DEB-TKTD FOR BIRDS (DEBIRDS)

Equations writing, state variables and parameters

Authors

KAAG Miléna, BAUDROT Virgile, CHARLES Sandrine

University Claude Bernard Lyon 1

Laboratory of Biometry - Evolutionary biology (UMR CNRS 5558)
43 boulevard du 11 novembre 1918
F-69622 Villeurbanne Cedex, France

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1 Introduction

The purpose of this document is to present all the equations, variables and parameters used in the DEB-TKTD model developed by [1] for the risk assessment of pesticides in birds. This model accounts for avian toxicity endpoints observed in regulatory studies using a standard DEB model extended to include bird behaviour and combined with a TKTD module. Pesticides are assumed to induce a reduction in in egg production efficiency, with both a direct effect (due to the mechanism of toxicity) and an indirect effect due to food avoidance.

2 Variables

Symbol	Unit	Definition	Equation
C^*_{int}	$\mu g_{ai}.g_{bw}^{-1}$	Scaled internal concentration of active ingredient	Equation 18
E	J	Reserve energy	Equation 5
E_H	J	Maturation level	Equation 24
$[E_m]$	$J.cm^{-3}$	Maximum energy density	Equation 14
E_R	J	reproductive buffer	Equation 19
E_R^0	J	Unripe reproductive buffer	Equations 10 and 15
E_R^1	J	Ripe reproductive buffer	Equations 11 and 16
f_{tot}	-	Total scaled food functional response	Equation 1
f	-	Scaled food functional response for the assimilation flux $\dot{p}_A$	Equation 2
f_R	-	Scaled food functional response for the upregulated assimilation flux $\dot{p}_{AR}$	Equation 3
J_X	$g_{food}.d^{-1}$	Food ingestion rate	Interpolated from data
κ_R	-	Reproductive efficiency parameter	Equation 23
L	cm	Structural body length	Equation 7
N	#	Cumulative number of eggs	Equations 13 and 17
$\dot{p}_A$	$J.d^{-1}$	Assimilation rate	Equation 4
$\dot{p}_C$	$J.d^{-1}$	Mobilisation rate	Equation 6
$\dot{p}_{Cm}$	$J.d^{-1}$	Mobilisation rate when $f = 1$	Equation 14
$\dot{r}$	d^{-1}	Growth rate	Equations 7, 8 and 9
s	-	Stress factor	Equation 22
W_w	g	Wet weight	Equation 21

Table 1: Model variables.
Subscript “ai” stands for active ingredient, while subscript “bw” stands for body weight.

3 Parameter list

Below is the table with parameter values as used to run the model simulations. They have been taken either from the paper by [1], or from the online database add_my_pet.
*: add_my_pet data from the supplementary material. It is unclear which parameter values were estimated and which were not. Only a few parameters have their value and status confirmed in the actual paper.
**: Debber data. The value returned by the `DEBtool` estimation function `initial_scaled_reserve()` is unknown.

Symbol	Unit	Definition	mallard duck	AmP mallard duck	bobwhite quail
c_0	$\mu g_{ai} \cdot g_{bw}^{-1}$	Resistance threshold concentration	See details	-	See details
c_T	$\mu g_{ai} \cdot g_{bw}^{-1}$	Tolerance gradient	See details	-	See details
C_X	$\mu g_{ai} \cdot g_{food}^{-1}$	Concentration of pesticide in the food	See details	-	See details
d_E	$g.cm^{-3}$	Density of the reserve E	0.28*	0.28	0.28*
d_{vw}	$g_{wet\ weight}.cm^{-3}$	Specific density to convert volume into wet weight	1*	*NA*	1*
d_X	$g.cm^{-3}$	Density of food X	0.28*	0.28	0.28*
E_0	J	Energy in one egg	3.39e+05**	2.63e+05	8.97e+04**
$[E_G]$	$J.cm^{-3}$	Specific cost for structure	7236	7283.68	7985
E_H^b	J	Maturity at birth	2.668e+04	1.648e+04	5466
E_H^p	J	Maturity at puberty	5.952e+06	8.892e+05	9.91e+05
k_e	d^{-1}	Elimination rate	1	-	1
$\dot{k}_J$	d^{-1}	Maturity maintenance rate coefficient	0.002	5.7217e-3	0.002
κ	-	Allocation fraction to soma	0.6837	0.8122	0.657
κ_G	-	Growth efficiency under starvation	See details	0.8042	See details
κ_{R0}	-	Reproduction efficiency in control group	0.95	0.95	0.95
κ_X	-	Digestion efficiency from food to reserve	See details	0.8	See details
μ_X	$J.Cmol^{-1}$	Chemical potential of food X	5.25e+05*	5.25e+05	5.25e+05*
μ_E	$J.Cmol^{-1}$	Chemical potential of the reserve E	5.5e+05*	5.5e+05	5.5e+05*
$\dot{\nu}$	$cm.d^{-1}$	Energy conductance	0.03064	0.044778	0.2093
$\{\dot{p}_{Am}\}$	$J.d^{-1}.cm^{-2}$	Surface-specific assimilation rate	3360	1055.14	2858.3
$[\dot{p}_M]$	$J.d^{-1}.cm^{-3}$	Volume-specific somatic maintenance	574.6	138.072	870.6
t_{init}	d	Time between hatching and start of the experiment	See details	-	See details
t_s	d	Time of start of reproduction induction	See details	-	See details
w_E	$g.Cmol^{-1}$	Molecular weight of the reserve E	16*	23.9	16*
w_X	$g.Cmol^{-1}$	Molecular weight of dehydrated food X	12*	23.9	12*

Table 2: Model parameters. Subscript “ai” stands for active ingredient, while subscript “bw” stands for body weight.

4 Equations

4.1 Experiment model

4.1.1 Intake, growth and somatic maintenance

$$f_{tot}(t) = \frac{1}{\{\dot{p}_{Am}\}L(t)^2}\kappa_X \mu_X \frac{J_X(t)}{d_{vw}}\frac{d_X}{w_X} \tag{1}$$

EQUATION DIMENSION

$$f_{tot}(t) = \frac{1}{\text{J.d}^{-1}.\text{cm}^{-2} \times \text{cm}^2} \times \text{nd} \times \text{J.Cmol}^{-1} \times \frac{\text{g}_{wet\ food}.\text{d}^{-1}}{\text{g}_{wet\ food}.\text{cm}^{-3}} \times \frac{\text{g}_{dry\ food}.\text{cm}^{-3}}{\text{g}_{dry\ food}.\text{Cmol}^{-1}}$$
$$= \text{Dimentionless}$$

$$f(t) = \begin{cases} f_{tot}(t) & \text{if } t < t_s \\ \min(1, f_{tot}(t)) & \text{otherwise} \end{cases} \tag{2}$$

$$f_R(t) = \begin{cases} 0 & \text{if } t < t_s \text{ or } E_H < E_H^p \\ \max(0, f_{tot}(t) - f(t)) & \text{otherwise} \end{cases} \tag{3}$$

After the onset of reproduction, the functional response representing food intake is bifurcated under the hypothesis that the increase in food intake brought about by the onset of reproduction is allocated directly to the ripe (or mature) reproductive buffer without passing through the reserve compartment.

Ingestion rate The feeding or intake rate, $\dot{p}_A(t)$, is a function of food density as expressed by the theory of functional responses.

$$\dot{p}_A(t) = f(t)\{\dot{p}_{Am}\}L(t)^2 \tag{4}$$

EQUATION DIMENSION

$$\dot{p}_A(t) = \text{Dimentionless} \times \text{J.d}^{-1}.\text{cm}^{-2} \times \text{cm}^2 = \text{J.d}^{-1}$$

Reserve dynamics The time course of the reserve energy E can be written as:

$$\frac{dE(t)}{dt} = \dot{p}_A(t) - \dot{p}_C(t) \tag{5}$$

In the previous equation (5), it is assumed that the mobilisation rate of the reserve, $\dot{p}_C(t)$ is a function of the reserve energy E and the structural volume only.

$$\dot{p}_C(t) = E(t)\frac{\frac{[E_G]\dot{\nu}}{L(t)} + [\dot{p}_M]}{\kappa[E(t)] + [E_G]} \tag{6}$$

Equation dimension

$$\dot{p}_C(t) = \text{J} \times \frac{\frac{\text{J.cm}^{-3}\times\text{cm.d}^{-1}}{\text{cm}} + \text{J.d}^{-1}.\text{cm}^{-3}}{\text{nd} \times \text{J.cm}^{-3} + \text{J.cm}^{-3}} = \text{J} \times \frac{\text{J.d}^{-1}.\text{cm}^{-3}}{\text{J.cm}^{-3}} = \text{J.d}^{-1}$$

$$\frac{dL(t)}{dt} = \frac{\dot{r}}{3}L(t) \text{ with } \dot{r}(t) = \begin{cases} \dot{r}_1(t) & \text{if } \kappa\dot{p}_C(t) \geqslant [\dot{p}_M]L(t)^3 \\ \dot{r}_2(t) & \text{if } \kappa\dot{p}_C(t) < [\dot{p}_M]L(t)^3 \text{ and } E_R^0(t) = 0 \\ 0 & \text{if } \kappa\dot{p}_C(t) < [\dot{p}_M]L(t)^3 \text{ and } E_R^0(t) > 0 \end{cases} \quad (7)$$

If there is enough energy for somatic maintenance, the growth rate is normal ($\dot{r}_1$). If not, then there is no growth if maintenance energy can be found in the unripe (or immature) reproductive buffer to maintain the structure, or a negative growth at a different rate ($\dot{r}_2$) otherwise.

$$\dot{r}_1(t) = \frac{\frac{[E(t)]\dot{\nu}}{L(t)} - [\dot{p}_M]/\kappa}{[E(t)] + [E_G]/\kappa} \quad (8)$$

$$\dot{r}_2(t) = \frac{\frac{[E(t)]\dot{\nu}}{L(t)} - [\dot{p}_M]/\kappa}{[E(t)] + \kappa_G[E_G]/\kappa} \quad (9)$$

See Section 5.4 for details on parameter κ_G.

Equation dimension

$$\dot{r}(t) = \frac{\frac{\text{J.cm}^{-3}\times\text{cm.d}^{-1}}{\text{cm}} - \text{J.d}^{-1}.\text{cm}^{-3}/\text{nd}}{\text{J.cm}^{-3} + (\text{nd}) \times \text{J.cm}^{-3}/\text{nd}} = \text{d}^{-1}$$

4.1.2 Reproduction

Reproductive dynamics depends on the successful somatic maintenance, which takes precedence over all other processes.

- **If $\kappa\dot{\mathbf{p}}_{\mathbf{C}}(\mathbf{t}) \geq [\dot{\mathbf{p}}_{\mathbf{M}}]\mathbf{L}(\mathbf{t})^{\mathbf{3}}$:** (enough energy for somatic maintenance)

$$\frac{dE_R^0(t)}{dt} = \max\left(0, (1-\kappa)\dot{p}_C(t) - \dot{k}_J E_H^p\right) - (E_R^0(t) > 0)(t > t_s)\left((1-\kappa)\dot{p}_{Cm}(t) - \dot{k}_J E_H^p\right) \quad (10)$$

$$\frac{dE_R^1(t)}{dt} = (E_R^0(t) > 0)(t > t_s)\left((1-\kappa)\dot{p}_{Cm}(t) - \dot{k}_J E_H^p\right) + f_R(t)\{\dot{p}_{Am}\}L(t)^2 \quad (11)$$

We define the time of laying t_l as the time where $E_R^1(t) \geqslant \frac{E_0}{\kappa_R(t)}$. At laying, we have:

$$E_R^1(t_l + dt) = E_R^1(t_l) - \frac{E_0}{\kappa_R(t_l)} \quad (12)$$

and

$$N(t_l + dt) = N(t_l) + 1, \text{ with } N(0) = 0 \quad (13)$$

$$\dot{p}_{Cm}(t) = [E_m(t)]\frac{[E_G]\dot{\nu}L(t)^2 + [\dot{p}_M]L^3}{\kappa[E_m(t)] + [E_G]} \text{ with } [E_m(t)] = \frac{\{\dot{p}_{Am}\}}{\dot{\nu}}f(t) \tag{14}$$

The energy allocated to reproduction, minus the energy for maintaining maturity, goes into the unripe reproductive buffer. The ripe reproductive buffer receives energy from the unripe buffer only if reproduction has been induced ($t > t_s$) and the unripe reproductive buffer is not empty. It also receives energy directly from the increase in food intake that occurs when reproduction is induced (f_R). Egg production will only occur if there is at least enough energy for one egg in the ripe reproductive buffer.

EQUATION DIMENSION

$$[E_m(t)] = \frac{\text{J.d}^{-1}.\text{cm}^{-2}}{\text{cm.d}^{-1}} \times \text{nd} = \text{J.cm}^{-3}$$

$$\dot{p}_{Cm}(t) = \text{J.cm}^{-3} \times \frac{\text{J.cm}^{-3} \times \text{cm.d}^{-1} \times \text{cm}^2 + \text{J.d}^{-1}.\text{cm}^{-3} \times \text{cm}^3}{\text{nd} \times \text{J.cm}^{-3} + \text{J.cm}^{-3}} = \text{J.d}^{-1}$$

- **Else:**

$$\frac{dE_R^0(t)}{dt} = \max(0, (1-\kappa)\dot{p}_C(t) - \dot{k}_J E_H^p) - (E_R^0(t) > 0)([\dot{p}_M]L(t)^3 - \kappa\dot{p}_C(t)) \tag{15}$$

$$\frac{dE_R^1(t)}{dt} = 0 \tag{16}$$

$$\frac{dN(t)}{dt} = 0 \tag{17}$$

When there is not enough energy for somatic maintenance, reproduction is paused. The unripe buffer still receives energy but it's energy is used for the lacking somatic maintenance, if possible. If not, then negative growth occurs.

4.1.3 Toxicokinetic-Toxicodynamic

$$\frac{dC^*_{int}(t)}{dt} = \frac{I(t)}{W_w(t)} - k_e C^*_{int}(t) - \frac{C^*_{int}(t)}{W_w(t)}\left(d_{vw}\left(\frac{dV}{dt} + \frac{w_E}{d_E\mu_E}\frac{dE}{dt}\right) + \frac{w_E}{\mu_E}\frac{dE_R}{dt}\right) \tag{18}$$

Variable $C^*_{int}(t) = \frac{1}{F}C_{int}(t)$ with F the bioavailability of the compound. Here $F = 1$.

The dynamics of the internal concentration is based first on the uptake rate then on the elimination rate, as well as on the dilution of the compound (by standard growth and by variation of the energy buffers).

$$\frac{dE_R}{dt} = \frac{dE_R^0}{dt} + \frac{dE_R^1}{dt} \tag{19}$$

$$I(t) = J_X(t)C_X \tag{20}$$

Equation dimension

$$I(t) = \text{g.d}^{-1} \times \mu\text{g.g}^{-1} = \mu\text{g.d}^{-1}$$

$$W_w(t) = d_{vw}\left(V(t) + E(t)\frac{w_E}{d_E\mu_E}\right) + E_R(t)\frac{w_E}{\mu_E} \text{ with } V(t) = L(t)^3 \tag{21}$$

"Dry weights of both buffers were included in the total wet weight of the females, taking into account that ***reproductive buffers do not contain water****"*. Therefore, the reserve energy is not converted using the specific density to convert volume into wet weight (d_{vw}).

Equation dimension

$$W_w(t) = \text{g}_{bw}.\text{cm}^{-3}\left(\text{cm}^3 + J\frac{\text{g.Cmol}^{-1}}{\text{g.cm}^{-3} \times \text{J.Cmol}^{-1}}\right) + \text{J}\frac{\text{g.Cmol}^{-1}}{\text{J.Cmol}^{-1}}$$
$$= \text{g}_{bw} + \text{g} = \text{g}$$

Equation dimension

$$\frac{dC^*_{int}(t)}{dt} = \frac{\mu\text{g.d}^{-1}}{\text{g}} - \text{d}^{-1} \times \mu\text{g} - \frac{\mu\text{g}}{\text{g}} \times$$
$$\left(\text{g.cm}^{-3} \times \left(\frac{\text{cm}^3}{\text{d}} + \frac{\text{g.Cmol}}{\text{g.cm}^{-3} \times \text{J.Cmol}^{-1}} \times \frac{\text{J}}{\text{d}}\right) + \frac{\text{g.Cmol}^{-1}}{\text{J.Cmol}^{-1}} \times \frac{\text{J}}{\text{d}}\right)$$
$$= \mu\text{g.d}^{-1}$$

Stress function Stress occurs once the scaled internal compound concentration exceeds threshold c_0. Based on [1], the relevant physiological mode of action for capturing what was observed on reproductive outputs was an increase in the reproductive costs. Consequently:

$$s(t) = \frac{1}{c_T}\max(0, C^*_{int}(t) - c_0) \tag{22}$$

$$\kappa_R(t) = \frac{\kappa_{R0}}{1 + s(t)} \tag{23}$$

Equation dimension

$$s(t) = \frac{1}{\mu g.\text{g}^{-1}}\left(\mu g.\text{g}^{-1} - \mu g.\text{g}^{-1}\right) = \text{Dimentionless}$$

4.2 Hatching to start of the experiment model

The maturation process of an organism is represented by the maturation level (variable E_H). For birds, three stages of development are considered: embryo/egg, juvenile and adult. The transition between these stages is represented by two maturation level thresholds: maturity at birth E_H^b and maturity at puberty E_H^p. Once the maturation level reaches the threshold of maturity at puberty, it remains constant. Before that, its dynamics for a juvenile can be described with the following equation:

$$\frac{dE_H(t)}{dt} = \max\Big(0, (1-\kappa)\dot{p}_C(t) - \dot{k}_J E_H(t)\Big)\,(E_H(t) < E_H^p) \tag{24}$$

To simulate the period between hatching and the start of the experiment, f is set to 1 in the absence of data on food ingestion rates.

There are no reproduction dynamics until puberty:

$$\frac{dE_R^0(t)}{dt} = 0 \tag{25}$$

The other equations are identical to those found in the experiment model.

4.3 Initial conditions

At hatching ($t = 0$), we have the following initial conditions:

$$C_{int}^*(0) = 0, \quad E_H(0) = E_H^b, \quad E_R(0) = 0, \quad N(0) = 0, \quad V(0) = L(0)^3$$

From Kooijman [2], equation 2.32, and the parameter values from add_my_pet, the length at hatching $L(0)$ for the mallard duck can be calculated as follows:

$$\begin{aligned} L(0)^3 &= \frac{E_H^b/[E_m]}{(1-\kappa)[E_G]/\kappa[E_m]} = \frac{\kappa E_H^b}{(1-\kappa)[E_G]} \\ &= \frac{0.8122 \times 1.648.10^4}{(1-0.8122) \times 7283.68} = 9.785 \text{ cm}^3 \\ \Leftrightarrow L(0) &= 2.139 \text{ cm} \end{aligned}$$

In addition, from Kooijman [2] and the equation given on page 52, we get:

$$E(0) = [E_b]L(0)^3$$

where $[E_b]$ the reserve density at birth can be approximated to $[E]$ the reserve density of the mother at egg formation.

Due to the lack of information on the condition of the mother at the time of egg formation, we use the observed wet weight at birth, $W_w(0)$, to estimate $E(0)$. Species-specific $W_w(0)$ values for the mallard duck and the bobwhite quail) can be found in the add_my_pet database.

For example, for the mallard duck, we get:

$$W_w(0) = d_{vw}\left(V(0) + E(0)\frac{w_E}{d_E\mu_E}\right)$$
$$\Leftrightarrow E(0) = \frac{d_E\mu_E}{w_E}\left(\frac{W_w(0)}{d_{vw}} - V(0)\right)$$
$$\Leftrightarrow E(0) = \frac{0.28 \times 5.5.10^5}{23.9}\left(\frac{30.8}{1} - (2.139)^3\right) \approx 135\,400 \text{ J}$$

5 Details on parameters values

5.1 c_0 and c_T

Symbol	Substance	Value for mallard duck	Value for bobwhite quail
c_0	Azoxystrobin	68.93	47.49
c_0	Atrazine	2.7e-3	1.1e-4
c_0	Adepidyn	1.162	1.80
c_0	Abamectin	1.32	-
c_T	Azoxystrobin	540.8	751.4
c_T	Atrazine	195	148.9
c_T	Adepidyn	387.1	200.6
c_T	Abamectin	46.97	-

5.2 Exposure concentration C_X

5.2.1 Azoxystrobin

mallard duck: 500, 1200, 3000
bobwhite quail: 500, 1200 3000

5.2.2 Abamectin

mallard duck: 1, 8, 64
bobwhite quail: 5, 10, 20

5.2.3 Adepidyn

mallard duck: 200, 1000, 5000
bobwhite quail: 200, 1000, 5000

5.2.4 Atrazine

mallard duck: 75, 225, 675
bobwhite quail: 75, 225, 675

5.2.5 Diquat

mallard duck: 5, 25, 50
bobwhite quail: 5, 25, 50

5.3 Parameter κ_X

Symbol	Substance	Value for mallard duck	Value for bobwhite quail
κ_X	Azoxystrobin	0.4094	0.7912
κ_X	Atrazine	0.6492	0.6579
κ_X	Adepidyn	0.541	0.730
κ_X	Abamectin	0.6266	0.5584
κ_X	Diquat	0.5916	0.6622

5.4 Parameter κ_G

According to Augustine et al. 2012, the growth efficiency under starvation is the following:

$$\kappa_G = \frac{\bar{\mu}_V d_V}{[E_G] w_v} \tag{26}$$

With $\bar{\mu}_V$ the chemical potential of the structure, d_V the density of the structure, $[E_G]$ the cost of synthesis of a unit of structure and w_v the molar weight of structure. We do not know the chemical potential and the molar weight of the structure from [1]. From add_my_pet, parameter values can be extracted:

$d_v = 0.28$ g.cm^3, $w_v = 23.9$ g.Cmol^{-1}, and $\bar{\mu}_V = 5.10^5$ J.Cmol^{-1}

Given $[E_G]$ value in Table 2, we get $\kappa_G = 0.8042$ (-).

5.5 Start of the experiment t_{init}

Note: these values correspond to the number of days between hatching and the start of the exposure experiment.

Symbol	Substance	Value for mallard duck	Value for bobwhite quail
t_{init}	Azoxystrobin	210	119
t_{init}	Atrazine	165	146
t_{init}	Adepidyn	168	147
t_{init}	Abamectine	217	?
t_{init}	Diquat	180	180

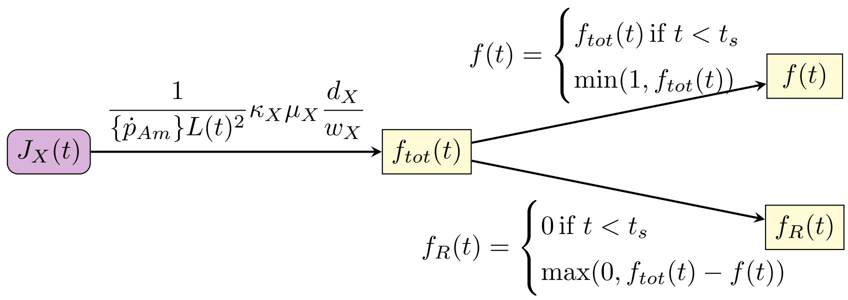
5.6 Time of reproduction induction t_s

Note: these values correspond to the number of days between hatching and the start of the reproduction induction.

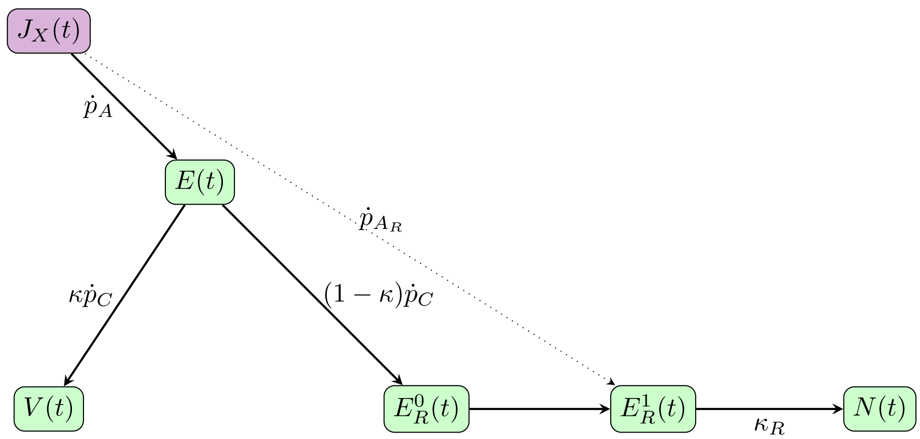
Symbol	Substance	Value for mallard duck	Value for bobwhite quail
t_s	Azoxystrobin	231	168
t_s	Atrazine	221	202
t_s	Adepidyn	231	204
t_s	Abamectine	217	?
t_s	Diquat	229	229

5.7 Directed Acyclic Graph (DAG)

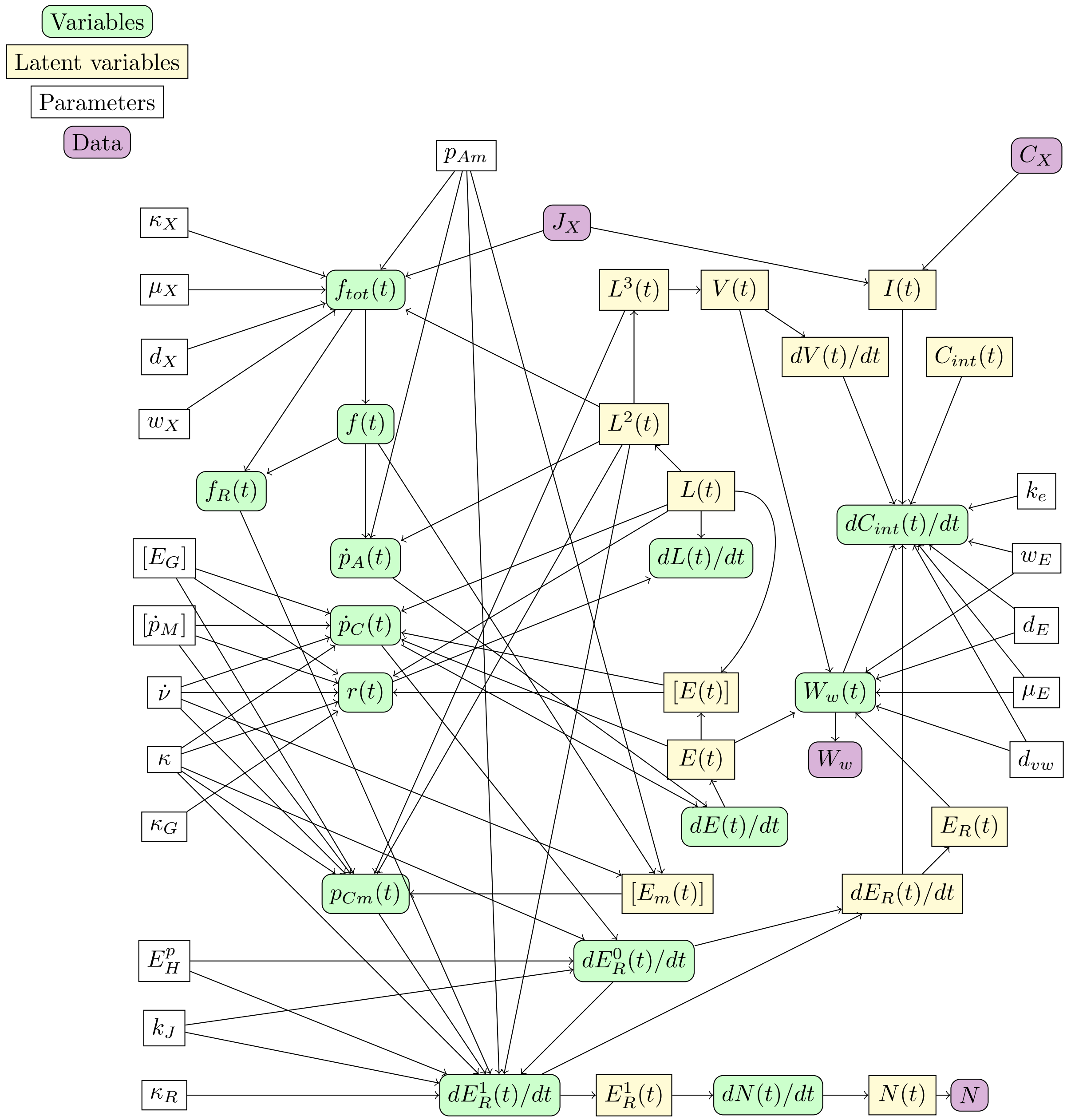
Feeding



Energy fluxes



Full DAG



References

[1] M. Trijau, B. Goussen, R. Brain, J. Maul, and N. Galic, "Development of a mechanistic model for analyzing avian reproduction data for pesticide risk assessment," *Environmental Pollution*, p. 121477, 2023.

[2] S. A. L. M. Kooijman, *Dynamic Energy Budget theory for metabolic organisation*, 3rd ed. Cambridge, UK: Cambridge university press, 2010. [Online]. Available: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2981979{&}tool=pmcentrez{&}rendertype=abstract