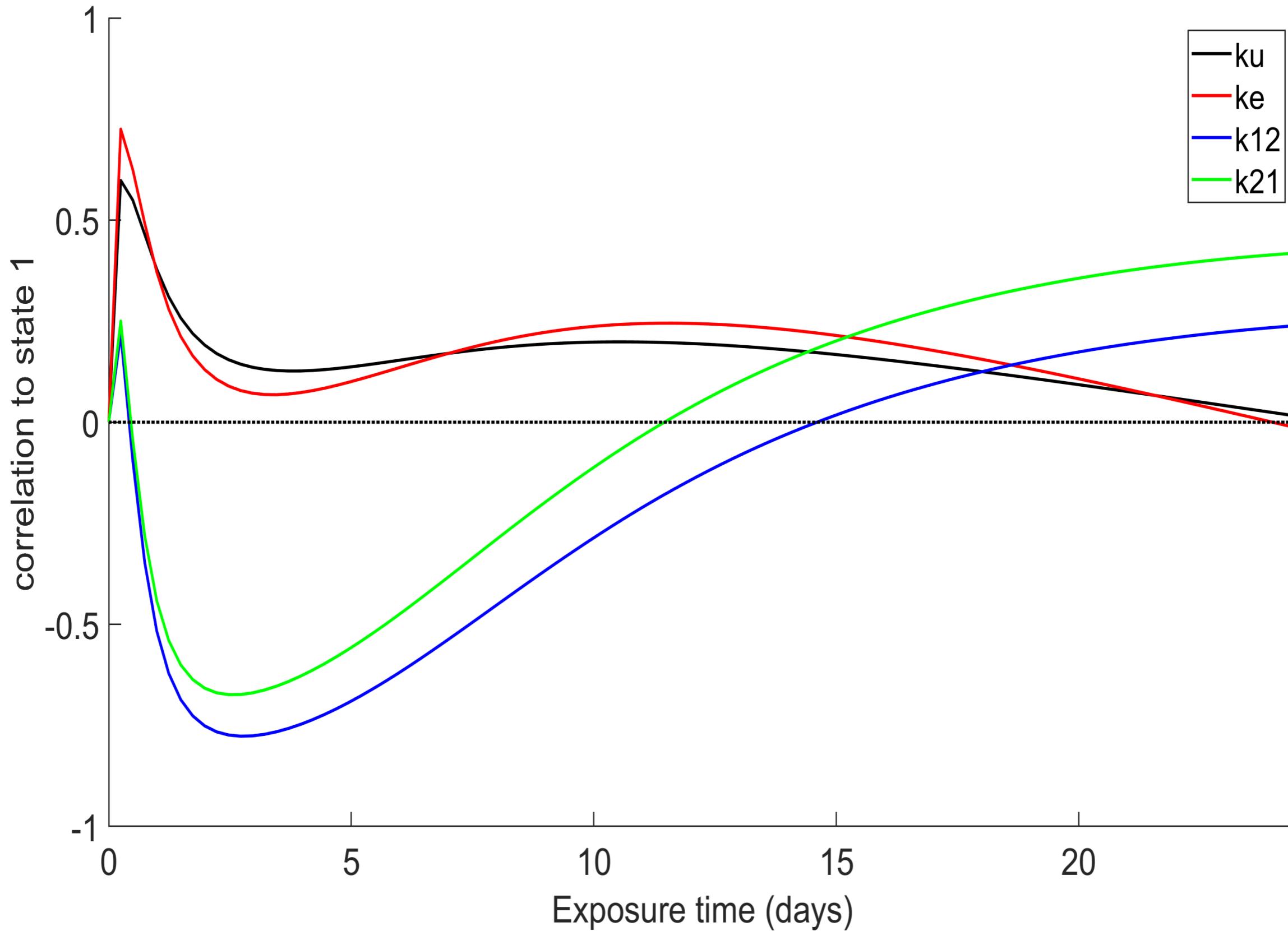


Two-compartment toxicokinetic model: calibration

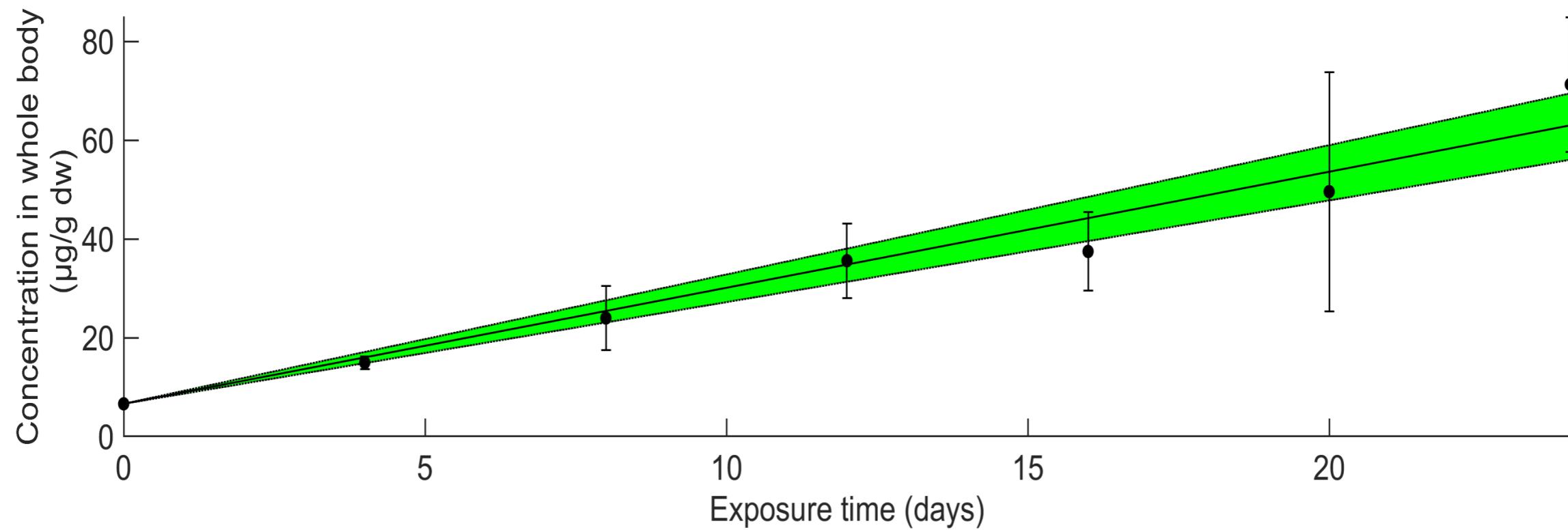
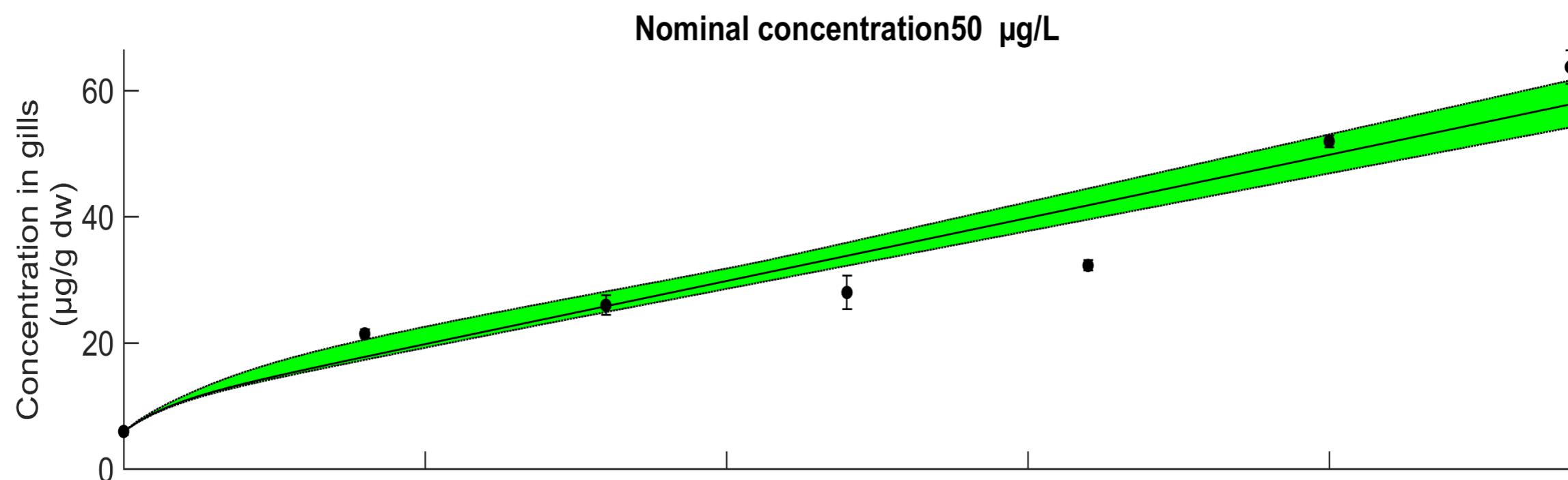


Two-compartment toxicokinetic model: sensitivity

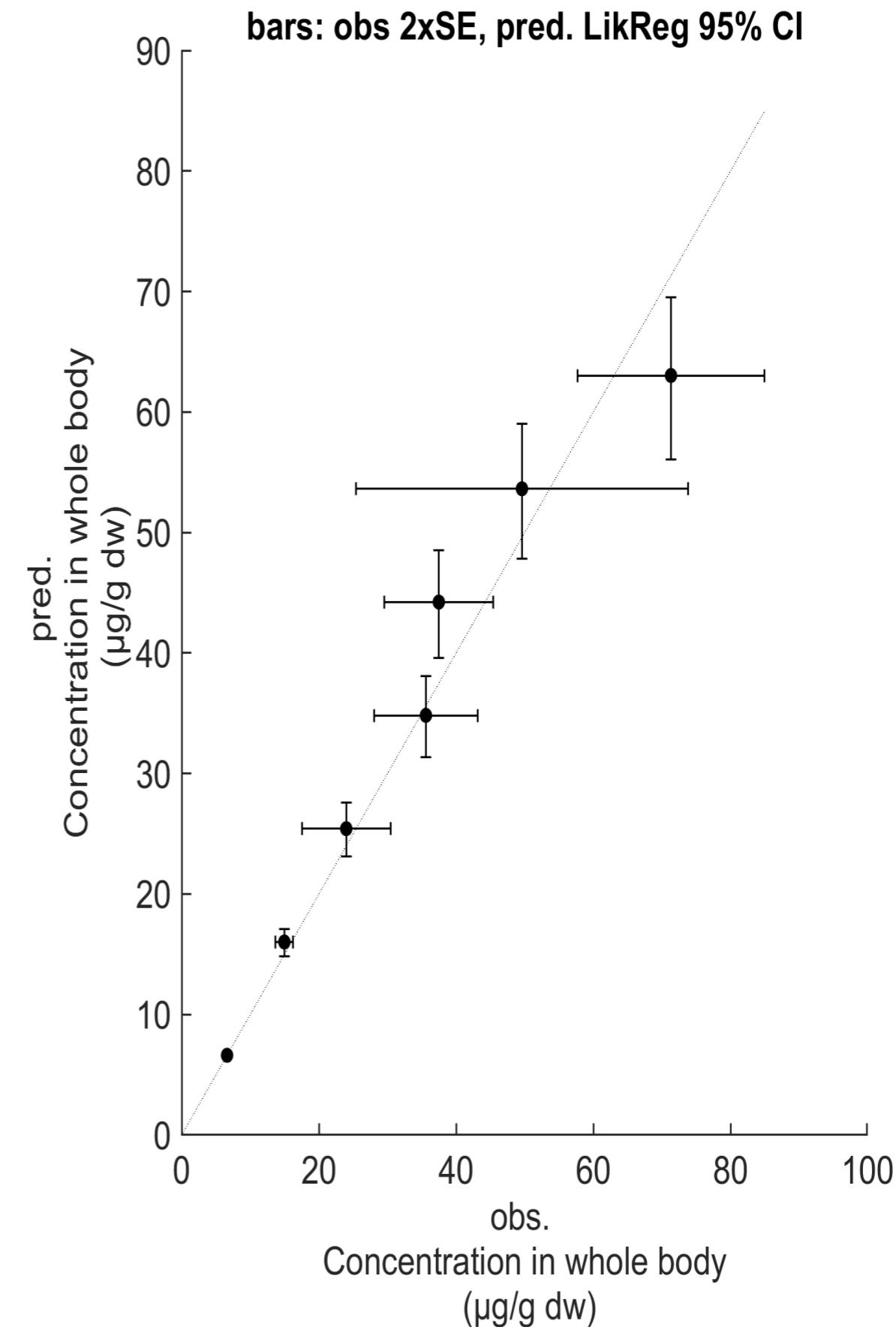
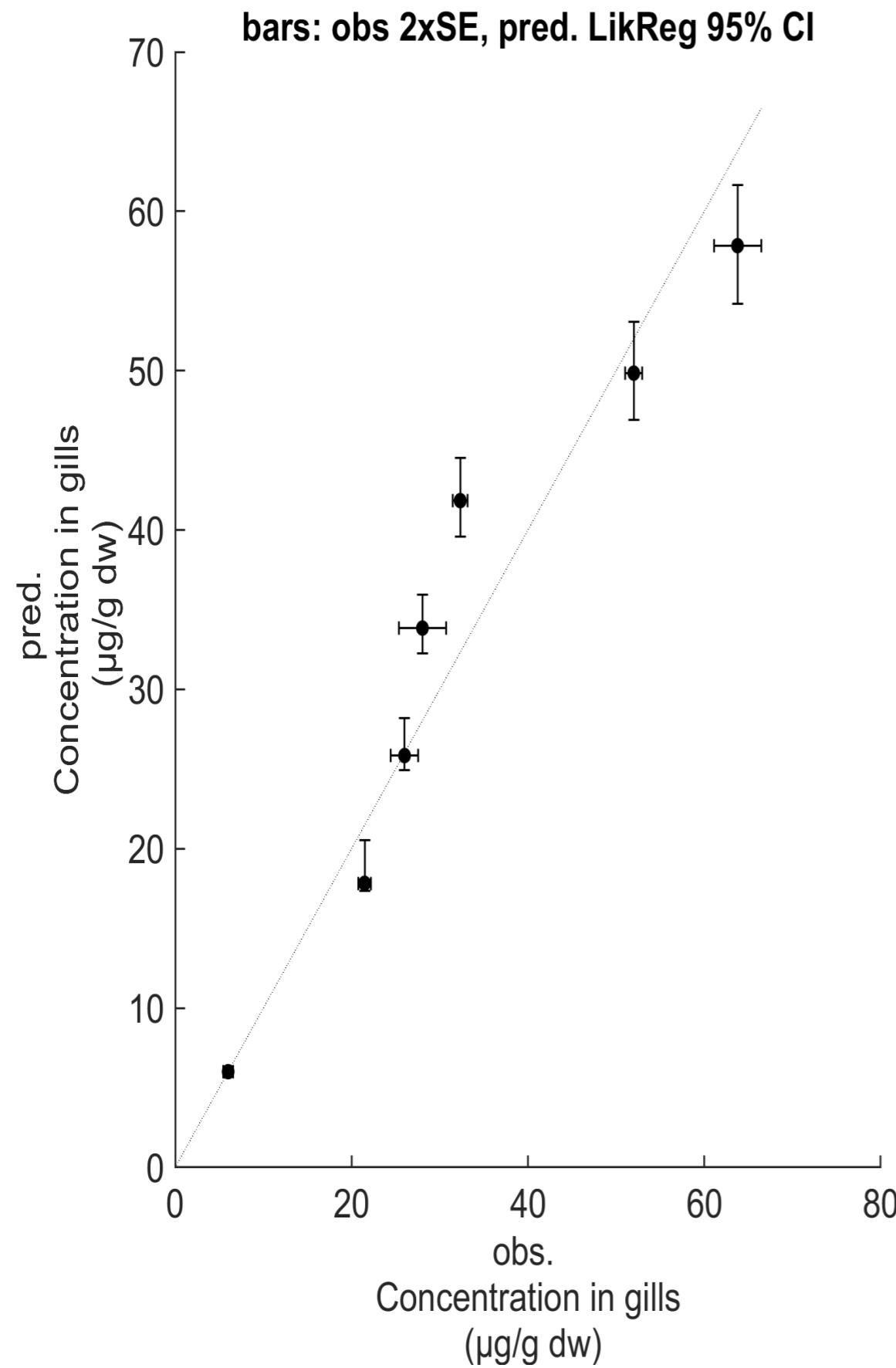
Contribution to uncertainty state 1



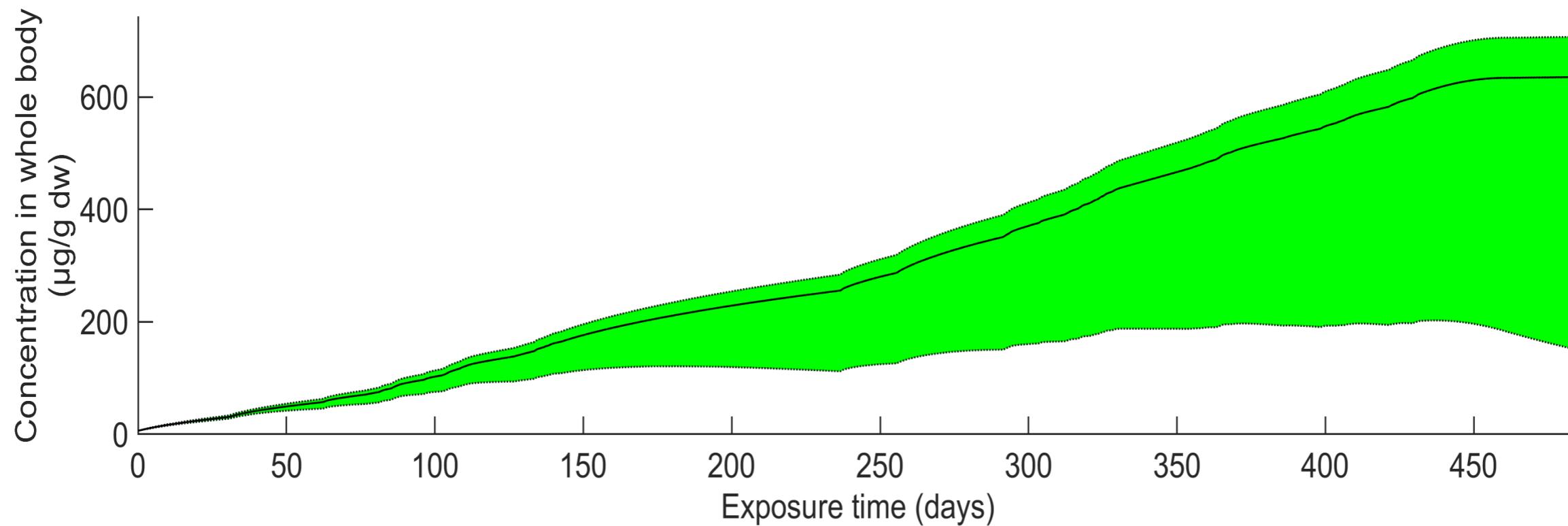
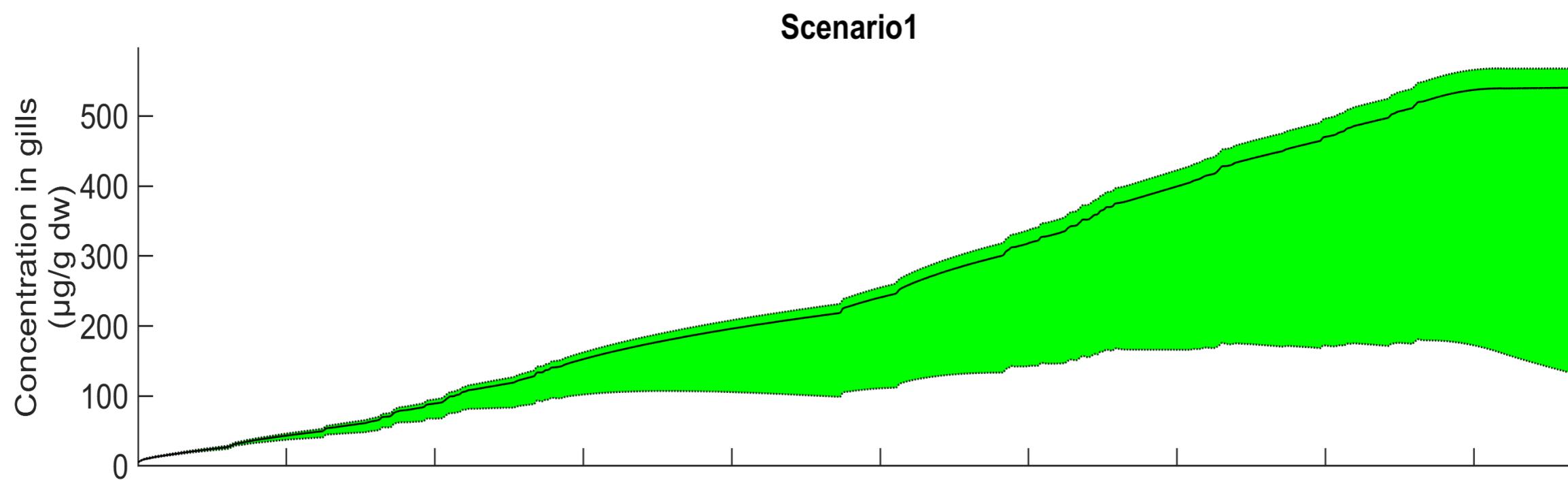
Two-compartment toxicokinetic model: calibration

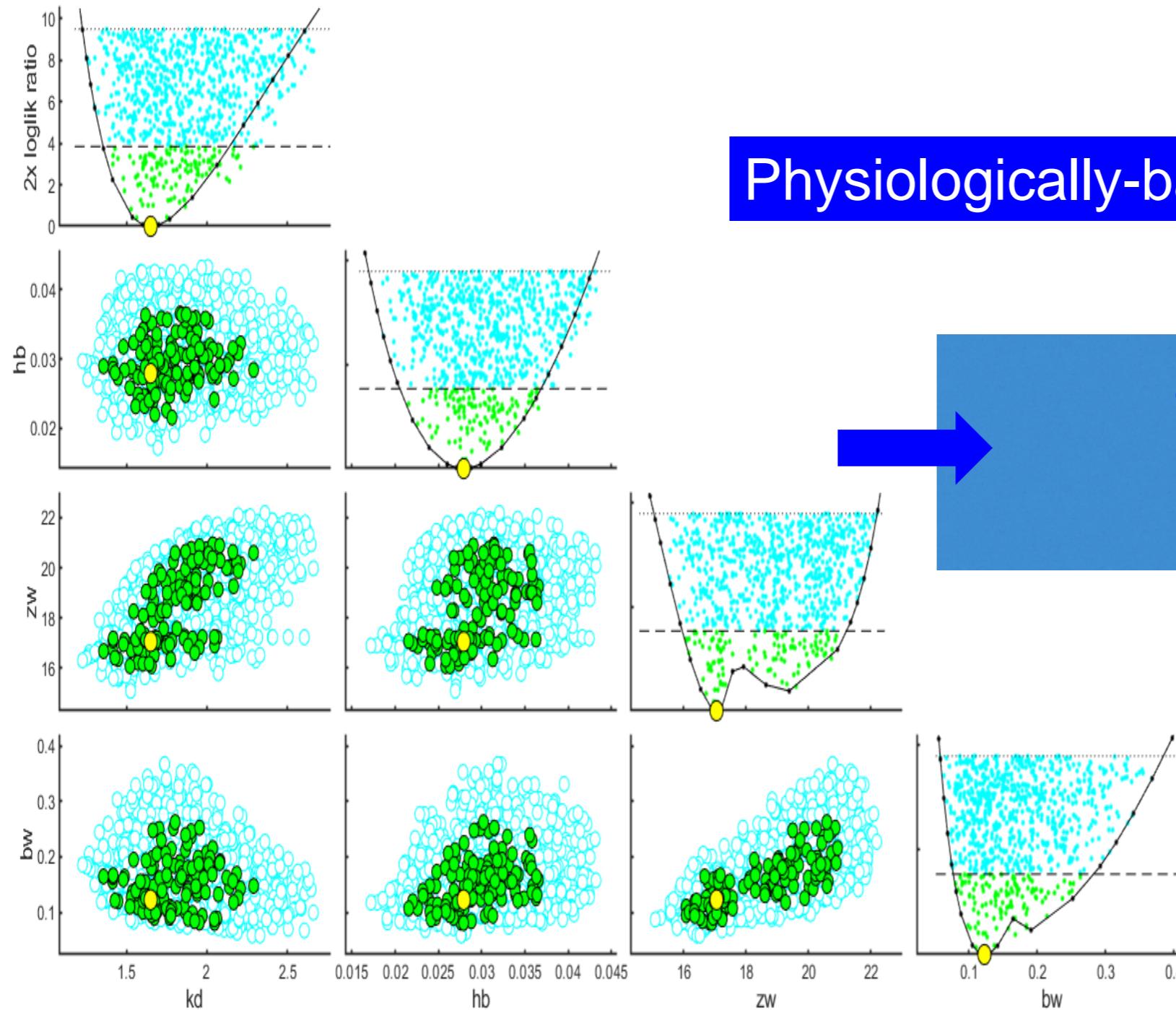


Two-compartment toxicokinetic model: calibration

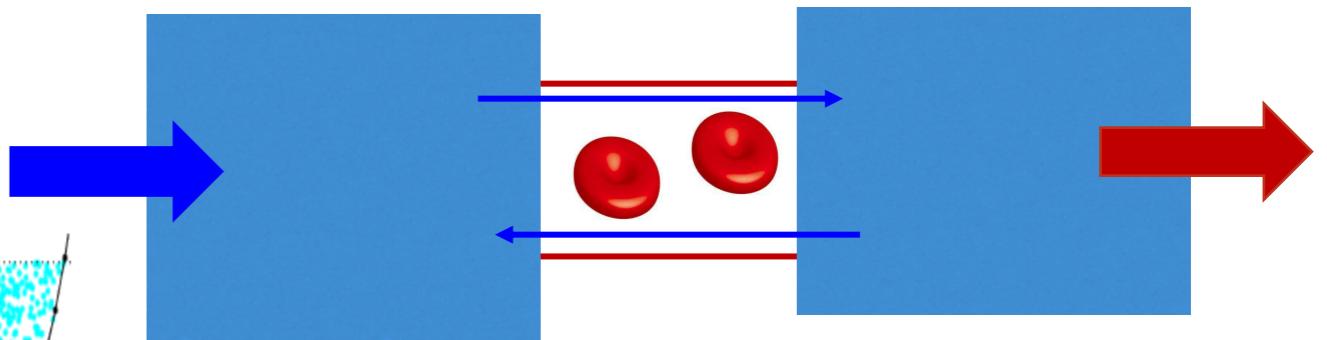


Two-compartment toxicokinetic model: validation

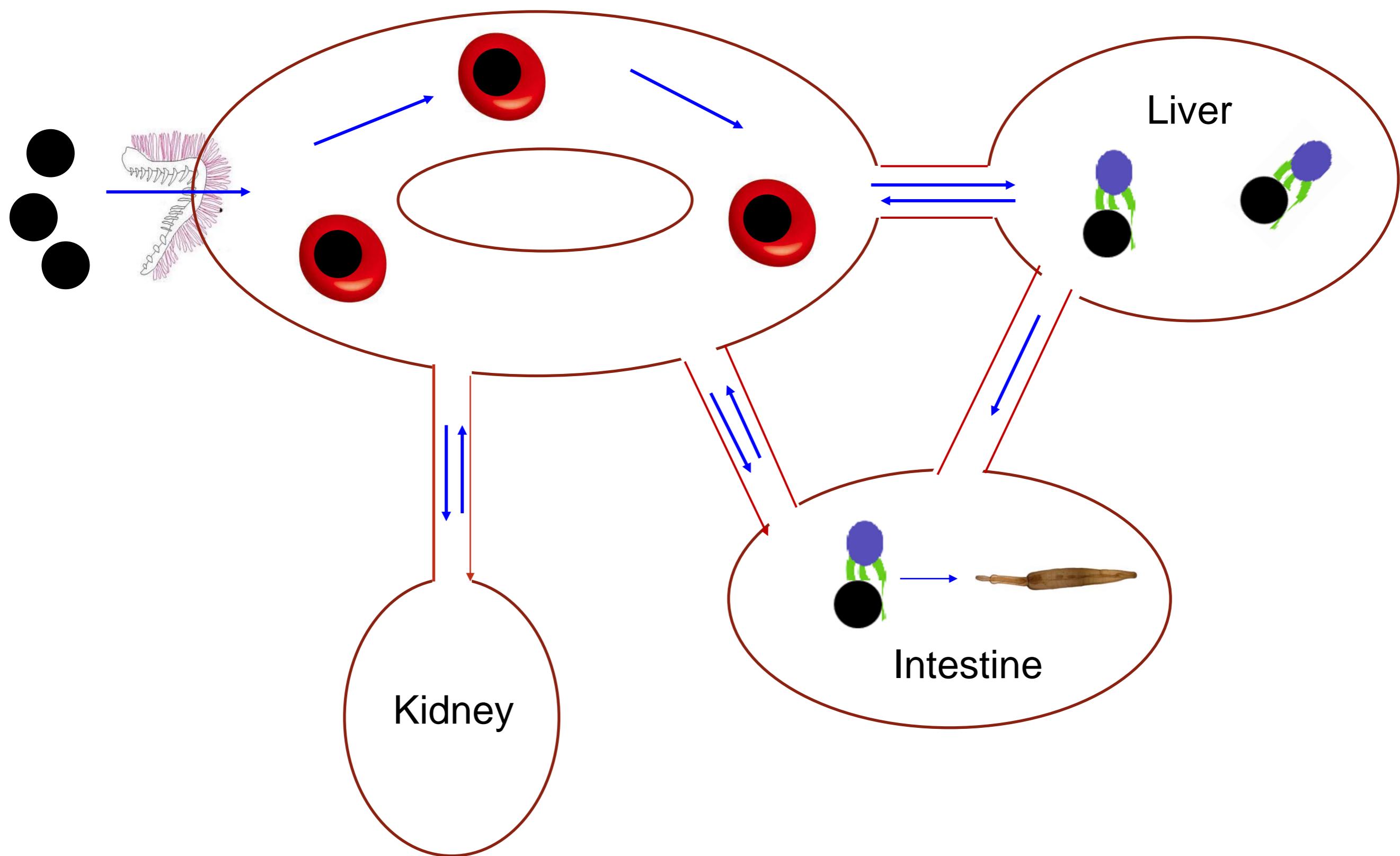




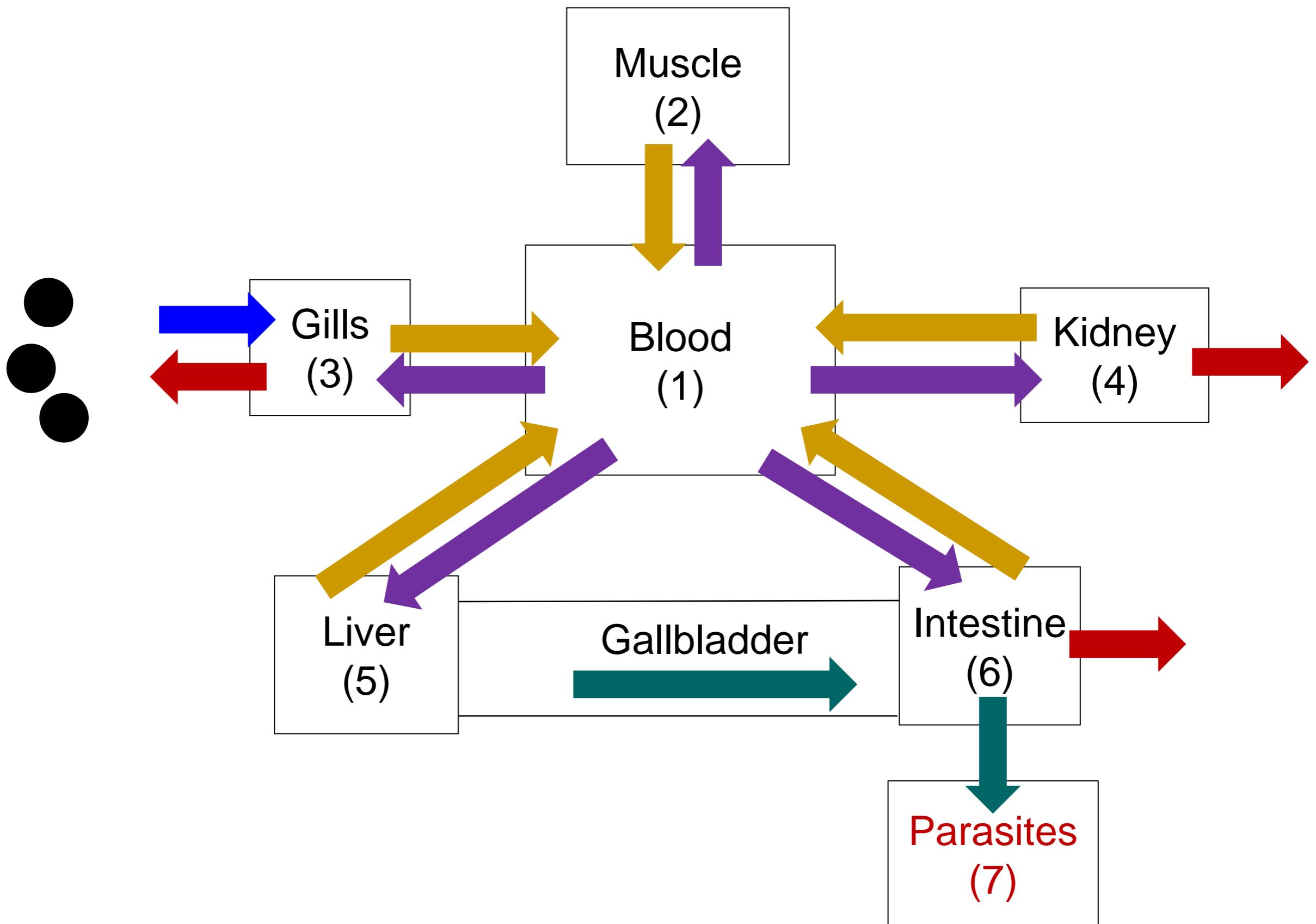
Physiologically-based toxicokinetic model



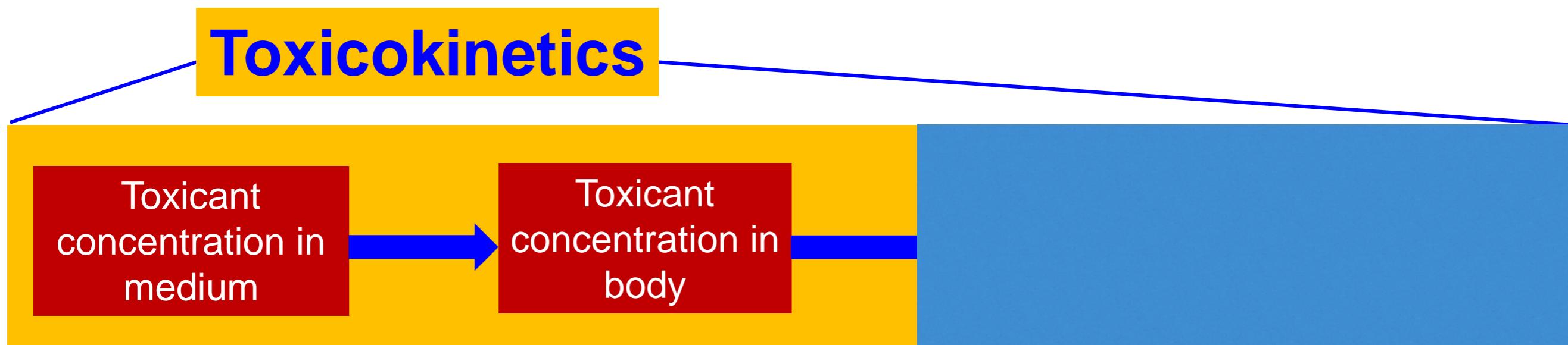
Physiologically-based toxicokinetic modelling



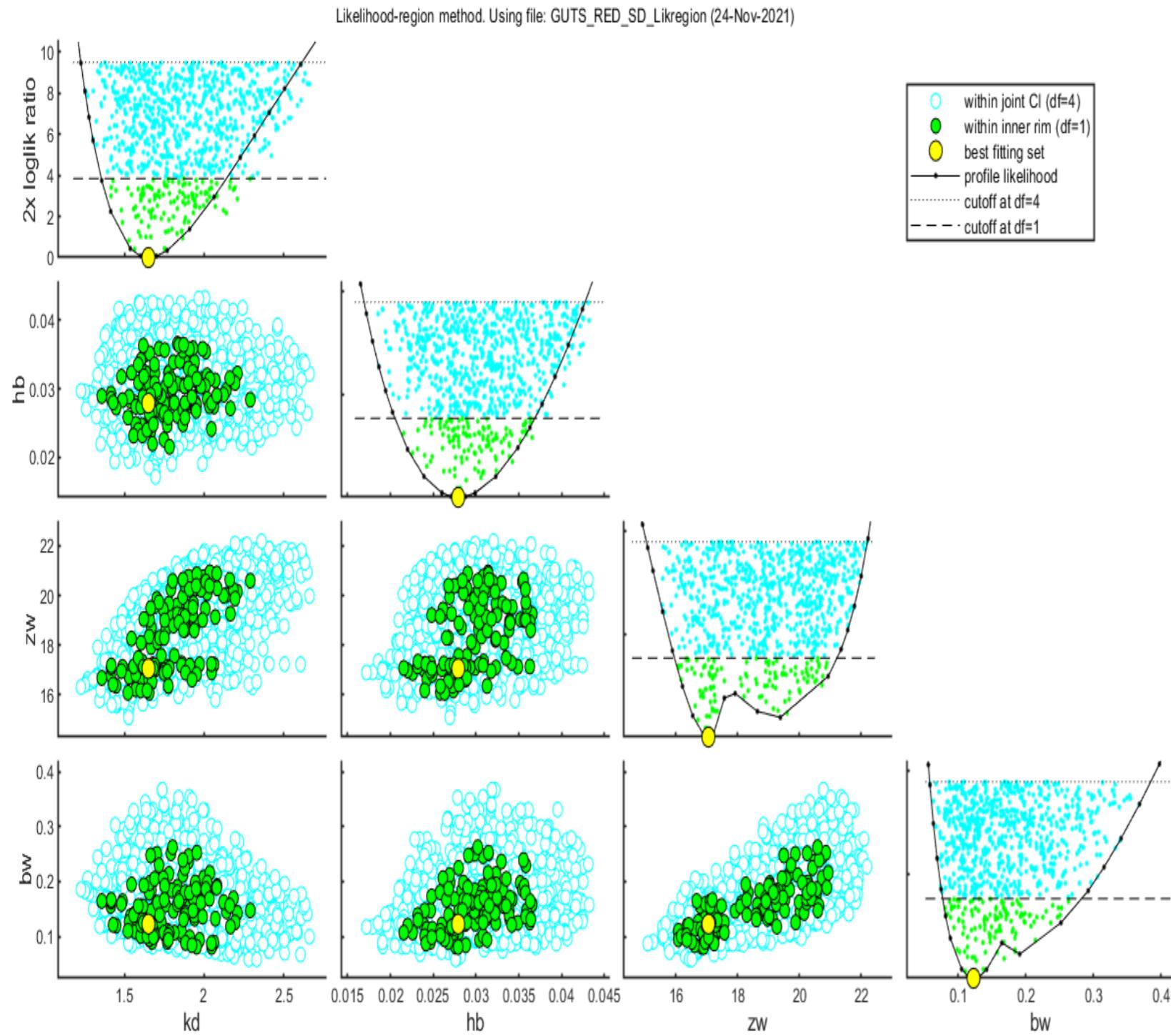
Physiologically-based toxicokinetic model



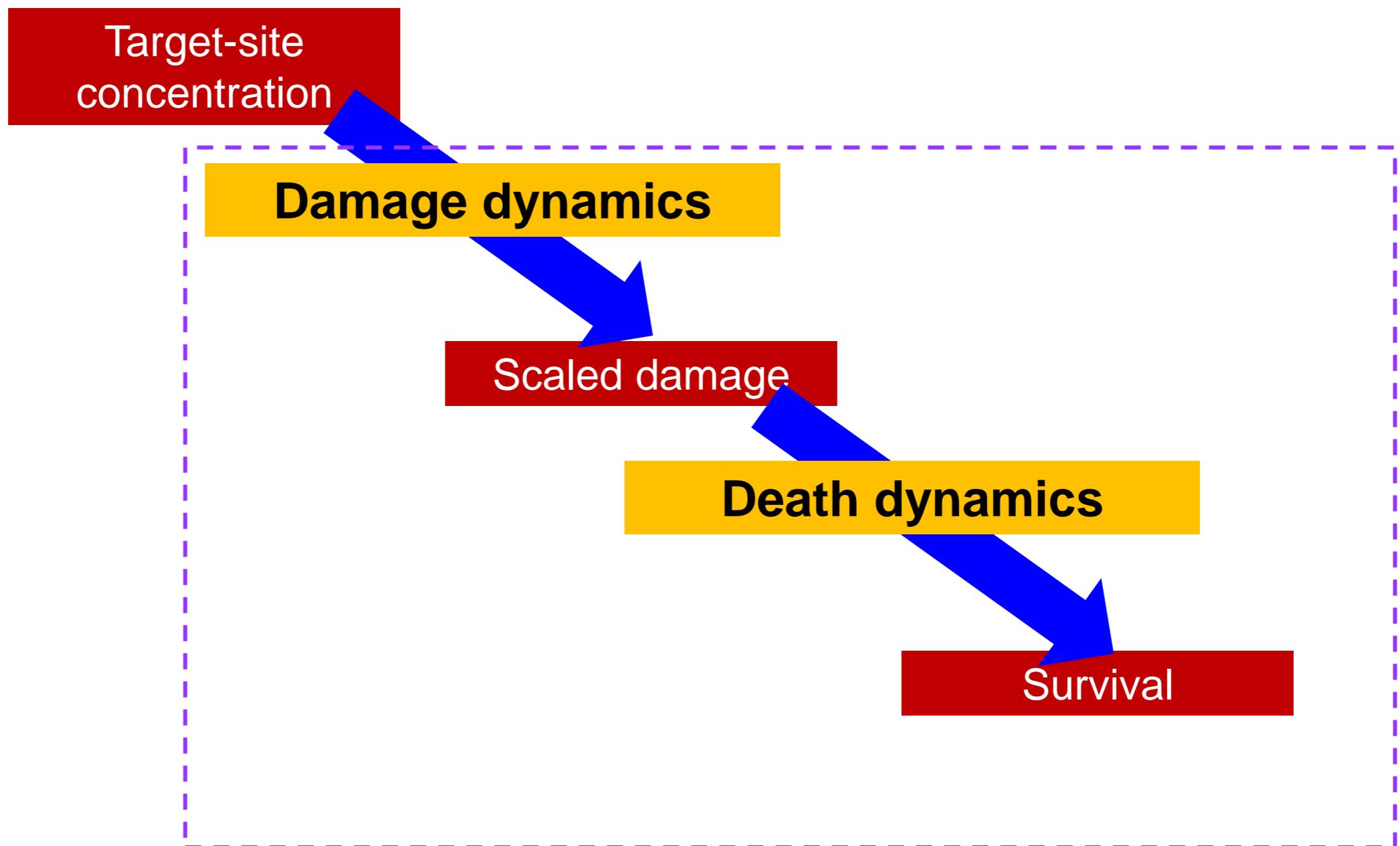
Toxicokinetic module



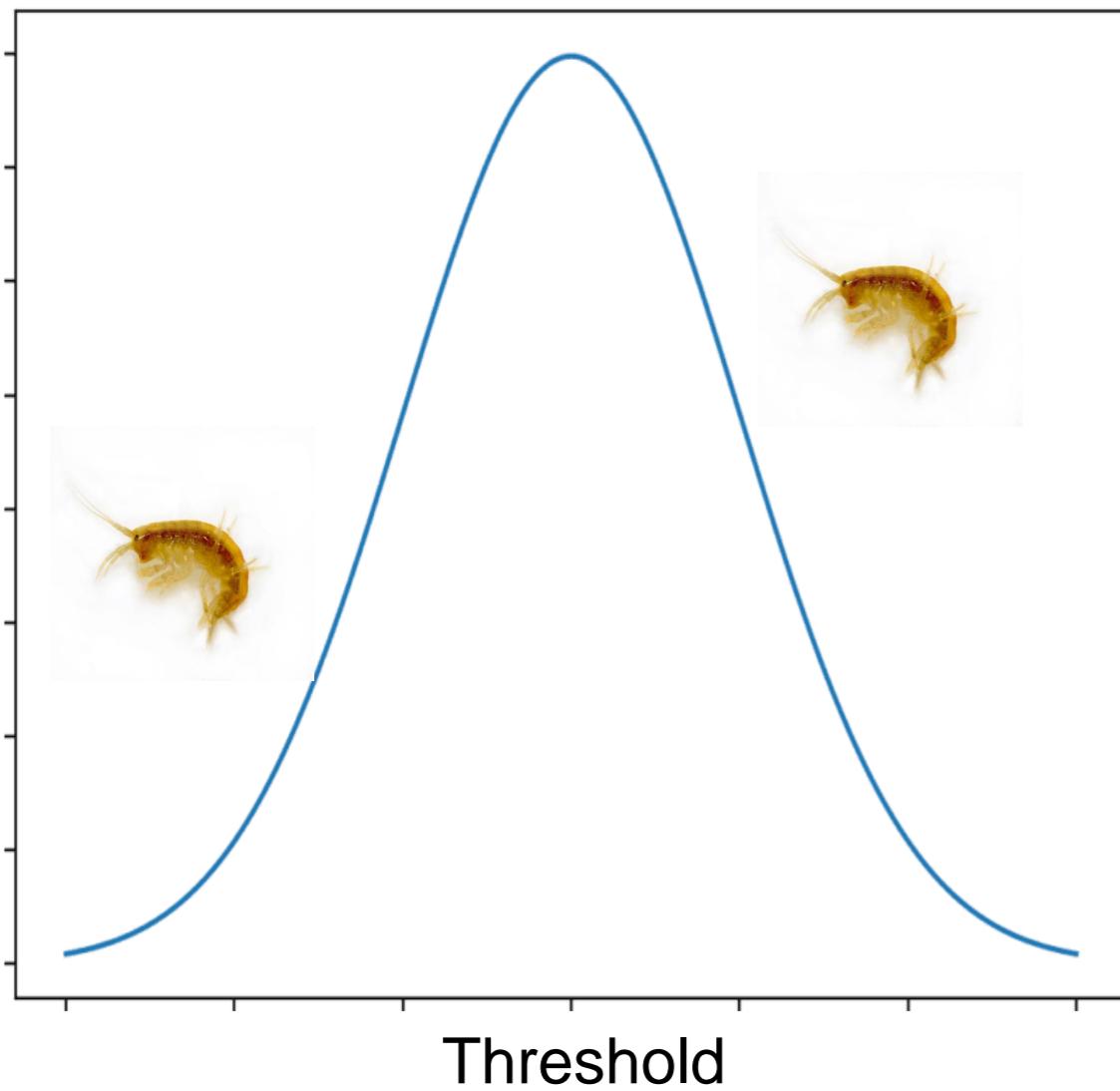
Toxicodynamic modelling



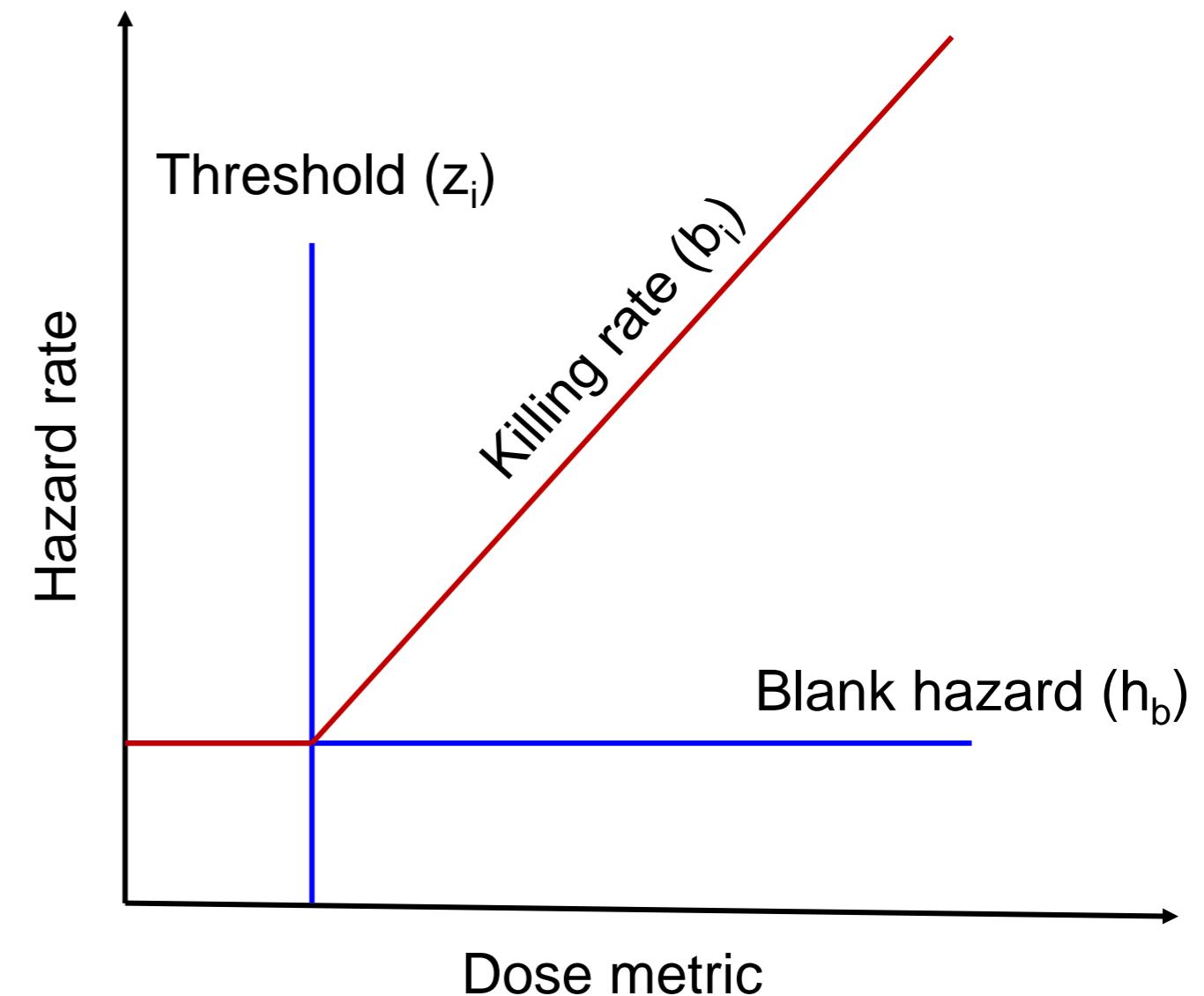
Toxicodynamic modelling



Individual tolerance VS Stochastic death

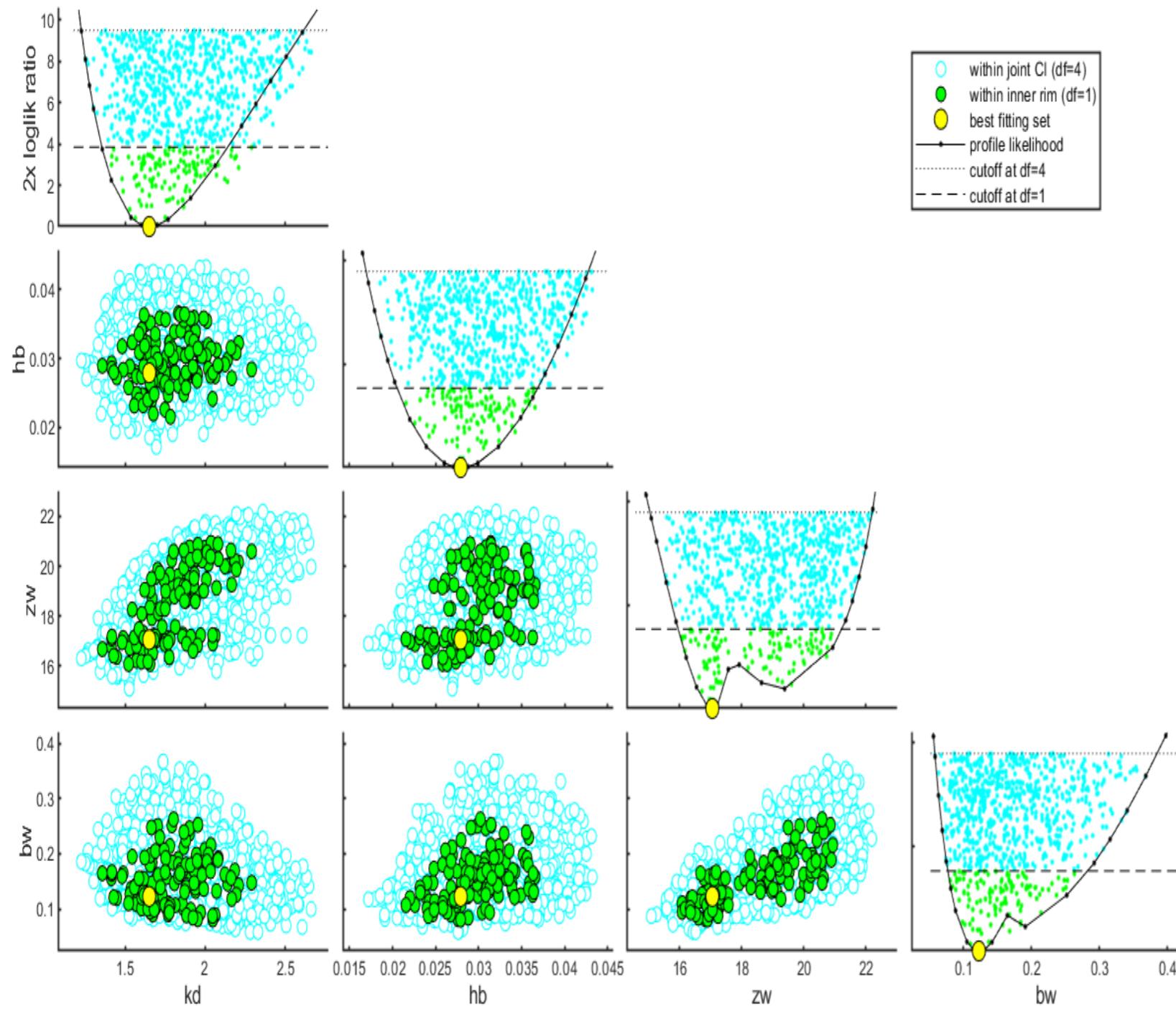


Individual tolerance

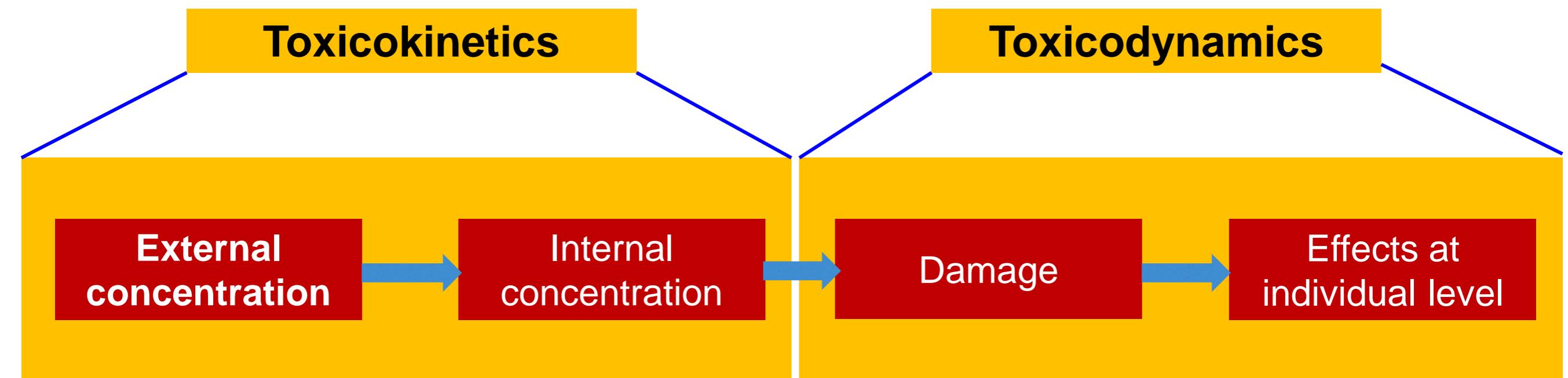


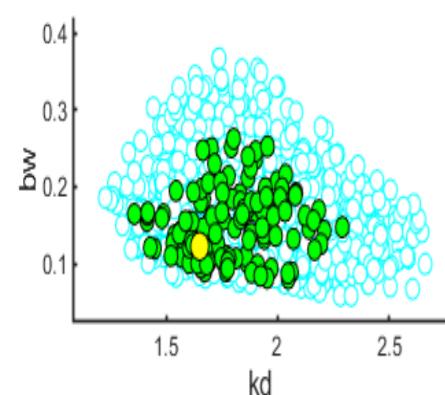
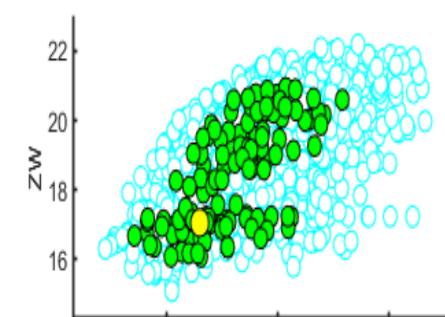
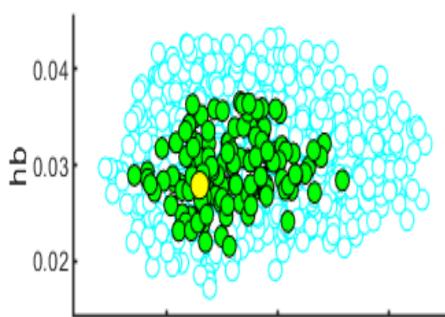
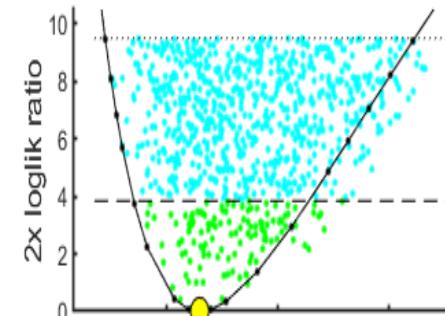
Stochastic death

TK-TD modelling

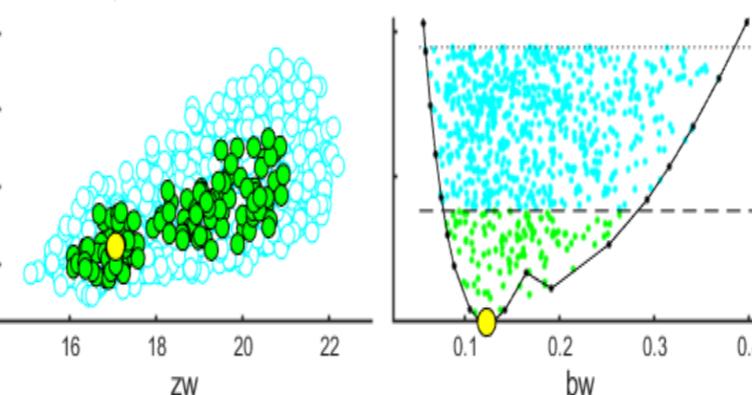
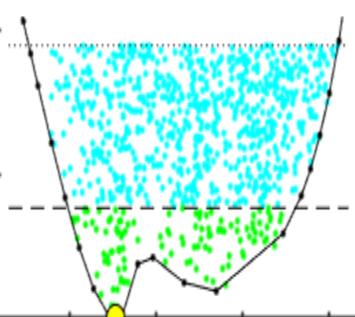
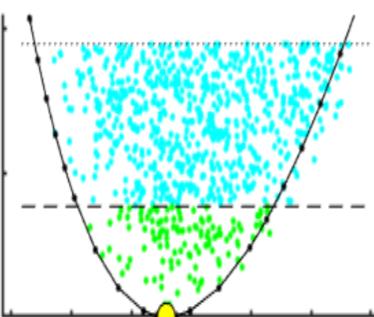


Toxicodynamic-Toxicokinetic modelling





Lethal toxicokinetic-toxicodynamic modelling



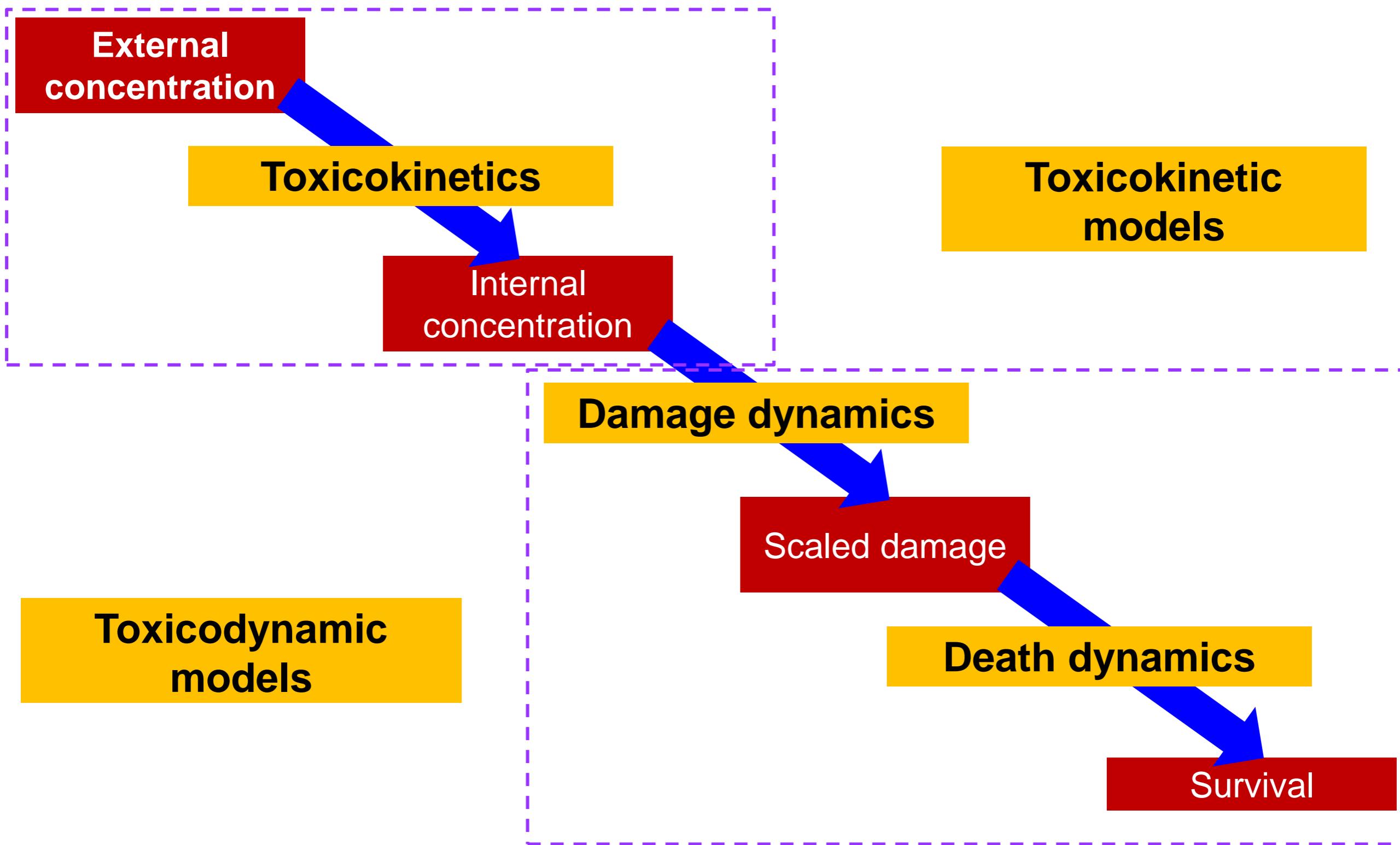
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hb

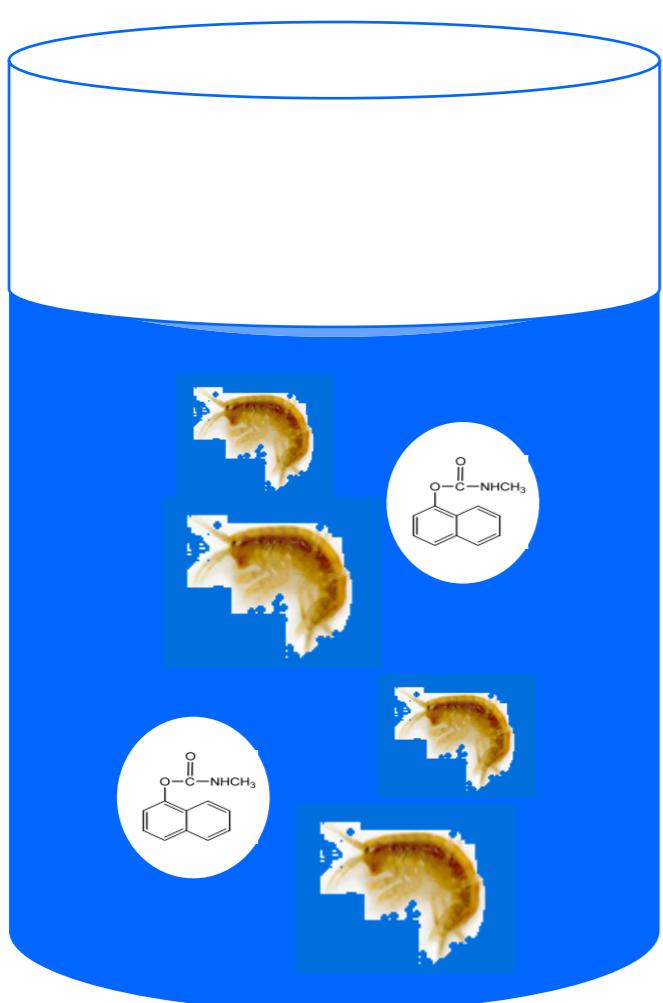
zw

bw

General Unified Threshold model of Survival (GUTS)

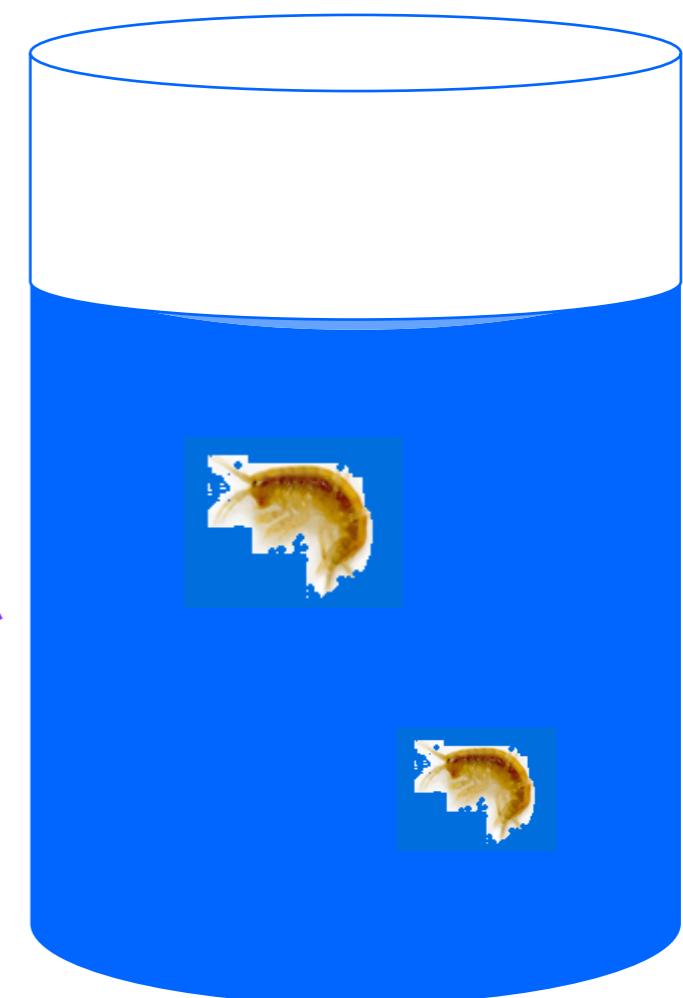


Exposure experiment for *Gammarus pulex*

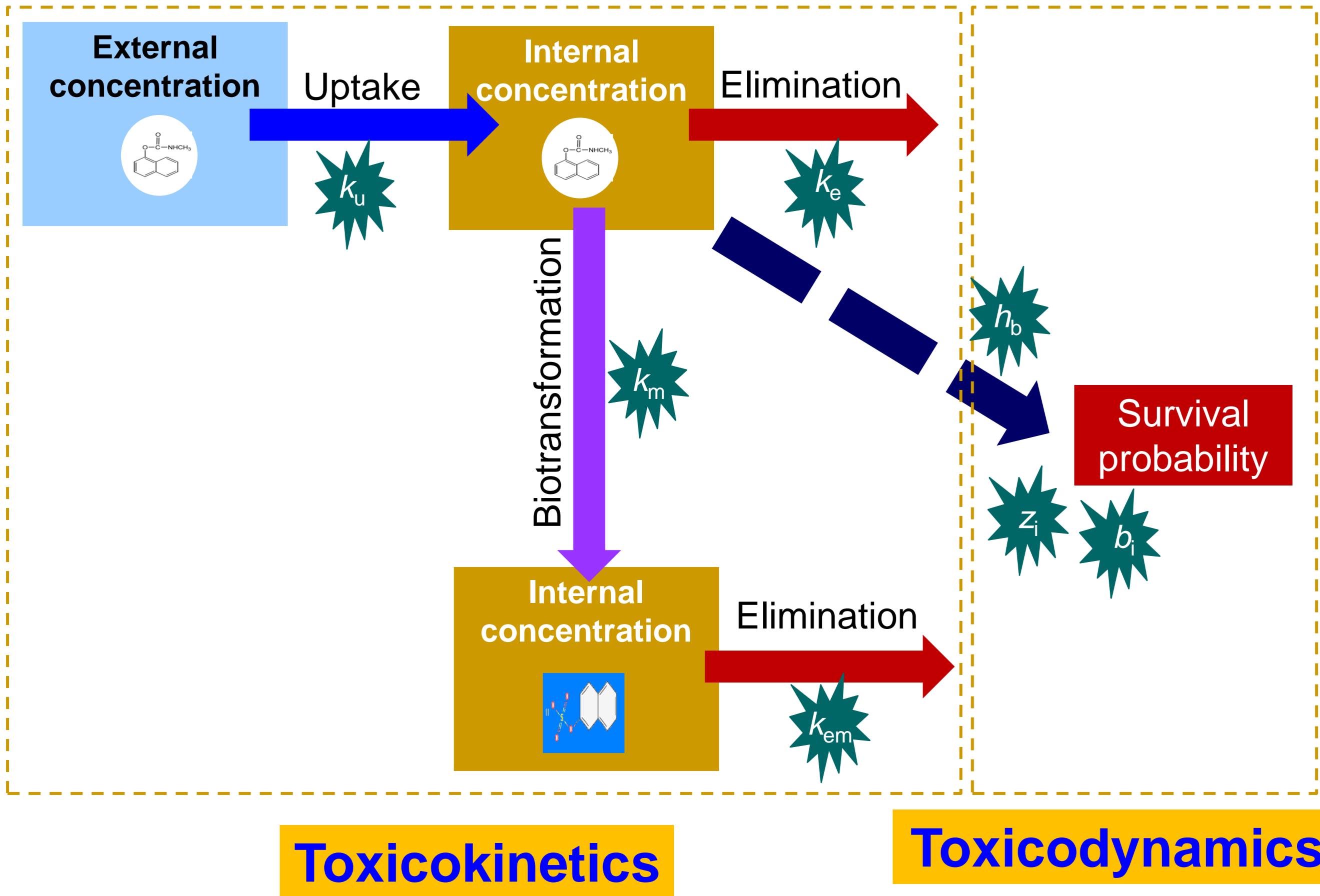


Internal concentration

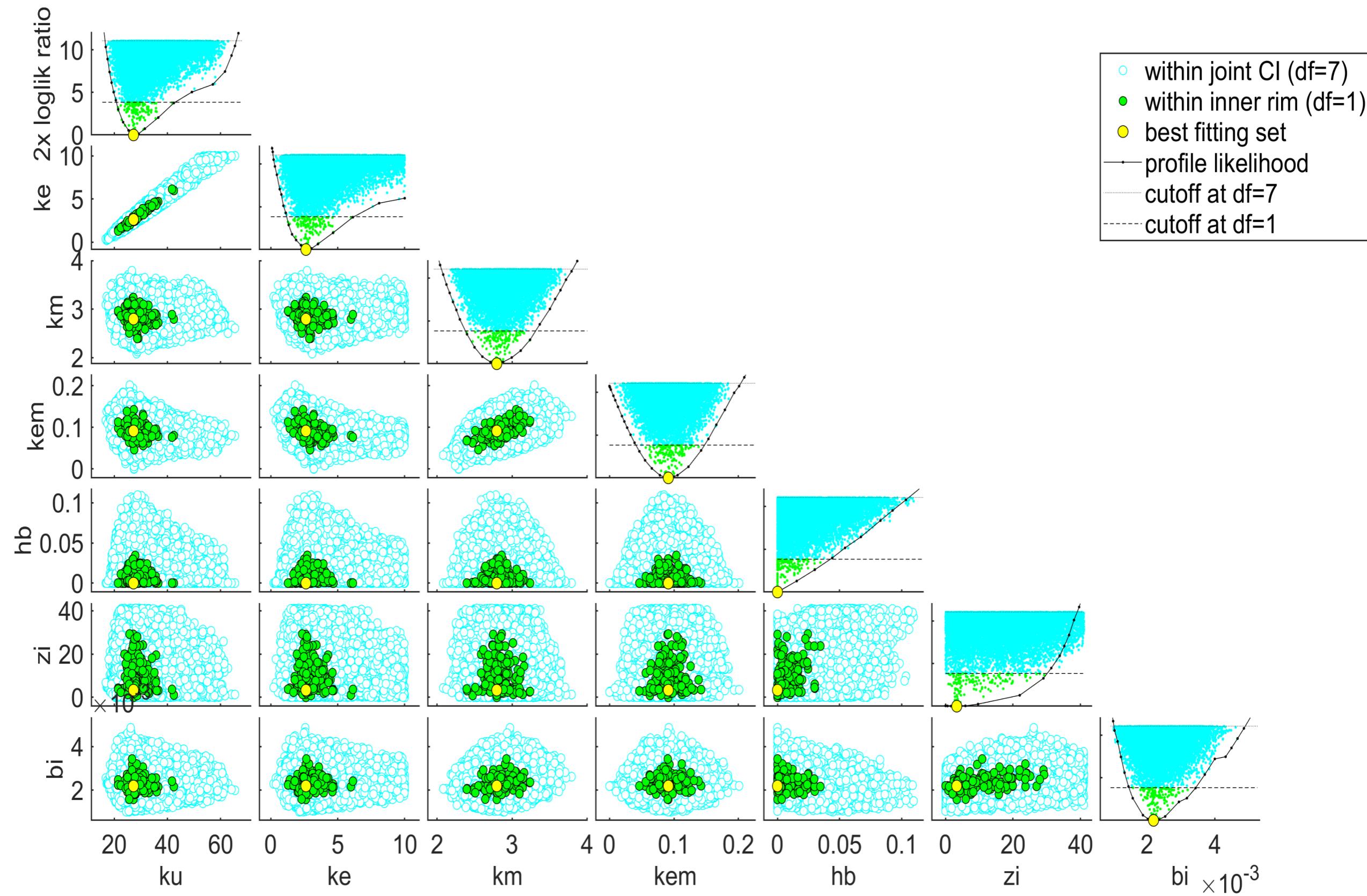
Survival



General Unified Threshold model of Survival (GUTS)



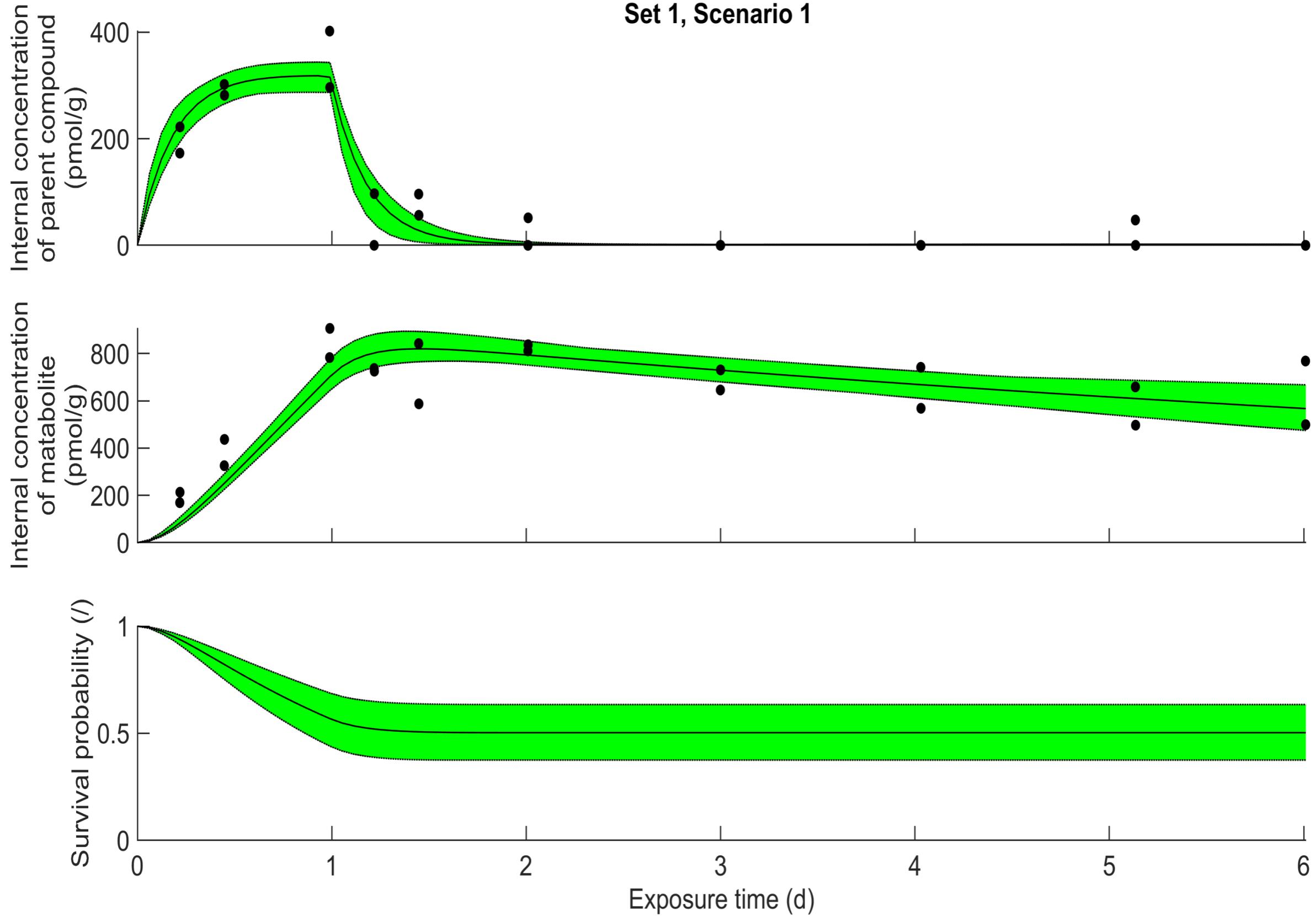
General Unified Threshold model of Survival (GUTS)



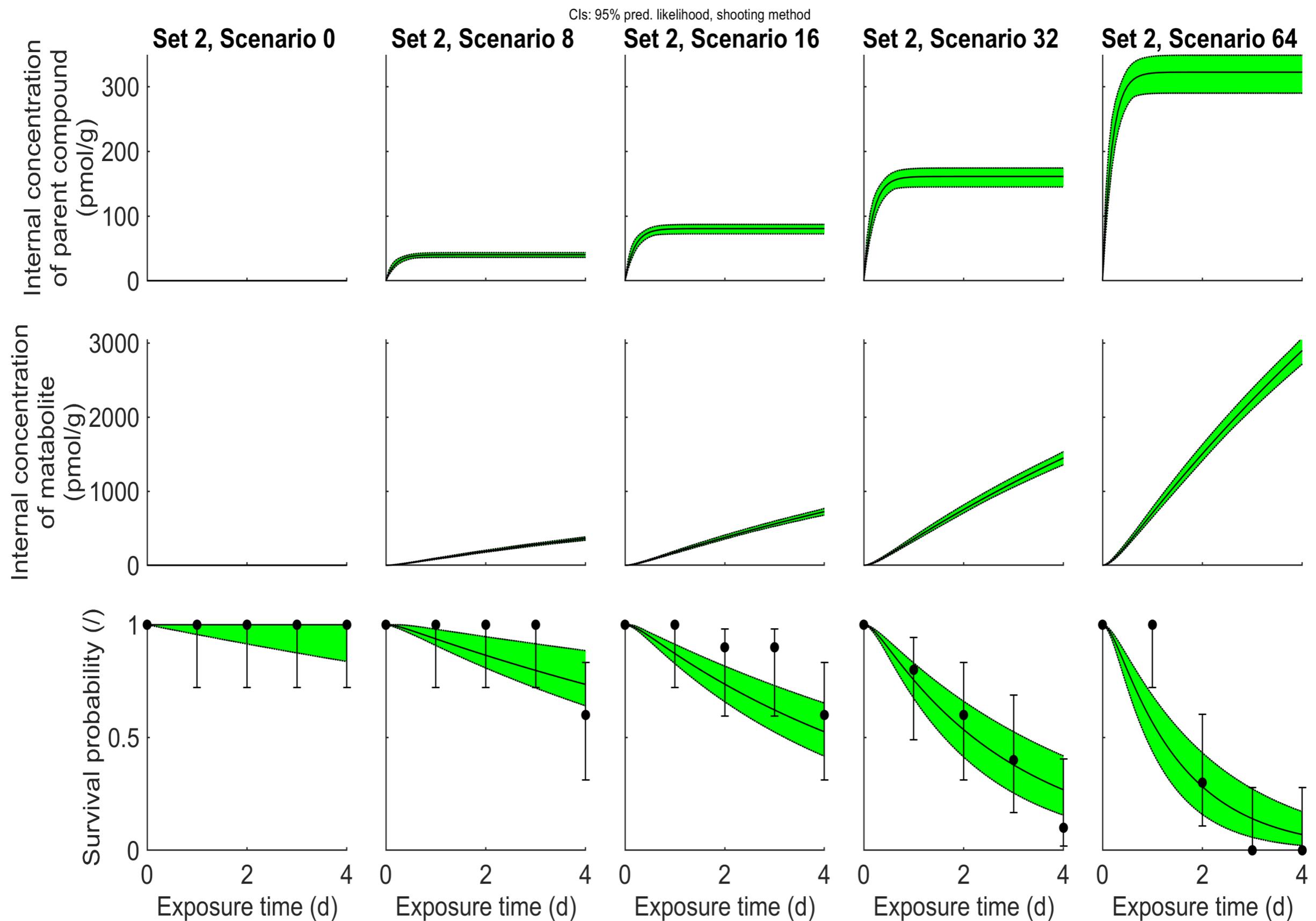
General Unified Threshold model of Survival (GUTS)

CIs: 95% pred. likelihood, shooting method

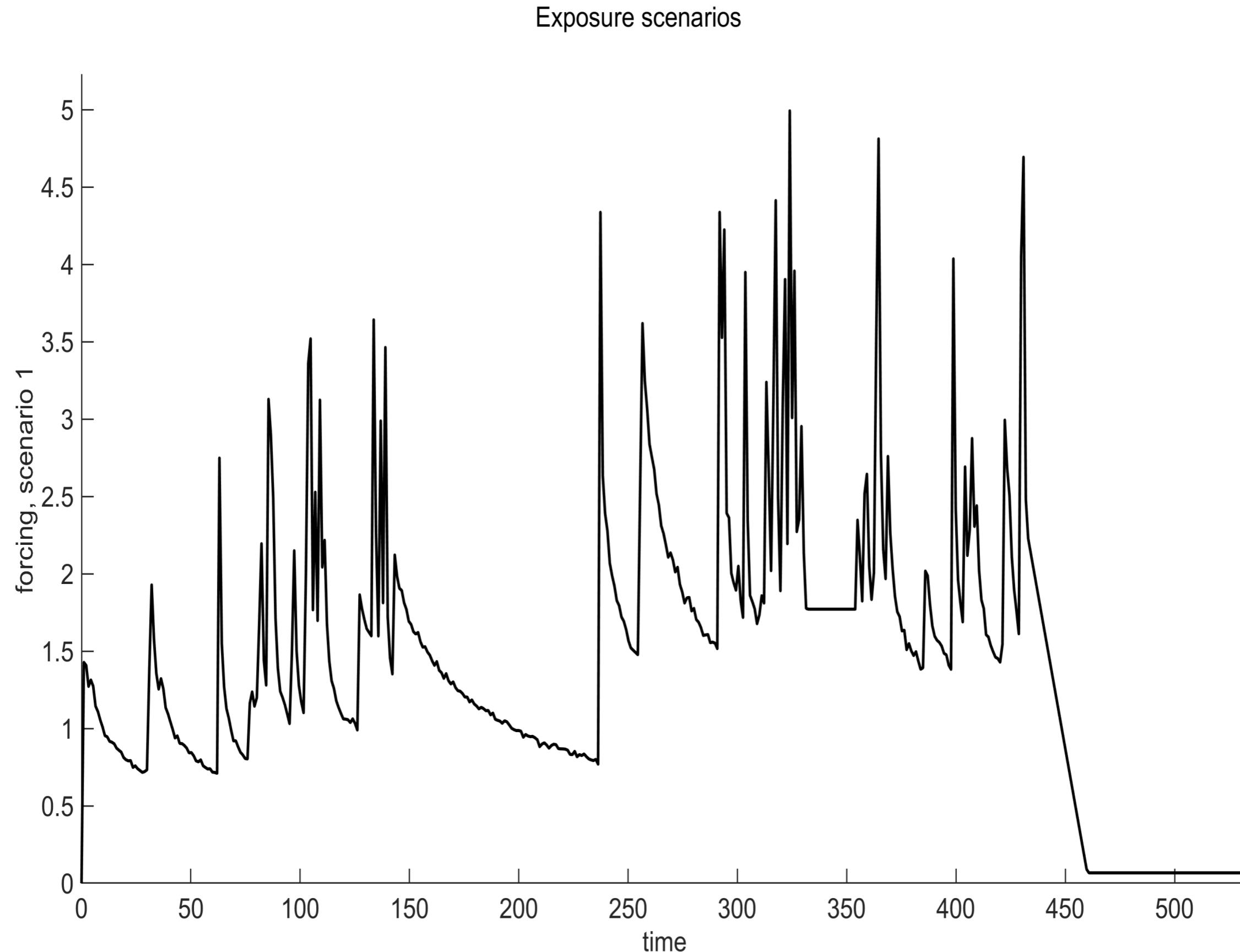
Set 1, Scenario 1



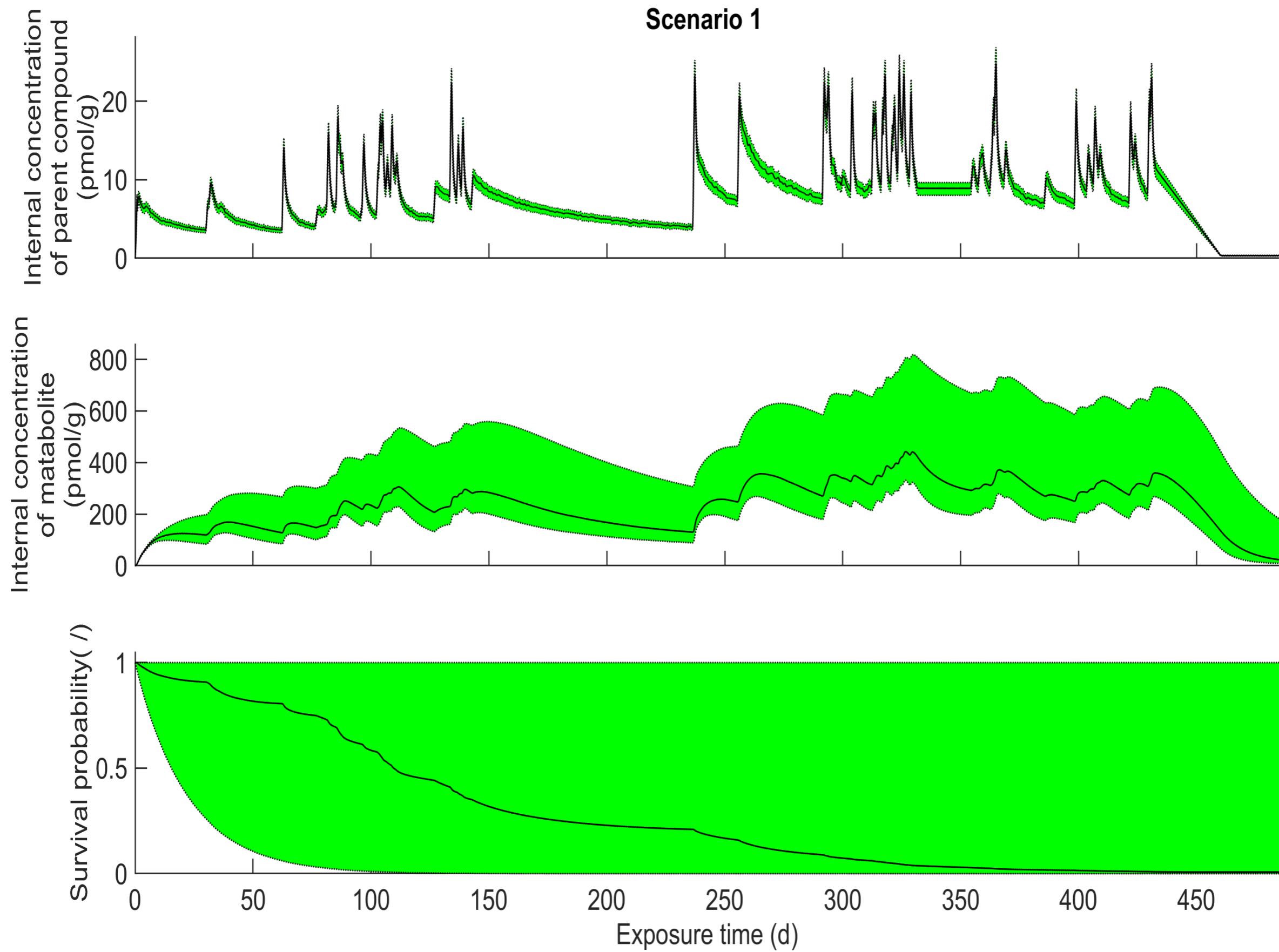
General Unified Threshold model of Survival (GUTS)

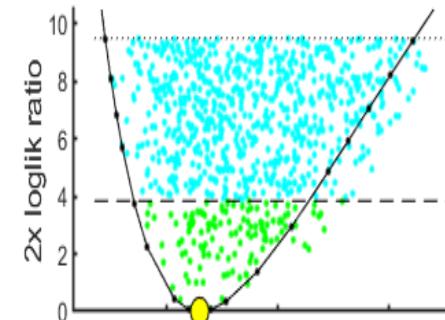


General Unified Threshold model of Survival (GUTS)

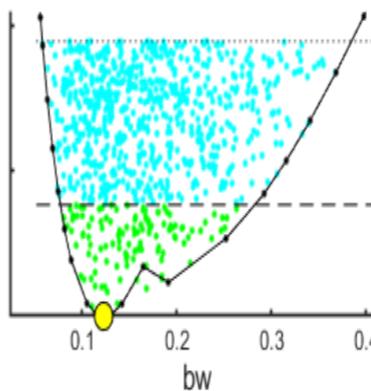
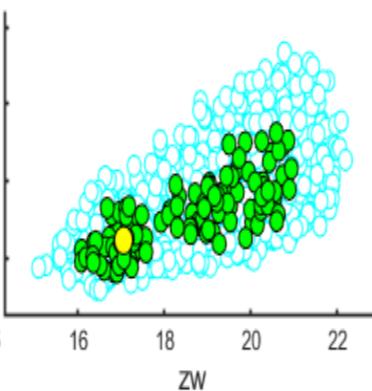
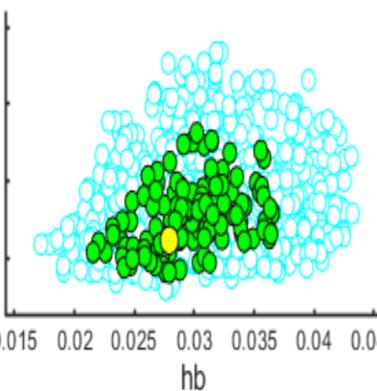
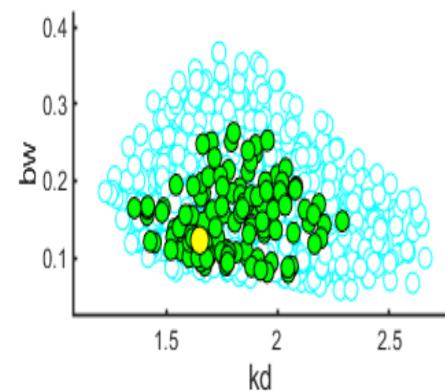
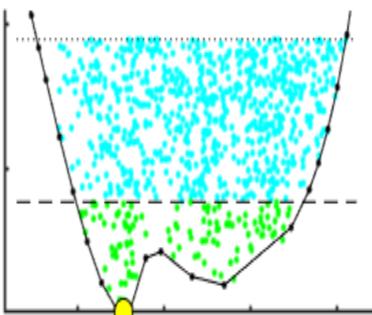
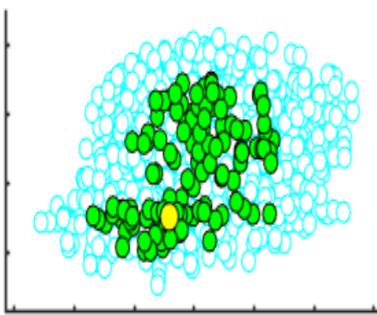
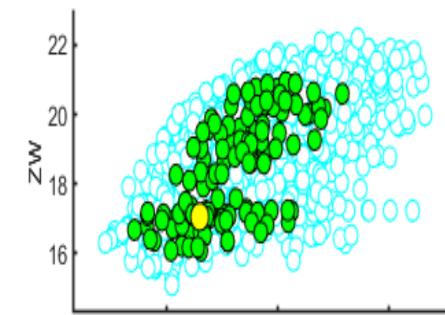
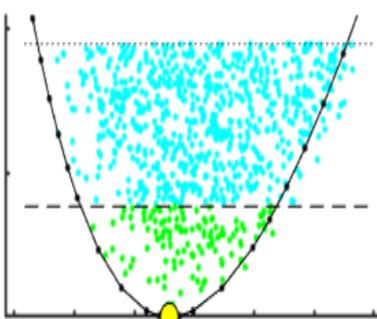
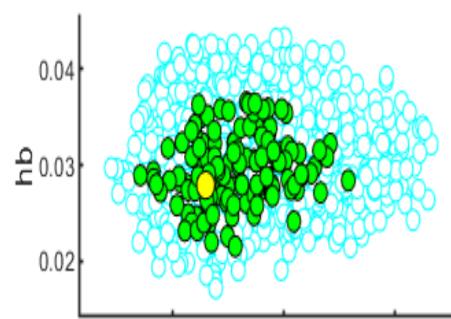


General Unified Threshold model of Survival (GUTS)

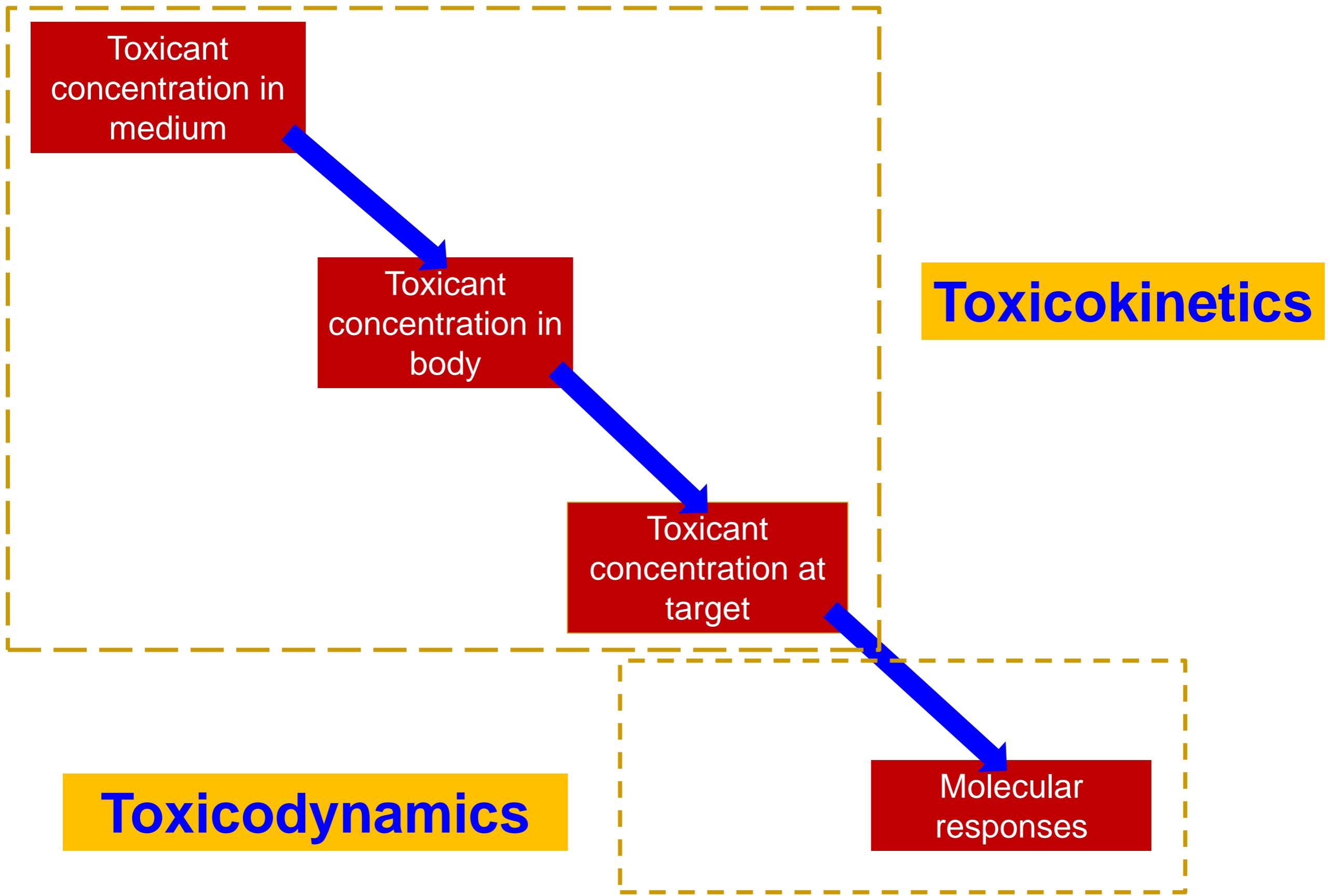




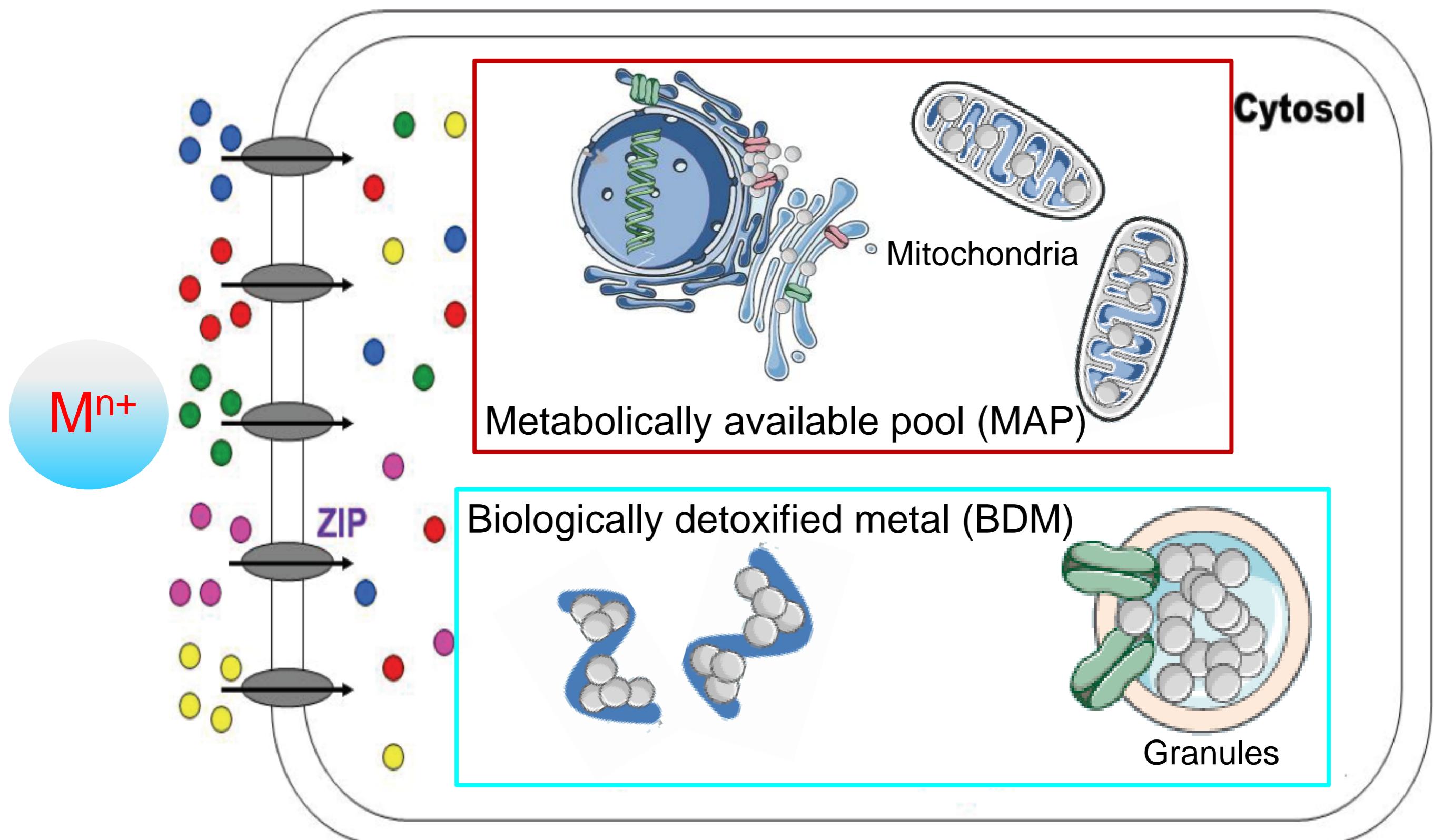
Sub-lethal toxicokinetic-toxicodynamic modelling



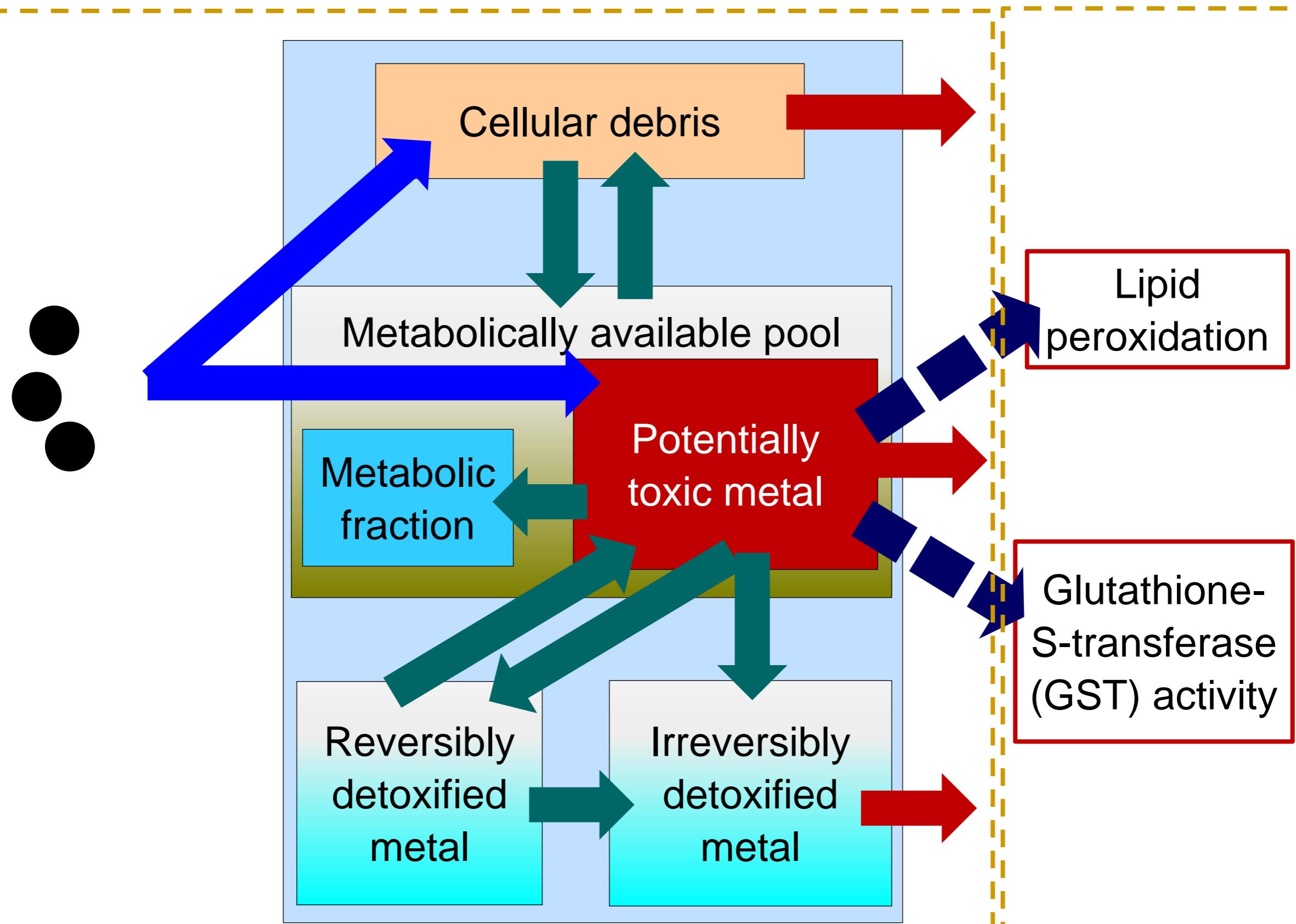
TK-TD for sub-lethal effects



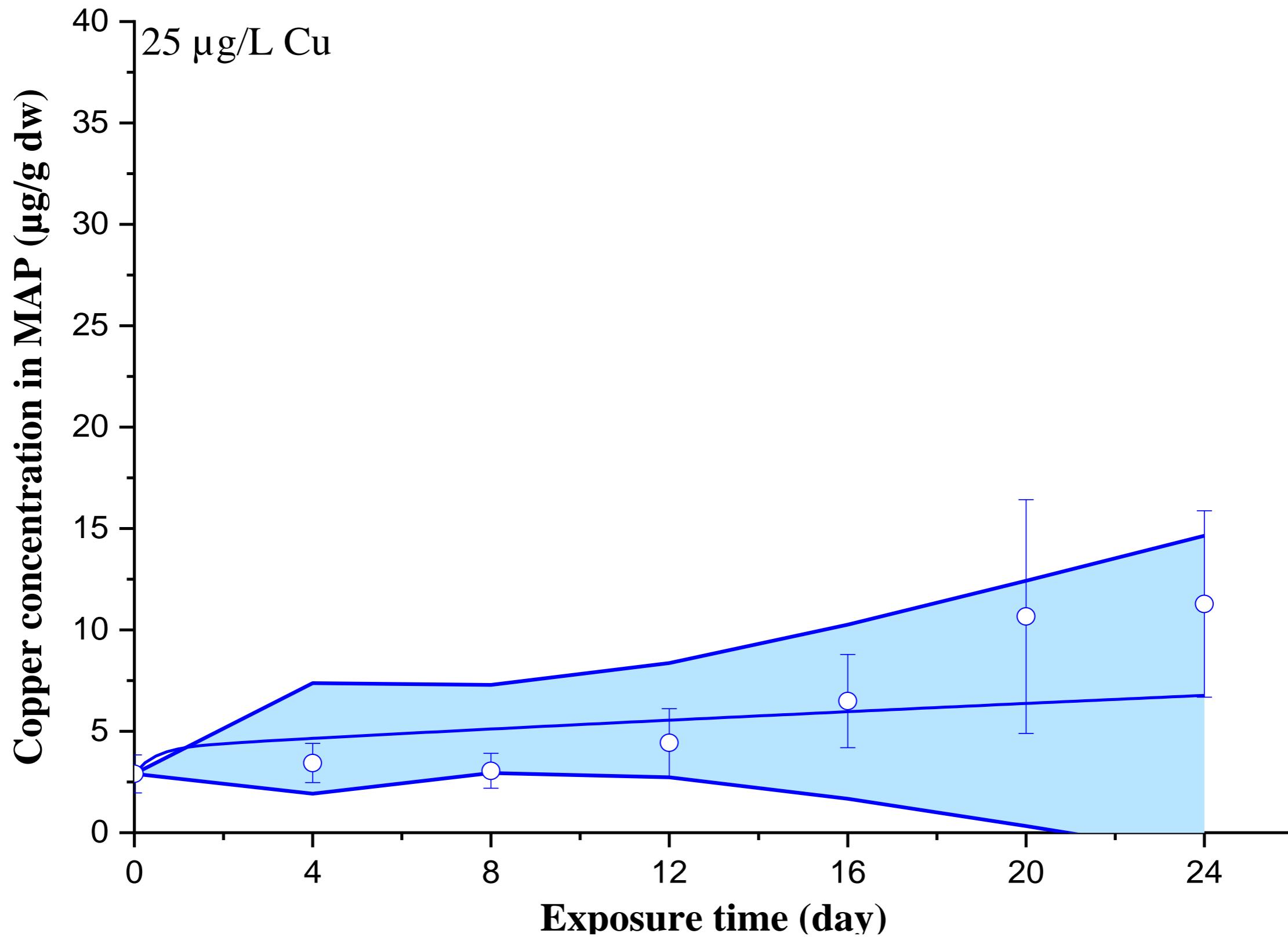
TK-TD for sub-lethal effects



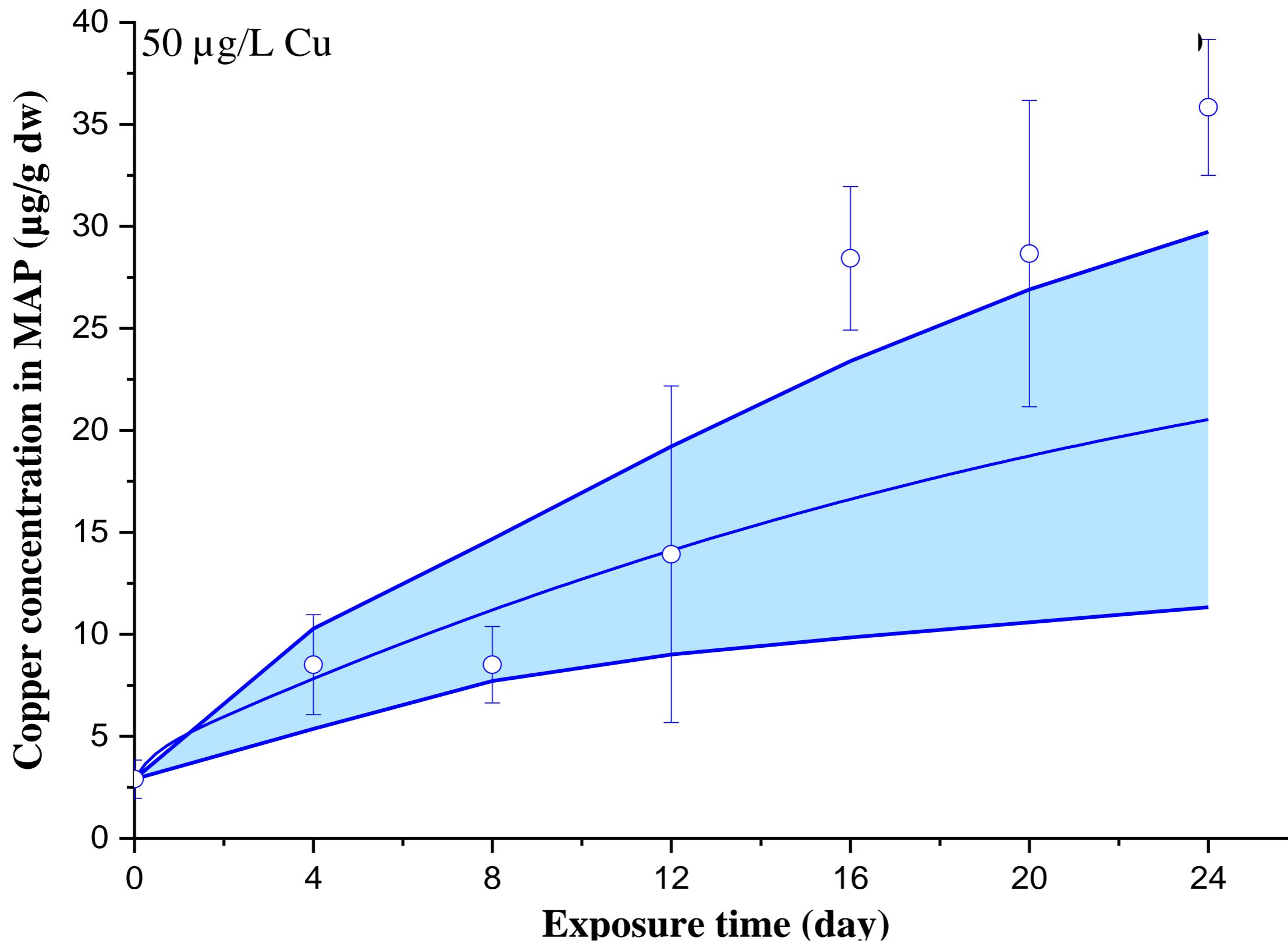
TK-TD for sub-lethal effects



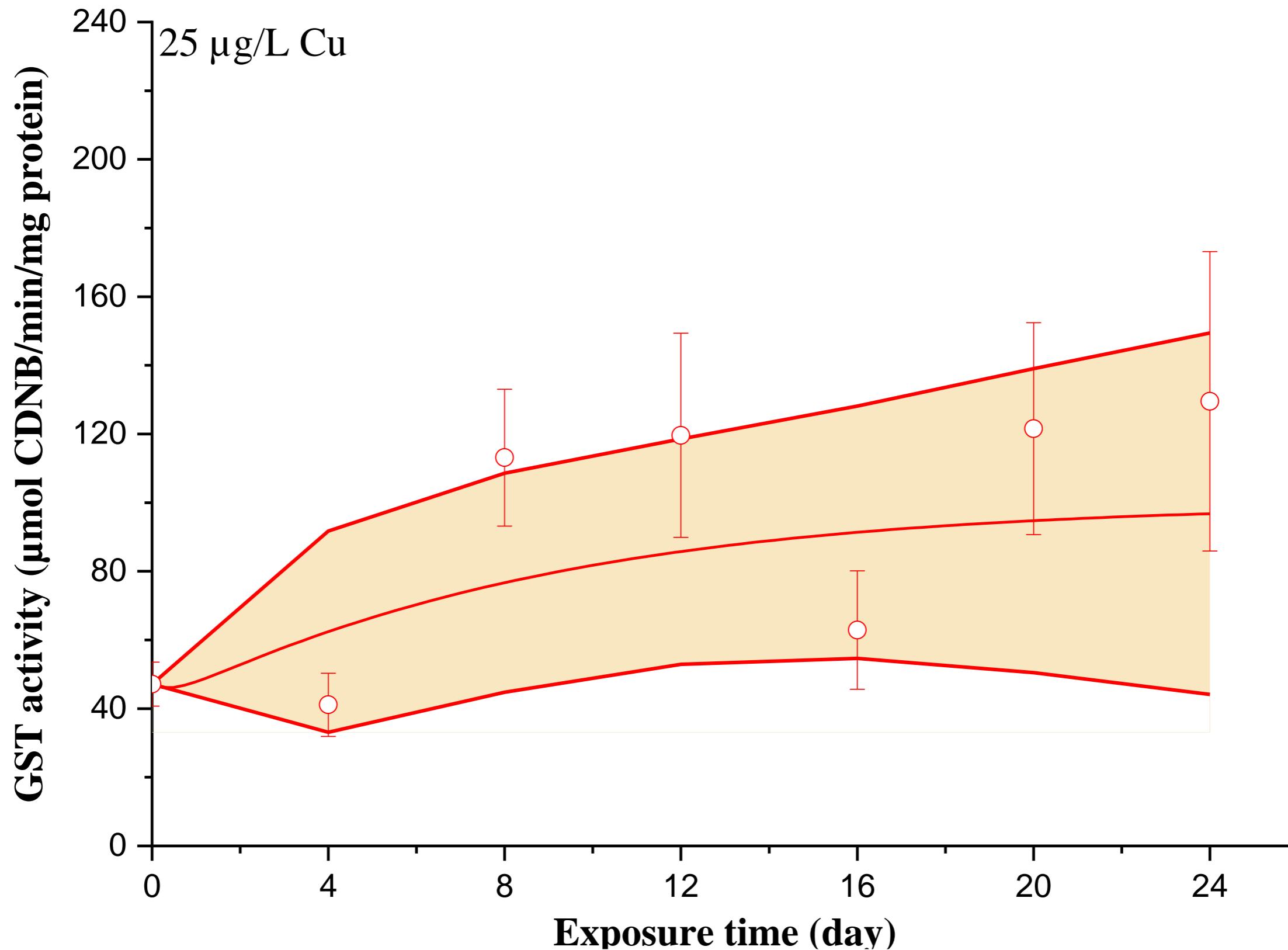
TK-TD for sub-lethal effects



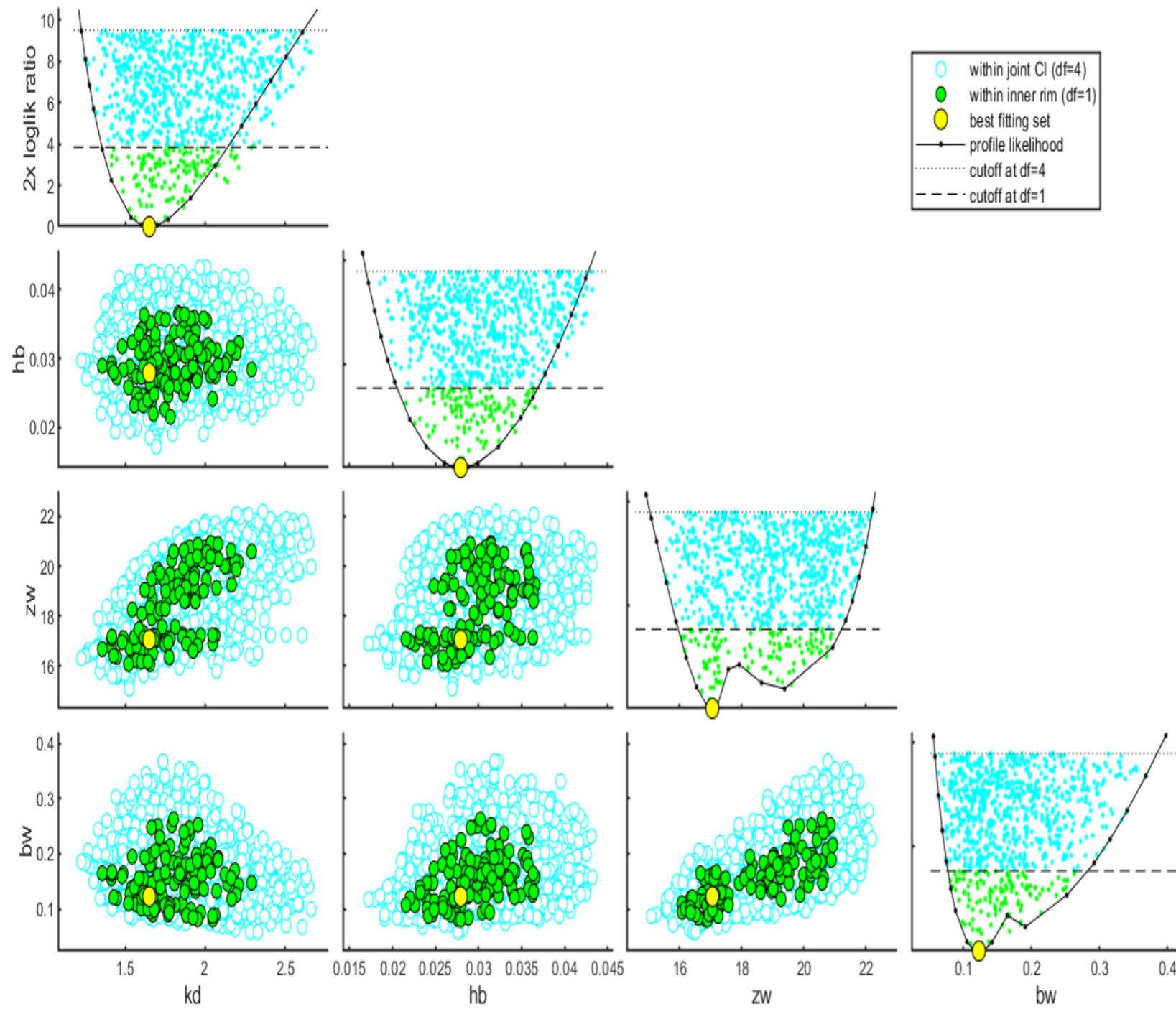
TK-TD for sub-lethal effects



TK-TD for sub-lethal effects



Discussion



Mechanistic modelling in ecotoxicology

What is a mechanistic model?

One-compartment models vs Multi-compartment models?

Combine individual tolerance and stochastic death?