Effects of depleted uranium on the metabolism of zebrafish, *Danio rerio*

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Introduction

The increasing demand for nuclear energy results in heightened levels of uranium (U) in aquatic ecosystems which present a potential health hazard to resident organisms. We address the effects of U on a well studied model organism: zebrafish, *Danio rerio*. Our objective was to mechanistically assess how chronic exposure to environmentally relevant concentrations of U perturbs the complex interplay between feeding, growth, maintenance, maturation and reproduction (= energetics) throughout the life-cycle of an individual.

To this end we analyzed literature-based and original zebrafish toxicity data within a same mass and energy balancing conceptual framework: Dynamic Energy Budget (DEB) theory [5]. The general philosophy is that effects are linked to the amount of internalized compound. Thus in order to quantify effects we must first quantify the uptake-elimination behavior of uranium and second understand which physiological process is perturbed by uranium.

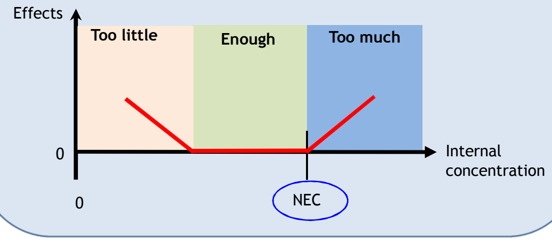
In this study we included a one compartment toxico-kinetic model with time varying coefficients [6] into a fully parameterized zebrafish DEB model [1]. The biomass of an individual is partitioned into two types of material: reserve and structure. Uptake and elimination is through structure and once inside uranium is assumed to be instantaniously partioned between both reserve and structure.

The model was applied to toxicity data in order to detect how the metabolism of zebrafish is affected by uranium.

Modeling toxic effects

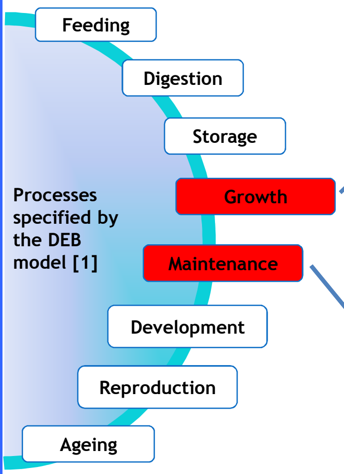
All internalized compounds are present in three ranges: enough, too little and too much [5]. Above and below the enough ranges effects are taken proportional to internal concentration.

Uranium being a non essential elements there is no too little range. The No effect internal Concentration, NEC, represents the internalized concentration after which a certain process is affected.



Results

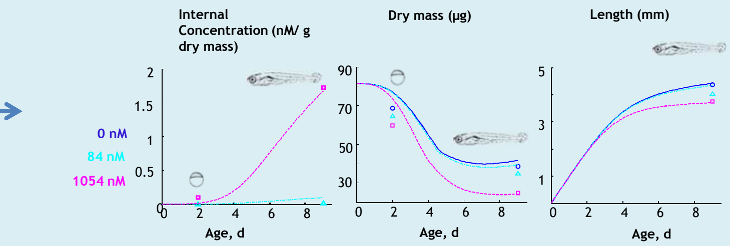
Uranium targets both somatic maintenance and growth processes



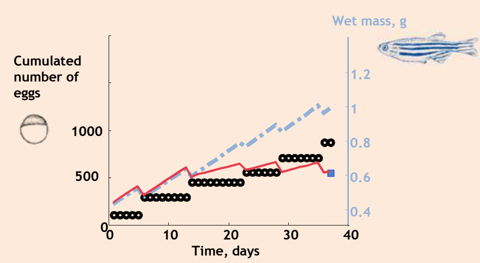
No effect internal concentration for growth: 28.9 nM per cm^3 of structure => 1.5 nM per litre of water

No effect internal concentration for maintenance: 32 nM per cm^3 of structure => 1.6 nM per litre of water

Symbols: mean values from [4]
Lines: DEB model predictions assuming an increase in costs for growth.



Final observed wet mass
Zebrafish DEB model prediction for wet mass assuming no effect of uranium
Zebrafish DEB model predictions for wet mass assuming that uranium increases somatic maintenance costs

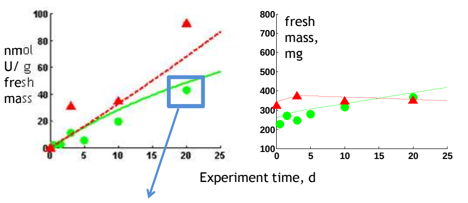


Individual female exposed to 84 nM uranium for 37 days (this study)

Energy invested in reproduction is resorbed to pay for increased somatic maintenance costs

Energetics affects toxico-kinetics

20 day exposure to 420 nM from two separate literature studies. The model explains the difference in observed mean bioaccumulation between both studies by dilution by growth (top row) and partly of the large inter-individual variability by inter-individual differences in prior feeding history (bottom row)

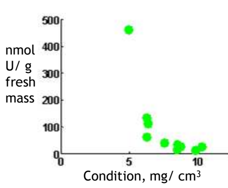


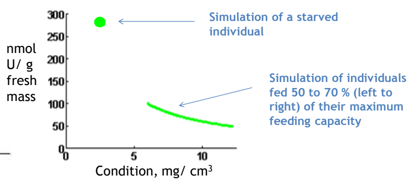
mean values from [2]
mean values from [3]

Lines: DEB model predictions

Observed values of internal concentration for each individual sampled at the last time point (from [3]) as a function of its condition (wet mass over cubed length):

DEB model predictions for internal concentration after 20 d exposure to 420 nM U assuming inter-individual differences in prior feeding history:





Conclusions

The Zebrafish DEB model [1] enables us to do the book keeping on mass/ energy flows in and out of each compartment. The dynamics of each of the compartments is very much dependent on the nutritional status of the individual = FEEDING.

Bioaccumulation data shows a very high inter-individual variability. Part of this variability is explained by the DEB model as resulting from dilution by growth and prior feeding history.

Thus energetics affects toxico-kinetics and so effects of uranium. Alternatively effects of uranium affects toxico-kinetics. The significance of this work is that we address how these issues are related and derive conclusions which are independent of experimental protocol and coherent with a very large body of literature on zebrafish eco-physiology.

The amount of initial reserve and amount of reproduction material in combination with feeding for a given female conditions the intensity of effects. Thus growth and reproduction for adult data should not be averaged for groups of adults if we want to make sense of toxicity data and derive No internal Effect concentrations.

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Acknowledgements: This research was supported by the IRSN project ENVIROM and the Provence-Alpes-Côtes d'Azur region