A general modelling framework for environmental risk assessment – sublethal effects and starvation

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Objectives

Standard risk assessment can be further developed

- For environmental and human risk assessment chemicals are tested in standardised biotests on representative species
- These biotests use different species and different test designs to answer different questions:
  i.e. we measure bioconcentration in bluegill sunfish, survival in rainbow trout, effects on growth in medaka and effects on reproduction in zebrafish → all endpoints are used in the risk assessment, but not linked to each other mechanistically
- *We can gain important insights on the effects of chemicals if we can mechanistically link the effects on different species*

Nutritional status interacts with toxicity

- The nutritional status of organisms interacts with toxicity, e.g., starvation might change the metabolism which leads to higher intrinsic toxicity.
- This can lead to a comparably much higher toxicity due to the added effects of starvation.
- *It is thus crucial to understand the effects of starvation in the standard test organisms.*

Project aim: expand testing and better predictions

- We develop tools:
  - for 11 standard vertebrate test species,
  - that can be used to make best use out of already existing data to reduce the need for new animal tests,
  - that allow a mechanistic interpretation of standard studies,
  - that enable us to extrapolate to untested species and untested scenarios/exposure situations including starvation
- *We will make these tools publicly available to facilitate risk assessment based on mechanistic effect modelling*

Framework: Dynamic Energy Budget theory

The conceptual model for all species is fundamentally the same

- For all 11 species, we are using the same modelling framework, based on Dynamic Energy budget (DEB) theory
- All organisms have the same general metabolic organization (scheme presented below).
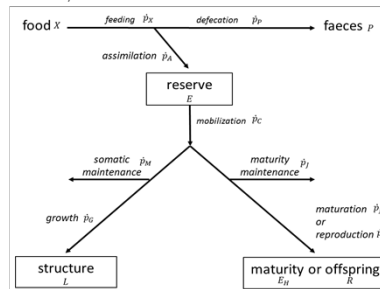
- Effects of chemicals are included as deviations on the energy allocated to the different processes.

The model account for differences in life history

- The standard DEB model assumes that organisms do not change their shape during ontogeny.
- While the basic metabolic organization is the same for all species, the models for the three different groups are different to accommodate for the differences in life-history.

| Group	Life-history fact	Model modification
Fish	Larval stage / metamorphosis	Metabolic acceleration
Mammals	Weaning	Fetal development
Birds	No specifics	None needed

The tools: Add-my-pet and DEBtool

We are using a publicly available toolbox and database

- The so-called Add-my-pet (AmP) database aims to collect and share:
  - referenced data on the energetics of animal species, such that the parameters of the standard Dynamic Energy Budget (DEB) model, can be estimated,
  - code for estimating DEB parameters from these data,
  - DEB parameter estimates,
- New entries are curated by an international board of 5 curators – scientists who apply and develop DEB in different disciplines
- All material is also publicly available and access is free.
- The published code mainly uses the toolbox DEBtool, which is a collection of well-tested Matlab routines that can be used to predict the life-history of organisms.

The parameters and models developed in the project will be made publicly available on the AmP database.

- The add-my-pet collection started at 2009/02/12 as part of the DEB tele course. It has 683 entries at 2017/04/21.
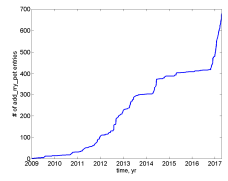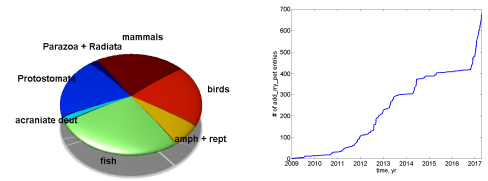
Species and life history

Endpoint	D. rerio	O. latipes	P. promelas	O. mykiss	O. cuniculus (new Zealand white)	R. norvegicus	M. arvalis	A. sylvaticus	M. musculus	A. Platyrhynchos	C. virginianus
Maximum body weight [g]	1	0.91	4	25400	5000	820	50	44	50	1100	250
Maximum body length [cm]	5	3.6	10	120	50	30	12	11	10	58	25
Age at birth [d]	5	11	6	54	32	22	21	24	20	25	23
Weight at birth [g]	2.3 10⁻³	6.5 10⁻⁴	7.4 10⁻⁴	0.032	70	7	2	2.5	1	40	6
Age at puberty [d]	75	60	200	628	168	38	11	60	26	365	168
Weight at puberty [g]	0.4	0.2	0.8	3500	3577	152	5	20	10	?	194
Maximum reproduction rate [#/d]	240	46	30	174	0.06	0.1	0.05	0.16	0.1	0.03	0.1
Maximum life span [yr]	3	6	5	11	9	4	5	6	4	29	10

2 birds

Bobwhite quail
Colinus virginianus

Mallard duck
Anas platyrhynchos

4 fish

5 mammals

Wood mouse
Apodemus sylvaticus

Common vole
Microtus arvalis

Rainbow trout
Oncorhynchus mykiss

House mouse
Mus musculus

Fathead minnow
Pimephales promelas

Zebrafish
Danio rerio

Medaka
Oryzias latipes
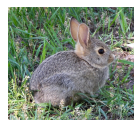
Rabbit
Oryctolagus cuniculus

Brown rat
Rattus norvegicus

Challenges and opportunities

Including starvation: are there general pattern across species and groups?

- Under starvation, organisms deviate from their usual metabolic behavior.
- For each of the groups, we will need different and very specific ways to model starvation responses.
- Some examples:
  - Fish can re-use part of their reproduction buffer under starvation, mammals. How do they do it? And is there any long-term damage connected to it?
  - Some birds deal with starvation during the migrations on regular basis. Does this mean that birds in general have a higher starvation tolerance?

Can we compare the laboratory species / strains to the wild type?

- The long-term aim of the project is to develop models that can be used for predicting effects of compounds under natural conditions. Is this possible for all species? If not, are there patterns in how parameters deviate between the wild type and the laboratory type?

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