Three perspectives on modelling for ecological risk assessment

A toy example with a simple one-compartment toxicokinetic model

Sandrine Charles and Roman Ashauer

2023-02-08

Abstract

We provide here a toy example based on the use of a simple one-compartment toxicokinetic model to describe the bioaccumulation of chemical substances within the whole body of living organisms. From a simple ODE model, we will illustrate : (P1) how to simulate both accumulation and depuration phases under constant exposure and to compare model outputs to observed data; (P2) how to fit such a model on data without using any prior information on the model (Frequentist point of view); (3) how to benefit of prior information in combination with knowledge in data to update the calibration results (Bayesian point of view).

Introduction

Perform calculations under the three perspectives as described within the main document

Case study

Based on (Ashauer et al. 2010). Data set on Malathion

```
# Load the data set
df <- read.table("data.txt", header = TRUE, sep = "")
# Plot the raw data
ggplot(data = df, aes(x = time, y = conc)) +
  geom_point() +
  xlab("Time (hours)") +
  ylab("Internal measured concentration (picomol/g wet weight)") +
  geom_vline(xintercept = 1, linetype="dashed")
```

A toxicokinetic (TK) model simply describing bioaccumulation of chemical substances within the whole body of living organisms is based on a set of two differential equations (Charles, Ratier, and Lopes 2021):

$$\begin{cases} \dfrac{dC}{dt}(t) = k_u \times C_w - k_e \times C(t) \quad \forall\, 0 \leq t \leq t_c & \text{(1a)} \\ \dfrac{dC}{dt}(t) = -k_e \times C(t) \quad \forall\, t > t_c & \text{(1b)} \end{cases}$$

where t_c stands for the duration of the accumulation phase (namely the end of the exposure period, before organisms are transferred into a clean medium). Quantity C_w stands for the exposure concentration in water, while variable $C(t)$ corresponds to the internal concentration within the whole body of organisms over time t. Parameters k_u and k_e are the uptake and the elimination rates, respectively.

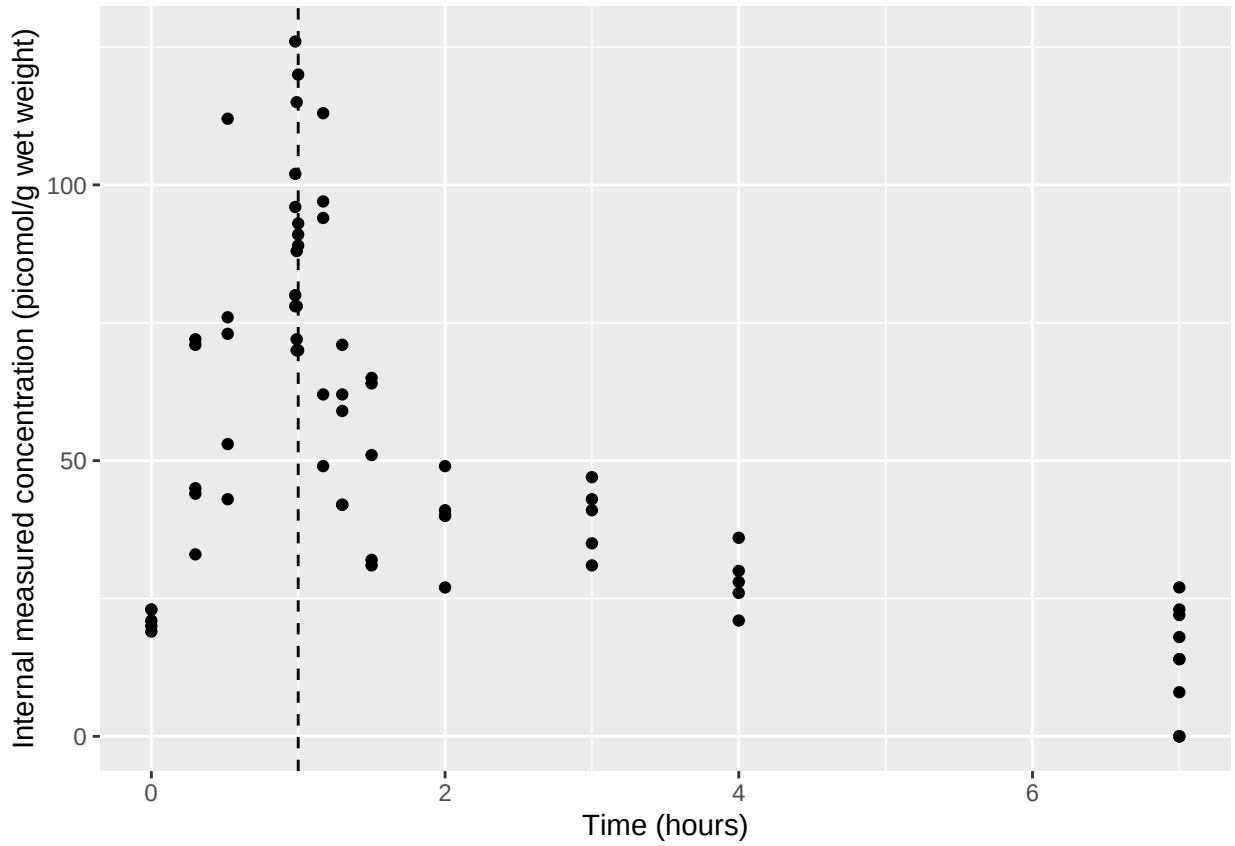

Figure 1: Raw data vizualisation. the vertical dashed line stands for the end of the accumulation phase ($t_c = 1$ day. Exposure concentration equals 1.485 picomol/ml.

Perspective 1

Perspective 2

Perspective 3

Fit the one compartment model under a Bayesian framework, with the R-package `rbioacc` (Ratier and Charles 2022). The same calculation can be easily reproduced on-line with the MOSAIC web platform and the `bioacc` module: https://mosaic.univ-lyon1.fr/bioacc

```
# Prepare the data to be use in the `rbioacc` package
mdf <- modelData(df, time_accumulation = 1, )
# fit the TK model built by default from the data
fit <- fitTK(mdf, refresh = 0)
```

```
# Display the corresponding equation of the model
equations(fit, df)
```

```
[1] "$\\frac{dC_{p}(t)}{dt} = k_{uw}\\times c_{w} - (k_{ee}) \\times C_{p}(t),\\ for\\ 0 \\leq t \\leq
[2] "$\\frac{dC_{p}(t)}{dt} = -(k_{ee}) \\times C_{p}(t),\\ for\\ t > t_{c}$"
```

```
# Check accordance with equations
```

References

Appendix: Raw data

```
df <- read.table("data.txt", header = TRUE, sep = "")
kable(head(df), format="latex")
```

time	conc	replicate	expw
0.0	23	1	1.485
0.0	19	2	1.485
0.0	20	3	1.485
0.0	21	4	1.485
0.0	23	5	1.485
0.3	44	1	1.485

Ashauer, Roman, Ivo Caravatti, Anita Hintermeister, and Beate Escher. 2010. "Bioaccumulation kinetics of organic xenobiotic pollutants in the freshwater invertebrate Gammarus pulex modeled with prediction intervals." *Environmental Toxicology and Chemistry* 29 (7): 1625–36. https://doi.org/10.1002/etc.175.

Charles, Sandrine, Aude Ratier, and Christelle Lopes. 2021. "Generic Solving of One-compartment Toxicokinetic Models." *Journal of Exploratory Research in Pharmacology* 6 (4): 158–67. https://doi.org/10.14218/jerp.2021.00024.

Ratier, Aude, and Sandrine Charles. 2022. "Accumulation-depuration data collection in support of toxicokinetic modelling." *Nature, Scientific Data* 9 (1): 130. https://doi.org/10.1038/s41597-022-01248-y.