



# *Applying criteria for model evaluation to TKTD models*

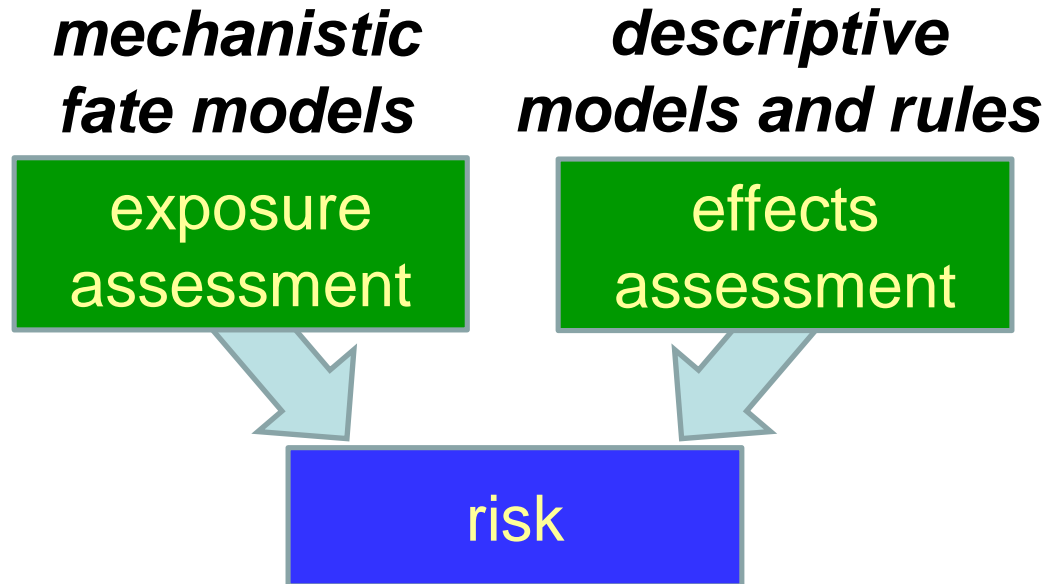
Tjalling Jager



*SETAC Brussels, May 2017*

# Context

---



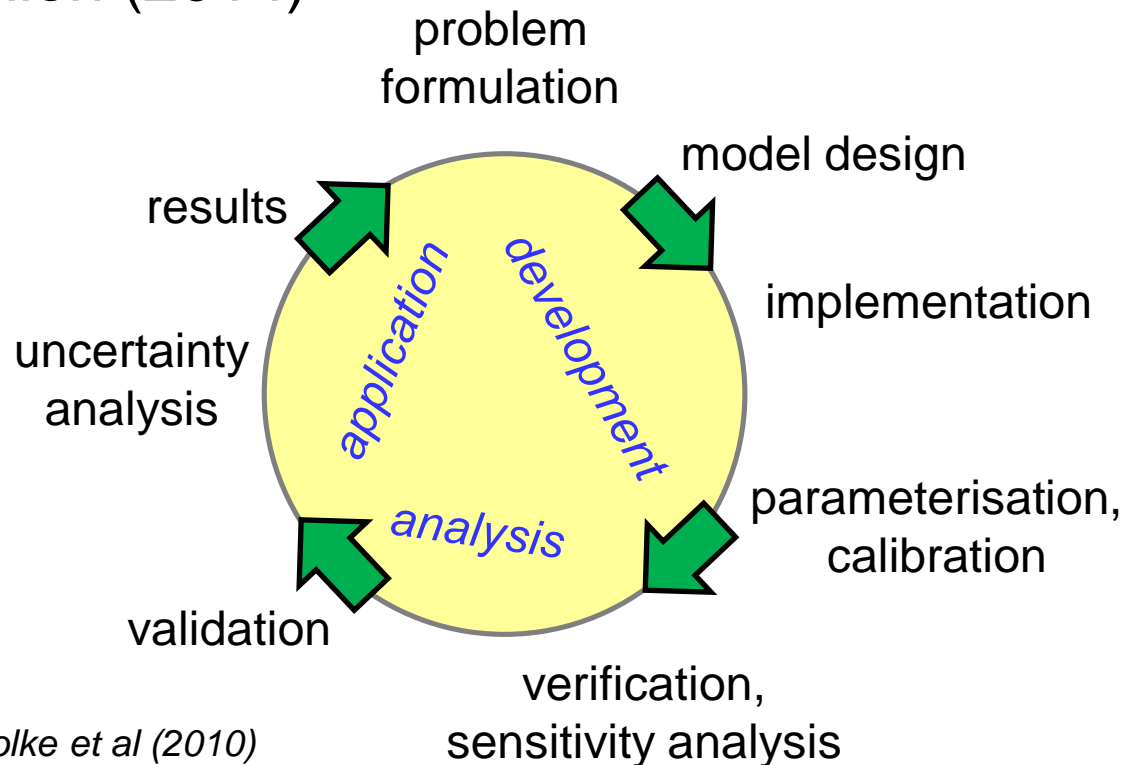
- Mechanistic effects models may improve ERA ...
- What is the 'quality' of these effects models?

# Context

---

## ‘Good modelling practice’

- TRACE (Schmolke *et al* 2010, Grimm *et al* 2014)
- EFSA scientific opinion (2014)



*Modified from Schmolke et al (2010)*

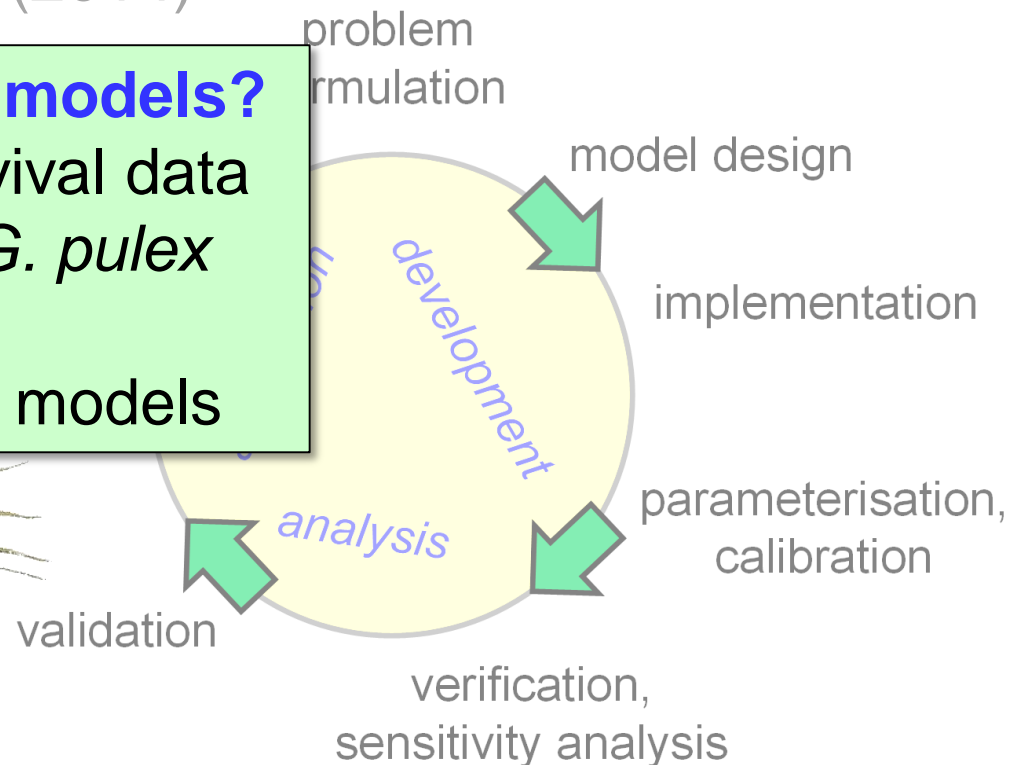
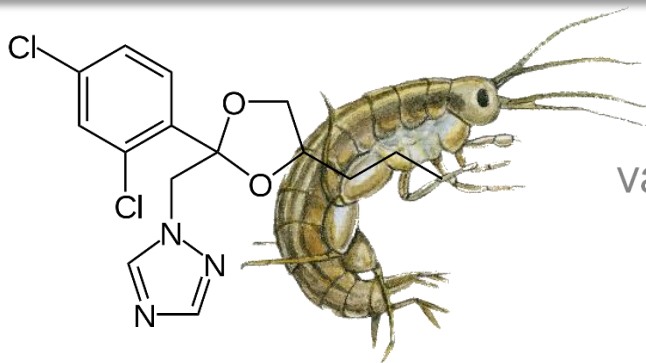
# Context

## ‘Good modelling practice’

- TRACE (Schmolke *et al* 2010, Grimm *et al* 2014)
- EFSA scientific opinion (2014)

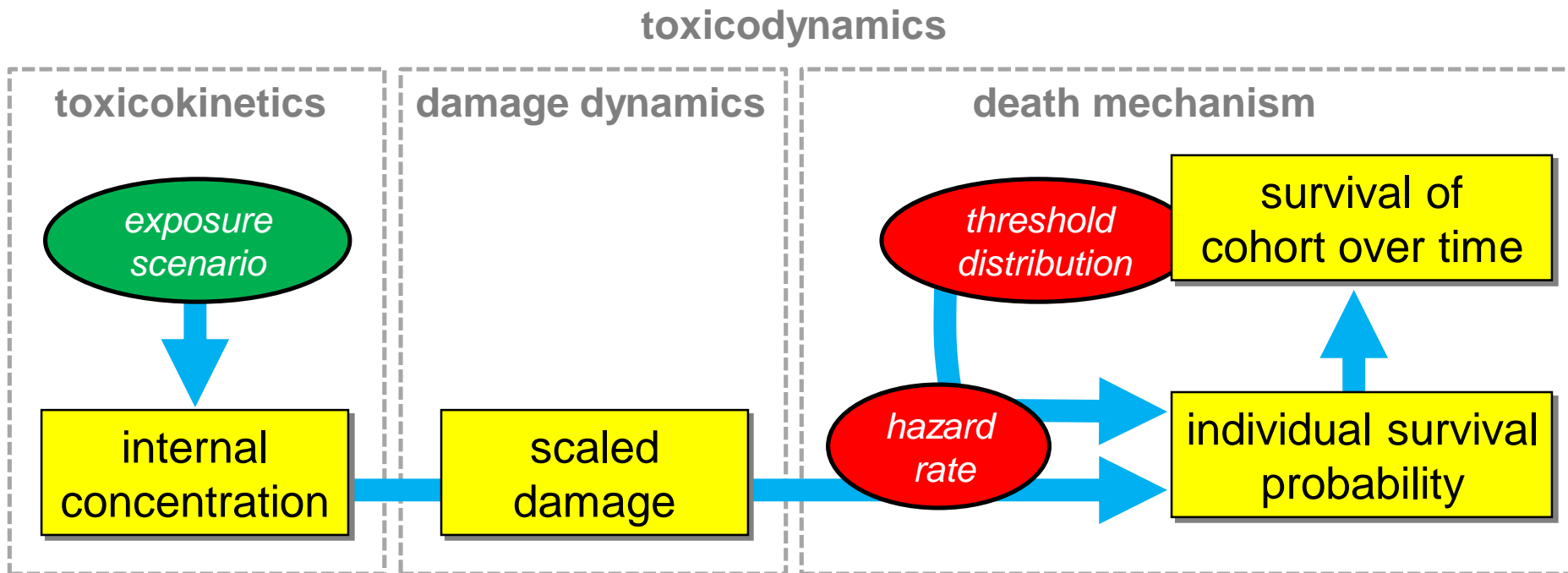
### How does this fit TKTD models?

- example: GUTS for survival data
- data: propiconazole in *G. pulex* (Nyman *et al* 2012)
- contrast with population models



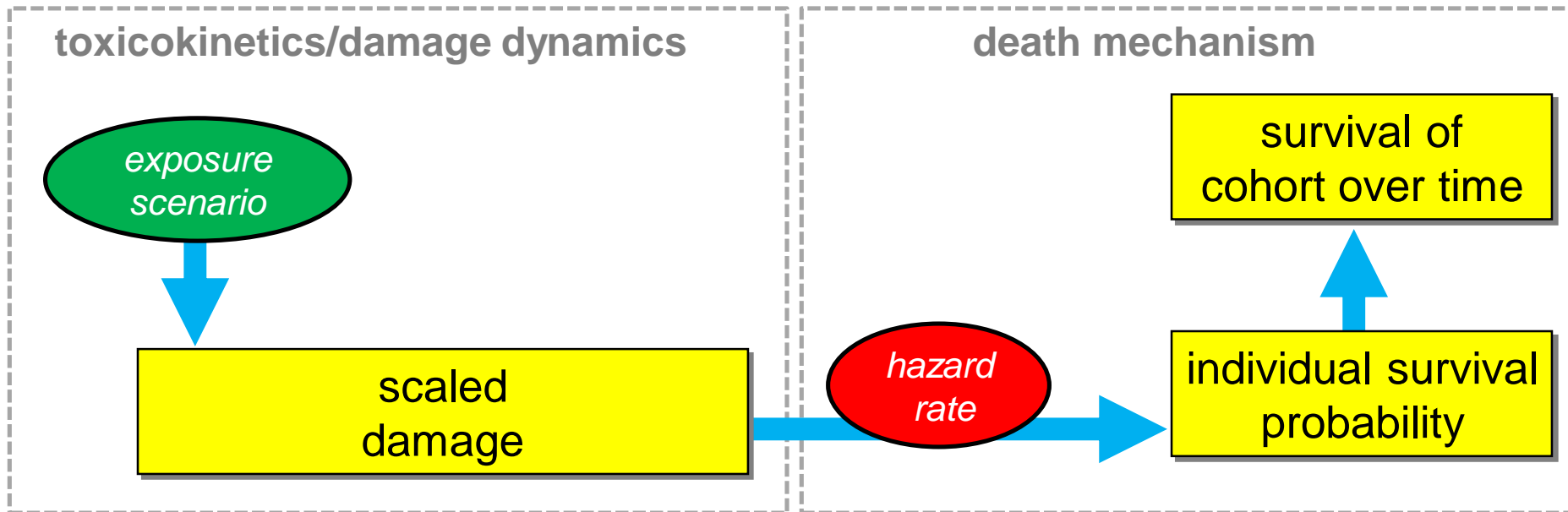
# GUTS framework

- General Unified Threshold model for Survival
  - Jager, Albert, Preuss and Ashauer (2011)



# GUTS framework

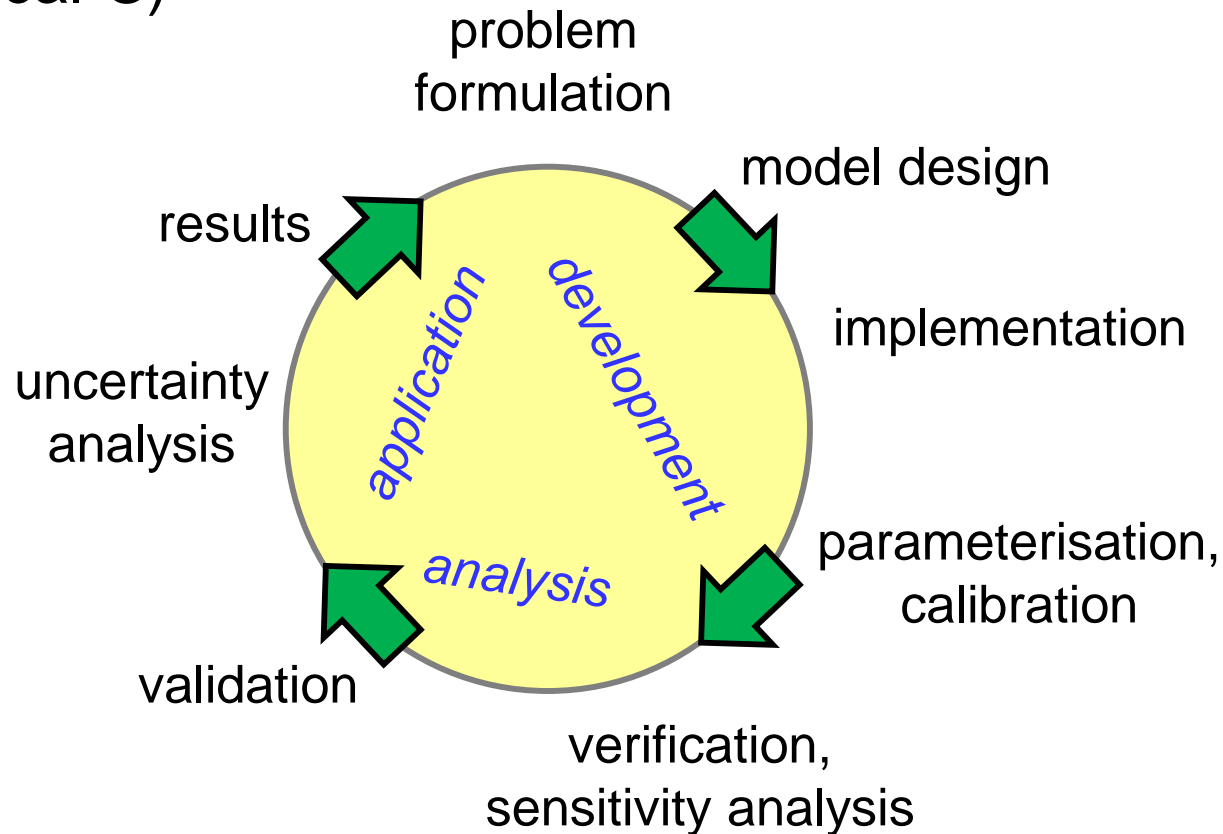
- General Unified Threshold model for Survival
  - Jager, Albert, Preuss and Ashauer (2011)
- Special case: GUTS-reduced SD



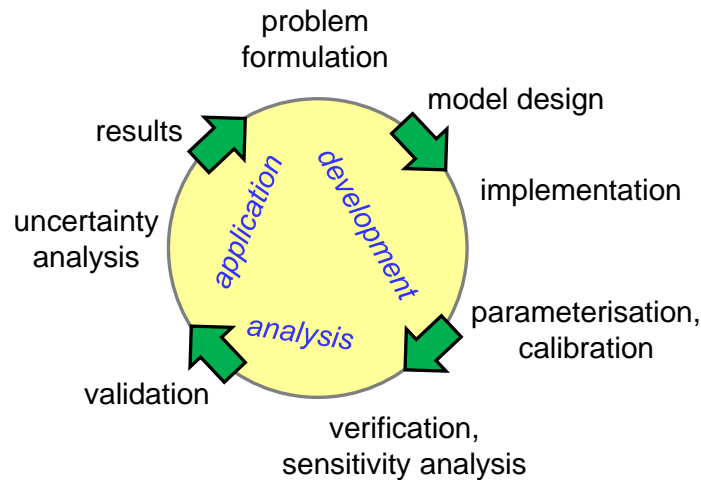
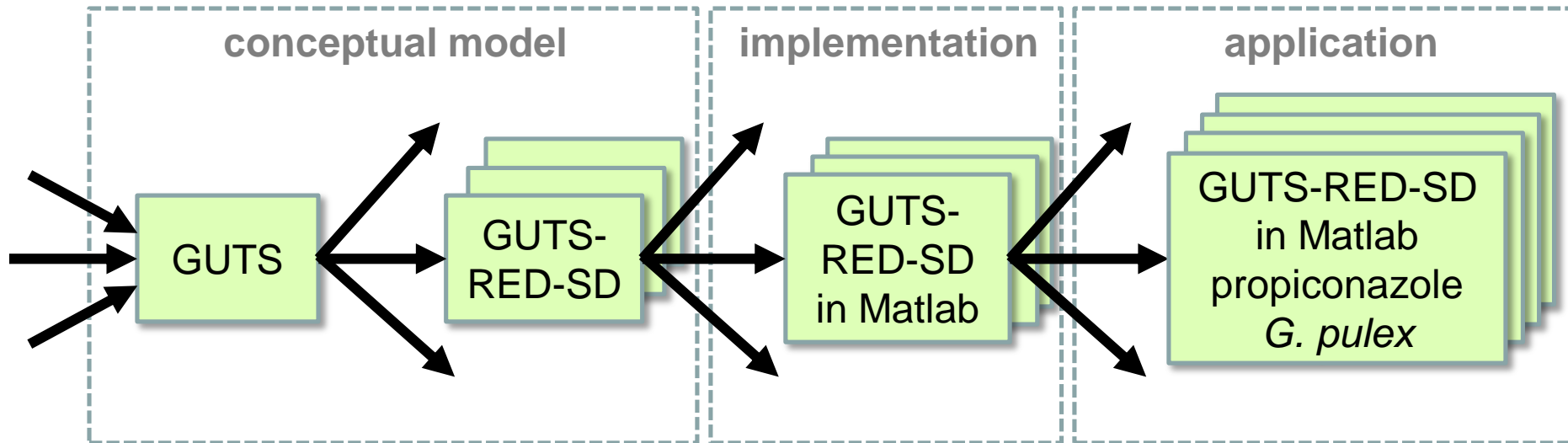
# For population models ...

---

- Develop model for species *A* in landscape *B* (for chemical *C*)

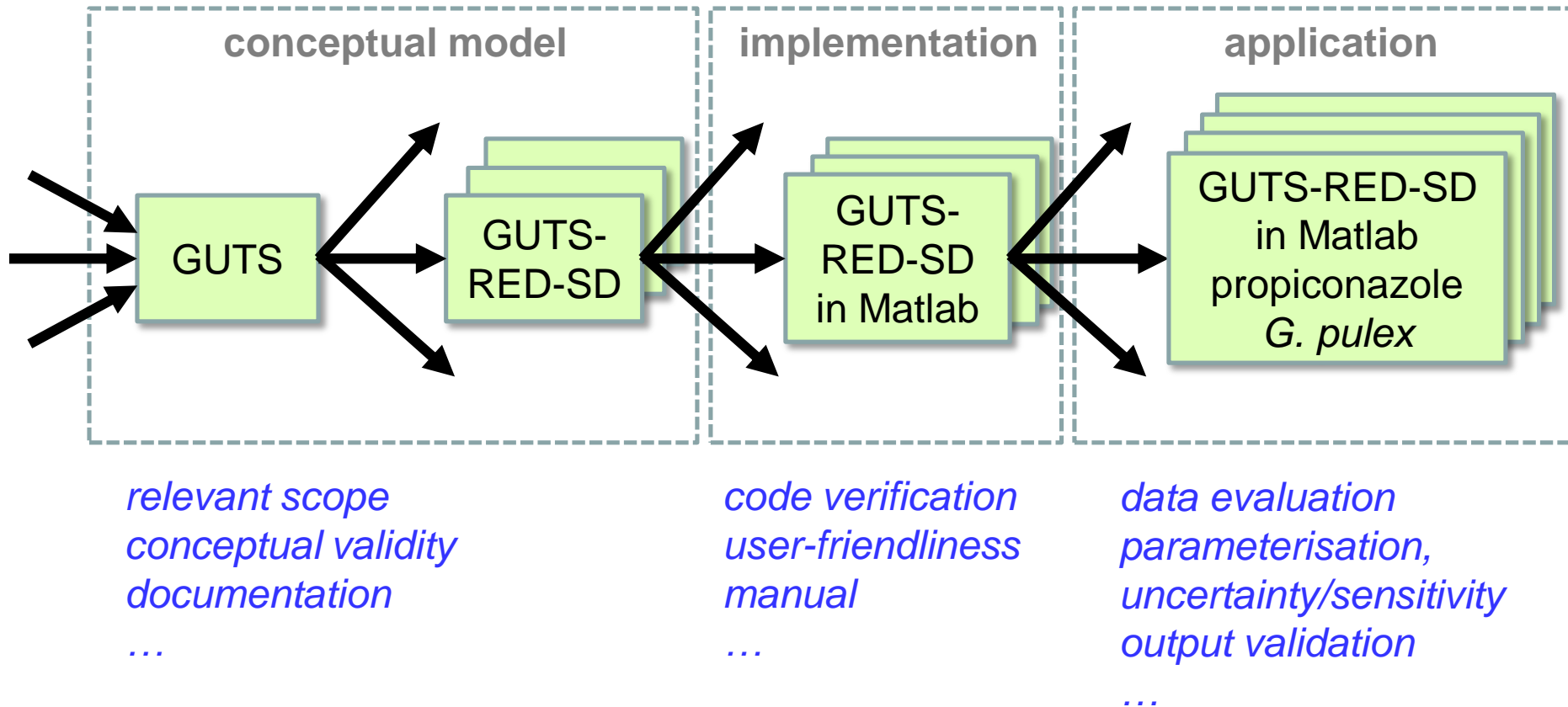


# What is *THE* model?



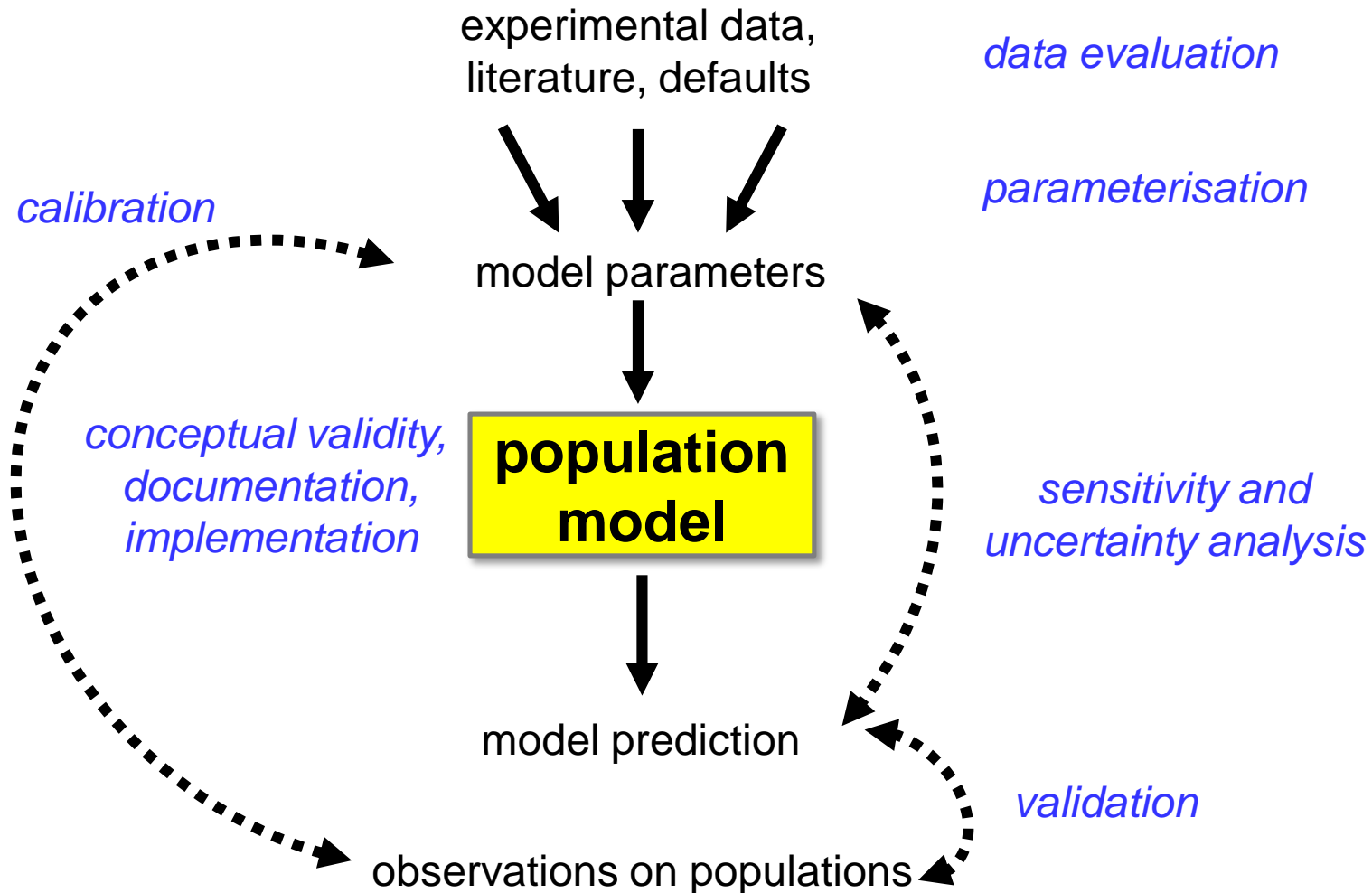


# What is *THE* model?

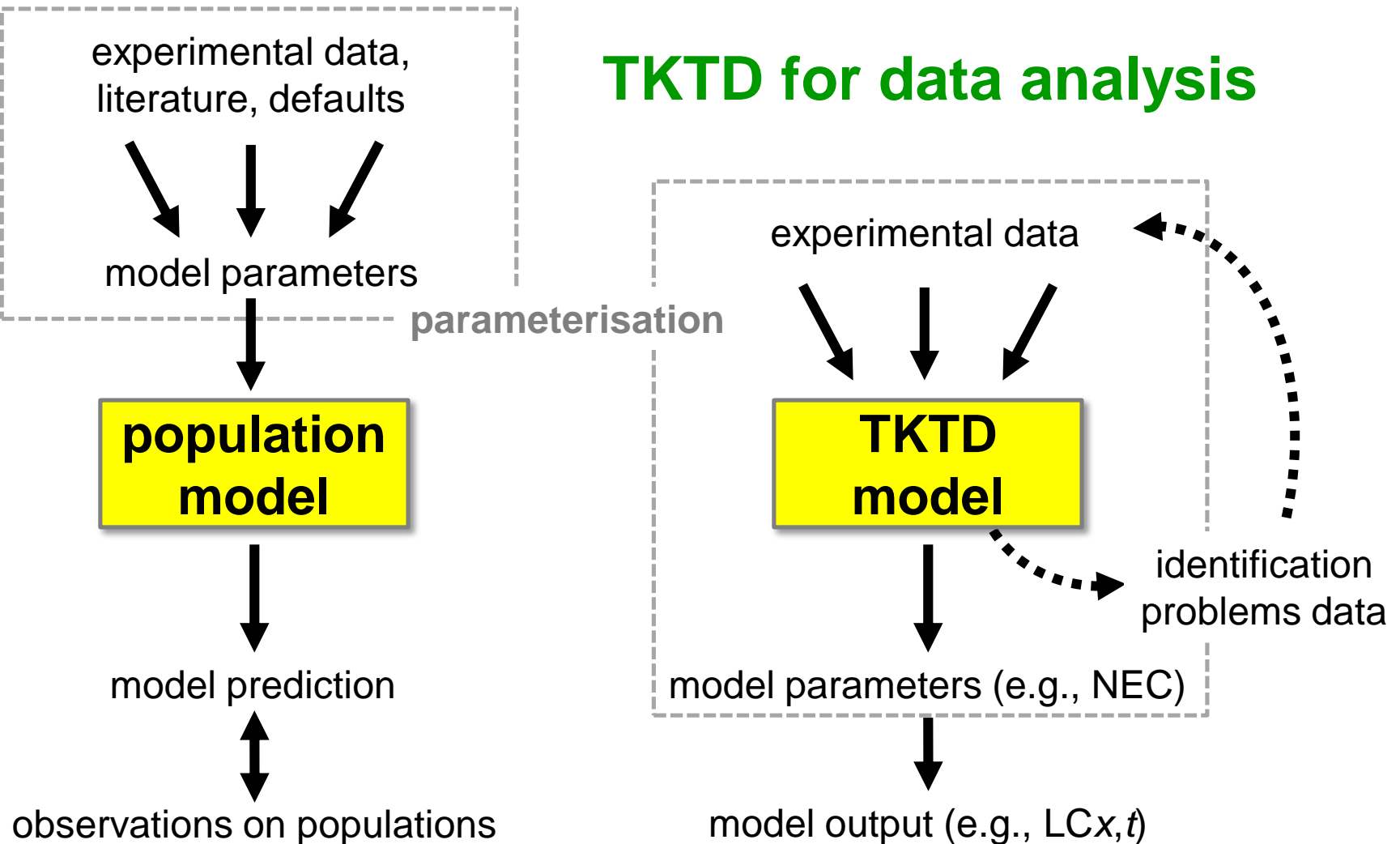


# What do quality elements mean?

---



# What do quality elements mean?

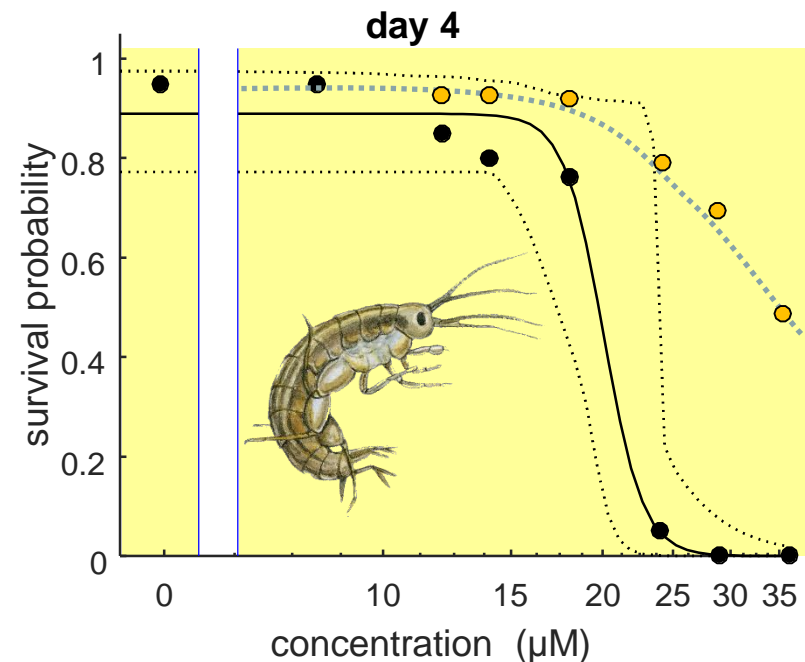


# What do quality elements mean?

## ➤ Model: classic log-logistic curve

- conceptual validation ...
- data evaluation ...
- calibration methods ...
- sensitivity analysis ...
- uncertainty analysis ...
- validation of model output ...

*proper statistical treatment  
generally fits well ...*



4d-LC50	= 20	(19-24) $\mu\text{M}$
S(0)	= 0.89	(0.81-0.95)
$\beta$	= 16	(>8.3)

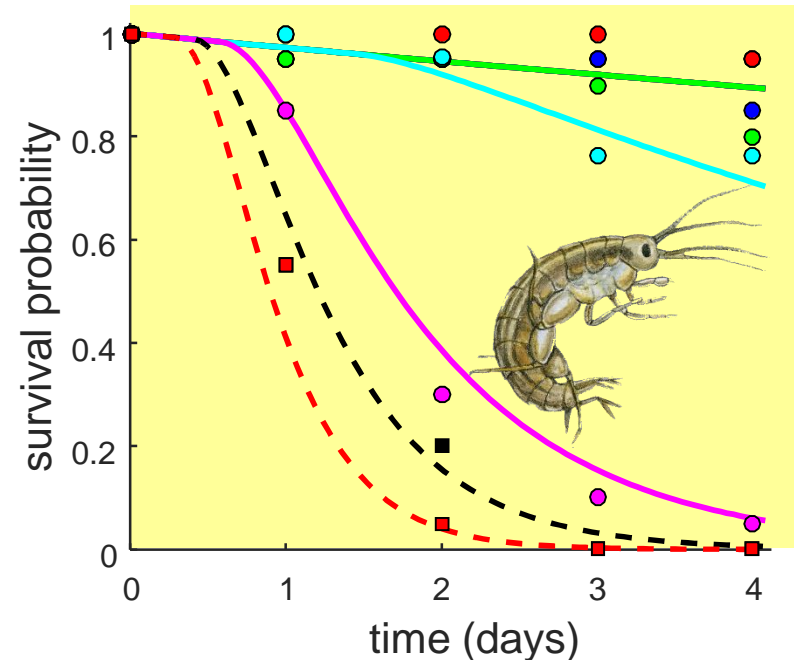
# What do quality elements mean?

## ➤ Model: GUTS-reduced SD

- conceptual validation ...
- data evaluation ...
- calibration methods ...
- sensitivity analysis ...
- uncertainty analysis ...
- validation of model output ...

*proper statistical treatment  
generally fits well ...*

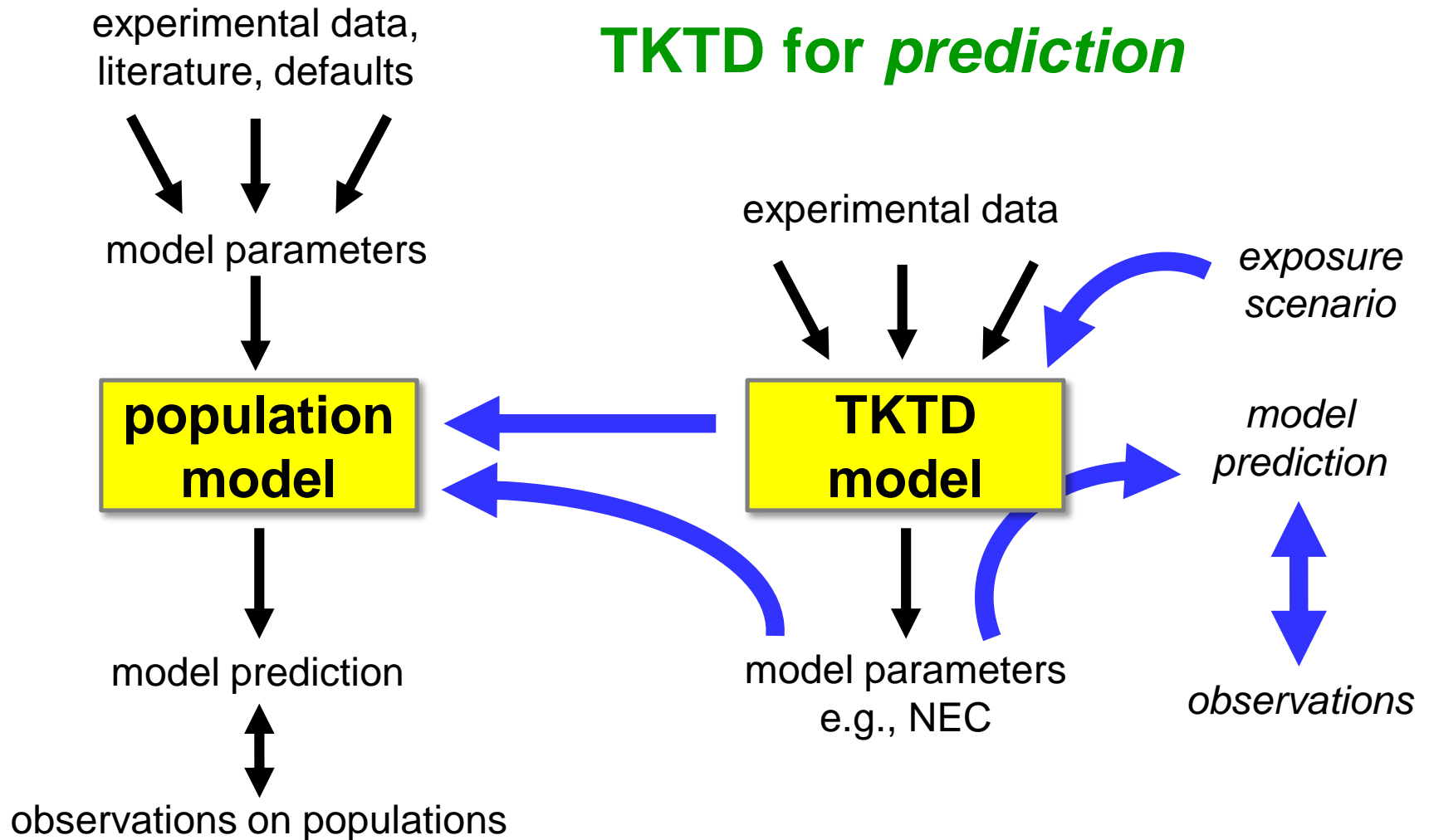
2d-LC50 = 23 (22-25)  $\mu\text{M}$   
 4d-LC50 = 19 (18-21)  $\mu\text{M}$   
 8d-LC50 = 18 (17-20)  $\mu\text{M}$



$k_d = 2.2$  (1.6-3.4)  $\text{d}^{-1}$   
 $m_w = 17$  (16-18)  $\mu\text{M}$   
 $b_w = 0.13$  (0.088-0.20)  $\mu\text{M}^{-1} \text{d}^{-1}$   
 $h_b = 0.028$  (0.013-0.050)  $\text{d}^{-1}$

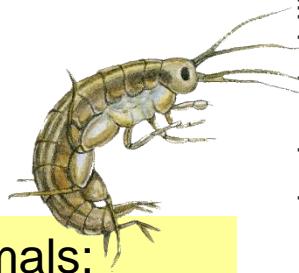
# What do quality elements mean?

---



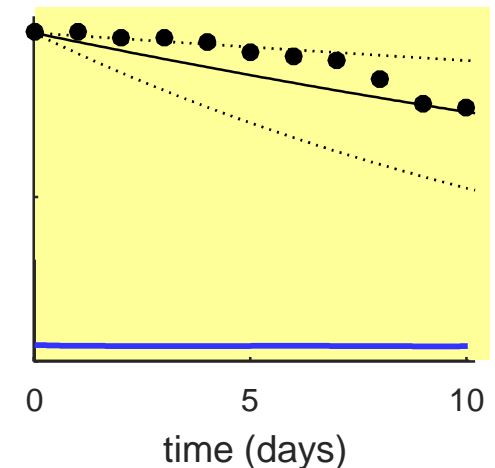
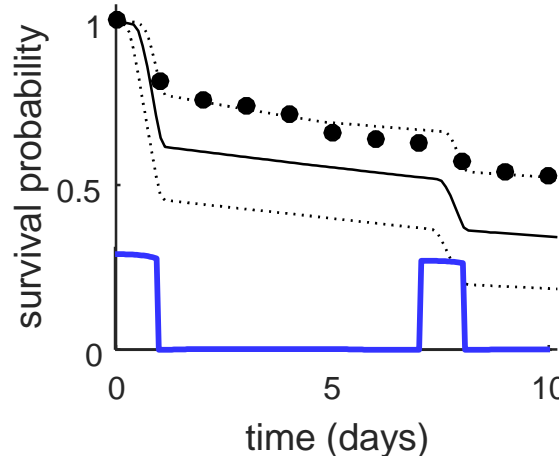
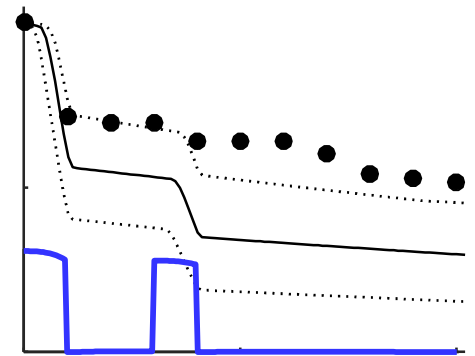
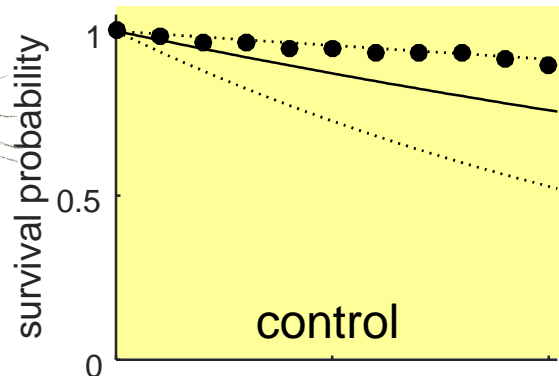
# Output validation possible

- Data *not* used for model calibration, incl. pulses
  - parameter uncertainty propagated to predictions



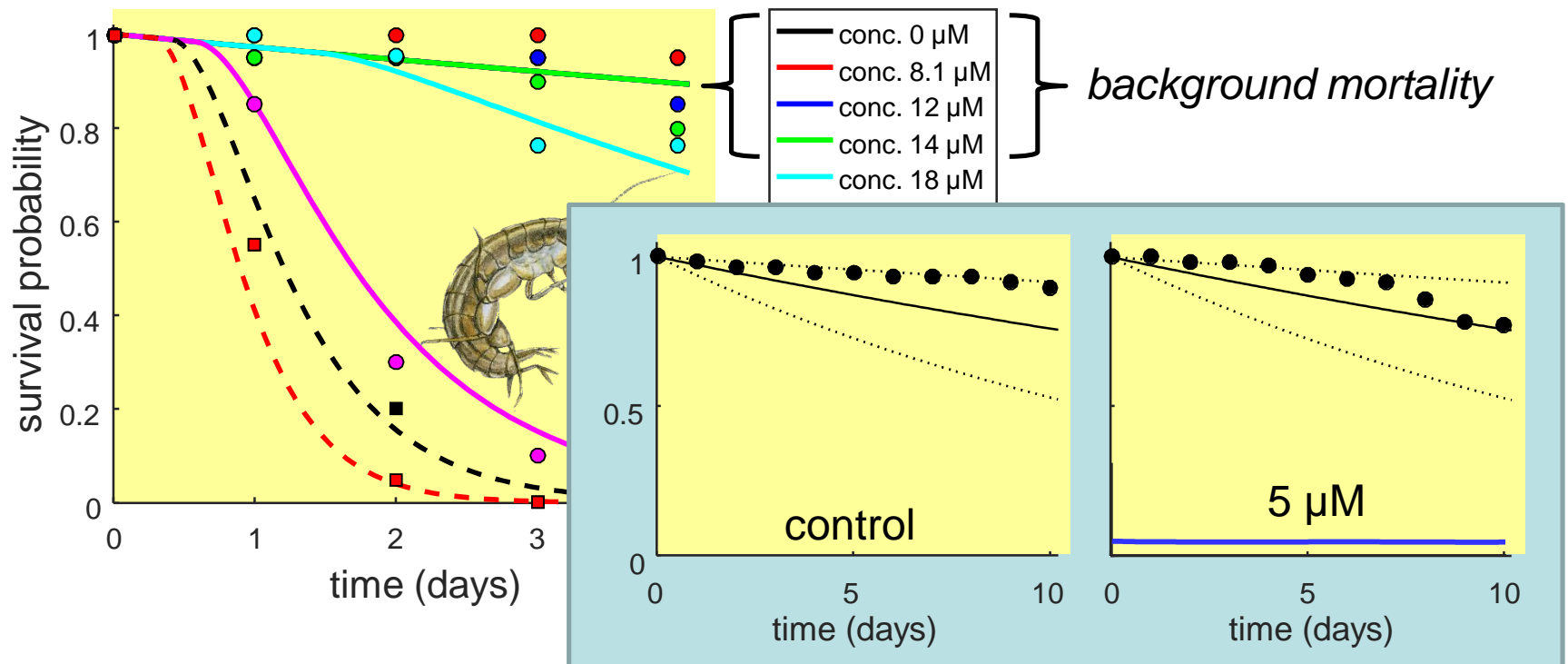
field-caught animals:

- calibration data spring
- validation data autumn



# Insight into data

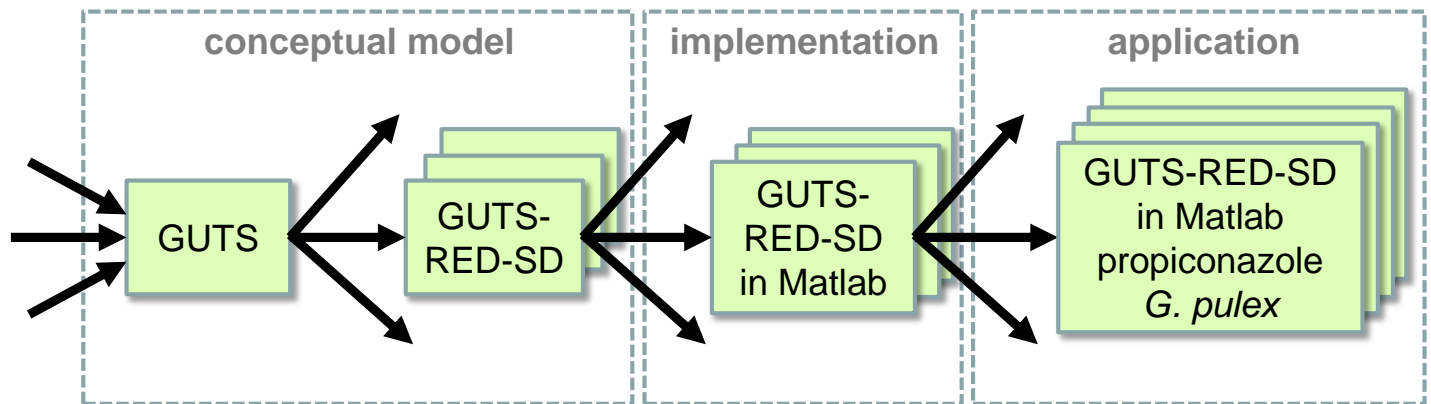
- Low doses: additional slow effect of propiconazole?
- 'Misfits' identify potentially relevant issues ...





# Concluding remarks 1

- Model quality *is* important, but ...
  - guidelines cannot be used in same way for TKTD models
  - separate conceptual model, implementations, applications
  - criteria should depend on intended model use
  - what to do with modularity in models?



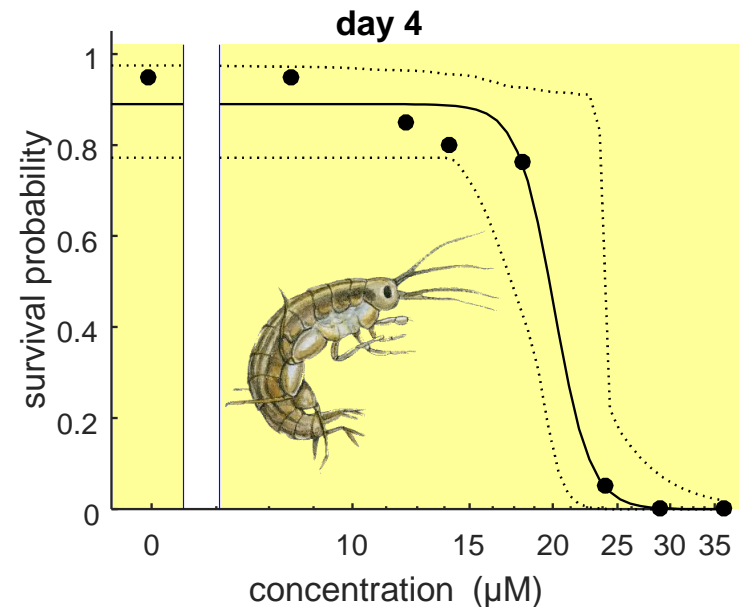
# Concluding remarks 2

- What quality does ERA need?
  - what is quality of current models?
  - requirements model and statistical treatment?
- Evaluate *current* models in same way and use the ones with the ‘highest quality’?

## OECD acute fish:

*“Normal statistical procedures are then employed ...”*

*“Confidence limits ... are determined using standard procedures ...”*



# Concluding remarks 2

---

- What quality does ERA need?
  - what is quality of current models?
  - requirements model and statistical treatment?
- Evaluate *current* models in same way and use the ones with the ‘highest quality’?

## Way forward

- Make a selection of most-promising models/modules
- evaluate/increase quality geared to intended use in ERA

# Thanks!

---

## CEFIC-LRI for funding project ECO39

- Ring testing of GUTS implementations
- E-book: description and guidance for GUTS
- see: [www.cefic-lri.org/projects/ ...](http://www.cefic-lri.org/projects/...) (ECO39)



UNIVERSITY  
*of York*



**Summer course:** Dynamic modelling of toxic effects,  
August 2018 (DK), see: [www.debtox.info](http://www.debtox.info)