



HAL
open science

A brief review on models for birds exposed to chemicals

Dominique Lamonica, Lison Charvy, Dave Kuo, Clémentine Fritsch, Michael Coeurdassier, Philippe Berny, Sandrine Charles

► To cite this version:

Dominique Lamonica, Lison Charvy, Dave Kuo, Clémentine Fritsch, Michael Coeurdassier, et al.. A brief review on models for birds exposed to chemicals. 2024. hal-04438562v1

HAL Id: hal-04438562

<https://univ-lyon1.hal.science/hal-04438562v1>

Preprint submitted on 5 Feb 2024 (v1), last revised 15 Feb 2024 (v2)

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

1 A brief review on models for birds exposed to
2 chemicals

3 Dr. Dominique LAMONICA^{1,2*}, Mrs. Lison CHARVY³, Dr.
4 Dave KUO⁴, Dr. Clémentine FRITSCH⁵, Dr. Michaël
5 COEURDASSIER⁵, Prof. Philippe BERNY⁶ and Prof.
6 Sandrine CHARLES¹

7 ¹University Lyon 1, Laboratory of Biometry and Evolutionary
8 Biology - UMR CNRS5558, 43 boulevard du 11 novembre 1918,
9 Villeurbanne Cedex, 69622, France.

10 ^{2*}Research Institute for Development, BotAny and Modeling of
11 Plant Architecture and Vegetation - UMR AMAP, TA A51/PS2,
12 Montpellier Cedex 05, 34398, France.

13 ³INSA Lyon, Biosciences department, 20 avenue Albert Einstein,
14 Villeurbanne, 69100, France.

15 ⁴Institute of Environmental Engineering (GIEE), National Taiwan
16 University, No. 1, Sec. 4, Roosevelt Rd., Taipei, 106, Taiwan.

17 ⁵UMR 6249 Chrono-environnement, CNRS - Université de
18 Franche-Comté Usc INRAe, 16 route de Gray, Besançon cedex,
19 25030, France.

20 ⁶UR ICE, VetAgro Sup Campus Vétérinaire de Lyon, 1 Avenue
21 Bourgelat, Marcy l'étoile, F-69280, France.

22 ^{*}Corresponding author(s). E-mail(s): dominique.lamonica@ird.fr;

23 **Abstract**

24 *“A Who’s Who of pesticides is therefore of concern to us all. If we are going to*
25 *live so intimately with these chemicals eating and drinking them, taking them*
26 *into the very marrow of our bones - we had better know something about their*
27 *nature and their power.” — Rachel Carson, Silent Spring.*
28

29 In her day, Rachel Carson was right: plant protection products
30 (PPP) like all the other chemical substances that humans increas-
31 ingly release into the environment without further precaution, are
32 among our worst enemies today (Bruhl and Zaller, 2019; Naidu
33 et al, 2021; Tang et al, 2021; Topping et al, 2020). All com-
34 partments of the biosphere, air, soil and water, are potential
35 reservoirs within which all species that live there are impaired.
36 Birds are particularly concerned: PPP are recognized as a fac-
37 tor in the decline of their abundance and diversity predominantly
38 in agricultural landscapes. Due to the restrictions on vertebrates
39 testing, *in silico* based approaches are an ideal choice alterna-
40 tive given input data are available. This is where the problem
41 lies as we will illustrate in this paper. We performed an extensive
42 literature search covering a long period of time, a wide diver-
43 sity of bird species, a large range of chemical substances and as
44 many model types as possible to encompass all our future need
45 to improve environmental risk assessment of chemicals for birds.
46 In the end, we show that poultry species exposed to pesticides
47 are the most studied at the individual level with physiologically
48 based toxicokinetic models. To go beyond, with more species, more
49 chemical types, over several levels of biological organization, we
50 show that observed data are crucially missing (Gilbert, 2011).
51 As a consequence, improving existing models or developing new
52 ones could be like climbing Everest if no additional data can be
53 gathered, especially on chemical effects and toxicodynamic aspects.

54 **Keywords:** ecotoxicology, avian species, toxicokinetic-toxicodynamic models,
55 drug, diet.

56 1 Introduction

57 As early as 1962, Rachel Carson warned about the devastating effects of plant
58 protection products (PPP) on terrestrial vertebrates in her pioneering book
59 *Silent Spring* (Carson, 1962). Later in 1967, Ratcliffe reported that birds
60 ingesting the synthetic pesticide DDT (dichloro-diphenyl-trichloroethane) had
61 a tendency to lay eggs with thin shells that broke prematurely in the nest.
62 This was confirmed by Cade et al (1971) as resulting in marked population

63 declines, a problem that has driven bald eagles, the national symbol of the
64 United States, along with peregrine falcons and other bird species, to the
65 brink of extinction, with populations collapsing by up to 80%. Since then,
66 all around the world, extensive studies have been carried out to understand
67 the mechanisms underlying this phenomenon. The results of these studies
68 are summarized in a recent collective expertise (ESCo, [Pesce et al \(2021\)](#)),
69 especially chapter 9 ([Mamy et al \(2022\)](#), p623-720) focusing on terrestrial
70 vertebrates to report on the state-of-the-art about: (i) active substances,
71 types or families of PPP for which effects on wildlife are proven, probable,
72 possible or null; (ii) the relationship between the exposure features in different
73 groups of terrestrial vertebrates and the induced effects; (iii) the main mech-
74 anisms (in particular direct and indirect ones) inducing the main effects; (iv)
75 the identification of the most influential environmental factors (agronomic,
76 ecological...); (iv) the impact of PPP on functions and ecosystem services
77 provided by terrestrial vertebrates.

78

79 Basically, [Mamy et al \(2022\)](#) identified as highly probable the causal link
80 between the use of PPP and the decline in invertebrate and bird populations
81 observed over several decades, particularly in agricultural areas, in interaction
82 with landscape simplification. Depending on the bird species and their diet,
83 PPP impacts are mainly the result of either a direct effect (*e.g.*, ingestion
84 of PPP-treated seeds by granivorous birds) or an indirect effect (*e.g.*, reduc-
85 tion of food resources due to the decline of prey); see Chapter 9 in [Mamy](#)

86 [et al \(2022\)](#) for more details. Environmental monitoring networks in various
87 European countries, including France, have revealed a large number of cases
88 of PPP poisoning of birds in the vicinity of agro-ecosystems. For granivorous
89 birds, the recorded cases since the beginning of the 2000s are mostly caused
90 by the ingestion of seeds treated with neonicotinoids ([Bishop et al, 2018](#)),
91 more specifically imidacloprid ([Rogers et al, 2019](#)). For insectivorous birds,
92 the impact of PPP is mainly expressed indirectly, through the decline in
93 food resources. Several studies in Europe have **demonstrated the existence of**
94 **significant correlations** between the use of PPP and the concomitant decline
95 in insect communities and bird populations ([Hallmann et al, 2014](#); [Bowler](#)
96 [et al, 2019](#); [Møller, 2019](#)). **In addition to these correlations, effects through**
97 **the consumption of contaminated prey have recently been demonstrated by**
98 **a multi-residue analysis of the diet of nestlings** ([Poisson et al, 2021](#)); these
99 **effects, which lead to the decline of certain populations, are mainly due to the**
100 **presence of neonicotinoids in the environment** ([Humann-Guilleminot et al,](#)
101 [2021](#)). **Apart from the lethal effects of PPP, flight efficiency and orientation**
102 **of birds may also be impaired in response to exposure. Such sublethal effects**
103 **have been observed, for example, in migratory birds stopping over in agricul-**
104 **tural areas, thus compromising the smooth running of the critical migration**
105 **period** ([Eng et al, 2017, 2019](#)).

107 The field of modeling has been particularly prolific in recent years, for example
108 in the prediction of contaminant transfer based on the physico-chemical char-
109 acteristics of the substances involved, combined with scenarios incorporating
110 different types of crops, climate and soil (Servien et al, 2022). But numerous
111 models have also been developed to better describe how organisms accumulate
112 the chemicals and how the internal damages translate into effects on their life
113 history traits (Larras et al, 2022b). Modeling is also repeatedly mentioned as
114 a potential solution for integrating the processes involved at different spatial
115 and temporal scales. For example, it is not uncommon in the literature to
116 find work that combines ecotoxicological models, to describe the impacts of
117 PPP, with ecological models, which describe the links between organisms and
118 the functions they ensure within ecosystems. In particular, there are spatially
119 explicit models that take into account not only the exposure of organisms,
120 but also the toxic potential of PPP and the adverse effects they have on
121 demography, while taking into account variability in both the landscape and
122 exposure (Topping et al, 2005, 2016; Topping and Weyman, 2018; Topping
123 et al, 2020). Nevertheless, as modeling strongly relies on the collection of
124 experimental data and the metadata to which they are associated, data avail-
125 ability is the major constraint to which model building and the testing of
126 their performances faces, especially at large spatial and temporal scales. All of
127 this finally prevents a wider use of models in environmental risk assessment.

129 An interesting perspective of the use of population modeling is the possibility
130 to extrapolate bio-monitoring data related to PPP bioaccumulation or specific
131 effects in terms of population risk of extinction. Based on a matrix population
132 model, [Goutte et al \(2018\)](#) provided a nice illustration with the South polar
133 skua, a large seabird, for which long term demographic monitoring disclosed
134 a possible effect of an organochlorine insecticide on the breeding success, thus
135 compromising the population viability. One of the key points of population
136 models is their ability to support extrapolation from one species to another,
137 as illustrated for birds by [Etterson et al 2017](#). Such a rapid cross-species
138 transposition of population models (especially stage-structured ones) benefits
139 from the recent construction of large ecological databases gathering together
140 demographic traits particularly helpful in conservation science. For instance,
141 [De Zwaan et al.](#) have recently compiled a huge data set of alpine breeding
142 records for 1,310 bird species, representing 12.0% of extant species and cover-
143 ing all major mountain regions across the five continents, except Antarctica
144 ([de Zwaan et al, 2022](#)). **Benefiting of such data collections is the condition to**
145 **support parameter inference for population models, especially when a large**
146 **number of species is involved. Such data bases are also particularly helpful**
147 **when ranking species vulnerabilities is required in relationship with the dif-**
148 **ferent uses of PPP** ([Forbes et al, 2015](#); [Etterson et al, 2017](#)).

149

150 The EU Regulation 1107/2009 defines all requirements before placing PPP on
151 the market, in association with data requirements from regulations 283/2013

152 and 284/2011. In particular, an assessment is required regarding the risks
153 for bird reproduction when they are exposed to PPP. In this perspective,
154 the OECD guideline 206 provides the way data must be collected through
155 standard toxicity test protocols whereby birds are exposed to the active
156 substance of interest for a period of 20 weeks. However, the expected expo-
157 sure period of active substances and their numerous degradation products in
158 field (as determined by EFSA guidelines), can be much shorter thus creating
159 disparities between both methodologies. For non-vertebrate species, such an
160 issue can be overcome by additional testing. However, owing to the need to
161 avoid vertebrate testing, this option is not valid for birds. Therefore, the use
162 of *in silico* approaches predicting toxicity endpoints for birds can be helpful
163 ([European Food Safety Authority et al, 2023](#)). In particular, toxicokinetic
164 (TK) models, relating the exposure concentration to the fate of chemicals
165 within an organism, coupled with toxicodynamic (TD) models, that make the
166 link between cellular, biochemical and physiological damages and individual
167 effects on life history traits, are potentially useful tools to refine risk assess-
168 ment of PPP for birds, especially under a regulatory framework where such
169 models remain still underused.

170

171 EFSA recently formulated recommendations to develop open source generic
172 physiologically based TK (PBTK) models for a range of relevant species
173 among which birds play an important role ([European Food Safety Authority
174 et al, 2023](#)). [Larras et al \(2022a\)](#) also established how huge is the gap between

175 the set of models used in PPP regulatory reports and those existing in the
176 literature, thus highlighting the need for the implementation of more sophis-
177 ticated models into PPP regulation. With the idea of describing the whole
178 cascade of impairments, from the exposure conditions to the apical effects,
179 PBTKTD models clearly appear as the most appropriate tool to focus with
180 effects at the individual level in the perspective of moving towards the next
181 generation risk assessment practice. Nevertheless, accounting for molecular
182 initiating events (usually based on omic-type data) and the subsequent series
183 of intermediate steps and key events leading to an adverse outcome is also
184 of great interest to provide a clear-cut mechanistic representation of critical
185 toxicological effects; this is what are allowing Adverse Outcome Pathways
186 (AOP) approaches ([Vinken, 2013](#)). Hence, combining AOP with PBTKTD
187 models could help in finely refining risk assessment. Similarly, linking individ-
188 ual effect models such as PBTKTD models with population and community
189 ones could complement protection schemes including both direct and indirect
190 effects ([Forbes et al, 2017](#)). One inside the other, PBTKTD models are the
191 key pillars of a comprehensive approach along the gradient of effects at all
192 levels of biological organization ([European Food Safety Authority et al, 2023](#)).

193

194 However, as already stated above, moving towards more complex models
195 necessarily means benefiting of more data. In particular, no generic PBTKTD
196 models are available for refined environmental risk assessment of birds and
197 mammals, since data requirements are very high ([Astuto et al, 2022](#)). Here

198 lies the dilemma facing PPP risk assessors for birds, *i.e.* discourage the use
199 of additional vertebrate testing, while acquiring sufficient and appropriate
200 data to improve assessment models. Clearly, the way forward seems to be
201 an intensive search of the literature for information already collected. In this
202 context, this paper presents a state-of-the-art of the different kinds of models
203 that have been developed in the last decades to sustain the deciphering of
204 chemical effects on birds. Notice that we do not detail the different types of
205 model (done by [Larras et al \(2022b\)](#); [Astuto et al \(2022\)](#)) to focus on where
206 reusable data feeding these models can be caught up.

207

208 After giving full details on the bibliographical methodology we adopted, we
209 present the general trends that emerge from our corpus of articles. We give a
210 breakdown of models by type (e.g., TD, food web) and by level of organiza-
211 tion (e.g., individual, community), before specifically examining bird models
212 crossing model type with their inputs (e.g., exposure routes) and outputs (e.g.,
213 measured internal concentration). Then, we conclude in identifying the main
214 gaps, as well as some ideas for overcoming them, and to go beyond.

215 **2 Methods**

216 Scientific articles were screened within several bibliographic databases includ-
217 ing Clarivate Web of Science ©, PubMed ([McEntyre and Ostell, 2002](#)),
218 Google Scholar ([López-Cózar et al, 2019](#)), Scopus ([Baas et al, 2020](#)), and the
219 co-authors' personal databases (those provided by [Kuo et al \(2022\)](#), > 500

220 entries, and [Mamy et al \(2022\)](#), > 2500 entries). The final paper collection
221 was achieved in February 2023, covering a period from the end of the seventies
222 until today.

223
224 The bibliographic queries were performed following several steps summarized
225 in [Figure 1](#). Google Scholar was first requested with an initial Scopus keyword
226 equation (data not shown) providing a preliminary collection of few papers that
227 were scrutinized through titles and abstracts to refine the final query equation.
228 Then, the above-mentioned bibliographic databases were all required with the
229 final Scopus keyword equation ([Figure 1](#)). From there, we excluded references
230 of books, book chapters, editorials and notes, to only keep peer-reviewed jour-
231 nal articles. Finally, we excluded all papers not referring to modeling issues. In
232 particular, we excluded papers without any model, or containing pure descrip-
233 tive models, such as those with only basic hypothesis testing methods. Purely
234 general papers without case studies were also removed from our collection.

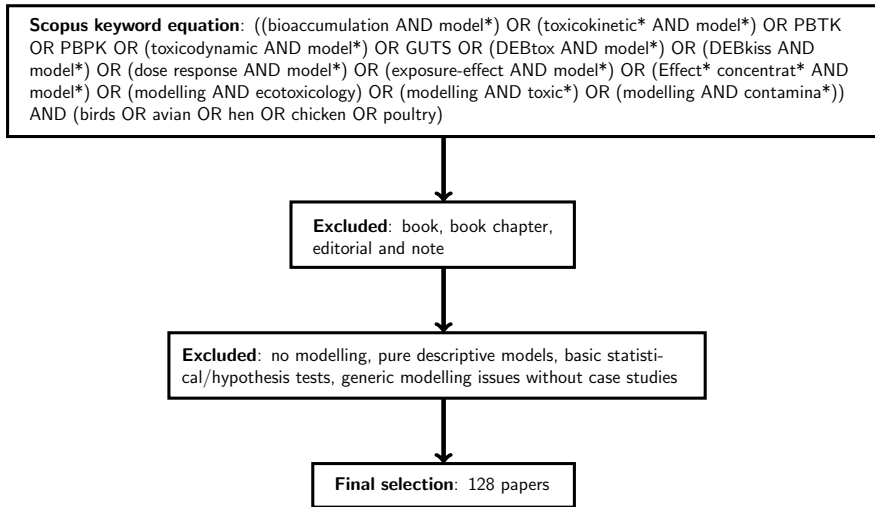


Fig. 1 Diagram of the bibliographic method we used to build the final corpus of scientific papers analyzed in this review.

235 Additionally to the terms we used in our query, our paper collection was
 236 only limited to research and review papers published in peer-reviewed jour-
 237 nals and written in English. At the end of the process, we had a total
 238 of 130 papers (97 from the bibliographic databases and 33 from the co-
 239 authors' personal databases). All these papers have been gathered together
 240 within a metadata file (in comma separator value format) available at
 241 <https://doi.org/10.5281/zenodo.7685817>. In addition to the classical fields
 242 defining a bibliographic reference, this metadata file records information
 243 about the biological species (wild/domestic, feeding regime, common and
 244 Latin names), the chemical substances (group, name, CAS number) and/or
 245 the models (model type, level of biological organization that is concerned)
 246 that have been used by the authors. The metadata file also inventories the

247 exposure routes and the measured endpoints provided in the papers. In the
248 end, the metadata file has 130 rows and 59 columns. A critical step in the
249 assembly of this metadata was the identification of the model type used by
250 the authors. To proceed, we first separated models processing at the individ-
251 ual level, that is the most employed. Among them, dose-response models were
252 easy to classify. For the rest of the papers, a careful check within the different
253 sections of the papers finally allowed us to clearly identified the type of model.

254

255 The paper collection, no reference being duplicated, was imported into the R
256 software (R Core Team, 2022) and analyzed to quantify the scientific produc-
257 tion per year, feeding groups (distinguishing between carnivores, frugivores,
258 granivores, herbivores, insectivores, omnivores, and piscivores), chemical
259 groups (according to their usage), level of biological organization (individual,
260 population community)) and model types (see Table 1 hereafter). **In the end,**
261 **our paper collection led us to identify the main research tendencies related to**
262 **the employment of models in support of a better deciphering of the impacts**
263 **of chemical substances on birds. This also allowed us to highlight advantages**
264 **and drawbacks of these models.**

265

266 Additionally to the metadata file, the supplementary material provided at
267 <https://doi.org/10.5281/zenodo.7685817> contains all resources to identically
268 reproduce the figures we are presenting below.

3 Results

Without claiming exhaustivity, our collection of papers (fully listed at the end of the manuscript) shows that studies involving models in bird ecotoxicology started to be published during the late seventies, with a slight increase from 2000, then only few papers each year (Figure 2). Half of the 130 papers focused on granivores (namely, seed-eating birds (Anadón et al, 2011; Fournier et al, 2015; Pollet et al, 1985)). Among wild species, groups of carnivores (*i.e.*, predatory birds, such as raptors (Azmanis et al, 2021; Engelman et al, 2012; Rattner et al, 2020)) and piscivores (*i.e.*, birds foraging for and eating fish or other sea life (An et al, 2006; Goutte et al, 2018; Sánchez et al, 2019)) are similarly represented (between 9 and 14 %) (Figure 3, upper panel). A bit less than one third of the papers investigated drugs, while around 20% of them focused on PPP (Figure 3, lower panel). Regarding trace metallic elements, mercury and derivatives have been the most studied (Smith et al, 2009; Nichols et al, 2010; Jackson et al, 2011). Exposure routes, all chemical substances combined, covered the full range of bird feeding regimes via their food sources. Exposure via injection or oral administration were the most widely studied regarding toxicokinetic-toxicodynamic aspects. Last but not least, exposure models describing the contamination routes, dealt with environment (*i.e.*, exposure via air, or not specified), food, or more rarely water *via* drinking (Nelson et al, 1998; Conder et al, 2009; Moore et al, 2018).

291 The salient point, which is not directly visible from Figure 3 but which follows
292 directly from it, is the total absence of studies that address the effects of PPP
293 on bird species of interest for the regulatory environmental risk assessment.
294 For example, European regulations 283/20134 and 284/20135 recommend
295 determining the acute oral toxicity of an active substance to a quail species
296 (Japanese quail, *Coturnix coturnix japonica* or bobwhite quail, *Colinus vir-*
297 *ginianus*), while data on additional species, such as *Serinus canaria*, may be
298 requested by other legislative frameworks ([European Food Safety Authority](#)
299 [et al, 2023](#)). These quail and canary species were totally absent from our set of
300 studies. On the contrary, poultry species are studied a lot, and the most, with
301 a majority of the related papers employing toxico-/pharmaco-kinetic (TPK)
302 models. Laying hens and broiler chicken species were both studied, the latter
303 being much more used (47 out of 130 papers). Regarding chicken, exposures
304 to drugs and PPP were the most investigated contaminants, while modeling
305 speaking, TPK models are almost exclusively used among the 47 papers.

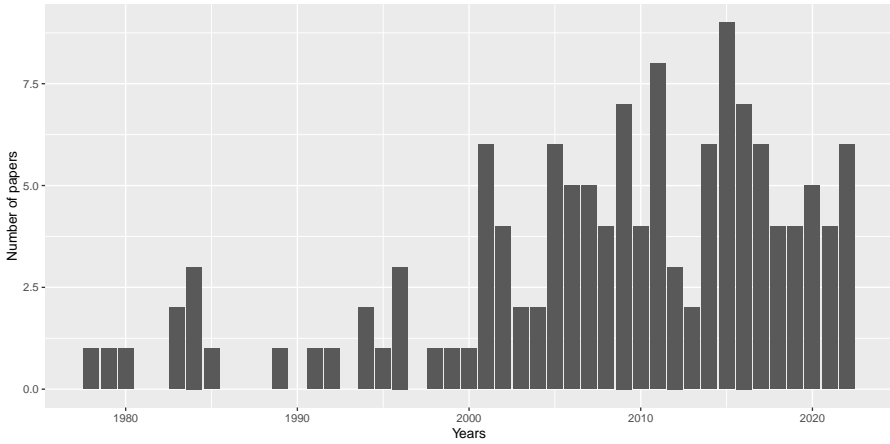


Fig. 2 Number of papers published per year among our collection of 130 scientific articles.

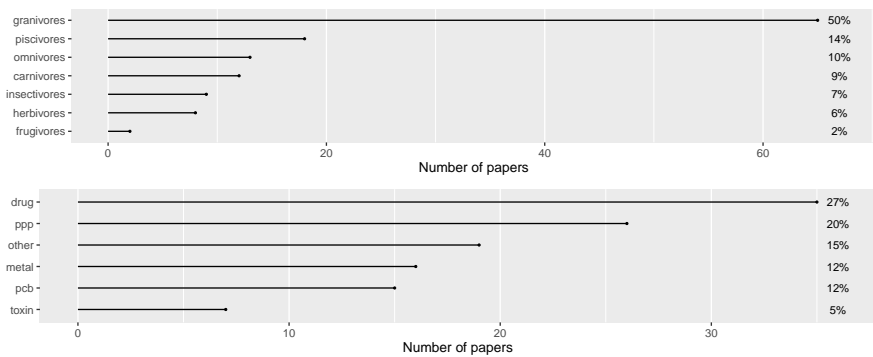


Fig. 3 Number of papers per feeding groups (upper panel) and chemical groups (lower panel) among our collection of 130 scientific articles.

306 About 80% of the studies were conducted at the individual level (Table 1, left
 307 panel). Those papers mainly addressed toxicokinetics or bioaccumulation of
 308 one or several substances in the organisms, leading to model concentration
 309 changes over time either in the whole body ([Abou-Donia, 1979](#); [Tarazona et al,](#)

310 2015), or in different organs (Bean et al, 2019; Suknikom et al, 2016), includ-
311 ing eggs (MacLachlan, 2010; Hekman and Schefferlie, 2011). Toxicokinetic
312 aspects of drugs in chicken or laying hens were the most frequent combination
313 (Furusawa et al, 1996; Henri et al, 2017), investigating residues of chemical in
314 muscles or eggs, which suggested food consumption purpose. Toxicodynamic
315 and dose-response studies have also been conducted, describing the effect of
316 a chemical at the individual level, over time or not (Eagles-Smith et al, 2009;
317 Zhao et al, 2014). However, Toxicodynamic and dose-response studies were
318 rarer, probably because they would imply experiments with vertebrates that
319 are subject to restrictions. Another plausible explanation could be a lack
320 of interest in toxic effects on laboratory species themselves, contrary to the
321 indirect effects that its diet may have on human health (Rani et al, 2021). In
322 this perspective, TPK models are the appropriate tools.

323

324 At the population level, several model frameworks have been employed such
325 as individual-based models (Hallam et al, 1996), matrix demographic models
326 (Goutte et al, 2018), or Monte Carlo Markov Chain models (Bennett and
327 Etterson, 2007). Such models describe the effect of a chemical at the popula-
328 tion level, either by incorporating critical effect concentrations on the chosen
329 endpoints (*e.g.*, survival, reproduction, behavior) together with an exposure
330 scenario (Etterson and Bennett, 2013), or by directly negatively impacting

331 one or several vital rates, such as survival rate or reproductive success, com-
332 pared to a scenario without contamination ([An et al, 2006](#)).

333

334 At higher levels of biological organization and/or with spatially explicit mod-
335 els, studies are much rarer (less than 5%) (Table 1, right panel). Community
336 level papers from our collection used food chain models to investigate bioac-
337 cumulation via two case studies (organochlorine accumulated in Arctic birds
338 ([Borgå et al, 2004](#)) and polychlorinated biphenyls accumulated in eggs of
339 San Francisco bay birds ([Gobas and Arnot, 2010](#))). In our database spatially
340 explicit models were population models including a compartment describing
341 environmental changes and/or where birds were located in space, allowing to
342 investigate for example habitat modification impact ([Nacci et al, 2005](#)), feed-
343 ing habits ([Matsinos and Wolff, 2003](#)), or crop rotation ([Topping et al, 2005](#)).

344

Table 1 Number (#) of papers per model type (left) and per level of organization (right), among our collection of 130 scientific articles.

Model type	Meaning or Based on	#	Biological level	#
TPK	Toxico-/Pharmaco-Kinetic	89	Individual	104
TD	Toxico-Dynamic	12	Population	22
DR	Dose response	4	Community	2
Energy-based	Dynamic Energy Budget theory	5	Landscape	3
ODE based	Ordinary Differential Equations	11		
IBM	Individuals or Agents	3		
Food web	Multiple trophic interactions	2		
Spatial	Spatially explicit	3		
Exposure	Exposure profile feature	13		
Other	Any other type	6		

345 By crossing views on our paper collection, classified by both model types
346 (columns) and either model outputs (measured internal concentration, pink
347 lines / measured endpoints, blue lines) or model inputs (exposure routes,
348 orange lines), we finely deciphered what were the main objectives of most
349 of the studies on birds exposed to chemicals. As shown in Figure 4, most of
350 the studies employed TPK models to investigate drug effects on birds after
351 injection or oral administration (Kuo et al, 2022), by measuring the time
352 course of internal concentrations at the whole organism level (Gögebakan and
353 Eraslan, 2015), or distinguishing target organs (Yang et al, 2014).

355 Figure 4 (second column and blue lines) also clearly demonstrates that
356 toxico/pharmaco-dynamics and dose-response analyses are under-represented
357 (see also Table 1, left panel), which points to a crucial gap in observed data of
358 chemical effects on bird life history traits. While the lack of toxico/pharmaco-
359 dynamic models can be understood easily enough (due to their difficult
360 handling and implementation), it is much more surprising to find so few
361 studies involving dose-response models, while they are today the basis of the
362 regulatory environmental risk assessment. Moreover, there are today no gen-
363 eral accepted methods that are currently available for how to calibrate and
364 validate toxicokinetic-toxicodynamics (TKTD) models without animal testing
365 ([European Food Safety Authority et al, 2023](#)). As a consequence, due to the
366 3R requirements ([European Parliament and European Council, 2010](#)), such a
367 lack in effect quantifier models prevents to attempt interconnecting individual
368 and population levels in the perspective of gaining in ecological relevance,
369 while still including information for which it is easier to obtain experimental
370 observations. Contamination via food represented the main exposure route
371 ($\sim 45\%$) within studies covered by our 130 papers (Figure 4, fourth orange
372 line). For example, Meda *et al.* developed a physiologically based pharma-
373 cokinetic model to investigate the main factors involved in the transfer of
374 α -hexabromocyclododecane to broiler meat ([Méda et al, 2020](#)); [Fournier et al](#)
375 ([2015](#)) assessed the impact of physiological characteristics of laying hen on
376 the transfer of ingested PCBs to their eggs. Regarding exposure models, they
377 have been developed to address levels of chemical contamination in the field,

378 mainly for PPP. For example, Moore *et al.* developed probabilistic models to
379 estimate, during the breeding season and the spring and fall migrations, how
380 many chlorpyrifos and malathion granules Kirtland's warblers ingest and,
381 from that, the quantity of pesticide ingested (Moore *et al.*, 2018).

382

383 Among the 130 papers, some studies were generic in scope, but for differ-
384 ent reasons. A total of 41 papers (31.5%) concerned several biological species
385 that were simultaneously studied as exposed to a same chemical (Newsted
386 *et al.*, 2006; Samuels and Ladino, 1984). A total of 45 papers (34.6%) reported
387 effects of several chemicals on one bird species (Topping *et al.*, 2005; Wayland
388 *et al.*, 2008). And only 8 papers out the 130 were general reviews covering a
389 wide spectrum of species-compound combinations (see for example Kuo *et al.*
390 (2022)). It is worth to note that only two papers dealt with the impacts of
391 multiple stressors: the first on white-tailed eagle populations (Korsman *et al.*,
392 2012); the second on the common loon (Nacci *et al.*, 2005). One of the most
393 striking points of our review is that only 9 papers (~7%) gave access to raw
394 data, potentially reusable for further studies.



Fig. 4 Cross-view of the 130 papers analyzed in this review, categorized by model type (columns) and model outputs (measured internal concentration, pink lines, measured endpoints, blue lines) or model inputs (exposure routes, orange lines). At column-line intercepts, histograms show the number of papers as a function of the studied chemical(s).

395 Results displayed in Figure 4 also appeared in a limpud manner within the title-
 396 based word cloud provided as graphical abstract. This word cloud specifically

397 emphasizes how frequent TPK studies applied to chickens were, as well as that
398 toxico/pharmaco-kinetic models were equally frequently employed, while no
399 chemical substances appeared more studied than another one.

400 **4 Conclusion**

401 Our bibliographic corpus showed a certain diversity in model types, chemicals,
402 exposure routes and feeding groups. Nevertheless, we identified a huge gap in
403 models dealing with chemical effects on birds at the individual level, even if
404 we found a large collection of papers on toxico/pharmaco-kinetic aspects. This
405 is far from being a negligible source of information. However, originally inter-
406 ested in toxicokinetic-toxicodynamic models on birds exposed to PPP, it was
407 clear that we would have very few previous studies at our disposal on which to
408 capitalize. Focusing on bird species targeted by the regulatory environmental
409 risk assessment and their exposure to PPP in addition, we ended up with no
410 dedicated resources to draw on. Both bad and good news in the end. Indeed,
411 we had found a new niche in which to innovate and develop new modeling tools
412 to support next generation risk assessment for birds. In such a perspective, the
413 key point will undoubtedly be the availability of raw data to build clever and
414 comprehensible mechanistic effects models, generic enough to be employed for
415 a wide battery of bird species and chemical compound combinations. Under
416 the umbrella of Open Science, achieving such dreamed tools, should manda-
417 torily imply full compliance to the FAIR data principles. To do so, we could
418 recommend adding non invasive endpoint measurements on birds together with

419 the current practice of TPK studies, or *in vitro* studies that are considered
420 as a good alternative to *in vivo* testing to better decipher TPK properties.
421 Such data could advantageously support further development of the TPK part
422 of TPK-TPD models, tools that now make sense to our community, which
423 more broadly advocates the need to modernize wildlife risk assessment through
424 improved collaboration, data sharing, application of standardized exposure
425 scenarios, better communication of assumptions and uncertainties of models,
426 and post-regulatory monitoring (Morrissey et al, 2023).

427 5 Supplementary Information

428 All supplementary information mentioned in this manuscript is available at
429 <https://doi.org/10.5281/zenodo.7685817>.

430 6 Acknowledgment

431 This work was : (i) part of a tender project financially supported by EFSA
432 (OC/EFSA/SCER/2021/07); (ii) based on a preliminary work performed by
433 experts among co-authors within the framework of the collective scientific
434 assessment commissioned by the French Ministries for Ecology, for Research,
435 and for Agriculture on the effects of plant protection products on biodiversity
436 and ecosystem services and published in May 2022; (iii) performed under
437 the umbrella of the French GDR "Aquatic Ecotoxicology" framework which
438 aims at fostering stimulating scientific discussions and collaborations for more
439 integrative approaches in ecotoxicology. The authors would like to thank Dr.

440 Raphaël Pelissier & Dr. Philippe Verley from IRD (UMR AMAP, Montpellier,
441 France) who supported the participation of Dr. Dominique Lamonica once
442 she started in her new position as IT engineer in ecology.

443

444 **Ethics approval** Not applicable.

445

446 **Consent to participate** Not applicable.

447

448 **Consent for publication** All authors contributed to and agreed on the final
449 version of the manuscript.

450

451 **Authors contributions** Dominique Lamonica and Lison Charvy: Paper
452 collection, Metadata collection and curation. Dominique Lamonica: Metadata
453 investigation, Methodology, Visualization, Analysis. Dominique Lamonica
454 and Sandrine Charles: Writing - Original draft preparation. Sandrine Charles:
455 Investigation, Supervision, Validation, Writing - Reviewing and Editing. Dave
456 Kuo, Clementine Fritsch, Michaël Coeurdassier and Philippe Berny: Investi-
457 gation, Reviewing and Editing.

458

459 **Funding** EFSA (OC/EFSA/SCER/2021/07).

460

461 **Competing interests** The authors declare no competing interests.

462

463 **Data, Material and/or Code availability** Data and code are available at
464 <https://doi.org/10.5281/zenodo.7685817>.

465 References

- 466 Astuto MC, Nicola MRD, Tarazona JV, et al (2022) *In Silico* Methods for
467 Environmental Risk Assessment: Principles, Tiered Approaches, Applica-
468 tions, and Future Perspectives. In: Benfenati E (ed) *In Silico* Methods for
469 Predicting Drug Toxicity, Methods in Molecular Biology, vol 2425. Springer
470 Nature, p 589–636, <https://doi.org/10.1016/B978-0-12-811037-9.00023-0>
- 471 Baas J, Schotten M, Plume A, et al (2020) Scopus as a curated, high-
472 quality bibliometric data source for academic research in quantitative science
473 studies. *Quantitative science studies* 1(1):377–386. [https://doi.org/10.1162/](https://doi.org/10.1162/qss_a_00019)
474 [qss_a_00019](https://doi.org/10.1162/qss_a_00019)
- 475 Bishop CA, Moran AJ, Toshack MC, et al (2018) Hummingbirds and bumble
476 bees exposed to neonicotinoid and organophosphate insecticides in the fraser
477 valley, british columbia, canada. *Environmental toxicology and chemistry*
478 37(8):2143–2152. <https://doi.org/https://doi.org/10.1002/etc.4174>
- 479 Bowler DE, Heldbjerg H, Fox AD, et al (2019) Long-term declines of European
480 insectivorous bird populations and potential causes. *Conservation Biology*
481 33(5):1120–1130. <https://doi.org/10.1111/cobi.13307>

- 482 Bruhl CA, Zaller JG (2019) Biodiversity Decline as a Consequence of
483 an Inappropriate Environmental Risk Assessment of Pesticides. *Frontiers*
484 in *Environmental Science* 7:2013–2016. [https://doi.org/10.3389/fenvs.2019.](https://doi.org/10.3389/fenvs.2019.00177)
485 [00177](https://doi.org/10.3389/fenvs.2019.00177)
- 486 Cade TJ, Lincer JL, White CM, et al (1971) DDE residues and eggshell changes
487 in Alaskan falcons and hawks. *Science* 172(3986):955–957. [https://doi.org/](https://doi.org/10.1126/science.172.3986.955)
488 [10.1126/science.172.3986.955](https://doi.org/10.1126/science.172.3986.955)
- 489 Carson R (1962) *Silent Spring*. Fawcett Publications, Inc., Greenwich, Conn.,
490 [https://doi.org/10.1016/0027-5107\(77\)90059-8](https://doi.org/10.1016/0027-5107(77)90059-8)
- 491 Eng ML, Stutchbury BJ, Morrissey CA (2017) Imidacloprid and chlorpyrifos
492 insecticides impair migratory ability in a seed-eating songbird. *Scientific*
493 *Reports* 7(1):1–9. <https://doi.org/10.1038/s41598-017-15446-x>
- 494 Eng ML, Stutchbury BJ, Morrissey CA (2019) A neonicotinoid insecticide
495 reduces fueling and delays migration in songbirds. *Science* 365(6458):1177–
496 1180. <https://doi.org/10.1126/science.aaw9419>
- 497 European Food Safety Authority, Aagaard A, Berny P, et al (2023) Peer review
498 of the pesticide risk assessment of the active substance *Reynoutria sach-*
499 *linensis* extract. *EFSA Journal* 21(2):7790. [https://doi.org/10.2903/j.efsa.](https://doi.org/10.2903/j.efsa.2023.7790)
500 [2023.7790](https://doi.org/10.2903/j.efsa.2023.7790)

- 501 European Parliament, European Council (2010) Directive 2010/63/EU on the
502 protection of animals used for scientific purposes. Official Journal of the
503 European Union L 276/33(20.10.2010):33–79
- 504 Forbes VE, Brain R, Edwards D, et al (2015) Assessing pesticide risks to
505 threatened and endangered species using population models: Findings and
506 recommendations from a CropLife America Science Forum. Integrated Envi-
507 ronmental Assessment and Management 11(3):348–354. [https://doi.org/10.](https://doi.org/10.1002/ieam.1628)
508 [1002/ieam.1628](https://doi.org/10.1002/ieam.1628)
- 509 Forbes VE, Salice CJ, Birnir B, et al (2017) A Framework for Predict-
510 ing Impacts on Ecosystem Services From (Sub)Organismal Responses to
511 Chemicals. Environmental Toxicology and Chemistry 36(4):845–859. [https:](https://doi.org/10.1002/etc.3720)
512 [//doi.org/10.1002/etc.3720](https://doi.org/10.1002/etc.3720)
- 513 Gilbert N (2011) Data gaps threaten chemical safety law. Nature
514 475(7355):150–151. <https://doi.org/10.1038/475150a>
- 515 Hallmann CA, Foppen RP, Van Turnhout CA, et al (2014) Declines in insec-
516 tivorous birds are associated with high neonicotinoid concentrations. Nature
517 511(7509):341–343. <https://doi.org/10.1038/nature13531>
- 518 Humann-Guillemot S, Laurent S, Bize P, et al (2021) Contamination by
519 neonicotinoid insecticides in barn owls (*Tyto alba*) and alpine swifts (*Tachy-*
520 *marptis melba*). Science of The Total Environment 785:147,403. [https://doi.](https://doi.org/https://doi.org/10.1016/j.scitotenv.2021.147403)
521 [org/https://doi.org/10.1016/j.scitotenv.2021.147403](https://doi.org/https://doi.org/10.1016/j.scitotenv.2021.147403)

- 522 Larras F, Beaudouin R, Berny P, et al (2022a) A meta-analysis of ecotoxi-
523 cological models used for plant protection product risk assessment before
524 their placing on the market. *Science of the Total Environment* p 157003.
525 <https://doi.org/10.1016/j.scitotenv.2022.157003>
- 526 Larras F, Charles S, Chaumot A, et al (2022b) A critical review of modelling
527 approaches for environmental risk assessment due to pesticides. *Environ-*
528 *ment Science and Pollution Research* 29:43,448–43,500. [https://doi.org/10.](https://doi.org/10.1007/s11356-022-19111-3)
529 [1007/s11356-022-19111-3](https://doi.org/10.1007/s11356-022-19111-3)
- 530 Li L, Li D (2021) Inter-Individual Variability and Non-linear Dose-Response
531 Relationship in Assessing Human Health Impact From Chemicals in LCA:
532 Addressing Uncertainties in Exposure and Toxicological Susceptibility. *Fron-*
533 *tiers in Sustainability* 2:1–12. <https://doi.org/10.3389/frsus.2021.648138>
- 534 López-Cózar ED, Orduña-Malea E, Martín-Martín A (2019) Google scholar as
535 a data source for research assessment. In: *Springer handbook of science and*
536 *technology indicators*. Springer, p 95–127
- 537 Mamy L, Pesce S, Sanchez W, et al (2022) Impacts des produits phytophar-
538 maceutiques sur la biodiversité et les services écosystémiques. Rapport de
539 l'expertise scientifique collective. <https://doi.org/10.17180/0gp2-cd65>
- 540 McEntyre J, Ostell J (2002) *The NCBI handbook*. Bethesda (MD): National
541 Center for Biotechnology Information (US)

- 542 Morrissey C, Fritsch C, Fremlin K, et al (2023) Advancing exposure assessment
543 approaches to improve wildlife risk assessment. *Integrated Environmental*
544 *Assessment and Management* 00:1–25. <https://doi.org/10.1002/ieam.4743>
- 545 Møller AP (2019) Parallel declines in abundance of insects and insectivorous
546 birds in denmark over 22 years. *Ecology and Evolution* 9(11):6581–6587.
547 <https://doi.org/https://doi.org/10.1002/ece3.5236>
- 548 Naidu R, Biswas B, Willett IR, et al (2021) Chemical pollution: A growing
549 peril and potential catastrophic risk to humanity. *Environment International*
550 156:106,616. <https://doi.org/10.1016/j.envint.2021.106616>
- 551 Pesce S, Mamy L, Achard AI, et al (2021) Collective scientific assessment as
552 a relevant tool to inform public debate and policy-making : an illustration
553 about the effects of plant protection products on biodiversity and ecosystem
554 services. *Environmental Science and Pollution Research* 28:38,448–38,454.
555 <https://doi.org/10.1007/s11356-021-14863-w>
- 556 Poisson MC, Garrett DR, Sigouin A, et al (2021) Assessing pesticides exposure
557 effects on the reproductive performance of a declining aerial insectivore. *Eco-*
558 *logical Applications* 31(7):e02,415. [https://doi.org/https://doi.org/10.1002/](https://doi.org/https://doi.org/10.1002/eap.2415)
559 [eap.2415](https://doi.org/https://doi.org/10.1002/eap.2415)
- 560 R Core Team (2022) R: A Language and Environment for Statistical Com-
561 puting. R Foundation for Statistical Computing, Vienna, Austria, URL
562 <https://www.R-project.org/>

- 563 Rani L, Thapa K, Kanojia N, et al (2021) An extensive review on the conse-
564 quences of chemical pesticides on human health and environment. *Journal*
565 *of Cleaner Production* 283:124,657. [https://doi.org/10.1016/j.jclepro.2020.](https://doi.org/10.1016/j.jclepro.2020.124657)
566 [124657](https://doi.org/10.1016/j.jclepro.2020.124657)
- 567 Ratcliffe D (1967) Decrease in Eggshell Weight in Certain Birds of Prey. *Nature*
568 215(8):208–210
- 569 Rogers KH, McMillin S, Olstad KJ, et al (2019) Imidacloprid Poisoning of
570 Songbirds Following a Drench Application of Trees in a Residential Neigh-
571 borhood in California, USA. *Environmental Toxicology and Chemistry*
572 38:1724–1727. <https://doi.org/10.1002/etc.4473>
- 573 Servien R, Latrille E, Patureau D, et al (2022) Machine learning models based
574 on molecular descriptors to predict human and environmental toxicological
575 factors in continental freshwater. *Peer Community In Ecotoxicology and*
576 *Environmental Chemistry* 2:e15
- 577 Tang FH, Lenzen M, McBratney A, et al (2021) Risk of pesticide pollution at
578 the global scale. *Nature Geoscience* 14(4):206–210. [https://doi.org/10.1038/](https://doi.org/10.1038/s41561-021-00712-5)
579 [s41561-021-00712-5](https://doi.org/10.1038/s41561-021-00712-5)
- 580 Topping CJ, Weyman GS (2018) Rabbit population landscape-scale simulation
581 to investigate the relevance of using rabbits in regulatory environmental risk
582 assessment. *Environmental Modeling and Assessment* 23:415–457

583 Topping CJ, Dalby L, Skov F (2016) Landscape structure and management
584 alter the outcome of a pesticide ERA: Evaluating impacts of endocrine
585 disruption using the ALMaSS European Brown Hare model. *Science of the*
586 *Total Environment* 541:1477–1488. [https://doi.org/10.1016/j.scitotenv.](https://doi.org/10.1016/j.scitotenv.2015.10.042)
587 [2015.10.042](https://doi.org/10.1016/j.scitotenv.2015.10.042)

588 Topping CJ, Aldrich A, Berny P (2020) Overhaul environmental risk assess-
589 ment for pesticides. *Science* 367(6476):360–363. [https://doi.org/10.1126/](https://doi.org/10.1126/science.aay1144)
590 [science.aay1144](https://doi.org/10.1126/science.aay1144)

591 Vinken M (2013) The adverse outcome pathway concept: A pragmatic tool in
592 toxicology. <https://doi.org/10.1016/j.tox.2013.08.011>

593 de Zwaan DR, Scridel D, Altamirano TA, et al (2022) GABB: A global dataset
594 of alpine breeding birds and their ecological traits. *Scientific Data* 9:627.
595 <https://doi.org/10.1038/s41597-022-01723-6>

596 **Bibliographic corpus of the review**

597 Abou-Donia MB (1979) Pharmacokinetics and metabolism of a topically
598 applied dose of O-4-bromo-2,5-dichlorophenyl O-methyl phenylphospho-
599 nothioate in hens. *Toxicology and Applied Pharmacology* 51(2):311–328.
600 [https://doi.org/10.1016/0041-008X\(79\)90474-5](https://doi.org/10.1016/0041-008X(79)90474-5)

- 601 Ackerman JT, Eagles-Smith Ca, Heinz G (2014) Mercury in San Francisco
602 Bay-Delta Birds: Trophic Pathways, Bioaccumulation and Ecotoxicologi-
603 cal Risk to Avian Reproduction. U.S. Geological Survey Open-File Report
604 2014-1251, <https://doi.org/10.3133/ofr20141251>, URL [http://dx.doi.org/](http://dx.doi.org/10.3133/ofr20141251)
605 [10.3133/ofr20141251](http://dx.doi.org/10.3133/ofr20141251)
- 606 Ahrens FA, Dyer DC, Lloyd WE (1980) Mirex kinetics in chickens. Journal
607 of Toxicology and Environmental Health 6(4):835–842. [https://doi.org/10.](https://doi.org/10.1080/15287398009529901)
608 [1080/15287398009529901](https://doi.org/10.1080/15287398009529901)
- 609 An W, Hu JY, Yao F (2006) A method of assessing ecological risk
610 to night heron, *Nycticorax nycticorax*, population persistence from
611 dichlorodiphenyltrichloroethane exposure. Environmental Toxicology and
612 Chemistry 25(1):281–286. <https://doi.org/10.1897/05-043R.1>
- 613 Anadón A, Bringas P, Martínez-Larranaga MR, et al (1994a) Bioavailability,
614 pharmacokinetics and residues of chloramphenicol in the chicken. Journal of
615 Veterinary Pharmacology and Therapeutics 23:52–58
- 616 Anadón A, Martínez-Larranaga MR, Diaz MJ, et al (1994b) Pharmacokinetics
617 of doxycycline in broiler chickens. Avian Pathology 23(1):79–90. [https://](https://doi.org/10.1080/03079459408418976)
618 doi.org/10.1080/03079459408418976
- 619 Anadón A, Martínez-Larranaga MR, Diaz MJ, et al (1996) Pharmacokinetics
620 of amoxicillin in broiler chickens. Avian Pathology 25(3):449–458. [https:](https://doi.org/10.1080/03079459608419154)
621 [//doi.org/10.1080/03079459608419154](https://doi.org/10.1080/03079459608419154)

- 622 Anadón A, Martínez-Larrañaga MR, Iturbe J, et al (2001) Pharmacokinetics
623 and residues of ciprofloxacin and its metabolites in broiler chickens.
624 *Research in Veterinary Science* 71(2):101–109. [https://doi.org/10.1053/rvsc.](https://doi.org/10.1053/rvsc.2001.0494)
625 [2001.0494](https://doi.org/10.1053/rvsc.2001.0494)
- 626 Anadón A, Martínez MA, Martínez M, et al (2008a) Oral bioavailability,
627 tissue distribution and depletion of flumequine in the food producing ani-
628 mal, chicken for fattening. *Food and Chemical Toxicology* 46(2):662–670.
629 <https://doi.org/10.1016/j.fct.2007.09.086>
- 630 Anadón A, Martínez MA, Martínez M, et al (2008b) Plasma and tissue
631 depletion of florfenicol and florfenicol-amine in chickens. *Journal of Agricultural*
632 *and Food Chemistry* 56(22):11,049–11,056. [https://doi.org/10.1021/](https://doi.org/10.1021/jf802138y)
633 [jf802138y](https://doi.org/10.1021/jf802138y)
- 634 Anadón A, Suárez FH, Martínez MA, et al (2011) Plasma disposition and
635 tissue depletion of difloxacin and its metabolite sarafloxacin in the food
636 producing animals, chickens for fattening. *Food and Chemical Toxicology*
637 49(2):441–449. <https://doi.org/10.1016/j.fct.2010.11.021>
- 638 Antonissen G, De Baere S, Novak B, et al (2020) Toxicokinetics of hydrolyzed
639 fumonisin B1 after single oral or intravenous bolus to broiler chickens fed a
640 control or a fumonisins-contaminated diet. *Toxins* 12(6):1–13. [https://doi.](https://doi.org/10.3390/toxins12060413)
641 [org/10.3390/toxins12060413](https://doi.org/10.3390/toxins12060413)

- 642 Ares J (2003) Time and space issues in ecotoxicology: Population models,
643 landscape pattern analysis, and long-range environmental chemistry. *Envi-*
644 *ronmental Toxicology and Chemistry* 22(5):945–957. [https://doi.org/10.](https://doi.org/10.1002/etc.5620220501)
645 [1002/etc.5620220501](https://doi.org/10.1002/etc.5620220501)
- 646 Azmanis P, Pappalardo L, Sara ZA, et al (2021) Disposition of posaconazole
647 after single oral administration in large falcons (*Falco spp*): Effect of meal
648 and dosage and a non-compartmental model to predict effective dosage.
649 *Medical Mycology* 59(9):901–908. <https://doi.org/10.1093/mmy/myab019>
- 650 Baier V, Paini A, Schaller S, et al (????) *Environment International* 169. [https:](https://doi.org/10.1016/j.envint.2022.107547)
651 [//doi.org/10.1016/j.envint.2022.107547](https://doi.org/10.1016/j.envint.2022.107547)
- 652 Bakir A, O'Connor IA, Rowland SJ, et al (2016) Relative importance of
653 microplastics as a pathway for the transfer of hydrophobic organic chemi-
654 cals to marine life. *Environmental Pollution* 219:56–65. [https://doi.org/10.](https://doi.org/10.1016/j.envpol.2016.09.046)
655 [1016/j.envpol.2016.09.046](https://doi.org/10.1016/j.envpol.2016.09.046)
- 656 Bean TG, Gross MS, Karouna-Renier NK, et al (2019) Toxicokinetics of
657 Imidacloprid-Coated Wheat Seeds in Japanese Quail (*Coturnix japonica*)
658 and an Evaluation of Hazard. *Environmental Science and Technology*
659 53(7):3888–3897. <https://doi.org/10.1021/acs.est.8b07062>
- 660 Benlashehr I, Repussard C, Jouglar JY, et al (2011) Toxicokinetics of fumonisin
661 B2 in ducks and turkeys. *Poultry Science* 90(8):1671–1675. [https://doi.org/](https://doi.org/10.3382/ps.2011-01434)
662 [10.3382/ps.2011-01434](https://doi.org/10.3382/ps.2011-01434)

- 663 Bennett RS, Etterson MA (2007) Incorporating Results of Avian Toxicity Tests
664 into a Model of Annual Reproductive Success. *Integrated Environmental*
665 *Assessment and Management* 3(4):498–507
- 666 Bistoletti M, Alvarez L, Lanusse C, et al (2013) Disposition kinetics of alben-
667 dazole and metabolites in laying hens. *Journal of Veterinary Pharmacology*
668 *and Therapeutics* 36(2):161–168. [https://doi.org/10.1111/j.1365-2885.2012.](https://doi.org/10.1111/j.1365-2885.2012.01401.x)
669 [01401.x](https://doi.org/10.1111/j.1365-2885.2012.01401.x)
- 670 Borgå K, Fisk AT, Hoekstra PF, et al (2004) Biological and chemical fac-
671 tors of importance in the bioaccumulation and trophic transfer of persistent
672 organochlorine contaminants in arctic marine food webs. *Environmental*
673 *Toxicology and Chemistry* 23(10):2367–2385
- 674 Broekaert N, Devreese M, De Mil T, et al (2015) Oral Bioavailability,
675 Hydrolysis, and Comparative Toxicokinetics of 3-Acetyldeoxynivalenol and
676 15-Acetyldeoxynivalenol in Broiler Chickens and Pigs. *Journal of Agricul-*
677 *tural and Food Chemistry* 63(39):8734–8742. [https://doi.org/10.1021/acs.](https://doi.org/10.1021/acs.jafc.5b03270)
678 [jafc.5b03270](https://doi.org/10.1021/acs.jafc.5b03270)
- 679 Broekaert N, Devreese M, De Boevre M, et al (2017) T-2 Toxin-3 α -glucoside in
680 Broiler Chickens: Toxicokinetics, Absolute Oral Bioavailability, and *In vivo*
681 Hydrolysis. *Journal of Agricultural and Food Chemistry* 65(23):4797–4803.
682 <https://doi.org/10.1021/acs.jafc.7b00698>

- 683 Bush PB, Tanner M, Kiker JT, et al (1978) Tissue residue studies on toxaphene
684 in broiler chickens. *Journal of Agricultural and Food Chemistry* 26(1):126–
685 130. <https://doi.org/10.1021/jf60215a064>
- 686 Capolongo F, Santi A, Tomasi L, et al (2002) Residues of oxytetracycline and
687 its 4'-epimer in edible tissues from turkeys. *Journal of AOAC International*
688 85(1):8–14. <https://doi.org/10.1093/jaoac/85.1.8>
- 689 Conder JM, Sorensen MT, Leitman P, et al (2009) Avian ecological risk
690 potential in an urbanized estuary: Lower Hackensack River, New Jersey,
691 U.S.A. *Science of the Total Environment* 407(3):1035–1047. [https://doi.org/](https://doi.org/10.1016/j.scitotenv.2008.09.043)
692 [10.1016/j.scitotenv.2008.09.043](https://doi.org/10.1016/j.scitotenv.2008.09.043)
- 693 Cornejo J, Lapierre L, Iragüen D, et al (2012) Study of enrofloxacin and
694 flumequine residues depletion in eggs of laying hens after oral administra-
695 tion. *Journal of Veterinary Pharmacology and Therapeutics* 35(1):67–72.
696 <https://doi.org/10.1111/j.1365-2885.2011.01283.x>
- 697 Cortright KA, Wetzlich SE, Craigmill AL (2009) A PBPK model for midazo-
698 lam in four avian species. *Journal of Veterinary Pharmacology and Thera-
699 peutics* 32(6):552–565. <https://doi.org/10.1111/j.1365-2885.2009.01073.x>
- 700 Crocker DR, Lawrence AJ (2018) Estimating the potential effects of pesticide
701 seed treatments on the reproductive success of arable birds. *Ecotoxicology
702 and Environmental Safety* 147:124–131. [https://doi.org/10.1016/j.ecoenv.](https://doi.org/10.1016/j.ecoenv.2017.08.035)
703 [2017.08.035](https://doi.org/10.1016/j.ecoenv.2017.08.035)

- 704 Dauwe T, Jaspers VL, Covaci A, et al (2006) Accumulation of organochlo-
705 rines and brominated flame retardants in the eggs and nestlings of great
706 tits, *Parus major*. Environmental Science and Technology 40(17):5297–5303.
707 <https://doi.org/10.1021/es060747a>
- 708 Delaski KM, Gehring R, Heffron BT, et al (2017) Plasma Concentrations of
709 Fentanyl Achieved with Transdermal Application in Chickens. Journal of
710 Avian Medicine and Surgery 31(1):6–15. <https://doi.org/10.1647/2015-153>
- 711 Drouillard KG, Norstrom RJ (2000) Dietary absorption efficiencies and toxi-
712 cokinetics of polychlorinated biphenyls in ring doves following exposure to
713 aroclor® mixtures. Environmental Toxicology and Chemistry 19(11):2707–
714 2714. <https://doi.org/10.1002/etc.5620191114>
- 715 Drouillard KG, Norstrom RJ (2001) Quantifying maternal and dietary sources
716 of 2,2',4,4',5,5'Hexachlorobiphenyl deposited in eggs of the ring dove (*Strept-*
717 *topelia risoria*). Environmental Toxicology and Chemistry 20(3):561–567.
718 <https://doi.org/10.1002/etc.5620200315>
- 719 Drouillard KG, Norstrom RJ (2003) The influence of diet properties and
720 feeding rates on PCB toxicokinetics in the ring dove. Archives of Envi-
721 ronmental Contamination and Toxicology 44(1):97–106. [https://doi.org/10.](https://doi.org/10.1007/s00244-002-1199-y)
722 [1007/s00244-002-1199-y](https://doi.org/10.1007/s00244-002-1199-y)
- 723 Drouillard KG, Fernie KJ, Smits JE, et al (2001) Bioaccumulation and tox-
724 icokinetics of 42 polychlorinated biphenyl congeners in American kestrels

725 (*Falco sparverius*). Environmental Toxicology and Chemistry 20(11):2514–
726 2522. <https://doi.org/10.1002/etc.5620201117>

727 Drouillard KG, Fernie KJ, Letcher RJ, et al (2007) Bioaccumulation and
728 biotransformation of 61 polychlorinated biphenyl and four polybrominated
729 diphenyl ether congeners in juvenile American kestrels (*Falco sparverius*).
730 Environmental Toxicology and Chemistry 26(2):313–324. [https://doi.org/](https://doi.org/10.1897/06-052R.1)
731 [10.1897/06-052R.1](https://doi.org/10.1897/06-052R.1)

732 Ducrot V, Ashauer R, Bednarska AJ, et al (2016) Using toxicokinetic-
733 toxicodynamic modeling as an acute risk assessment refinement approach in
734 vertebrate ecological risk assessment. Integrated Environmental Assessment
735 and Management 12(1):32–45. <https://doi.org/10.1002/ieam.1641>

736 Eagles-Smith CA, Ackerman JT, Julie YE, et al (2009) Mercury demethylation
737 in waterbird livers: Dose-response thresholds and differences among species.
738 Environmental Toxicology and Chemistry 28(3):568–577. [https://doi.org/](https://doi.org/10.1897/08-245.1)
739 [10.1897/08-245.1](https://doi.org/10.1897/08-245.1)

740 Ehrich M, Correll L, Strait J, et al (1992) Toxicity and toxicokinetics
741 of carbaryl in chickens and rats:a comparative study. Journal of Toxi-
742 cology and Environmental Health 36(4):411–423. [https://doi.org/10.1080/](https://doi.org/10.1080/15287399209531648)
743 [15287399209531648](https://doi.org/10.1080/15287399209531648)

- 744 Engelman CA, Grant WE, Mora MA, et al (2012) Modelling effects of chemical
745 exposure on birds wintering in agricultural landscapes: The western burrow-
746 ing owl (*Athene cunicularia hypugaea*) as a case study. *Ecological Modelling*
747 224(1):90–102. <https://doi.org/10.1016/j.ecolmodel.2011.10.017>
- 748 Eraslan G, Tekeli MY, Karabacak M (2017) Toxicokinetic of cypermethrin in
749 broiler chickens. *Fresenius Environmental Bulletin* 26(7):4704–4710
- 750 Etterson M, Garber K, Odenkirchen E (2017) Mechanistic modeling of insecti-
751 cide risks to breeding birds in North American agroecosystems. *Plos One*
752 12(5):e0176,998. <https://doi.org/10.1371/journal.pone.0176998>
- 753 Etterson MA (2022) Realism, Conservatism, and Tiered Ecological
754 Risk Assessment. *Ecologies* 3(2):131–144. [https://doi.org/10.3390/](https://doi.org/10.3390/ecologies3020011)
755 [ecologies3020011](https://doi.org/10.3390/ecologies3020011)
- 756 Etterson MA, Ankley GT (2021) Endogenous Lifecycle Models for Chemical
757 Risk Assessment. *Environmental Science and Technology* 55(23):15,596–
758 15,608. <https://doi.org/10.1021/acs.est.1c04791>
- 759 Etterson MA, Bennett RS (2013) Quantifying the effects of pesticide expo-
760 sure on annual reproductive success of birds. *Integrated environmental*
761 *assessment and management* 9:590–599. <https://doi.org/10.1002/ieam.1450>

- 762 Fournier A, Feidt C, Dziurla MA, et al (2010) Transfer kinetics to egg yolk and
763 modeling residue recovered in yolk of readily metabolized molecules: Poly-
764 cyclic aromatic hydrocarbons orally administered to laying hens. *Chemo-*
765 *sphere* 78(8):1004–1010. <https://doi.org/10.1016/j.chemosphere.2009.12.008>
- 766 Fournier A, Feidt C, Marchand P, et al (2012) Kinetic study of γ -
767 hexabromocyclododecane orally given to laying hens (*Gallus domesticus*).
768 *Environmental Science and Pollution Research* 19(2):440–447. [https://doi.](https://doi.org/10.1007/s11356-011-0573-6)
769 [org/10.1007/s11356-011-0573-6](https://doi.org/10.1007/s11356-011-0573-6)
- 770 Fournier A, Martin O, Travel A, et al (2015) Modeling PCB transfer into hen
771 eggs: Influence of physiological characteristics of the animal. *Environmental*
772 *Toxicology and Chemistry* 34(1):173–183. <https://doi.org/10.1002/etc.2781>
- 773 Fournier F, Karasov WH, Kenow KP, et al (2002) The oral bioavailabil-
774 ity and toxicokinetics of methylmercury in common loon (*Gavia immer*)
775 chicks. *Comparative Biochemistry and Physiology - A Molecular and Inte-*
776 *grative Physiology* 133(3):703–714. [https://doi.org/10.1016/S1095-6433\(02\)](https://doi.org/10.1016/S1095-6433(02)00140-X)
777 [00140-X](https://doi.org/10.1016/S1095-6433(02)00140-X)
- 778 Furusawa N, Mukai T, Ohori H (1996) Depletion of dietary sulpha-
779 monomethoxine and sulphadimethoxine from various tissues of laying
780 hens. *British Poultry Science* 37(2):435–442. [https://doi.org/10.1080/](https://doi.org/10.1080/00071669608417874)
781 [00071669608417874](https://doi.org/10.1080/00071669608417874)

- 782 García Ovando H, Gorla N, Luders C, et al (1999) Comparative pharmacoki-
783 netics of enrofloxacin and ciprofloxacin in chickens. *Journal of Veterinary*
784 *Pharmacology and Therapeutics* 22(3):209–212. [https://doi.org/10.1046/j.](https://doi.org/10.1046/j.1365-2885.1999.00211.x)
785 [1365-2885.1999.00211.x](https://doi.org/10.1046/j.1365-2885.1999.00211.x)
- 786 Gerletti P, Von Kleist M, Mielke H, et al (2020) Transfer kinetics of fipronil
787 into chicken (*Gallus gallus domesticus*) eggs. *Computational Toxicology*
788 15(February):100,131. <https://doi.org/10.1016/j.comtox.2020.100131>
- 789 Gilbert CM, Filippich LJ, McGeary RP, et al (2007) Toxicokinetics of the
790 active doxorubicin metabolite, doxorubicinol, in sulphur-crested cockatoos
791 (*Cacatua galerita*). *Research in Veterinary Science* 83(1):123–129. [https://](https://doi.org/10.1016/j.rvsc.2006.11.005)
792 doi.org/10.1016/j.rvsc.2006.11.005
- 793 Glaser D, Connolly JP (2002) A model of p,p'-DDE and total PCB bioac-
794 cumulation in birds from the Southern California Bight. *Continental*
795 *Shelf Research* 22(6-7):1079–1100. [https://doi.org/10.1016/S0278-4343\(01\)](https://doi.org/10.1016/S0278-4343(01)00119-4)
796 [00119-4](https://doi.org/10.1016/S0278-4343(01)00119-4)
- 797 Gobas FA, Arnot JA (2010) Food web bioaccumulation model for polychlo-
798 rinated biphenyls in san francisco bay, California, USA. *Environmental*
799 *Toxicology and Chemistry* 29(6):1385–1395. [https://doi.org/10.1002/etc.](https://doi.org/10.1002/etc.164)
800 [164](https://doi.org/10.1002/etc.164)

- 801 Gobas FA, Burkhard LP, Doucette WJ, et al (2016) Review of existing
802 terrestrial bioaccumulation models and terrestrial bioaccumulation model-
803 ing needs for organic chemicals. *Integrated Environmental Assessment and*
804 *Management* 12(1):123–134. <https://doi.org/10.1002/ieam.1690>
- 805 Gögebakan T, Eraslan G (2015) Single-dose toxicokinetics of permethrin in
806 broiler chickens. *British Poultry Science* 56(5):605–611. <https://doi.org/10.1080/00071668.2015.1085957>
- 807
- 808 Goudah A (2009) Pharmacokinetics and tissue residues of moxifloxacin in
809 broiler chickens. *British Poultry Science* 50(2):251–258. <https://doi.org/10.1080/00071660802710108>
- 810
- 811 Goutte A, Bustamante P, Barbraud C, et al (2014) Demographic responses
812 to mercury exposure in two closely related antarctic top predators. *Ecology*
813 95(4):1075–1086. <https://doi.org/10.1890/13-1229.1>
- 814 Goutte A, Barbraud C, Herzke D, et al (2015) Survival rate and breeding out-
815 puts in a high Arctic seabird exposed to legacy persistent organic pollutants
816 and mercury. *Environmental Pollution* 200:1–9. [https://doi.org/10.1016/j. envpol.2015.01.033](https://doi.org/10.1016/j.envpol.2015.01.033)
- 817
- 818 Goutte A, Meillère A, Barbraud C, et al (2018) Demographic, endocrine and
819 behavioral responses to mirex in the South polar skua. *Science of the Total*
820 *Environment* 631-632:317–325. <https://doi.org/10.1016/j.scitotenv.2018.02.326>
- 821

- 822 Grabowski T, Pasławska U, Poźniak B, et al (2017) Models describing metron-
823 idazole pharmacokinetics in relation to hemodynamics in turkeys. *Research*
824 *in Veterinary Science* 112:167–171. [https://doi.org/10.1016/j.rvsc.2017.03.](https://doi.org/10.1016/j.rvsc.2017.03.014)
825 [014](https://doi.org/10.1016/j.rvsc.2017.03.014)
- 826 Grant WE, Fraser SO, Isakson KG (1984) Effect of vertebrate pesticides on
827 non-target wildlife populations: Evaluation through modelling. *Ecological*
828 *Modelling* 21(1-2):85–108. [https://doi.org/10.1016/0304-3800\(84\)90026-7](https://doi.org/10.1016/0304-3800(84)90026-7)
- 829 Hallam TG, Trawick TL, Wolff WF (1996) Modeling effects of chemicals
830 on a population: Application to a wading bird nesting colony. *Ecological*
831 *Modelling* 92(2-3):155–178. [https://doi.org/10.1016/0304-3800\(95\)00204-9](https://doi.org/10.1016/0304-3800(95)00204-9)
- 832 Hamamoto K, Koike R, Machida Y (2000) Bioavailability of amprolium in
833 fasting and nonfasting chickens after intravenous and oral administration.
834 *Journal of Veterinary Pharmacology and Therapeutics* 23(1):9–14. <https://doi.org/10.1046/j.1365-2885.2000.00239.x>
835 [//doi.org/10.1046/j.1365-2885.2000.00239.x](https://doi.org/10.1046/j.1365-2885.2000.00239.x)
- 836 Hassan IZ, Duncan N, Adawaren EO, et al (2018) Could the environmen-
837 tal toxicity of diclofenac in vultures been predictable if preclinical testing
838 methodology were applied? *Environmental Toxicology and Pharmacology*
839 64(July):181–186. <https://doi.org/10.1016/j.etap.2018.10.006>
- 840 Hekman P, Schefferlie GJ (2011) Kinetic modelling and residue depletion of
841 drugs in eggs. *British Poultry Science* 52(3):376–380. [https://doi.org/10.](https://doi.org/10.1080/00071668.2011.577055)
842 [1080/00071668.2011.577055](https://doi.org/10.1080/00071668.2011.577055)

- 843 Hendriks AJ, Enserink EL (1996) Modelling response of single-species pop-
844 ulations to microcontaminants as a function of species size with examples
845 for waterfleas (*Daphnia magna*) and cormorants (*Phalacrocorax carbo*). Eco-
846 logical Modelling 88(1-3):247–262. [https://doi.org/10.1016/0304-3800\(95\)](https://doi.org/10.1016/0304-3800(95)00111-5)
847 [00111-5](https://doi.org/10.1016/0304-3800(95)00111-5)
- 848 Hendriks AJ, Maas-Diepeveen JL, Heugens EH, et al (2005) Meta-analysis
849 of intrinsic rates of increase and carrying capacity of populations affected
850 by toxic and other stressors. Environmental Toxicology and Chemistry
851 24(9):2267–2277. <https://doi.org/10.1897/05-122.1>
- 852 Henri J, Carrez R, Méda B, et al (2017) A physiologically based pharma-
853 cokinetic model for chickens exposed to feed supplemented with monensin
854 during their lifetime. Journal of Veterinary Pharmacology and Therapeutics
855 40(4):370–382. <https://doi.org/10.1111/jvp.12370>
- 856 Herman J, Vermeersch H, Remon JP, et al (1989) Pharmacokinetics and
857 bioavailability of ronidazole from a prolonged release tablet in the homing
858 pigeon (*Columba livid*). Journal of Veterinary Pharmacology and Therapeu-
859 tics 12(1):46–49. <https://doi.org/10.1111/j.1365-2885.1989.tb00640.x>
- 860 Hommen U, Forbes V, Grimm V, et al (2016) How to use mechanistic effect
861 models in environmental risk assessment of pesticides: Case studies and
862 recommendations from the SETAC workshop MODELINK. Integrated Envi-
863 ronmental Assessment and Management 12(1):21–31. [https://doi.org/10.](https://doi.org/10.1007/s11367-015-0361-1)

864 [1002/ieam.1704](https://doi.org/10.1002/ieam.1704)

865 Hutchinson TH, Madden JC, Naidoo V, et al (2014) Comparative metabolism
866 as a key driver of wildlife species sensitivity to human and veterinary phar-
867 maceuticals. *Philosophical Transactions of the Royal Society B: Biological*
868 *Sciences* 369:1656. <https://doi.org/10.1098/rstb.2013.0583>

869 Hüyük R, Eraslan G (2017) Toxicokinetics of the broad-spectrum pyrethroid
870 insecticide deltamethrin in broiler chickens. *British Poultry Science* 58:95–
871 99. <https://doi.org/10.1080/00071668.2016.1211253>

872 Jackson AK, Evers DC, Etterson MA, et al (2011) Mercury exposure affects
873 the reproductive success of a free-living terrestrial songbird, the carolina
874 wren (*Thryothorus Ludovicianus*). *Auk* 128(4):759–769. [https://doi.org/10.](https://doi.org/10.1525/auk.2011.11106)
875 [1525/auk.2011.11106](https://doi.org/10.1525/auk.2011.11106)

876 Karasov WH, Kenow KP, Meyer MW, et al (2007) Bioenergetic and phar-
877 macokinetic model for exposure of common loon (*Gavia immer*) chicks to
878 methylmercury. *Environmental Toxicology and Chemistry* 26(4):677–685.
879 <https://doi.org/10.1897/06-262.1>

880 Kongkapan J, Giorgi M, Poapolathep S, et al (2016) Toxicokinetics and tissue
881 distribution of nivalenol in broiler chickens. *Toxicon* 111:31–36. [https://doi.](https://doi.org/10.1016/j.toxicon.2015.12.013)
882 [org/10.1016/j.toxicon.2015.12.013](https://doi.org/10.1016/j.toxicon.2015.12.013)

- 883 Korsman JC, Schipper AM, Lenders HJ, et al (2012) Modelling the
884 impact of toxic and disturbance stress on white-tailed eagle (*Haliaeetus*
885 *albicilla*) populations. *Ecotoxicology* 21(1):27–36. [https://doi.org/10.1007/
886 s10646-011-0760-8](https://doi.org/10.1007/s10646-011-0760-8)
- 887 Kuo DTF, Rattner BA, Martinson SC, et al (2022) A Critical Review of
888 Bioaccumulation and Biotransformation of Organic Chemicals in Birds.
889 *Reviews of Environmental Contamination and Toxicology* 260:6–61. [https:
890 //doi.org/10.1007/s44169-021-00007-1](https://doi.org/10.1007/s44169-021-00007-1)
- 891 Lautz LS, Nebbia C, Hoeks S, et al (2020) An open source physiologically
892 based kinetic model for the chicken (*Gallus gallus domesticus*): Calibration
893 and validation for the prediction residues in tissues and eggs. *Environment*
894 *International* 136:105,488. <https://doi.org/10.1016/j.envint.2020.105488>
- 895 Liu X, Liu C, Wang P, et al (2019) Distribution, metabolism and metabolic
896 disturbances of alpha-cypermethrin in embryo development, chick growth
897 and adult hens. *Environmental Pollution* 249:390–397. [https://doi.org/10.
898 1016/j.envpol.2019.03.017](https://doi.org/10.1016/j.envpol.2019.03.017)
- 899 Lu Z, Xue M, Shen G, et al (2011) Accumulation dynamics of chlordanes and
900 their enantiomers in cockerels (*Gallus gallus*) after oral exposure. *Environ-*
901 *mental Science and Technology* 45(18):7928–7935. [https://doi.org/10.1021/
902 es201629p](https://doi.org/10.1021/es201629p)

- 903 MacLachlan DJ (2010) Physiologically based pharmacokinetic (PBPK) model
904 for residues of lipophilic pesticides in poultry. *Food Additives and Contam-*
905 *inants - Part A* 27(3):302–314. <https://doi.org/10.1080/19440040903296683>
- 906 Matsinos YG, Wolff WF (2003) An individual-oriented model for ecological risk
907 assessment of wading birds. *Ecological Modelling* 170(2-3):471–478. [https://doi.org/10.1016/S0304-3800\(03\)00246-1](https://doi.org/10.1016/S0304-3800(03)00246-1)
- 909 Méda B, Travel A, Guyot Y, et al (2020) A PBPK model to study the
910 transfer of α -hexabromocyclododecane (α -HBCDD) to tissues of fast- and
911 slow-growing broilers. *Food Additives and Contaminants - Part A Chem-*
912 *istry, Analysis, Control, Exposure and Risk Assessment* 37(2):316–331.
913 <https://doi.org/10.1080/19440049.2019.1681596>
- 914 Millot F, Berny P, Decors A, et al (2015) Little field evidence of direct acute
915 and short-term effects of current pesticides on the grey partridge. *Ecotoxicol-*
916 *ogy and Environmental Safety* 117:41–61. [https://doi.org/10.1016/j.ecoenv.](https://doi.org/10.1016/j.ecoenv.2015.03.017)
917 [2015.03.017](https://doi.org/10.1016/j.ecoenv.2015.03.017)
- 918 Monteiro LR, Furness RW (2001) Kinetics, dose-response, and excretion
919 of methylmercury in free-living adult Cory’s shearwaters. *Environmental*
920 *Science and Technology* 35(4):739–746. <https://doi.org/10.1021/es000114a>
- 921 Moore DRJ, Fischer D, Teed S, et al (2010) A Probabilistic Risk Assessment
922 Model for Birds Exposed to Granular Pesticides. *Integrated Environmen-*
923 *tal Assessment and Management* 6:83–101. https://doi.org/10.1897/ieam_

924 [2009-021.1](#)

925 Moore DRJ, Priest CD, Olson AD, et al (2018) A probabilistic risk assess-
926 ment for the Kirtland’s warbler potentially exposed to chlorpyrifos and
927 malathion during the breeding season and migration. *Integrated Envi-*
928 *ronmental Assessment and Management* 14(2):252–269. [https://doi.org/10.](https://doi.org/10.1002/ieam.2004)
929 [1002/ieam.2004](https://doi.org/10.1002/ieam.2004)

930 Nacci D, Pelletier M, Lake J, et al (2005) An approach to predict risks to
931 wildlife populations from mercury and other stressors. *Ecotoxicology* 14(1-
932 2):283–293. <https://doi.org/10.1007/s10646-004-6275-9>

933 Nelson YM, Thampy RJ, Motelin GK, et al (1998) Model for trace metal
934 exposure in filter-feeding flamingos at alkaline Rift Valley Lake, Kenya. *Envi-*
935 *ronmental Toxicology and Chemistry* 17(11):2302–2309. [https://doi.org/10.](https://doi.org/10.1897/1551-5028(1998)017<2302:MFTMEI>2.3.CO;2)
936 [1897/1551-5028\(1998\)017<2302:MFTMEI>2.3.CO;2](https://doi.org/10.1897/1551-5028(1998)017<2302:MFTMEI>2.3.CO;2)

937 Newsted JL, Beach SA, Gallagher SP, et al (2006) Pharmacokinetics and acute
938 lethality of perfluorooctanesulfonate (PFOS) to juvenile mallard and north-
939 ern bobwhite. *Archives of Environmental Contamination and Toxicology*
940 50(3):411–420. <https://doi.org/10.1007/s00244-005-1137-x>

941 Nichols JW, Larsen CP, McDonald ME, et al (1995) Bioenergetics-Based
942 Model for Accumulation of Polychlorinated Biphenyls by Nestling Tree
943 Swallows, *Tachycineta bicolor*. *Environmental Science and Technology*
944 29(3):604–612

- 945 Nichols JW, Echols KR, Tillitt DE, et al (2004) Bioenergetics-based modeling
946 of individual PCB congeners in nestling tree swallows from two contami-
947 nated sites on the Upper Hudson River, New York. *Environmental Science*
948 *and Technology* 38(23):6234–6239. <https://doi.org/10.1021/es0497734>
- 949 Nichols JW, Bennett RS, Rossmann R, et al (2010) A physiologically based
950 toxicokinetic model for methylmercury in female American kestrels. *Envi-*
951 *ronmental Toxicology and Chemistry* 29(8):1854–1867. [https://doi.org/10.](https://doi.org/10.1002/etc.241)
952 [1002/etc.241](https://doi.org/10.1002/etc.241)
- 953 Norstrom RJ, Clark TP, Enright M, et al (2007) ABAM, a model for bioaccu-
954 mulation of POPs in birds: Validation for adult herring gulls and their eggs
955 in Lake Ontario. *Environmental Science and Technology* 41(12):4339–4347.
956 <https://doi.org/10.1021/es062205z>
- 957 Ohlhoff B, Savvateeva D, Leisner J, et al (2022) Transfer of Non-Dioxin-Like
958 Polychlorinated Biphenyls (ndl-PCBs) from Feed and Soil into Hen Eggs.
959 *Journal of Agricultural and Food Chemistry* 70(29):8955–8962. [https://doi.](https://doi.org/10.1021/acs.jafc.2c02243)
960 [org/10.1021/acs.jafc.2c02243](https://doi.org/10.1021/acs.jafc.2c02243)
- 961 Opdycke JC, Menzer RE, Menzer RE (1984) Pharmacokinetics of difluben-
962 zuron in two types of chickens. *Journal of Toxicology and Environmental*
963 *Health* 13(4-6):721–733. <https://doi.org/10.1080/15287398409530534>
- 964 Pan Y, Chang J, Xu P, et al (2022) Twenty-four hours of Thiamethoxam:
965 *In vivo* and molecular dynamics simulation study on the toxicokinetic and

966 underlying mechanisms in quails (*Coturnix japonica*). Journal of Hazardous
967 Materials 427(October 2021):128,159. [https://doi.org/10.1016/j.jhazmat.
968 2021.128159](https://doi.org/10.1016/j.jhazmat.2021.128159)

969 Pant S, Rao GS, Sastry KV, et al (2005) Pharmacokinetics and tissue residues
970 of pefloxacin and its metabolite norfloxacin in broiler chickens. British
971 Poultry Science 46(5):615–620. <https://doi.org/10.1080/00071660500255323>

972 Pisani JM, Grant WE, Mora MA (2008) Simulating the impact of
973 cholinesterase-inhibiting pesticides on non-target wildlife in irrigated
974 crops. Ecological Modelling 210(1-2):179–192. [https://doi.org/10.1016/j.
975 ecolmodel.2007.07.017](https://doi.org/10.1016/j.ecolmodel.2007.07.017)

976 Poapolathep S, Klangkaew N, Arreesrisom P, et al (2015) Toxicokinetics and
977 absolute oral bioavailability of melamine in broiler chickens. Journal of Vet-
978 erinary Pharmacology and Therapeutics 38(1):101–104. [https://doi.org/10.
979 1111/jvp.12145](https://doi.org/10.1111/jvp.12145)

980 Pollet RA, Glatz CE, Dyer DC, et al (1983) Pharmacokinetics of chlortetra-
981 cycline potentiation with citric acid in the chicken. American Journal of
982 Veterinary Research 44(9):1718–1721

983 Pollet RA, Glatz CE, Dyer DC (1985) The pharmacokinetics of chlortetracy-
984 cline orally administered to turkeys: Influence of citric acid and *Pasteurella*
985 *multocida* infection. Journal of Pharmacokinetics and Biopharmaceutics
986 13(3):243–264. <https://doi.org/10.1007/BF01065655>

- 987 Rattner BA, Horak KE, Lazarus RS, et al (2014) Toxicokinetics and coag-
988 ulopathy threshold of the rodenticide diphacinone in eastern screech-owls
989 (*Megascops asio*). Environmental Toxicology and Chemistry 33(1):74–81.
990 <https://doi.org/10.1002/etc.2390>
- 991 Rattner BA, Volker SF, Lankton JS, et al (2020) Brodifacoum Toxicity in
992 American Kestrels (*Falco sparverius*) with Evidence of Increased Hazard on
993 Subsequent Anticoagulant Rodenticide Exposure. Environmental Toxicology
994 and Chemistry 39(2):468–481. <https://doi.org/10.1002/etc.4629>
- 995 Ratzlaff K, Papich MG, Flammer K (2011) Plasma concentrations of flu-
996 conazole after a single oral dose and administration in drinking water in
997 cockatiels (*Nymphicus hollandicus*). Journal of Avian Medicine and Surgery
998 25(1):23–31. <https://doi.org/10.1647/2009-044.1>
- 999 Roelofs W, Crocker DR, Shore RF, et al (2005) Case study part 2: Probabilistic
1000 modelling of long-term effects of pesticides on individual breeding success in
1001 birds and mammals. Ecotoxicology 14(8):895–923. [https://doi.org/10.1007/
1002 s10646-005-0035-3](https://doi.org/10.1007/s10646-005-0035-3)
- 1003 Samuels WB, Ladino A (1984) Calculations of seabird population recov-
1004 ery from potential oilspills in the mid-atlantic region of the united states.
1005 Ecological Modelling 21:63–84
- 1006 Sánchez CR, Zalesak S, Pich AA, et al (2019) Population pharmacokinetics
1007 of itraconazole solution after a single oral administration in captive lesser

- 1008 flamingos (*Phoeniconaias minor*). Journal of Veterinary Pharmacology and
1009 Therapeutics 42(1):1–6. <https://doi.org/10.1111/jvp.12721>
- 1010 Schefferlie GJ, Hekman P (2016) Prediction of the residue levels of drugs
1011 in eggs, using physicochemical properties and their influence on passive
1012 diffusion processes. Journal of Veterinary Pharmacology and Therapeutics
1013 39(4):381–387. <https://doi.org/10.1111/jvp.12290>
- 1014 Sibly RM, Akcakaya HR, Topping CJ, et al (2005) Population-level assess-
1015 ment of risks of pesticides to birds and mammals in the UK. Ecotoxicology
1016 14(8):863–876. <https://doi.org/10.1007/s10646-005-0033-5>
- 1017 Siegel DM, Giri SN (1983) Toxicokinetics, covalent binding and histopatho-
1018 logical features of [14C]2-chloro-4-acetotoluidide toxicity in the starling
1019 after intravenous administration. Experimental and Molecular Pathology
1020 39(2):194–206. [https://doi.org/10.1016/0014-4800\(83\)90051-5](https://doi.org/10.1016/0014-4800(83)90051-5)
- 1021 Smith JT, Walker LA, Shore RF, et al (2009) Do estuaries pose a toxic
1022 contamination risk for wading birds? Ecotoxicology 18(7):906–917. <https://doi.org/10.1007/s10646-009-0352-z>
- 1024 Suknikom P, Jermnak U, Poapolathep S, et al (2016) Dispositions and tissue
1025 depletion of melamine in ducks. Journal of Veterinary Pharmacology and
1026 Therapeutics 39(1):90–94. <https://doi.org/10.1111/jvp.12242>

- 1027 Sullivan JP, Scanlon PF (1991) A comparison between intubation and food
1028 addition as routes of oral exposure for northern bobwhites to DDT insecti-
1029 cide. *Journal of wildlife diseases* 27(3):435–440. [https://doi.org/10.7589/
1030 0090-3558-27.3.435](https://doi.org/10.7589/0090-3558-27.3.435)
- 1031 Tarazona JV, Rodríguez C, Alonso E, et al (2015) Toxicokinetics of per-
1032 fluorooctane sulfonate in birds under environmentally realistic exposure
1033 conditions and development of a kinetic predictive model. *Toxicology Letters*
1034 232(2):363–368. <https://doi.org/10.1016/j.toxlet.2014.11.022>
- 1035 Tavecchia G, Pradel R, Lebreton JD, et al (2001) The effect of lead exposure
1036 on survival of adult mallards in the Camargue, southern France. *Journal*
1037 *of Applied Ecology* 38(6):1197–1207. [https://doi.org/10.1046/j.0021-8901.
1038 2001.00684.x](https://doi.org/10.1046/j.0021-8901.2001.00684.x)
- 1039 Thompson CV, Firman JW, Goldsmith MR, et al (2021) A Systematic Review
1040 of Published Physiologically-based Kinetic Models and an Assessment of
1041 their Chemical Space Coverage. *ATLA Alternatives to Laboratory Animals*
1042 49(5):197–208. <https://doi.org/10.1177/02611929211060264>
- 1043 Topping CJ, Sibly RM, Akcakaya HR, et al (2005) Risk assessment of UK sky-
1044 lark populations using life-history and individual-based landscape models.
1045 *Ecotoxicology* 14(8):925–936. <https://doi.org/10.1007/s10646-005-0027-3>
- 1046 Van Eijkeren JC, Zeilmaker MJ, Kan CA, et al (2006) A toxicokinetic
1047 model for the carry-over of dioxins and PCBs from feed and soil to eggs.

1048 Food Additives and Contaminants 23(5):509–517. [https://doi.org/10.1080/](https://doi.org/10.1080/02652030500512045)
1049 [02652030500512045](https://doi.org/10.1080/02652030500512045)

1050 Waegeneers N, De Steur H, De Temmerman L, et al (2009) Transfer of soil
1051 contaminants to home-produced eggs and preventive measures to reduce
1052 contamination. *Science of the Total Environment* 407(15):4438–4446. <https://doi.org/10.1016/j.scitotenv.2008.12.041>
1053 [//doi.org/10.1016/j.scitotenv.2008.12.041](https://doi.org/10.1016/j.scitotenv.2008.12.041)

1054 Wang YS, Li M, Tell LA, et al (2021) Physiological parameter values for physi-
1055 ologically based pharmacokinetic models in food-producing animals. Part II:
1056 Chicken and turkey. *Journal of Veterinary Pharmacology and Therapeutics*
1057 44(4):423–455. <https://doi.org/10.1111/jvp.12931>

1058 Wayland M, Drake KL, Alisauskas RT, et al (2008) Survival rates and
1059 blood metal concentrations in two species of free-ranging North Ameri-
1060 can sea ducks. *Environmental Toxicology and Chemistry* 27(3):698–704.
1061 <https://doi.org/10.1897/07-321.1>

1062 Yang F, Yang Y, Wang L, et al (2014) Estimating marbofloxacin withdrawal
1063 time in broiler chickens using a population physiologically based pharma-
1064 cokinetics model. *Journal of Veterinary Pharmacology and Therapeutics*
1065 37:579–588. <https://doi.org/10.1111/jvp.12137>

1066 Yang F, Sun N, Liu YM, et al (2015) Estimating danofloxacin withdrawal
1067 time in broiler chickens based on physiologically based pharmacokinetics

- 1068 modeling. *Journal of Veterinary Pharmacology and Therapeutics* 38(2):174–
1069 182. <https://doi.org/10.1111/jvp.12162>
- 1070 Yuan L, Sun J, Wang R, et al (2011) Pharmacokinetics and bioavailability
1071 of cefquinome in healthy ducks. *American Journal of Veterinary Research*
1072 72(1):122–126. <https://doi.org/10.2460/ajvr.72.1.122>
- 1073 Yuan L, Chou WC, Richards ED, et al (2022) A web-based interac-
1074 tive physiologically based pharmacokinetic (iPBPK) model for meloxi-
1075 cam in broiler chickens and laying hens. *Food and Chemical Toxicology*
1076 168(August):113,332. <https://doi.org/10.1016/j.fct.2022.113332>
- 1077 Zeng D, Lin Z, Zeng Z, et al (2019) Assessing Global Human Exposure to
1078 T-2 Toxin via Poultry Meat Consumption Using a Lifetime Physiologically
1079 Based Pharmacokinetic Model. *Journal of Agricultural and Food Chemistry*
1080 67(5):1563–1571. <https://doi.org/10.1021/acs.jafc.8b07133>
- 1081 Zhao DH, Zhou YF, Yu Y, et al (2014) Integration of pharmacokinetic
1082 and pharmacodynamic indices of valnemulin in broiler chickens after a
1083 single intravenous and intramuscular administration. *Veterinary Journal*
1084 201(1):109–115. <https://doi.org/10.1016/j.tvjl.2014.05.010>