BODY-BURDEN MODEL (BBM) FOR BIRDS

Equations writing, state variables and parameters

Authors

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Introduction

The theoretical basis of the body burden modelling (BBM) is not new (Craig and Grzonka, 1991; Buckley et al., 1997). Originating in the field of pharmacology, the principle of this modelling approach was to model the individual accumulation of the chemical of interest (hereafter referred to as toxicokinetics) over time by a simple rate balance equation written as follows:

$$\{Dose\ rate\} = \{Intake\} - \{Elimination\ rate\}$$

Thus, the BBM allows comparison of the cumulative body burden with published values for the minimum toxic dose and derived values for the minimum guideline dose for the chemical of interest.

From the generic equation above, different assumptions lead to different versions of the BBM. To keep the model simple, the elimination rate is usually assumed to be proportional to the internal dose, which is a first order (linear) approximation of a non-linear dependence. This simplification is expected to hold to some extent for small doses.

Applied to birds, toxicokinetic (TK) modelling, together with information on feeding patterns in risk assessment, can help to reduce uncertainties associated with acute laboratory studies in terms of dosing and internal exposure, i.e. the bioavailability of the substance at the target site (EFSA et al., 2023).

Physiologically based toxicokinetics (PBTK) models may be preferred to mathematically describe the time course of the internal concentration as the net result of absorption, distribution, metabolism and excretion (ADME). Asd these models are usually complex and data intensive, relatively simple models that follow the total body burden may be more practical and sufficient for wildlife risk assessment of pesticides. Indeed, in such situations, it is more important to have operational models that can be applied in complex situations (Bednarska et al., 2013).

Body-Burden Model (BBM) for birds

This document intends to write all equations, state variables and parameters used in the body-burden model proposed by Ducrot et al., 2016 as an acute risk assessment refinement approach in vertebrates ecological risk assessment. This model is a simple one-compartment toxicokinetic model (1) running per intervals between two feeding bouts (2).

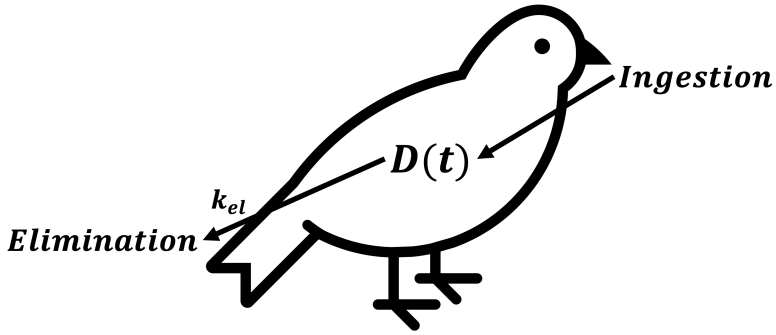

Figure 1: Schematic representation of the BBM principle.

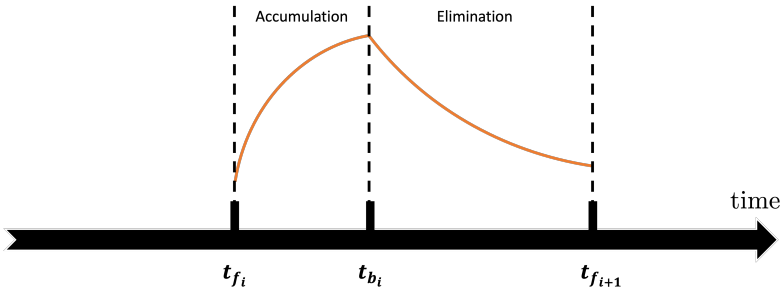

Figure 2: Time course between two feeding bouts.

Let t_{f_i}, $i = 1, 2 \text{ or } 8$, be the time points at which starts each feeding bout.

Let t_{b_i} be the time points at which birds stop feeding: $\forall i, t_{b_i} \in \left[t_{f_i}; t_{f_{i+1}}\right]$.

Between two feeding bouts, there are two kinetic phases: accumulation and depuration, that lead to the writing of the toxicokinetic model as given in equations (1).

$$\begin{cases} \frac{dD_{acc}(t)}{dt} = I - k_{e\ell}\, D_{acc}(t) & \text{if } t \in [t_{f_i}; t_{b_i}] \\ \frac{dD_{dep}(t)}{dt} = -k_{e\ell}\, D_{dep}(t) & \text{if } t \in \left[t_{b_i}; t_{f_{i+1}}\right] \end{cases} \tag{1}$$

Variables $D_{acc}(t)$ and $D_{dep}(t)$ stand for the internal dose within bird during the accumulation and the depuration phases respectively. Input I stand for the ingestion, that is the compound quantity ingested per time unit. Parameter $k_{e\ell}$ is the elimination rate constant (expressed per time unit).

For each interval, we need initial conditions as detailed in equations (2) below.

$$\begin{cases} D_{acc}(t_{f_i}) = D_{dep}(t_{f_i}) & \text{if } t \in [t_{f_i}; t_{b_i}] \\ D_{dep}(t_{b_i}) = D_{acc}(t_{b_i}) & \text{if } t \in \left[t_{b_i}; t_{f_{i+1}}\right] \end{cases} \tag{2}$$

The first initial condition translates the fact that the internal dose at the beginning of a feeding bout interval equals the internal dose at the end of the previous feeding bout interval. The second initial condition translates the fact that the depuration phase starts with an internal dose equals to the one at the end of the accumulation phase.

In the particular case of $i = 1$, $t_{f_i} = 0$ (beginning of the day) as well as $D_{acc}(t_{f_i}) = 0$ and $D_{dep}(t_{f_i}) = 0$.

The dynamical system defined by equations 1 can be analytically solved Charles et al., 2021. After few lines of calculations (see end of file), we get the exact solution given by equations (3):

$$\begin{cases} D_{acc}(t) = \frac{I}{k_{e\ell}} + \left(D_{dep}(t_{f_i}) - \frac{I}{k_{e\ell}}\right) e^{k_{e\ell}\left(t_{f_i} - t\right)} & \text{if } t \in [t_{f_i}; t_{b_i}] \\ D_{dep}(t) = \frac{I}{k_{e\ell}} e^{k_{e\ell}\left(t_{b_i} - t\right)} + \left(D_{dep}(t_{f_i}) - \frac{I}{k_{e\ell}}\right) e^{k_{e\ell}\left(t_{f_i} - t\right)} & \text{if } t \in \left[t_{b_i}; t_{f_{i+1}}\right] \end{cases} \tag{3}$$

In the particular case of $i = 1$, $t_{f_i} = 0$ (beginning of the day) and equations (3) can be simplified in equations (4).

$$\begin{cases} D_{acc}(t) = \frac{I}{k_{e\ell}} \left(1 - e^{-k_{e\ell} t}\right) & \text{if } t \in [0; t_{b_i}] \\ D_{dep}(t) = \frac{I}{k_{e\ell}} e^{k_{e\ell}(t_b - t)} - \frac{I}{k_{e\ell}} e^{-k_{e\ell} t} & \text{if } t \in [t_{b_i}; t_{f_2}] \end{cases} \tag{4}$$

Taking advantage of the exact solution, the model can be used to simulate the time course of the body burden in birds exposed to a chemical via diet.

Below are two example scenarios:

1. A continuous exposure all along the feeding period (Figure 3)
2. A 2 feeding bout scenarios (Figure 4)

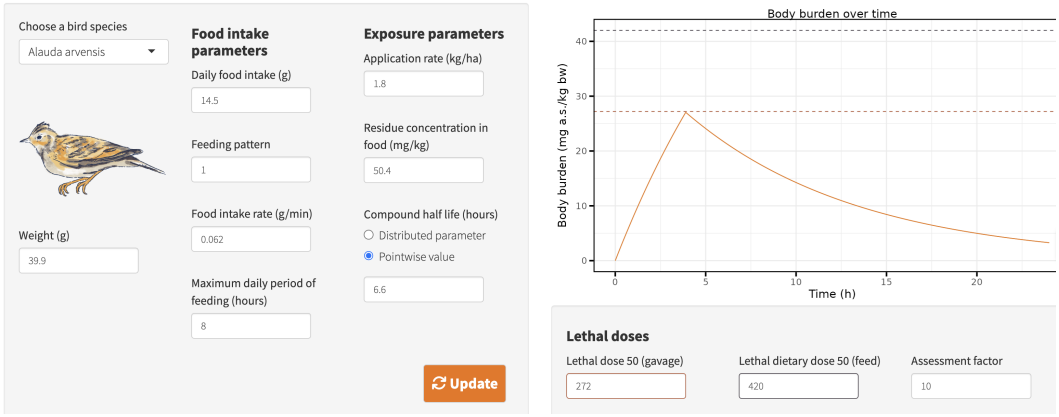

Figure 3: Time course of body burden over one day for a single feeding session of skylarks in a treated field. Dotted orange line: acute threshold; dotted grey line: dietary threshold. The solid orange line represents the time course of the internal dose in the bird body.

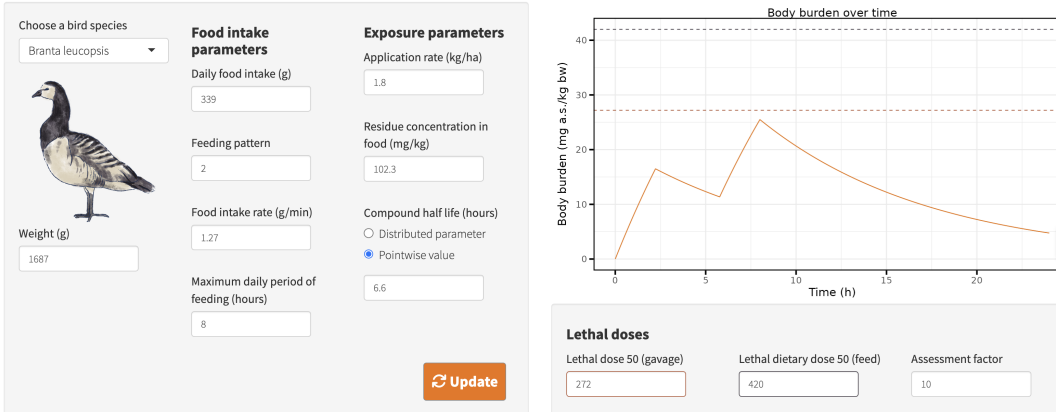

Figure 4: Time course of body burden over one day for two feeding sessions of barnacle gooses in a treated field. Dotted orange line: acute threshold; dotted grey line: dietary threshold. The solid orange line represents the time course of the internal dose in the bird body.

Analytical solution

- t_{fi} time at which birds feed
- t_{bi} time at which birds stop feeding, with $t_{bi} \in [t_{fi}; t_{fi+1}]$

Accumulation

For $t \in [t_{fi}; t_{bi}]$:

$$\begin{aligned} \frac{dD_{acc}(t)}{dt} &= I - k_{el} D_{acc}(t) \\ \Leftrightarrow D_{acc}(t) &= \frac{I}{k_{el}} + K\mathrm{e}^{-k_{el}t} \text{ with } K \in \mathbb{R} \end{aligned}$$

We can write:

$$\begin{aligned} D_{acc}(t_{fi}) &= \frac{I}{k_{el}} + K\mathrm{e}^{-k_{el}t_{fi}} = D_{dep}(t_{fi}) \\ \Leftrightarrow K\mathrm{e}^{-k_{el}t_{fi}} &= D_{dep}(t_{fi}) - \frac{I}{k_{el}} \\ \Leftrightarrow K &= \left(D_{dep}(t_{fi}) - \frac{I}{k_{el}} \right) \mathrm{e}^{k_{el}t_{fi}} \end{aligned}$$

Then we have:

$$D_{acc}(t) = \frac{I}{k_{el}} + \left(D_{dep}(t_{fi}) - \frac{I}{k_{el}} \right) \mathrm{e}^{k_{el}(t_{fi}-t)}$$

Note: if $t_{fi} = 0$, we get $D_{acc}(t) = \frac{I}{k_{el}}(1 - \mathrm{e}^{-k_{el}t})$

Elimination

For $t \in [t_{bi}; t_{fi+1}]$:

$$\begin{aligned} \frac{dD_{dep}(t)}{dt} &= -k_{el} D_{dep}(t) \\ \Leftrightarrow D_{dep}(t) &= K\mathrm{e}^{-k_{el}t} \text{ with } K \in \mathbb{R} \end{aligned}$$

We can write:

$$\begin{aligned} D_{dep}(t_{bi}) &= D_{acc}(t_{bi}) \\ \Leftrightarrow K\mathrm{e}^{-k_{el}t_{bi}} &= \frac{I}{k_{el}} + \left(D_{dep}(t_{fi}) - \frac{I}{k_{el}} \right) \mathrm{e}^{k_{el}(t_{fi}-t_{bi})} \\ \Leftrightarrow K &= \frac{I}{k_{el}} \mathrm{e}^{k_{el}t_{bi}} + \left(D_{dep}(t_{fi}) - \frac{I}{k_{el}} \right) \mathrm{e}^{k_{el}t_{fi}} \end{aligned}$$

Then we have:

$$D_{dep}(t) = \frac{I}{k_{el}} \mathrm{e}^{k_{el}(t_{bi}-t)} + \left(D_{dep}(t_{fi}) - \frac{I}{k_{el}} \right) \mathrm{e}^{k_{el}(t_{fi}-t)}$$

Note: if $t_{fi} = 0$, we get $D_{dep}(t) = \frac{I}{k_{el}} \mathrm{e}^{k_{el}(t_{bi}-t)} - \frac{I}{k_{el}} \mathrm{e}^{-k_{el}t}$

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