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1 Is structural sensitivity a problem of oversimplified 2 biological models? Insights from nested Dynamic 3 Energy Budget models.

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14 **Keywords** model sensitivity ; functional response ; metabolism ; bifurcations ; chemostat

15 Highlights

- 16 • Four predator-prey models in chemostat are built from Dynamic Energy Budget theory
- 17 • Structural sensitivity to functional response formulation is investigated
- 18 • The less detailed metabolic model (Monod) leads to higher structural sensitivity
- 19 • Structural sensitivity is lower in mass-balanced models including maintenance

20 **Authorship** CA performed the research. All authors contributed to the design and dis-
21 cussion. CA wrote the paper and all authors contributed to revisions.

22 **Conflicts of interest** none.

23 **Abstract**

24 Many current issues in ecology require predictions made by mathematical models, which
25 are built on somewhat arbitrary choices. Their consequences are quantified by sensitivity
26 analysis to quantify how changes in model parameters propagate into an uncertainty in model
27 predictions. An extension called structural sensitivity analysis deals with changes in the
28 mathematical description of complex processes like predation. Such processes are described
29 at the population scale by a specific mathematical function that is taken among similar
30 ones, a choice that can strongly drive model predictions. However, it has only been studied
31 in simple theoretical models. Here, we ask whether structural sensitivity is a problem of
32 oversimplified models. We found in predator-prey models describing chemostat experiments
33 that these models are less structurally sensitive to the choice of a specific functional response
34 if they include mass balance resource dynamics and individual maintenance. Neglecting
35 these processes in an ecological model (for instance by using the well-known logistic growth
36 equation) is not only an inappropriate description of the ecological system, but also a source
37 of more uncertain predictions.

1 Introduction

Facing current socio-environmental issues, such as species extinctions and loss of ecosystem services, requires to make ecological predictions with a level of accuracy that is not yet achieved (Mouquet *et al.*, 2015; Morozov, 2017; Pennekamp *et al.*, 2017). Uncertainty arises in predictions made by mathematical models, which are perceived as objective tools but remain simplified representations built on somewhat arbitrary choices (Anderson, 2005, 2010). Among these choices, two types can be distinguished. The first ones are the processes and components (e.g. species, nutrients) to include, which are often a consensus between scientists from different ecology-related disciplines (animal and plant biology, microbiology, chemistry, physics, Demongeot *et al.*, 2009). Those choices are assumptions that can be discussed, and testing their consequences on predictions helps to improve ecological theories. The second type of choices is still an open issue and is the mathematical function selected to model a given process (Lafferty *et al.*, 2015). A process can be described by many functions that fit available data with the same accuracy but that are based on different assumptions. Whereas different assumptions about the emerging process shape (e.g. density-dependence, group behaviour) have been widely considered in the literature, the choice between similar functions (i.e mechanisms) to model the same process shape (e.g. process rate increases with population abundance) has received only little attention in ecology. However, this attention has increased in the past decade since the preliminary work by Myerscough *et al.* (1996) and Wood & Thomas (1999), followed by Gross *et al.* (2004) and Fussmann & Blasius (2005). Recent studies indicate that this choice can deeply affect both qualitative and quantitative predictions (Cordoleani *et al.*, 2011), including those at the food web level or about system resilience (Aldebert *et al.*, 2016a,b). This concept extends the idea of parameter sensitivity, as it becomes the sensitivity of model predictions to any change in parameter values and/or model formulation (see Cordoleani *et al.*, 2011, for a proper mathematical formulation). This more general concept has been coined structural sensitivity.

Structural sensitivity emerges if several scales of organization, space and/or time are

65 entangled in a complex process. Such a process is for instance predation. Predation involves
66 individual to population level mechanisms that are often summarized at the population scale
67 by one function, the functional response (Solomon, 1949). Many functional responses can
68 be derived depending on the mechanisms considered (Jeschke *et al.*, 2002). A mechanism
69 underlying a formulation (e.g. prey handling) might be relevant, but additional assumptions
70 that translate it into mathematics (e.g. space homogeneity, no individual variability) are
71 almost always violated. Thus, the best formulation from a theoretical point of view might
72 not be the best quantitative description of data. As this uncertainty propagates into model
73 predictions, Gross & Feudel (2006) and Adamson & Morozov (2012) proposed approaches
74 based on generic (partially-specified) models. These generalized models avoid the issue
75 of structural sensitivity and are useful to draw widely applicable conclusions in theoretical
76 studies (Gross *et al.*, 2009). However, such models hardly consider non-equilibrium dynamics
77 (Kuehn & Gross, 2013) and tell nothing about the existence of alternative stable states, two
78 important characteristics of living systems (Fussmann *et al.*, 2000; Scheffer *et al.*, 2012) that
79 can be affected by structural sensitivity (Aldebert *et al.*, 2016b).

80 In this study, we suggest an alternative way to deal with structural sensitivity that
81 applies to systems with non-equilibrium dynamics and alternative stable states. Structural
82 sensitivity has only been studied in theoretical population models, where population growth
83 is logistic for the prey and proportional to the feeding rate for the predator. So, one may think
84 that structural sensitivity is a problem of oversimplified models. We test this hypothesis by
85 presenting the first study on structural sensitivity in ecosystem models (*sensu* with explicit
86 resource dynamics) that include various level of details to describe individual metabolism.

87 Modelling individual metabolism requires to add processes and create model sensitivity
88 to their formulation. Mechanistic formulations of metabolic processes can be derived from
89 Dynamic Energy Budget (DEB) theory (Kooijman, 2010; Jusup *et al.*, 2017). This reduc-
90 tionist theory focuses on the individual level, as it allows to make easy mass and energy
91 budgets. As a consequence, the formulation of metabolic processes is constrained by the

92 laws of thermodynamics. Another advantage of DEB theory is that it provides a level of
93 abstraction that allows generalization to many living organisms.

94 To test whether structural sensitivity is a result of model oversimplification, we focus on a
95 predator-prey system of dividing unicellular organisms living in a chemostat-like environment
96 (figure 1a). This system is modelled using different functional responses (figure 1b) and levels
97 of metabolic details (figure 1c). For the metabolism, we consider a predator-prey model
98 based on DEB theory (Kooi & Kooijman, 1994b) that describes chemostat experiments
99 and includes two buffers between feeding and population growth: an energy reserve and
100 maintenance costs. These two features are neglected at limit cases of this model, leading
101 to three simpler models: Droop (1973), Marr-Pirt (Marr *et al.*, 1963) and Monod (1942)
102 models. Thus, these four models are nested within the framework of DEB theory.

103 Next section presents the nested predator-prey models. Then, their predictions are ana-
104 lyzed and discussed in the light of the general question: Is structural sensitivity a problem
105 of the oversimplified biological models? Discussion ends with a synthesis of research on
106 structural sensitivity that leads to a guidance for ecologists in their modelling choices.

107 2 Models

108 2.1 Functional responses to model predation

109 To model predation, we consider the next three functions (figure 1b):

$$F^H(X) = \frac{j_{XAm}^H X}{X + K^H}, F^I(X) = j_{XAm}^I (1 - \exp(-X/K^I)), F^t(X) = j_{XAm}^t \tanh(X/K^t), \quad (1)$$

110 where X is prey biomass, j_{XAm} is the maximum assimilation rate and j_{XAm}/K is the
111 function slope at 0. The classical Holling functional response F^H assumes that a predator
112 splits its activity between searching and handling prey (Holling, 1965). It is equivalent to
113 Michaëlis-Menten function for enzyme kinetics. Ivlev functional response F^I is based on

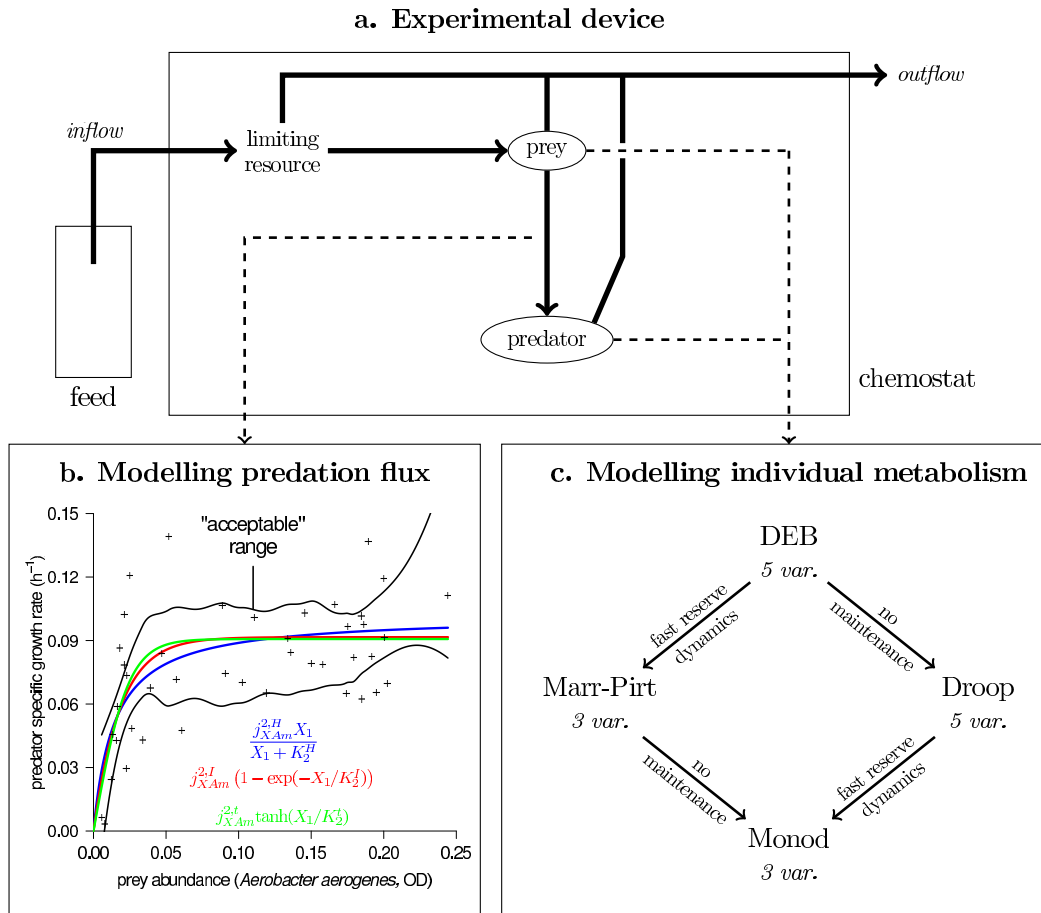


Figure 1. Sketch of the study. We compare predictions of predator-prey system in a chemostat-like environment (a) modelled with one of three mathematical functions (color, “acceptable range” is the 95 % confidence interval of a non-parametric kernel regression) to model predation (b) and one of four nested models to model individual metabolism (c).

114 digestion (Ivlev, 1955). Conversely, the hyperbolic tangent function F^t has no theoretical
 115 basis, but it happens to be an appropriate description of data (Jassby & Platt, 1976) and it
 116 is used in some population models (Fussmann & Blasius, 2005; Cordoleani *et al.*, 2011). The
 117 three prey-dependent functions (1) are type-II functional responses (they vanish at zero, are
 118 strictly increasing, concave and saturating). However, the same exercise can be performed
 119 with more complex functions like type-III (sigmoid) or ratio-dependent functional responses.

120 2.2 Predator-prey models

121 Starting from a DEB model for unicellular dividing individuals (Appendix A), Kooi & Kooi-
 122 jman (1994b) proposed the following model (referred as DEB model) to describe a predator-
 123 prey system living in an environment described by a chemostat:

$$\left\{ \begin{array}{l}
 \frac{de_1}{dt} = \dot{k}_E^1 (f_1(X_0) - e_1) \\
 \frac{de_2}{dt} = \dot{k}_E^2 (f_2(X_1) - e_2) \\
 \frac{dX_0}{dt} = \dot{h}(X_r - X_0) - F_1(X_0)X_1 \\
 \frac{dX_1}{dt} = \left(\frac{\dot{k}_E^1 e_1 - \dot{k}_M^1 g_1}{e_1 + g_1} - \dot{h} \right) X_1 - F_2(X_1)X_2 \\
 \frac{dX_2}{dt} = \left(\frac{\dot{k}_E^2 e_2 - \dot{k}_M^2 g_2}{e_2 + g_2} - \dot{h} \right) X_2.
 \end{array} \right. \quad (2)$$

124 The prey (structure X_1 and scaled reserve density e_1) feeds on an inorganic resource (con-
 125 centration X_0) and is eaten by a predator (structure X_2 and scaled reserve density e_2),
 126 with $f_i(X_{i-1}) := F_i(X_{i-1})/j_{X_{Am}}^i$, $i = 1, 2$ being scaled functional responses. The biological
 127 parameters \dot{k}_E^i (in h^{-1}), \dot{k}_M^i (in h^{-1}) and g_i (no unit) are the specific energy conductance,
 128 somatic maintenance rate and energy investment rate of species i respectively. Two envi-
 129 ronmental parameters describe the chemostat, its dilution rate \dot{h} (in h^{-1}) and the resource

130 concentration in the feed X_r . This model assumes that the predator digests only prey struc-
 131 ture, as adding reserve digestion does not improve the fit to data (Kooijman, 2010, p357).

132 Marr-Pirt model is a specific case of the DEB model (2) where reserve dynamics is
 133 assumed to be infinitely fast ($\dot{k}_E^i \rightarrow +\infty$). It implies that the scaled reserve density is a
 134 function of the available food ($e_i(t) = f_i(X_{i-1}(t))$) at the same time. Taking also $g_i \rightarrow +\infty$,
 135 the growth rate of structure becomes $\dot{\mu}_i f_i(X_{i-1}) - \dot{k}_M^i$, where $\dot{\mu}_i = \dot{k}_E^i/g_i$. The new parameter
 136 $\dot{\mu}_i$ (in h^{-1}) is the maximum growth rate of the population. Then, the DEB model (2)
 137 simplifies into the following three-dimensional system based on Marr-Pirt model:

$$\left\{ \begin{array}{l} \frac{dX_0}{dt} = \dot{h}(X_r - X_0) - f_1(X_0)j_{XAm}^1 X_1 \\ \frac{dX_1}{dt} = \left(\dot{\mu}_1 f_1(X_0) - \dot{k}_M^1 - \dot{h} \right) X_1 - f_2(X_1)j_{XAm}^2 X_2 \\ \frac{dX_2}{dt} = \left(\dot{\mu}_2 f_2(X_1) - \dot{k}_M^2 - \dot{h} \right) X_2. \end{array} \right. \quad (3)$$

138 Droop and Monod models are specific cases of the DEB and Marr-Pirt models respectively,
 139 where $\dot{k}_M^1 = \dot{k}_M^2 = 0$, i.e. maintenance costs are neglected for both species.

140 2.3 Analysis of model predictions

141 To get a global picture of model predictions, we focus on the type of predicted asymp-
 142 totic dynamics (the state that the system will reach after a sufficient amount of time) like
 143 species survival and equilibrium situation vs. predator-prey oscillations. A qualitative change
 144 between asymptotic dynamics, like a species extinction or the onset of predator-prey oscil-
 145 lations, occurs at a threshold on parameter values called bifurcation (Kuznetsov, 2004).
 146 Bifurcations that correspond to a sudden collapse or transition to an alternative state of
 147 the system are also known as tipping point and critical transition in the ecological litera-
 148 ture (Scheffer *et al.*, 2012). We provide some analytical results on bifurcations related to
 149 species extinction in Appendix B. The next section presents the full results with all the

150 model bifurcations as thresholds on environmental parameters (\dot{h} and X_r), computed using
151 numerical methods (Dhooge *et al.*, 2006) for a given functional response and given values of
152 the biological parameters.

153 Biological parameters are set to numerical values that describe a chemostat experiment
154 by Dent *et al.* (1976) where *Escherichia coli* grows on glucose and is eaten by *Dictyostelium*
155 *discoides*. This parameter estimation was performed by Kooi & Kooijman (1994b) for the
156 four chemostat models using Holling-II functional response for each species. As functional
157 response data were not available (Kooi & Kooijman fitted the predicted model dynamics
158 on temporal data), we mimic the situation in figure 1b following Aldebert *et al.* (2016a,b):
159 parameters of $F^I(X)$ and $F^t(X)$ were set to minimize the Euclidean distance between these
160 functions and the Holling-II functional response (Appendix A), which is equivalent to fit
161 all functions to data if functional response data were available. For Monod model, we
162 also used data from an experiment by Canale *et al.* (1973) where *Aerobacter aerogenes*
163 grows on carbohydrates and is eaten by *Tetrahymena pyriformis* (functional response data
164 were available and used to parameterize the three functional responses, see figure 1b). The
165 predictions by Monod models are qualitatively the same between both experiments, but
166 for numerical reasons (see next section) they are easier to visualize with parameter values
167 from the experiment by Canale *et al.* (1973). For each model, only the predator functional
168 response (flux from the prey to the predator) is changed. We kept Holling-II for the prey
169 functional response (flux from the resource to the prey) as changing it has only a little
170 quantitative effect on our results (data not shown). All parameter values are provided in
171 Appendix A.

172 **3 Results**

173 Overall, the three functional responses lead to the same qualitative pattern of predicted
174 dynamics (dynamics, type of bifurcations) in each predator-prey model, except for Monod

175 model (figures 2-3, Appendix C). Monod model together with the hyperbolic tangent can
176 predict the coexistence of two alternative stable states (figure 3d) corresponding to prey-
177 predator coexistence either at equilibrium or with oscillations. These alternative states are
178 not predicted with the two other functional responses in Monod model (figure 2d). Note
179 that results for Monod model are qualitatively the same with data from both Dent *et al.*
180 (1976) and Canale *et al.* (1973) experiments (Appendix C), and only the latter is presented
181 in figures 2d-3d as results are easier to visualize for numerical reasons. In DEB, Droop and
182 Marr-Pirt models, bifurcations occur at slightly different values between functional responses,
183 but only in a limited range of environmental conditions (low resource concentration in the
184 feed) corresponding to 1 % to ≈ 25 % of the bifurcation diagrams (details in Appendix C)
185 and bifurcation diagrams have the same general pattern.

186 The pattern of predicted dynamics is also affected by the level of metabolic details in-
187 cluded in the model. The DEB model can predict with all functional responses the co-
188 existence of alternative stable states (figures 2a-3a). These alternative dynamics were not
189 reported in the previous analysis of the DEB model (Kooi & Kooijman, 1994a), and they
190 are not predicted if either maintenance or reserve dynamics are not included. Not includ-
191 ing reserve dynamics also increases the range of dilution rates that predict species survival
192 (figures 2b-3b). Conversely, not including maintenance decreases the range of dilution rates
193 that predict species survival, especially for the prey (figures 2c-3c). In addition, species
194 are predicted to survive even at infinitely small dilution rates, as they do not have to pay
195 maintenance costs to survive. This last effect is also found if both maintenance and reserve
196 dynamics are not included to model the same species, but species are predicted to survive
197 in a larger range of dilution rates (Appendix C).

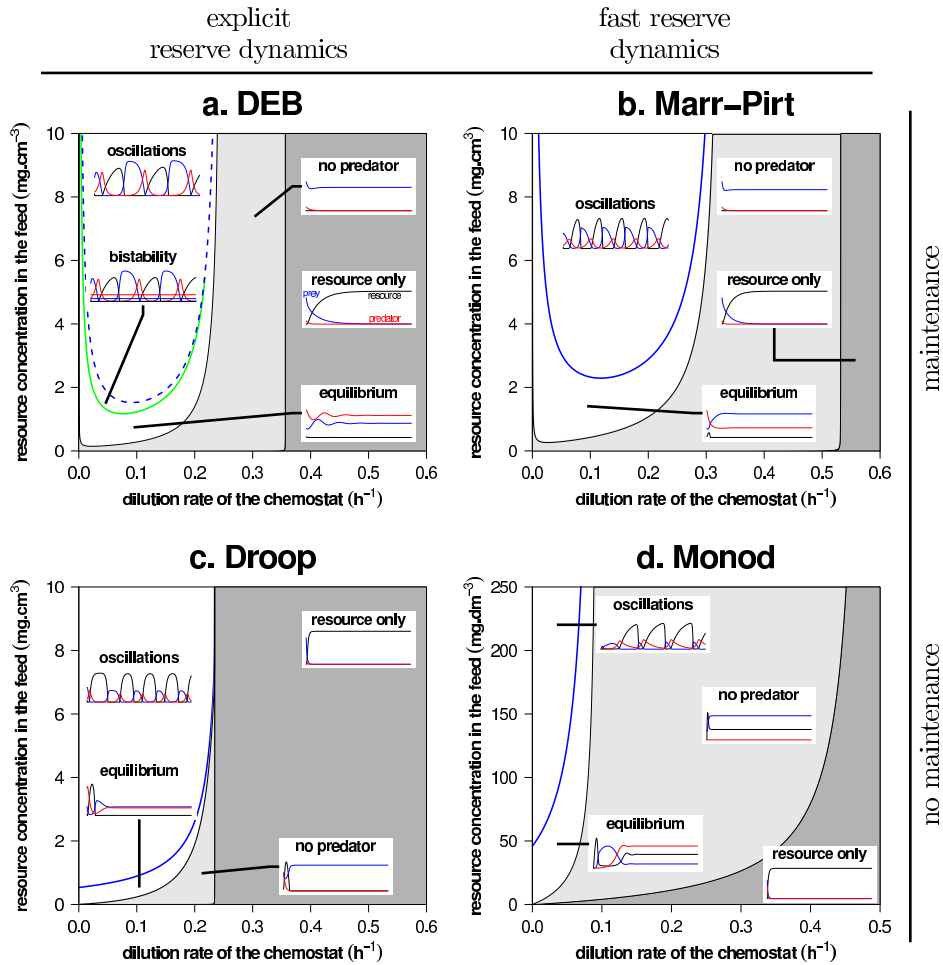


Figure 2. Predictions made with the four models of individual metabolism and Holling-II functional response. Predictions of each model are summarized by a bifurcation diagram which indicates the predicted qualitative dynamics (small panels) as a function of environmental parameters, the thresholds on environmental parameters are bifurcations (bif.) being indicated by the curves (black: transcritical bif. = species extinction, plain/dashed blue: supercritical/subcritical Hopf bif. = stable/unstable oscillations, green: limit point for cycles bif. = both stable and unstable oscillations). Biological parameters represent *Dictyostelium discoideum* feeding on *Escherichia coli* in (a-c) and *Tetrahymena pyriformis* feeding on *Aerobacter aerogenes* in (d). Qualitative differences between figures 2d and 3d drawn for the first species are the same but are harder to visualize (Appendix C). Results for Ivlev’s functional response are qualitatively the same (Appendix C).

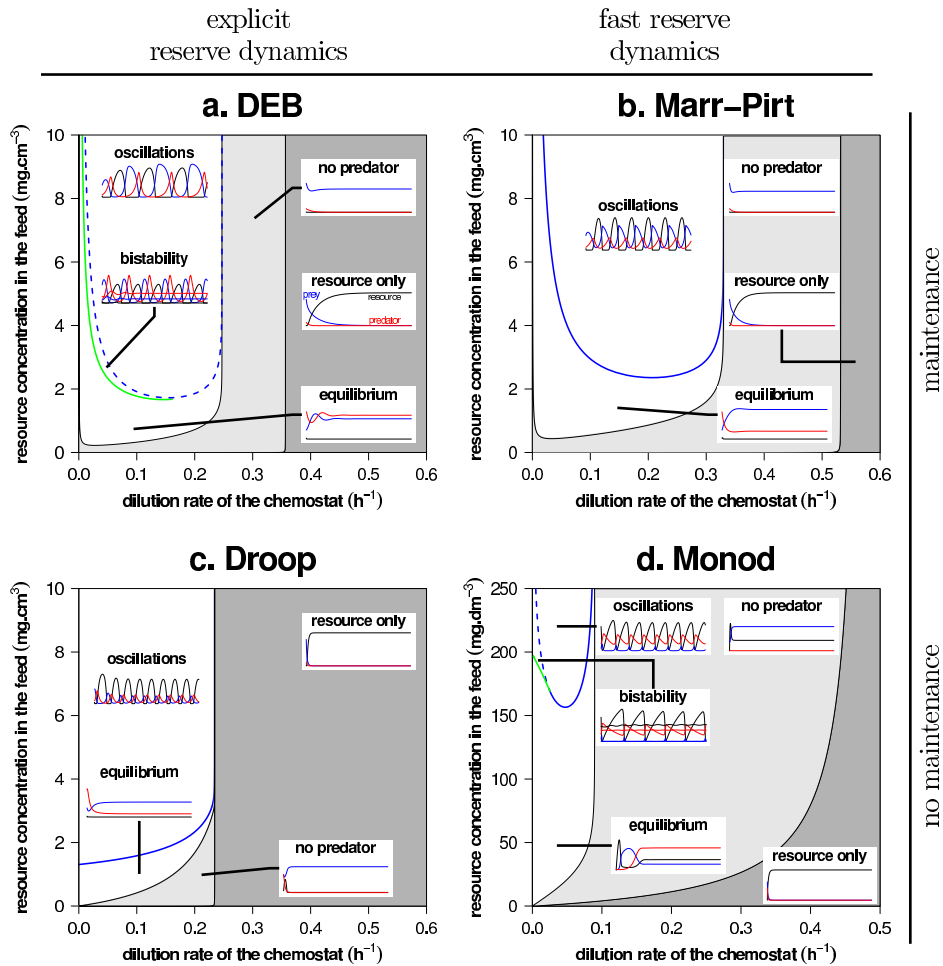


Figure 3. Predictions made with the four models of individual metabolism and an hyperbolic tangent functional response. Legend and modelled species are the same as in figure 2. In (d), there is a Bautin bifurcation point where the Hopf bifurcation (blue) switches from supercritical (plain) to subcritical (dashed) and a limit point for cycles bifurcation curve (green) emanates.

198 4 Discussion

199 Including more details on individual metabolism decreases the structural sensitivity of the
200 population model. Indeed, structural sensitivity is higher with Monod model, as functional
201 response formulation affects the qualitative pattern (type of bifurcations and predicted dy-
202 namics) of model predictions more than in the three more complex models: Marr-Pirt, Droop
203 and DEB models. Also, in these models, only 1 % to ≈ 25 % of a bounded part of the bifur-
204 cation diagrams is affected by the change of functional response. This is significantly lower
205 than the 26 % to 64 % of changes that we found in Bazykin’s predator-prey model (Aldebert
206 *et al.*, 2016b) where changes occur in a non-bounded subspace of parameter values. Here,
207 the three less sensitive models include at least maintenance or reserve dynamics.

208 Putting the previous conclusion into a broader framework of predator-prey models, an
209 additional requirement to avoid a strong structural sensitivity (i.e. changes in the type of bi-
210 furcations and dynamics) is to include an explicit description of resource dynamics (figure 4).
211 Explicit resource dynamics are used in mass-balance models (here chemostat), whereas other
212 models use a logistic growth equation for the prey. The logistic growth equation is phe-
213 nomenological, so its use may be less justified in comparison to a mechanistic mass-balance
214 equation of resource uptake (that might be a chemostat or not). These two approaches can
215 lead to very different dynamics in food chain models (Kooi *et al.*, 1998). In addition to these
216 limits of the logistic growth equation, we found that its use makes models more sensitive to
217 changes in the mathematical representation of trophic interactions. Here, we will not discuss
218 which model features (maintenance, reserve dynamics) make a model more or less sensitive
219 to predator functional response in terms of bifurcations location. Indeed, these quantitative
220 changes will depend on the biological parameter values that correspond here to two specific
221 experiments. Also, a deeper quantitative analysis including the predicted population size (as
222 in Cordoleani *et al.*, 2011, figure 5) across the whole bifurcation diagrams would require a too
223 high computational effort with two environmental parameters that vary and non-equilibrium
224 dynamics. In addition, existing metrics (Cordoleani *et al.*, 2011; Adamson & Morozov, 2012)

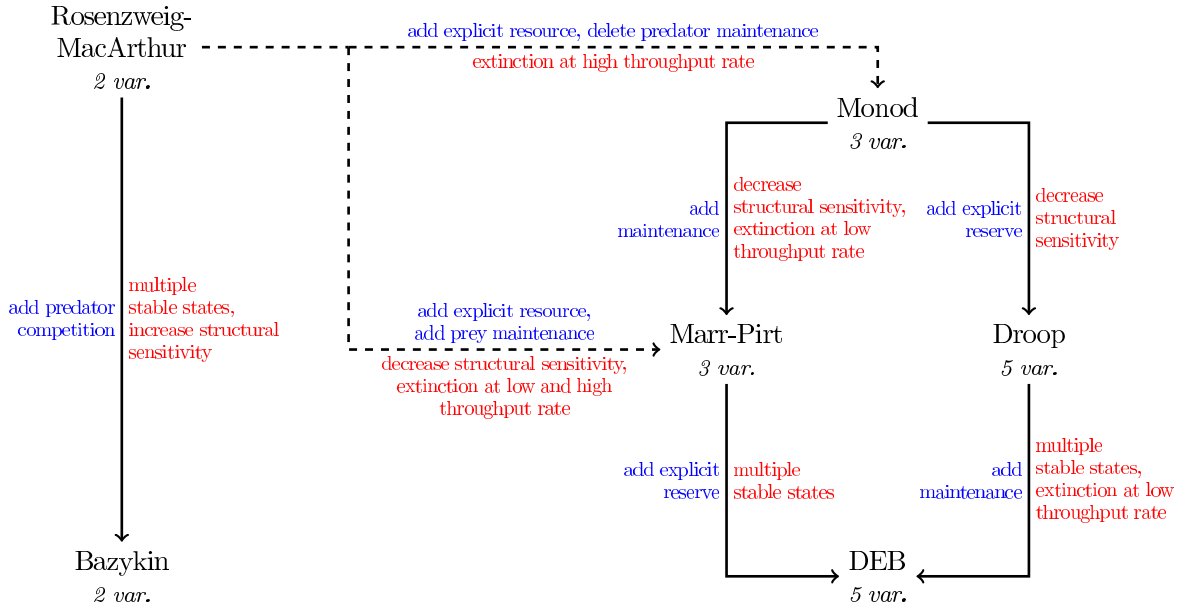


Figure 4. Changes in model assumptions (blue) and their consequences on model predictions (red). Structural sensitivity is here quantified in terms of qualitative change in bifurcations type. For Rosenzweig & MacArthur (1963) and Bazykin (1998) models, structural sensitivity analysis is presented in Fussmann & Blasius (2005) and Aldebert *et al.* (2016b) respectively. Arrows indicate either that the starting model is a limit case (plain) or an approximation (dashed) of the ending model. Details in Appendix D.

225 were designed to compare models with one stable and need to be first extend to compare
 226 models that might predict a different number of stable states (e.g. bistability area in figure 3d
 227 that does not exist in figure 2d, or in figure 2a vs. figure 2b).

228 The parameter values of Ivlev and the hyperbolic tangent functional responses are only
 229 estimated by fitting them to Holling-II functional response. The latter is not parameterized
 230 from functional response data, but by optimizing all parameter values so that model dynam-
 231 ics fit empirical data (Kooi & Kooijman, 1994b). Using this fitting procedure to estimate
 232 all parameters for each functional response would take into account the co-variation of some
 233 parameters (Lika *et al.*, 2011). Thus, a possible way to deal with structural sensitivity is to
 234 acquire data on both processes (here the functional response) and temporal dynamics of the
 235 system. Doing this would include the predicted location of thresholds like species extinction
 236 and the onset of predator-prey oscillations as constraints in functional response estimation.

237 Apart from the synergistic effect of maintenance and reserve on the coexistence of alter-
238 native stable states, reserve has a smaller impact on model predictions than maintenance.
239 Maintenance implies that a species disappears if resource input (here the dilution rate) is
240 not high enough to overcome its cost. This result was already known for models without
241 reserve (Nisbet *et al.*, 1983; Kooi, 2003), and we extend it here to models with explicit re-
242 serve. Note that the four models predict different thresholds of environmental parameters
243 for species invasion. Indeed, biological parameter values are optimized from one data set
244 corresponding to a single environmental condition. Thus, extrapolations from this reference
245 condition are likely to vary between models. From a biological point of view, maintenance
246 (linear mortality in community models) is a basic process that should be considered. In
247 addition, using explicit reserve without maintenance costs (Droop model) lead to the worst
248 fit to data (Kooi & Kooijman, 1994b). So, despite including reserve is relevant for many
249 reasons (Kooijman, 2010, section 1.1.3), it seems to be less important than maintenance.

250 When multiple resources limit the growth of the prey, the way their co-limited uptake is
251 modelled deeply affects the predicted dynamics of a predator-prey system (Poggiale *et al.*,
252 2010). These dynamics also change if maintenance is explicitly taken into account or not.
253 The uptake of multiple resources can be modeled in a mechanistic way through the concept
254 of Synthesising Units (Kooijman, 2010, chapter 3) that describe enzymatic pathways. Here,
255 we found that the predation formulation for the prey (i.e. resource uptake) has little effects
256 on model dynamics with one limiting resource. With multiple resources, model sensitivity
257 to the formulation of both predation and co-limited uptake remains to be assessed.

258 In addition to the number of limiting resources, the number of species in interaction
259 also influences system dynamics and structural sensitivity (Aldebert *et al.*, 2016a). Here,
260 we considered two species in interaction, but simple three-species food webs can have more
261 complicated dynamics with Monod and Marr-Pirt models (Kooi & Boer, 2001), and the sit-
262 uation might be more entangled for the DEB model (2). Moreover, the sensitivity functional
263 response formulation would be more complex to analyze for these models.

264 5 Conclusion

265 As a conclusion, the answer to the general question: *Is structural sensitivity problem of*
266 *oversimplified biological models?* is *Yes* in the context of our study. Here we found a
267 lower structural sensitivity in predator-prey models that include explicit resource dynamics
268 and maintenance (or reserve dynamics, figure 4). Thus, including these processes allows to
269 achieve three goals: (i) description of relevant processes, (ii) a better fit to available data
270 (Kooi & Kooijman, 1994b; Poggiale *et al.*, 2010), and (iii) more accurate predictions (fore-
271 cast of unknown situations) with respect to uncertainty in the mathematical formulation of
272 complex processes like predation. For this last point, one avoids the worst effect of struc-
273 tural sensitivity (qualitative change in predictions). However, some uncertainty in model
274 predictions (quantitative predictions, precise bifurcation values) remain, which motivate on-
275 going researches on the quantification of structural sensitivity to allow the communication
276 of model predictions together with their uncertainty. Finally, including explicit resource
277 dynamics and maintenance only slightly increases model complexity, which allows to keep
278 models tractable. Thus, including these processes is a promising way to deal with struc-
279 tural sensitivity, including in systems with non-equilibrium dynamics and alternative stable
280 states. So, the extension of our results to operational models based on multiple species and
281 resources is an open way of research. Another open way is to check that our guidance on the
282 use of predator-prey models holds for parameter values that describe data for a wide range
283 of species, which would be a critical advance toward more accurate predictions in ecology.

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