Développement d'un modèle toxicocinetique à base physiologique décrivant la bioaccumulation par voie alimentaire d'un acide perfluoroalkyl sulfonique chez la truite arc-en-ciel (oncorhynchus mykiss)

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Development of a Physiologically Based ToxicoKinetic (PBTK) model describing the bioaccumulation of a perfluorinated substance in rainbow trout (*Onchorynchus mykiss*)

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• INTRODUCTION

Due to their unique physico-chemical properties, such as good thermic and chemical stability, **perfluorinated compounds (PFASs)** are ubiquitous in the environment and bioaccumulate in aquatic organisms. However, mechanistic models explaining the PFAS fate are still limited in aquatic vertebrates. **PBTK model** is a powerful tool for describing the absorption, distribution, metabolisation and excretion processes of xenobiotics.

This study aims to calibrate a descriptive PBTK model applicable to the perfluorooctane sulfonate (PFOS) in adult rainbow trout thanks to an experimental data set (Goeritz et al., 2013).

• METHODOLOGY

STARTING MODELS

- **Nichols et al., 2004**

  Advantage: Dietary uptake modeled for rainbow trout

  Limitation: Not directly applicable to PFASs
- **Ng and Hungerbühler, 2013**

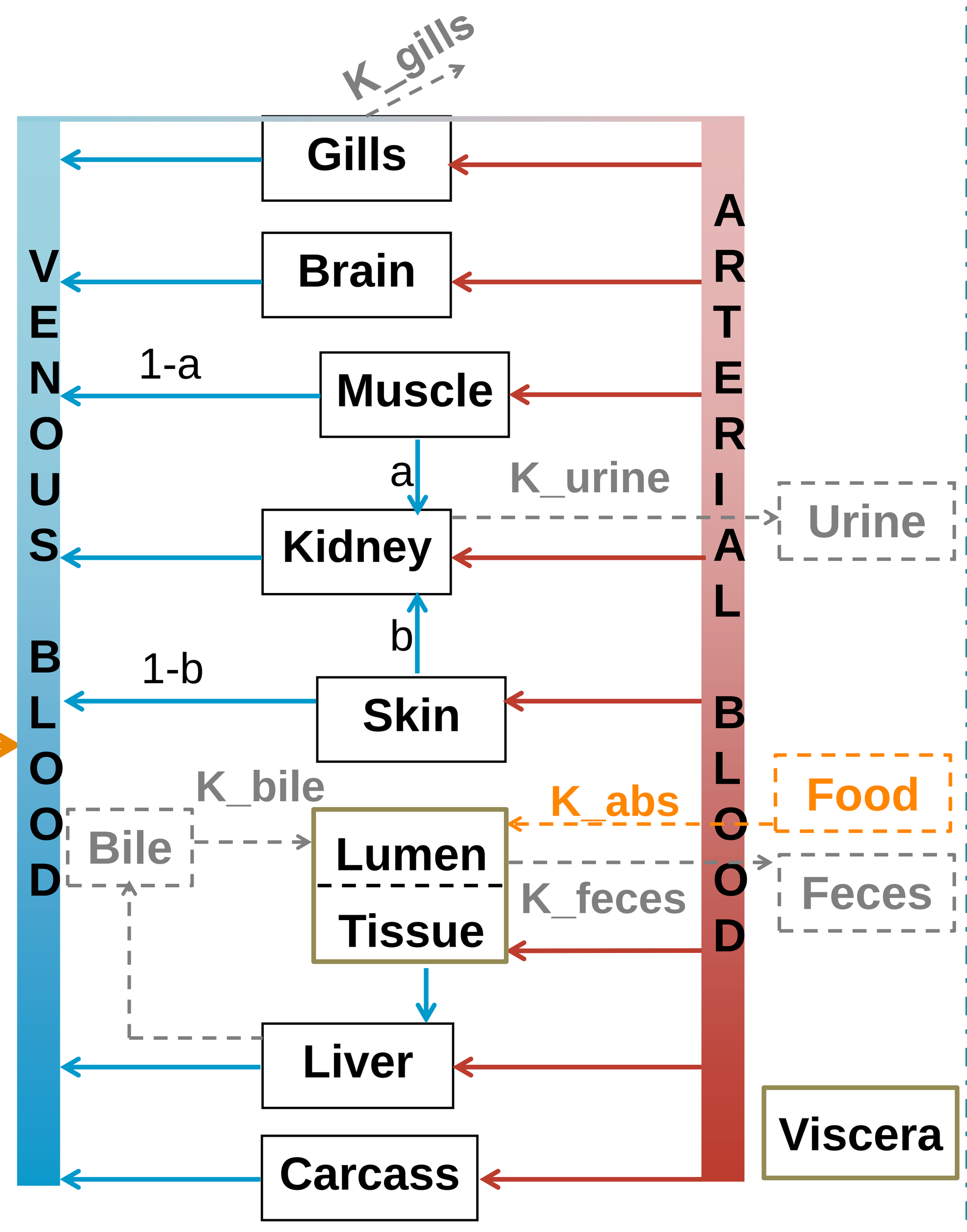
  Advantage: Applicable to PFAS

  Limitation: Complex model implemented with mammal protein parameters and absorption from water only

HYPOTHESES OF THE PRESENT MODEL

- Growth of individuals taken into account
- Elimination from feces in addition to urine, bile, gills
- Dietary uptake only (absorption from gills considered as negligible)
- No metabolisation of PFOS

CONCEPTUALISATION

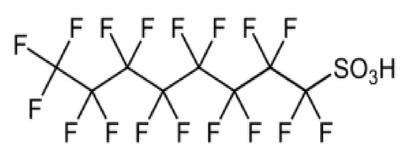


PARAMETRISATION & CALIBRATION

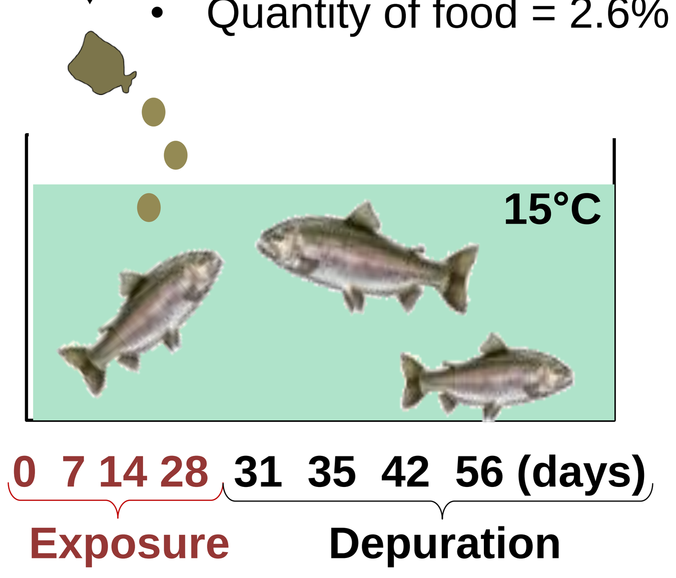
- Many physiological parameters for rainbow trout available
- Calibration with data from Goeritz et al., 2013 → Visual fitting

EXPERIMENTAL DESIGN

(Goeritz et al., 2013)



- [PFOS] in the food = 172 ng.g^{-1}
- Quantity of food = 2.6% of the total biomass (twice a day)

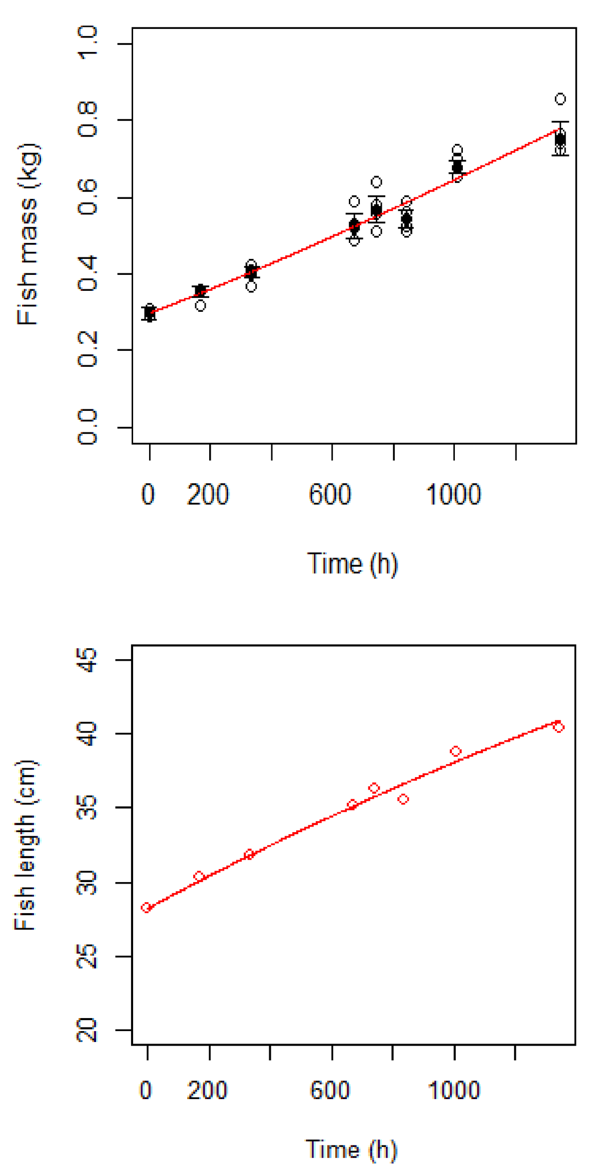


Sampled organs:
- ✓ Blood
- ✓ Gills
- ✓ Muscle
- ✓ Kidney
- ✓ Skin
- ✓ Liver
- ✓ Carcass

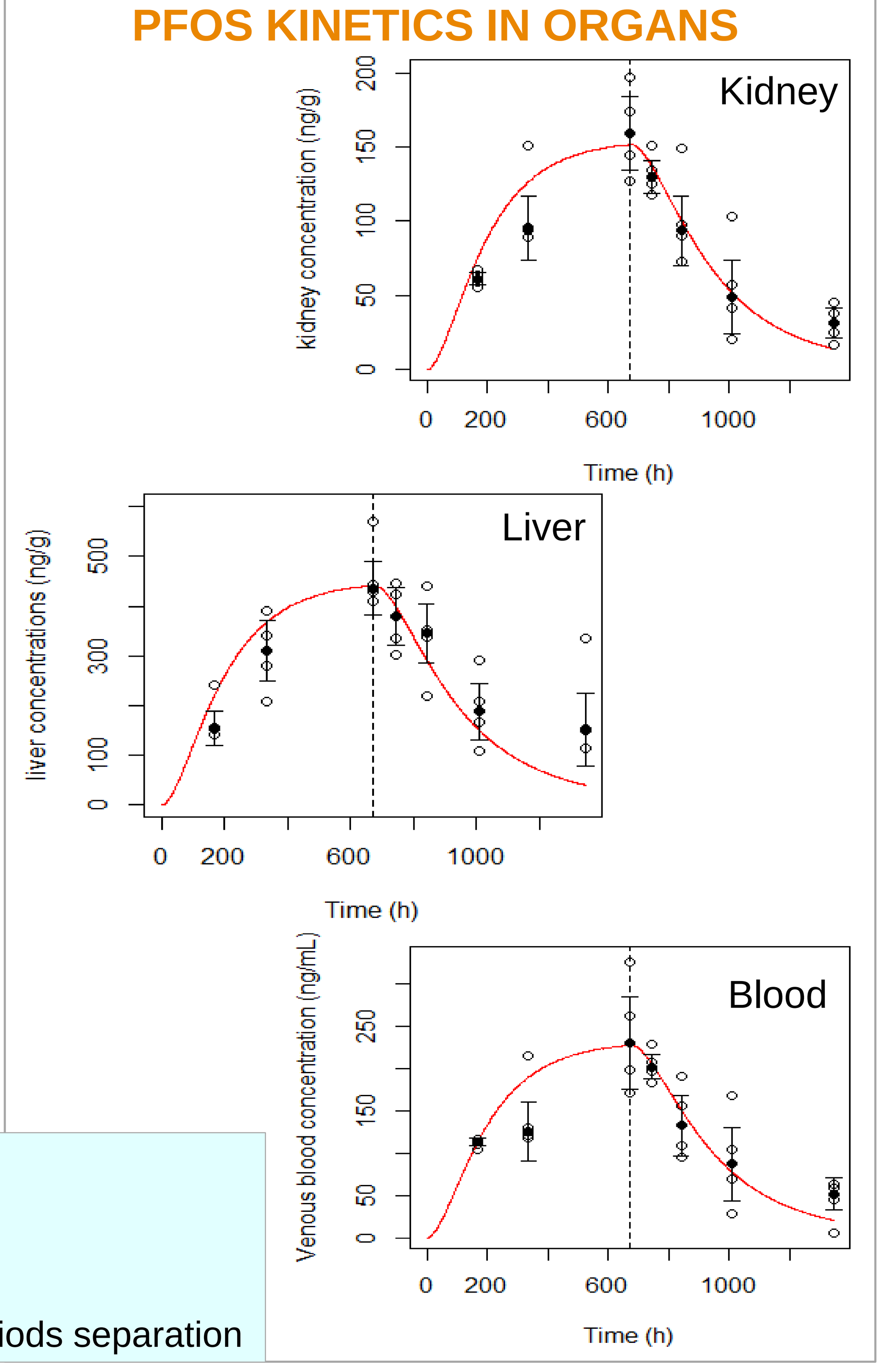
Analysis of PFOS: LC-MS/MS

• RESULTS OF MODELLING

FISH GROWTH



PFOS KINETICS IN ORGANS

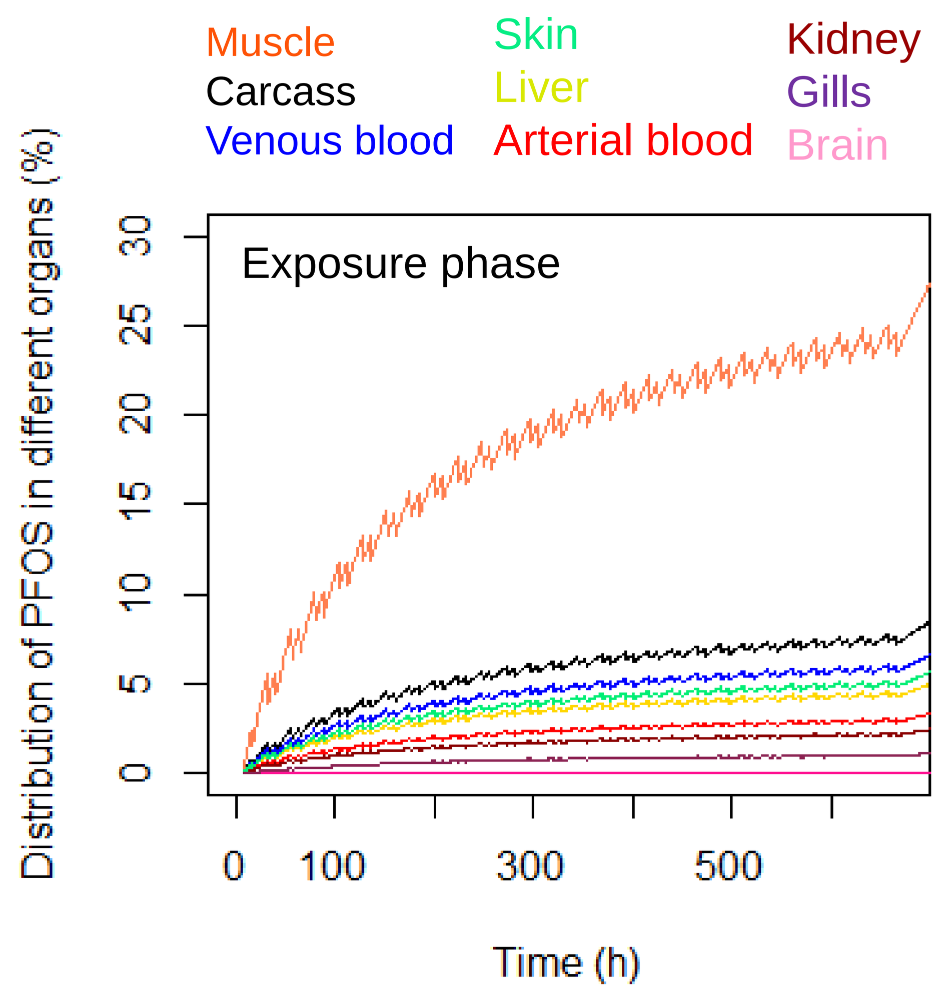


- ○ Observed data
- ● Mean of observed data
- ○ Prediction
- — Prediction
- ······ Exposure/depuration periods separation

CONTRIBUTION OF ORGANS IN THE DISTRIBUTION OF PFOS

Relative distribution (%) =

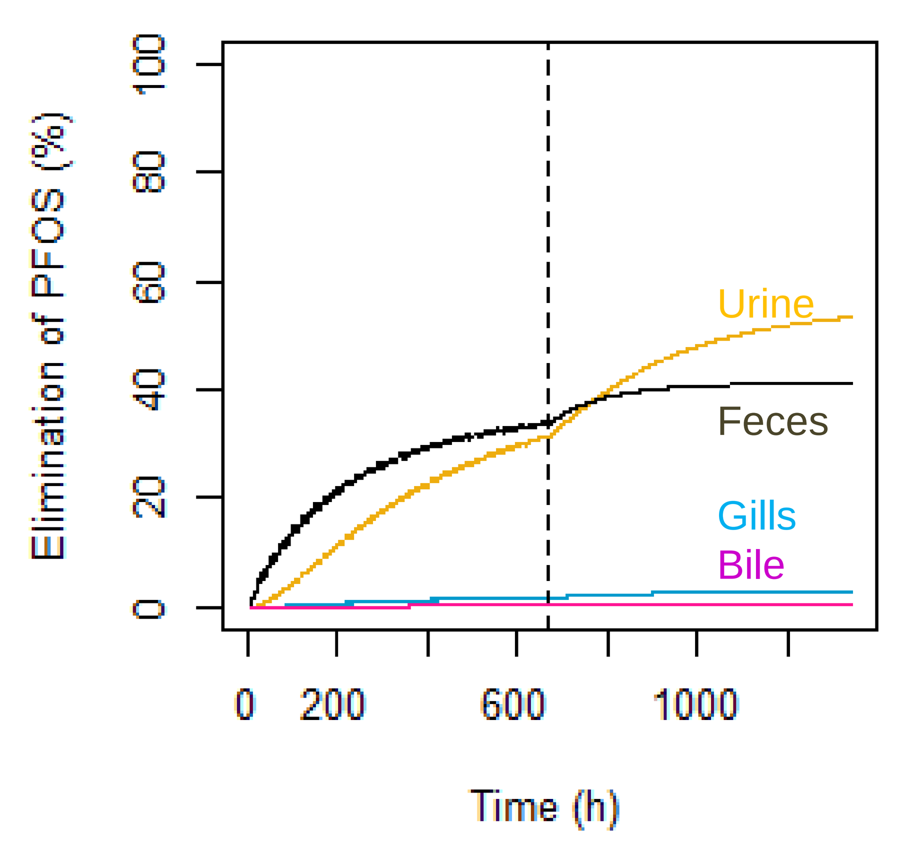
$$\frac{[PFOS]\ (ng.g^{-1}) \times \text{mass organ (g)}}{\text{Quantity of PFOS in all organs (ng)}}$$



CONTRIBUTION OF THE ELIMINATION PATHWAYS

Relative contribution (%) =

$$\frac{\text{Quantity of PFOS eliminated by urine, bile, feces or gills}}{\text{Quantity of PFOS administred to fish}}$$



• DISCUSSION & PERSPECTIVES

- Fish growth and PFOS kinetics in organs fit well with data of Goeritz and al. (2013)
- Fecal elimination is shown to be an important elimination pathway of PFOS for rainbow trout exposed to contaminated food

  However:
  - ➢ There are still some uncertainties of elimination rates and elimination pathways
  - ➢ The modeled kidney and liver elimination is faster than experimental data at the end of the experiment → Additional processes to consider, such as enterohepatic or urinary reabsorption (PFOS-Oats bindings)
  - ➢ The modeled blood elimination is faster than experimental data at the end of the experiment → Additional interactions to consider: PFAS-serum albumin and PFAS-L-FABP

Perspectives: **Water temperature controls many physiological processes in fish. Since this variable is important for mechanisms of absorption, distribution and elimination of contaminants, the present PBTK model will take into account variations of the water temperature**

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