



Roadmap for establishing DEBtox in environmental risk assessment (ERA) practice

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DEB symposium April 2019, Brest



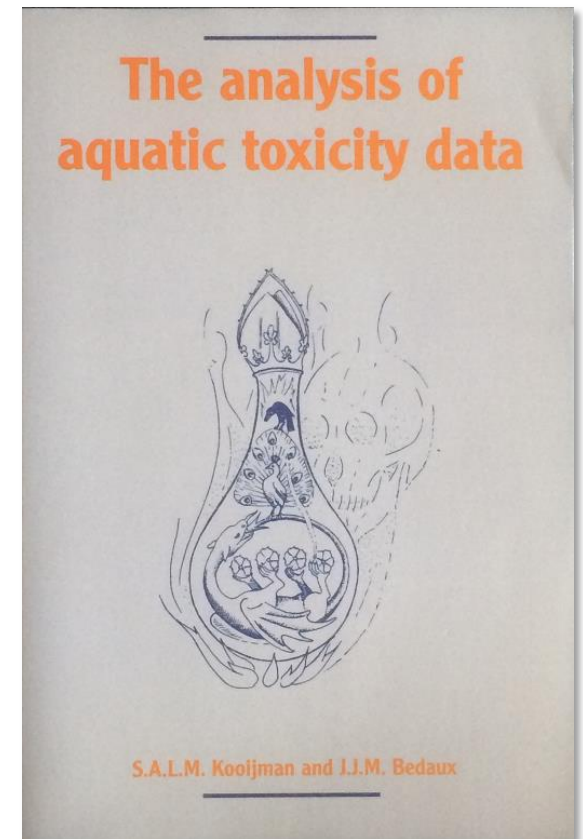
What is DEBtox?

Initially:

- Simplified DEB models as part of booklet/software:
 - Kooijman & Bedaux (1996)
 - updated by Billoir *et al* (2008) and Jager & Zimmer (2012)

More general:

- Application of *any* DEB-based model to toxicant stress
 - TKTD for sub-lethal effects



Recent developments

SCIENTIFIC OPINION



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doi: 10.2903/j.efsa.2018.5377

Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms

DEBtox

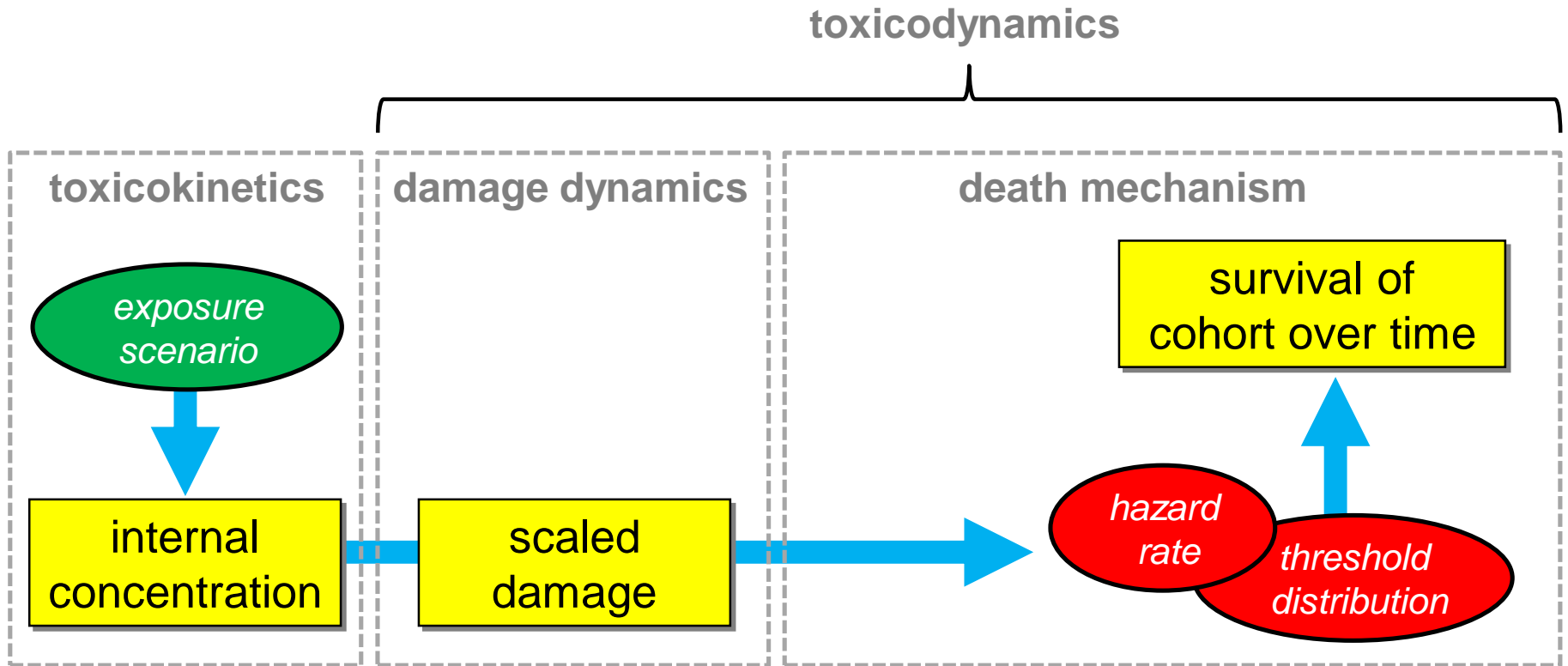
great potential ...
not ready for use

GUTS

ready for use in
risk assessment

What is GUTS?

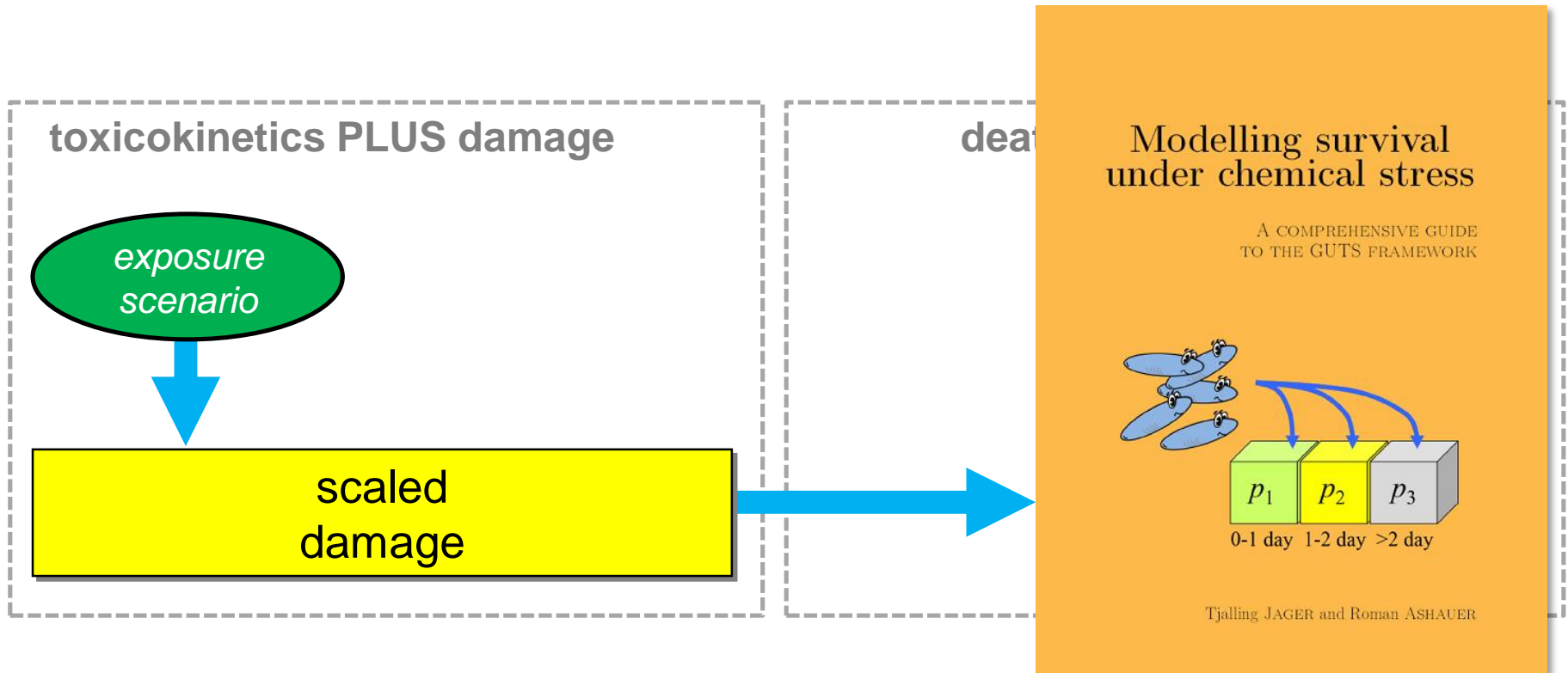
- Simple TKTD framework for effects on survival
 - death treated as a stochastic process



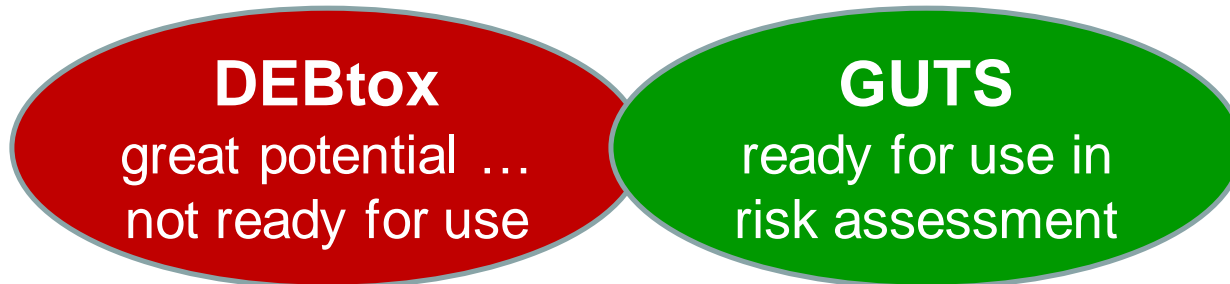
What is GUTS?

➤ Reduced models ...

- threshold distribution only → classic ‘CBR’ models
- hazard rate only → classic ‘DEBtox-acute’



Why is DEBtox 'not ready'?

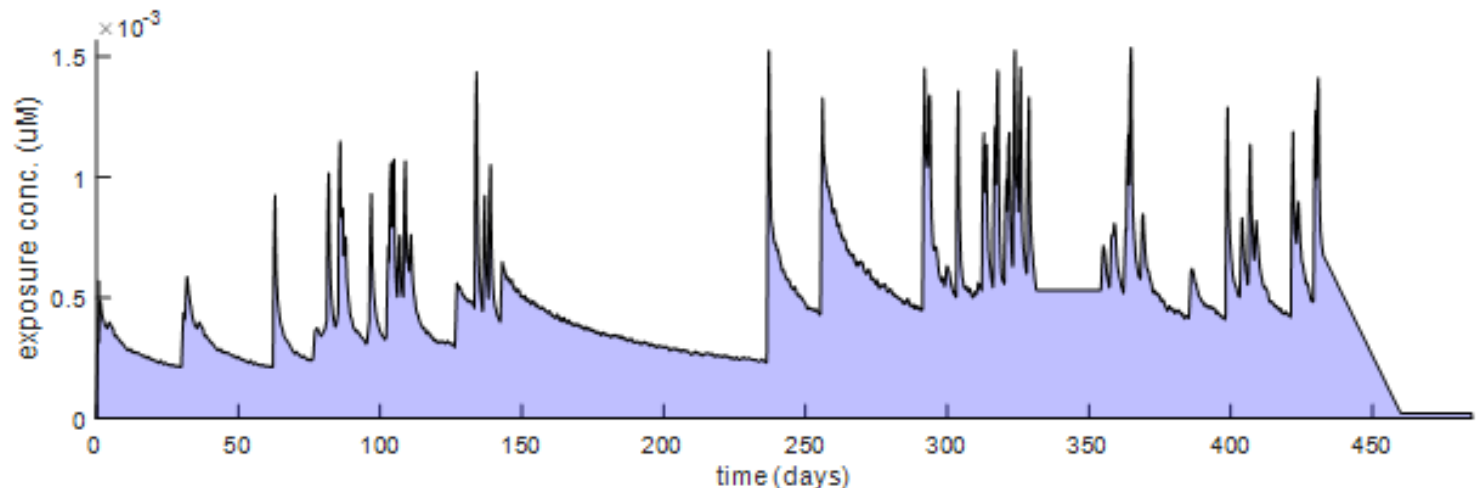


- EFSA mentions for DEBtox:
 - lack of relevant case studies published
 - lack of user-friendly software
- However, other issues require attention
 - application of DEBtox is more complex than GUTS ...

Why is DEBtox 'not ready'?

Context of my analysis

- ERA for pesticides following EFSA opinion
- Main workflow envisaged for TKTD models:
 - **parameterise** on lab. data (constant exposure)
 - **validate** on lab. data (pulsed exposure)
 - **predict** effects for output of fate model



Roadmap for DEBtox

most useful DEB model

revise toxicity module (GUTS)

strategy for time-varying exposure

case studies for ERA of pesticides



most useful DEB
model

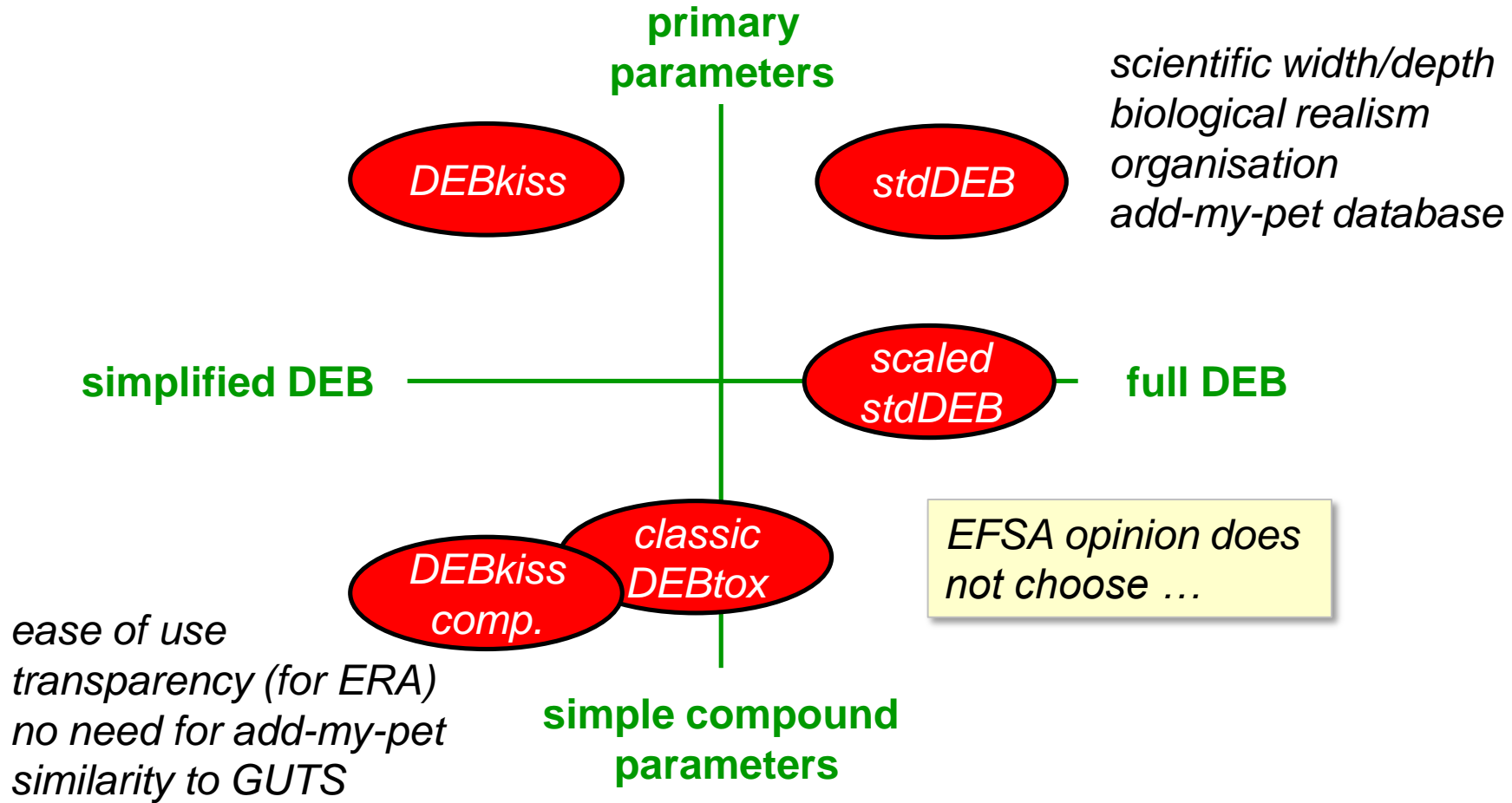
DEB-based models

What is DEBtox:

- Application of *any* DEB-based model to toxicant stress

most useful DEB model

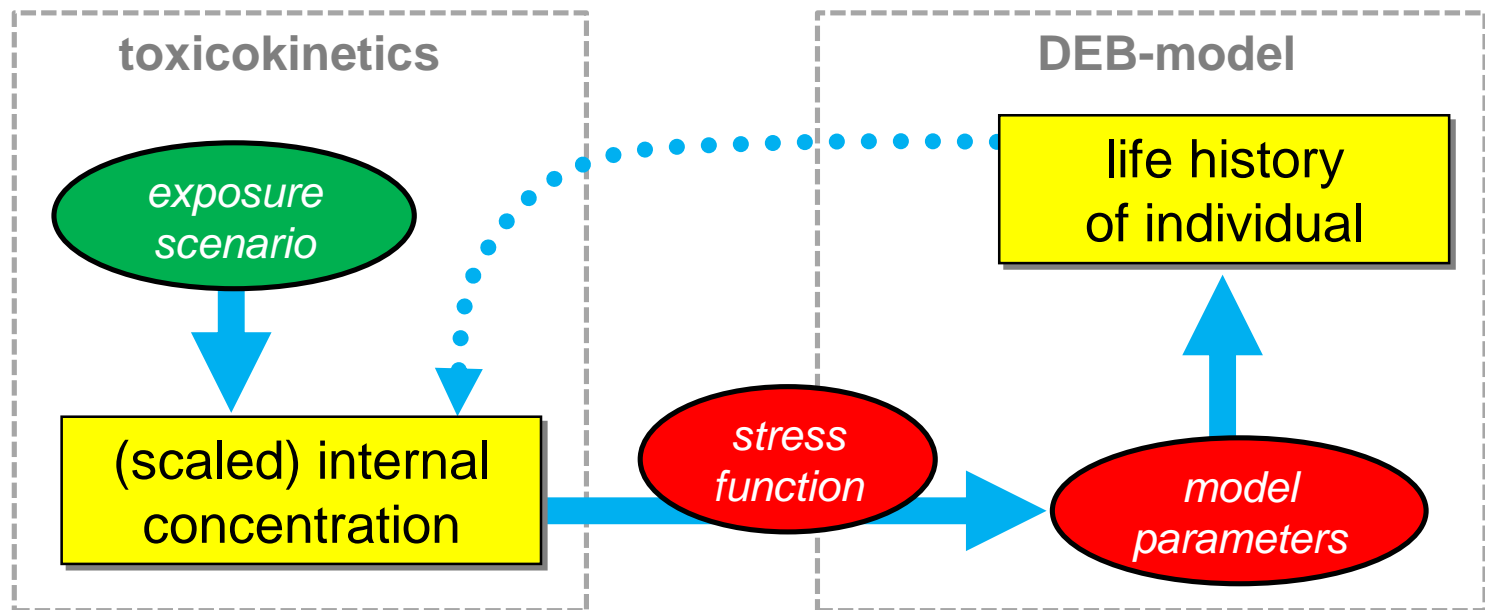
DEB-based models



Dealing with toxicants

➤ Classic DEBtox ...

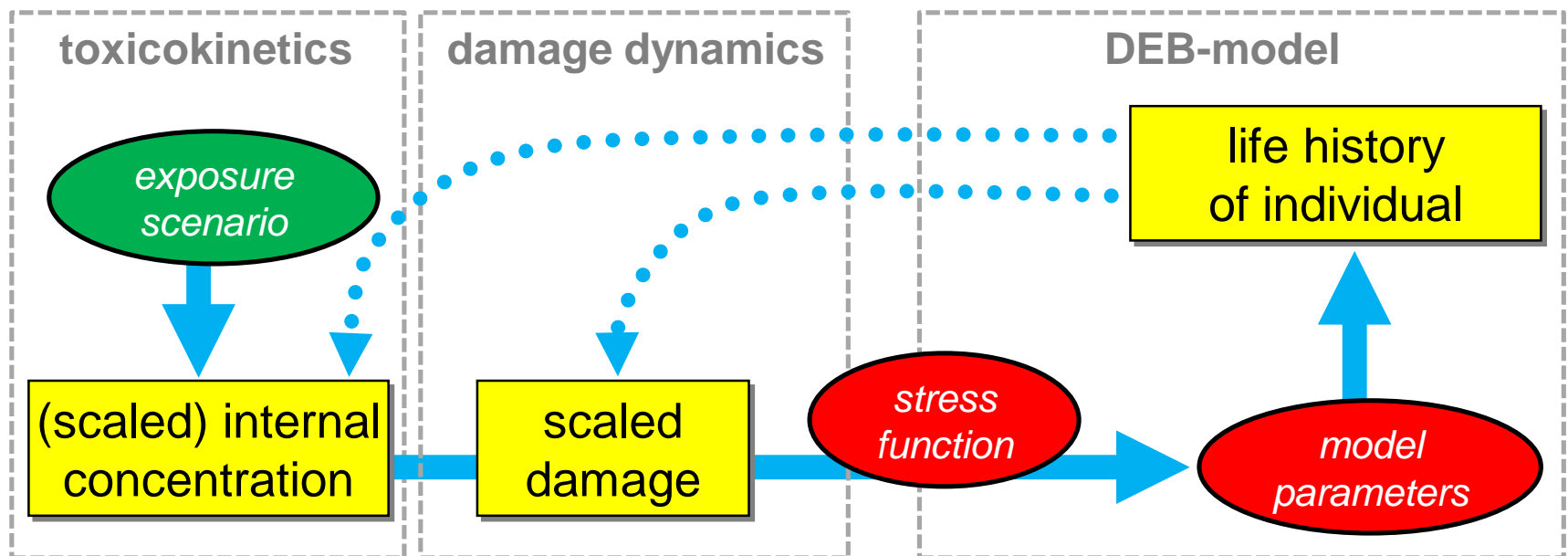
*dilution by growth
surface:volume ratio*



Dealing with toxicants

➤ Consider damage ...

dilution by growth
surface:volume ratio

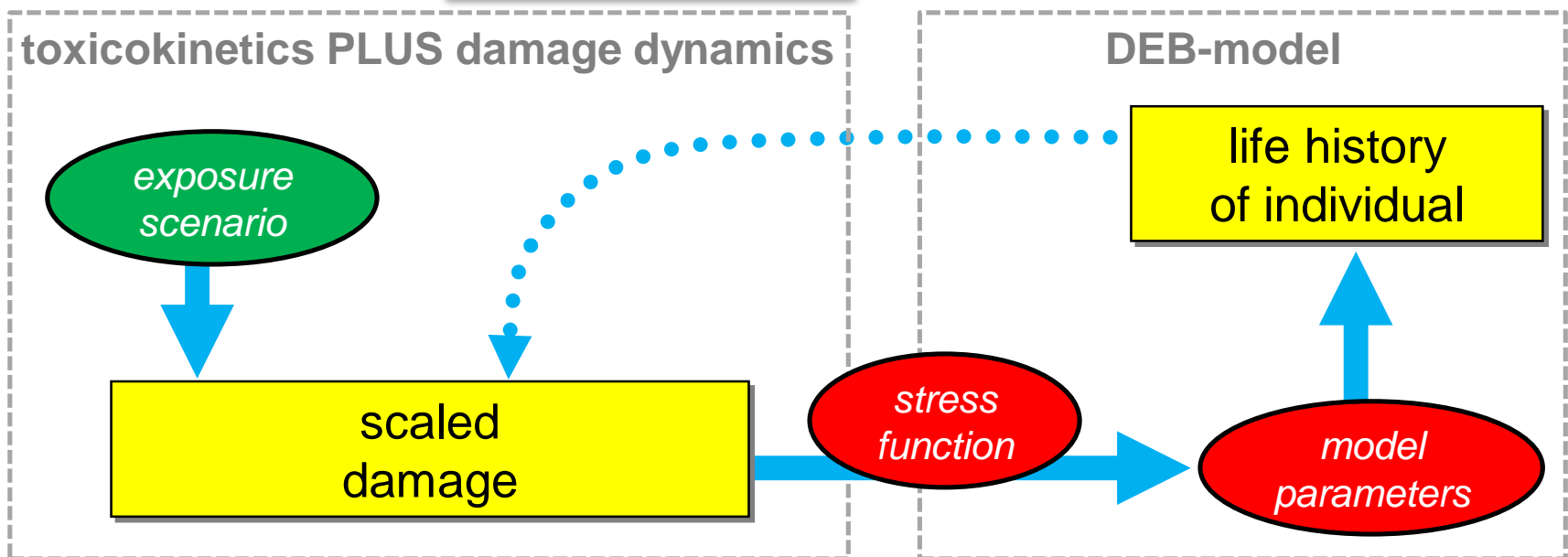


Dealing with toxicants

➤ Reduced model ...

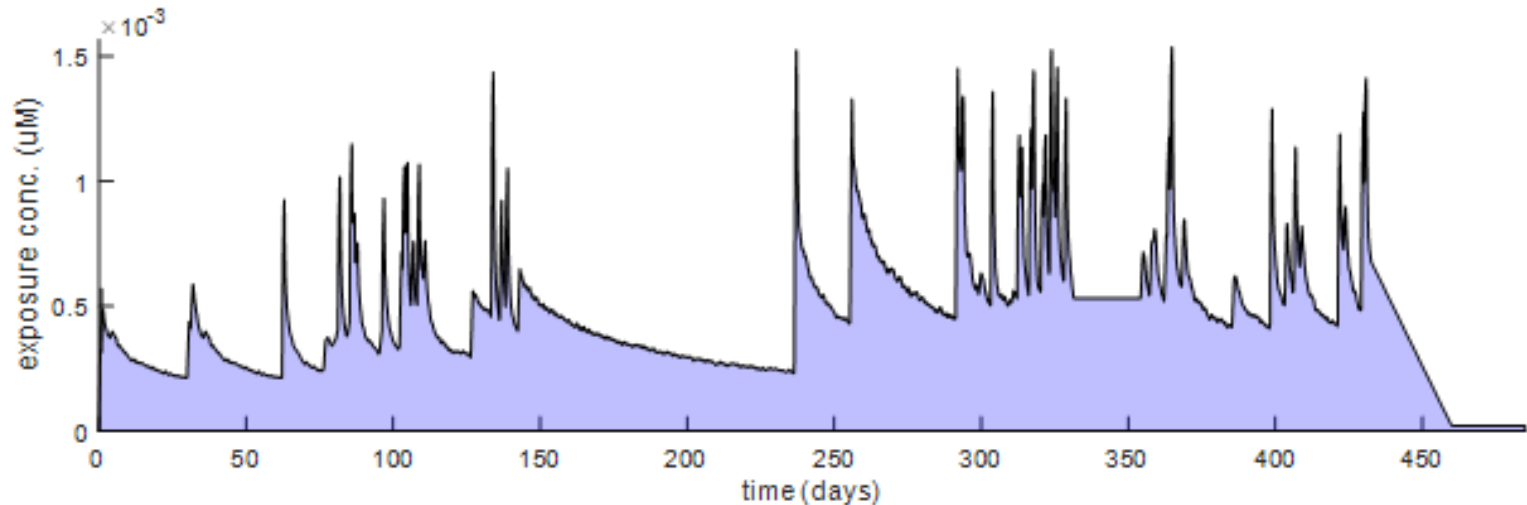
*dilution by growth?
surface:volume ratio?*

*losses with eggs?
reserve dynamics?*



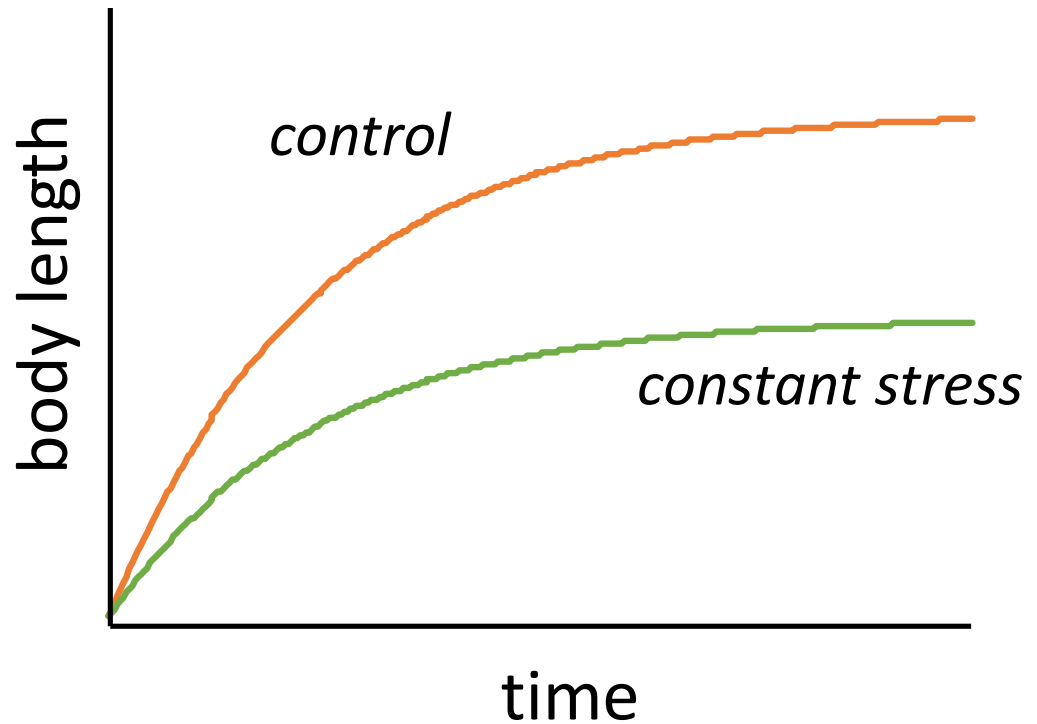
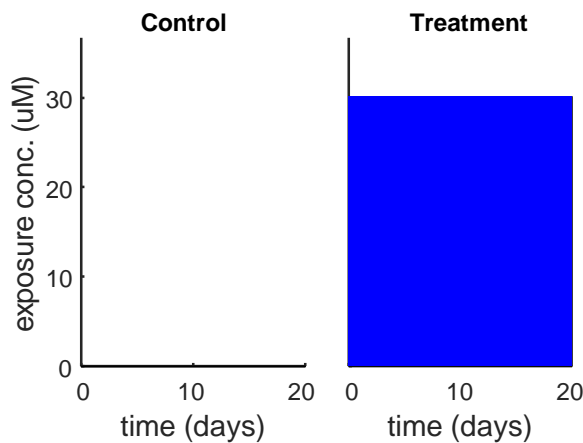
Time-varying exposure

- Most DEBtox applications: constant exposure
 - for pesticides, time-varying exposure is key
- Comes with challenges ...



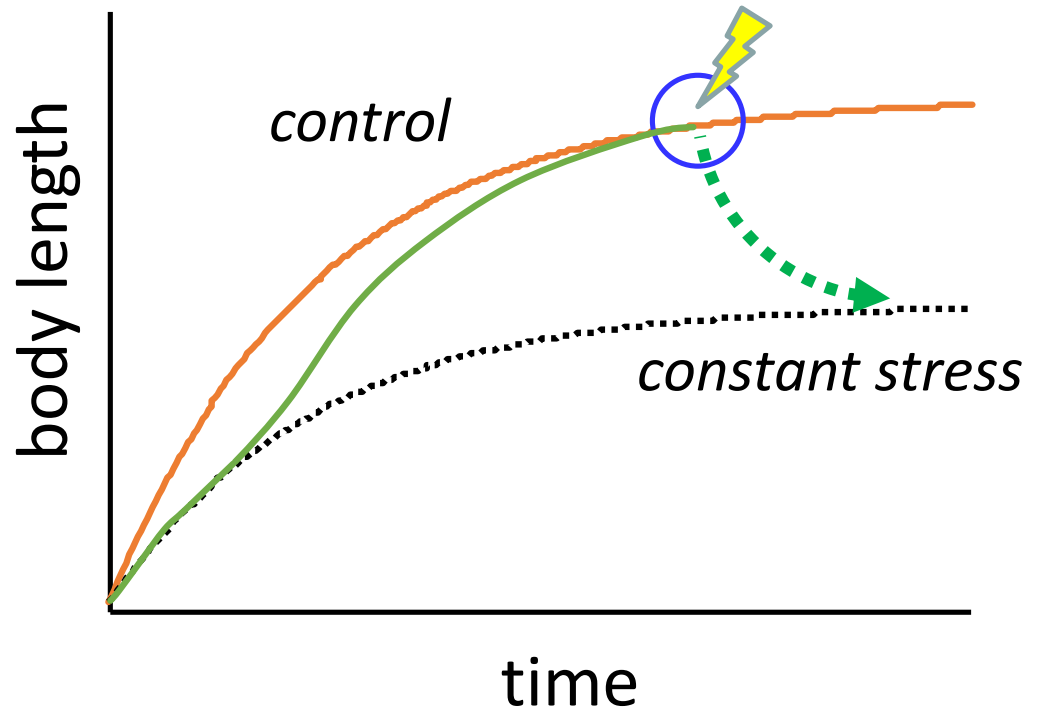
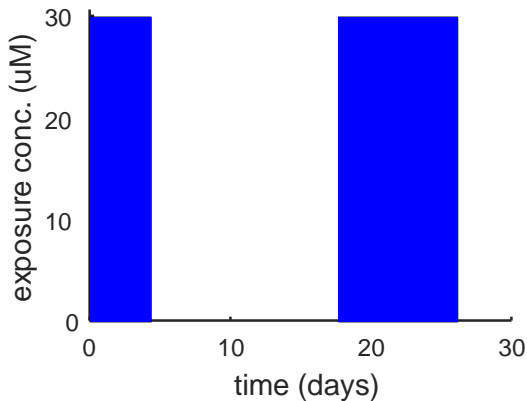
Starvation

- Constant stress on assimilation or maintenance leads to decrease in ultimate size



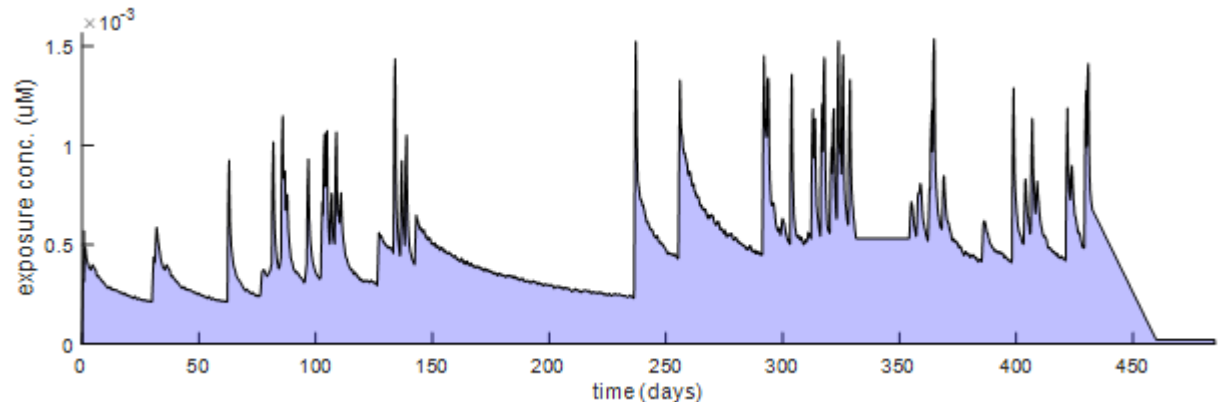
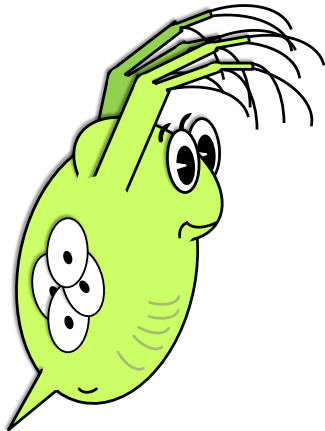
Starvation

- Constant stress on assimilation or maintenance leads to decrease in ultimate size
- For pulsed exposure, there can be recovery ...
- Starvation links to model choice ...



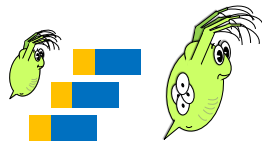
Long-term extrapolation

- EFSA: simulate individual over >1 year ...
- Life cycle *Daphnia* plays over several weeks ...
 - juvenile phase is short but very important

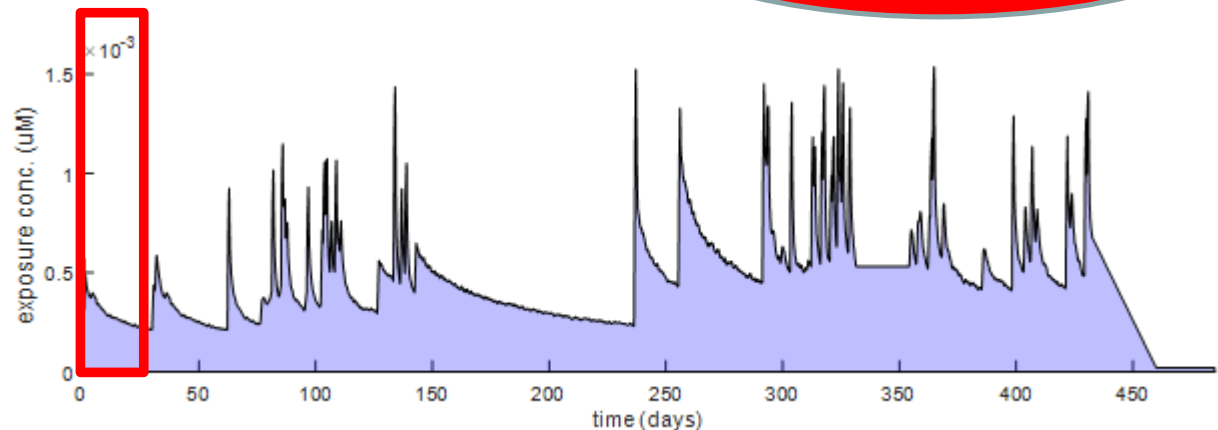
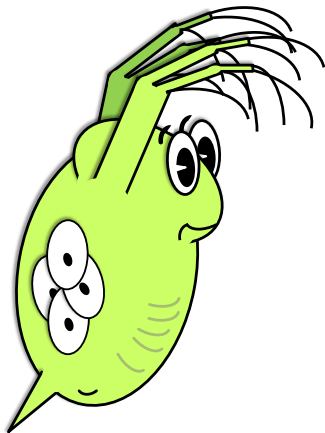


Long-term extrapolation

- EFSA: simulate individual over >1 year ...
- Life cycle *Daphnia* plays over several weeks ...
 - juvenile phase is short but very important
- Moving time window mentioned ...



Challenge
cross-generational
effects ...



Relevant case studies

>80 papers on 'DEBtox' (www.debtox.info/papers_debtox.html)

➤ Needs from ERA standpoint:

- pesticides and aquatic organisms
- extrapolation constant to pulsed exposure

➤ Additional needs:

- compare performance different models
- elucidate appropriate feedbacks
- measure size/quality of offspring
- test starvation rules

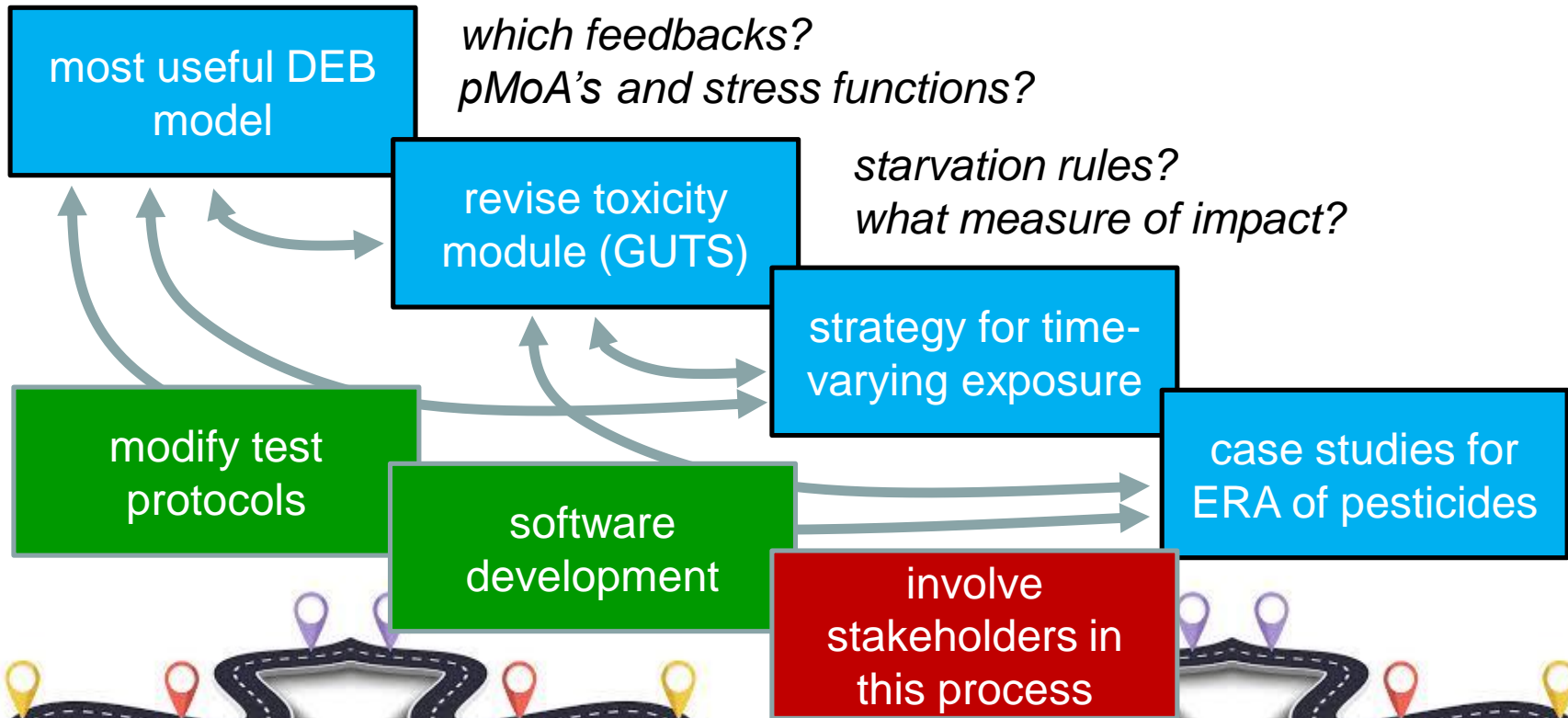
most useful DEB
model

revise toxicity
module

strategy for time-
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Roadmap for DEBtox

which one?





More information

On TKTD/DEBtox/GUTS: www.debtox.info

Several courses planned for 2019/2020 ...

Dedicated GUTS course 16-18 Oct. 2019

About DEBtox Research: www.debtox.nl

