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REGULATION OF REPRODUCTIVE PROCESSES WITH DYNAMIC ENERGY BUDGETS

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31KEYWORDS

33**ABSTRACT**

34 1. Linking organismal level processes to underlying suborganismal

35   mechanisms at the molecular, cellular and organ level constitutes a

36   major challenge for predictive ecological risk assessments. This

37   challenge can be addressed with the simple bioenergetic models in the

38   family of Dynamic Energy Budget (DEB), which consist of a small

39   number of state equations quantifying universal processes, such as

40   feeding, maintenance, development, reproduction and growth.

41 2. Motivated by the need for process-based models to evaluate the

42   impact of endocrine disruptors on ecologically relevant endpoints, this

43   paper develops and evaluates two general modeling modules

44   describing demand-driven feedback mechanisms within the DEB

45   modeling framework exerted by gonads on the allocation of resources

46   to production of reproductive matter.

47 3. These modules describe iteroparous, semelparous and batch-mode

48   reproductive strategies. The modules have a generic form with both

49   positive and negative feedback components; species and sex specific

50   attributes of endocrine regulation can be added without changing the

51   core of the modules.

52 4. We demonstrate that these modules successfully describe time-

53   resolved measurements of wet weight of body, ovaries and liver, egg

54   diameter and plasma content of vitellogenin and estradiol in rainbow

55   trout (*Oncorynchus mykiss*) by fitting these models to published and

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56   new data, which require the estimation of less than two parameters

57   per data type.

58 5. We illustrate the general applicability of the concept of demand-driven

59   allocation of resources to reproduction by evaluating one of the

60   modules with data on growth and seed production of an annual plant,

61   the common bean (*Phaseolis vulgaris*).

62Introduction

63Dynamic Energy Budget (DEB) theory offers a remarkably general 64mathematical and conceptual framework for physiological ecology. Originally 65formulated to describe growth and reproduction in animals, DEB theory now 66describes widespread empirical patterns in metabolic behavior of a steadily 67increasing number species (over 1,200 at the time of writing) from phyla 68from all three domains (Sousa, Domingos & Kooijman 2008; Kooijman 2010; 69Jusup *et al.* 2017; AmP 2018). Its core concepts are consistent with some 70general trends in evolutionary history (Kooijman 1986; Kooijman & Troost 712007) and with the principles of thermodynamics (Sousa *et al.* 2010; Jusup *et 72al.* 2017). In addition, the theory offers a powerful framework for modeling 73organismal response to environmental stress, notably in ecotoxicology 74(Kooijman & Bedaux 1996; Jager *et al.* 2014; Muller *et al.* 2014) and, more 75recently, in the context of ocean acidification (Muller & Nisbet 2014; Jager, 76Ravagnan & Dupont 2016), starvation (Gergs & Jager 2014) and crowding 77stress (Gergs, Preuss & Palmqvist 2014). The versatility of the theory is due 78to its modular structure, through which specific attributes or 'details' of a 79particular environment, stressor or species can be included without changing 80the core of the model. Here we follow a similar approach to accommodate 81life history strategies by which organisms allocate resources to reproduction. 82Since reproduction generally constitutes a major fraction of the total energy 83budget of an adult organism, the energetic implications of different

84reproductive strategies and their trade-offs play a fundamental role in life

85history theory (Stearns 1992).

86An important feature of most DEB models is that resources are first

87assimilated into somatic reserves, which are then committed to support

88somatic, developmental and/or reproductive functions, depending on

89nutritional status and life stage. In the standard formulation of DEB (stdDEB),

90applicable to animals, the rate at which reserves are allocated to

91reproduction depends only on the reserve density and the size of the animal

92(see Figure 1). Control mechanisms regulating the partitioning of reserves to

93favor growth over reproduction, or *vice versa*, are absent. Standard DEB

94ignores control mechanisms regulating the development of gonads, as the

95specifics of those mechanisms vary widely among taxa and sexes (but see

96Pecquerie, Petitgas and Kooijman (2009), Einarsson, Birnir and Sigurosson

97(2011), Augustine *et al.* (2012) and Llandres *et al.* (2015) for species or

98group specific DEB gonad loading modeling modules for anchovy, capelin,

99zebrafish and parasitic wasps, respectively). This lack of feedback simplifies

100the dynamics of resource allocation, with obvious mathematical advantages

101as a result. Yet, stdDEB quantifies reproductive output sufficiently accurately

102for many purposes, such as those that require estimates of reproductive

103output over longer time spans or those involving species that release

104gametes in a nearly continuous manner. However, it is important to consider

105feedback, e.g., mediated by endocrine regulation mechanisms, in order to

106capture the *dynamics* of gamete maturation in iteroparous and semelparous

107organisms, in which gametes mature during the later part of the

108reproductive cycle or near the end of the life cycle, respectively. In addition,

109this kind of feedback could provide an entry to mechanistic modeling of the

110impact of endocrine disruptors on growth and reproduction in the DEB

111framework.

112To more accurately accommodate the alternative reproductive strategies of

113iteroparous and semelparous organisms, we develop and evaluate the

114performance of two extensions of the standard DEB model. These extensions

115include demand-driven feedback mechanisms on gonad development,

116guided by the premise that hormones produced in the reproductive organs

117and other organs commonly mediate those feedback mechanisms. We

118center our evaluation of model performance on a single fish species, the

119rainbow trout (*Oncorynchus mykiss*), due to the expansive data set on its

120growth and reproductive biology. However, we argue that the model

121extensions are based on general principles, and therefore applicable to other

122species. As an illustration, we discuss how simplified formalism from one of

123the model extensions can be applied to describe the growth and

124reproductive patterns in a species very different from trout, namely the

125common bean (*Phaseolis vulgaris*). Beans have a reproductive strategy

126typical for many annual plants, namely an allocation strategy that favors

127seed production over somatic growth during the later phases of the life

128cycle. In addition, we discuss how these extensions can be useful in

129exploring physiological mechanisms by which stressors, in particular

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130endocrine disruptors, affect resource allocation, and ultimately adverse

131outcomes to reproduction and growth.

132

133**Materials and methods**

134DATA SOURCES

135Three data sets about female rainbow trout (*O. mykiss*) were analyzed to

136evaluate model performance. The most expansive set, referred to as main

137data set, was from Nagler *et al.* (2012) with additional data from Gillies *et al.*

138(2016), and concerns a reproductively synchronized autumn-spawning

139population obtained from a commercial supplier (Troutlodge, Inc., Sumner,

140WA) and maintained in a temperature controlled flow-through system under

141a natural lighting regime at the Battelle Marine Science Facility (Sequim,

142WA). The main data set included time-resolved measurements of wet weight

143of body, ovaries and liver, egg diameter and plasma content of vitellogenin

144and estradiol of 58 individuals. The two supplementary data sets, SD1 and

145SD2, were more limited in scope. SD1 included time resolved measurements

146of body weight and egg mass of 12 and 9 individuals, respectively, of a

147spring spawning strain obtained from Troutlodge Inc. (Sumner, WA). SD2

148included initial and final total body and egg weights as well as weights and

149diameters of individual eggs of 16 individuals of a fall-spawning strain

150obtained from Nisqually Trout Farm (Lacey, WA). Fish of SD1 and SD2 were

151kept in the same facility as those of the main set; see Nagler *et al.* (2012),

152Schultz *et al.* (2013) and the Supplemental Information for experimental

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153detail. All sets span a single breeding cycle of approximately 11-14 months

154starting immediately after the time of first spawning.

155The common bean, *Phaseolis vulgaris*, was used to evaluate the potential of

156the principle of demand driven resource allocation to reproduction (see next

157section) to capture the dynamics of growth and reproduction of a species

158wildly different from iteroparous rainbow trout; beans have a semelparous

159reproductive strategy typical for many annual plants, namely an allocation

160strategy that favors seed production over somatic growth during the later

161phases of the life cycle. Data are from Lima *et al.* (2005) and include time-

162resolved measurements of vegetative above ground biomass, leaf cover and

163pod biomass of 6 cultivars grown in a field setting in coastal Brazil from May

164to August (mean growing conditions: 21.2°C, 70% humidity, 6.9 h solar

165radiation per day; 12 seeds per row meter at 0.5 m row distance; plots

166fertilized with 2.5 g N, 4.0 g P and 4.0 g K per square meter).

167

168DYNAMIC ENERGY BUDGET THEORY

169This study uses the standard model of Dynamic Energy Budget (stdDEB)

170theory as a reference. Since Kooijman (2010) has described this theory and

171its standard formulation in detail and several other publications provide

172extensive summaries (Nisbet *et al.* 2000; Sousa, Domingos & Kooijman 2008;

173Jusup *et al.* 2017), we only present features of the theory that are essential

174to evaluate the models developed in this study.

175The stdDEB formulation (see Fig. 1), describes the rates at which a
176'generalized' animal acquires resources from its environment and uses the
177energy therein for somatic and maturity maintenance, growth, maturation
178(juveniles) and reproduction (adults). A 'generalized' animal is heterotrophic,
179grows isometrically (constant shape), does not encounter conditions of stress
180(including debilitating forms of starvation), and has three life stages:
181embryonic (during which it does not feed), juvenile (feeding but no
182reproduction) and adult. Since this study involves the adult stage only, from
183now on, all references to animals pertain to adults, unless other life stages
184are explicitly mentioned. stdDEB distinguishes three pools of biomass:
185structure, general reserve and material in the reproductive buffer. Structure
186is defined as the biomass requiring maintenance in order to remain viable.
187The reproductive buffer contains resources tagged for reproduction
188(irreversibly, except potentially during starvation conditions). General
189reserve is functionally defined as all other metabolizable biomass; in
190practice, general reserve typically includes conventional storage materials as
191well as compounds that are traditionally not thought of as reserve, such as
192ribosomes in excess of the minimal amount needed to ensure vitality of an
193organism of a given size (Nisbet *et al.* 2000). The gross biochemical
194composition of each pool is considered to be invariant, implying that the
195costs to produce a unit of each type of biomass and the cost to maintain a
196unit of structure are constant. The general reserve density, i.e., the ratio of
197general reserve and structure, stabilizes in a constant food environment.

198Environmental resources are first assimilated into general reserve, which is

199subsequently committed to somatic and developmental/ reproductive

200functions, with each set of functions receiving a constant fraction κ of

201committed general reserve (see Figure 1). In order to accommodate the

202changing rate of gamete development during a reproductive cycle in female

203rainbow trout, we studied two extensions to the standard model (see Figure

2041). In the first variant, the proportion of committed general reserve allocated

205to reproduction is subject to feedback regulation of the reproductive buffer,

206implying that the allocation of general reserve to reproduction is driven by

207demand of the reproductive buffer. This variant is denoted dDEB, with the '*d*'

208standing for 'demand-driven'. The second variant, a modified version of a

209capelin model by Einarsson, Birnir and Sigurosson (2011), assumes stdDEB

210but separates the reproductive buffer in pools of unspecified reproductive

211reserve and actual reproductive matter. A gonad loading modeling module

212describes the rate at which reproductive reserve are converted into actual

213reproductive matter. This variant will be denoted stdDEB+, with the '+'

214referring to the gonad loading module. Regulation of the allocation of

215reserves to the reproductive buffer in dDEB and of gonad loading in stdDEB+

216are subject to endocrine control.

217The derivations of the dDEB and stdDEB+ model equations in Table 1 are

218presented in full in the Supplementary Information. Here, only the

219assumptions that are not part of stdDEB are presented and evaluated. The

220following list contains assumptions shared by and specific to both model

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221variants, though it should be stressed that reproductive matter is defined

222differently in those variants. In dDEB, reproductive matter refers to all matter

223in the reproductive buffer regardless of location in the body, whereas

224reproductive matter roughly corresponds to gametes in stdDEB+. The

225assumptions are:

226 1. At the onset of a reproductive cycle, a small fraction of somatic
227   biomass is converted to reproductive matter, e.g., due to meiosis.
228   General reserve and structure contribute proportionally to the initial
229   formation of reproductive matter, and the costs of this conversion are
230   negligible. The latter two assumptions are rather arbitrary but
231   quantitatively insubstantial.
232 2. The initial density of reproductive matter is constant. This assumption
233   maintains parameter parsimony and model simplicity.
234 3. An adult has a bounded capacity to carry reproductive matter. In non-
235   starving adults, this capacity is proportional to the amount of structural
236   biomass, i.e., the maximum density of reproductive matter is a
237   constant. This assumption maintains parameter parsimony and model
238   simplicity.
239 4. dDEB only: the fraction of mobilized general reserve allocated to
240   reproduction and maturity maintenance in adults is proportional to (1)
241   the density of reproductive matter, and (2) the difference between the
242   maximum and actual density of reproductive matter. The first
243   proportionality introduces positive feedback and is based on the

244 general observation that the ovaries in fish produce estrogen, which

245 stimulates the production of vitellogenin, the precursor of egg reserve

246 material (Tyler & Sumpter 1996). The second proportionality provides a

247 simple negative feedback (i.e., deceleration) mechanism that causes

248 the accumulation of reproductive material in the gonads to slow down

249 towards the end of a reproductive cycle.

250 5. stdDEB+ only: the rate at which reproductive reserves are converted

251 to reproductive matter is proportional to (1) the density of reproductive

252 reserves, (2) the density of reproductive matter, (3) the difference

253 between the maximum and actual density of reproductive matter, and

254 (4) the amount of structural biomass. The first proportionality ensures

255 the density of reproductive reserves cannot become negative; for

256 arguments for the two subsequent proportionalities, see previous

257 assumption.

258 6. The efficiency with which reproductive reserves are converted into

259 reproductive matter is constant.

260 7. Spawning requires the density of reproductive matter to exceed a

261 threshold and, additionally, may be under the control of a time trigger

262 or environmental factor, depending on species.

263 LINK BETWEEN DEB QUANTITIES AND DATA

264 Variables in DEB models are abstract quantities and therefore do not

265 correspond directly with measurable quantities. The mapping of DEB

266 quantities onto the data analyzed in this study, including total body, ovary

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267and liver wet weights, follicle diameter and plasma levels of estradiol and

268vitellogenin, is achieved through auxiliary assumptions stated in this section;

269the corresponding equations, summarized in Table 1, are derived in the

270Supplementary Information. The relationship between measurable quantities

271pertaining to the common bean and those of a DEB model of bean growth

272and fecundity can be found in the Supplementary Information.

273In order to convert DEB mass quantities to wet weights, we use conversion

274factors from the rainbow trout entry in the DEB parameter database

275(Kooijman *et al.* 2017). Considering that the ovaries mainly consist of storage

276materials in eggs, we assume the contributions of structure and general

277reserves to the wet weight of the ovaries are negligible (to avoid confusion,

278we will use 'storage' to refer to physical materials and 'reserves' as the

279conceptual abstraction in the context of DEB). We also assume that the

280fraction of reproductive matter that is in the ovaries is constant.

281Furthermore, we assume that reproductive matter is either in the ovaries or

282in the liver, which produces the precursors of egg storage materials. It is

283prudent to consider also including plasma vitellogenin, the precursor of egg

284storage materials. However, plasma vitellogenin levels are especially high

285just prior and after ovulation, indicating that not all plasma vitellogenin ends

286up in eggs. Furthermore, the fraction of vitellogenin in plasma is relatively

287small. Plasma contributes 2.5% to 5.5% to body wet weight in teleost fish

288(Brill *et al.* 1998, and references therein) and contains about 25 mg

289vitellogenin/ ml during the phase of accelerating ovary growth in a typical

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290individual in this study (see figure 2F), which corresponds to only about 1.5-
2913.5 g vitellogenin in a 2.5 kg fish. Thus, it is reasonable to ignore the
292contribution of vitellogenin to reproductive matter, though its dynamics are
293informative and are modeled later. Furthermore, we assume that the
294fractions of structure and reserves that are part of the liver are constants for
295both model variants, and, for stdDEB+, in order to retain simplicity, that the
296amount of reproductive reserves in the liver is negligible.

297This leaves the follicle diameter and estradiol and vitellogenin plasma levels
298as the experimental quantities that need to be related to DEB variables. In
299order to relate the mean diameter of a follicle to reproductive matter, we
300assume that follicles are perfect spheres and that the specific gravity of
301biomass equals unity. Estradiol is produced by the ovaries and regulates the
302flow of vitellogenin to the ovaries. Accordingly, we link the gonad loading
303module of stdDEB+ and the reproduction flux in dDEB to the plasma
304estradiol concentration assuming simple proportionality.

305To model the dynamics of plasma vitellogenin, we assume that the volume of
306plasma is proportional to the amount of structural biomass, and that the rate
307at which vitellogenin is cleared from plasma is proportional to the amount of
308structural biomass (e.g., by structural mass in the ovaries). Furthermore, for
309dDEB, we assume that the rate at which vitellogenin is released into the
310blood stream is proportional to the rate at which somatic reserves are
311allocated to reproduction. For stdDEB+, we assume that the rate at which

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312vitellogenin is released into the blood stream is proportional to the rate at

313which reproductive reserves are allocated to reproductive matter.

314

315PARAMETERIZATION

316

317In the evaluation of model performance with trout data, the values of some

318or all parameters in Table 2 were fixed, depending on the information

319content of the data and on the purpose of the analysis (see legend to Figure

3204 for information about parameter values regarding the analysis of bean

321data). The main data set was used to parameterize the model variants;

322subsequently, this parameterization was used to predict the observations in

323the supplementary data sets SD1 and SD2 (with one exception – see next

324section). However, not all parameters were estimable from the main data set

325due to a lack of information about, e.g., elemental biomass composition and

326some conversion efficiencies, and therefore had to be fixed; similar values

327were used for fixed parameters that occur in both model variants. The values

328of eight fixed parameters, as marked in Table 2c, were taken or calculated

329from the rainbow trout entry in the DEB parameter database (Kooijman *et al.*

3302017). Among those was the somatic maintenance rate parameter, which

331could not be estimated as it strongly covaried with other parameters, notably

332the general reserve turnover rate. Since the value of the somatic

333maintenance rate parameter is relatively invariant across species (Kooijman

334 3342010), it was fixed at the value in the DEB parameter database, while the 335 latter was treated as a free parameter.

336 The reasoning for the remaining five fixed values is as follows. First, the 337 value for the scaled food density was set at 0.9, which is close to its 338 maximum of 1.0, as the fish were well fed. Second, according to the 339 parameter database, maturity maintenance costs would have been an 340 insubstantial fraction of the total energy budget of the fishes and were 341 therefore ignored. Third, the initial density of reproductive reserve in 342 stdDEB+ was assumed negligible, since there was no information available 343 that could be used to identify the reproductive reserve pool as a pool 344 separate from general reserve and reproductive matter in this model variant 345 (in contrast, this parameter could be estimated for dDEB – see Table 2d). 346 This assumption is supported by the fact the fish had recently matured and 347 were stripped before the experiment. Fourth, the maximum density of 348 reproductive matter in stdDEB+ strongly covaried with other parameters and 349 was therefore fixed; it was identical to the density of reproductive matter in 350 a female of ultimate size at optimal conditions after one year according to 351 the parameter database. Fifth, the conversion efficiency of reproductive 352 reserves to reproductive matter in stdDEB+ was set at unity, implying that 353 all the conversion overheads were subsumed in the conversion of general 354 into reproductive reserve.

355 Free parameters were estimated by maximizing likelihood considering all 356 data types in a set simultaneously, while assuming that discrepancies

357between data and model predictions were due to normally distributed

358homoscedastic error in the data. These estimations were done with a

359modified version of the BYOM platform coded in Matlab

360(www.debtox.info/byom). Confidence intervals were estimated from the

361likelihood profile of each parameter. Universally suitable goodness-of-fit

362measures are lacking for nonlinear models (see e.g. Shcherbakov *et al.*

3632013), which problem was compounded by the composite nature of the trout

364data sets analyzed in this study. Therefore, in the analysis of trout data sets,

365in addition to likelihood values, two goodness-of-fit measures were used to

366evaluate model performance: the symmetric mean scaled error, $SMScE_i$, and

367the model efficiency, ME - see Supplemental Information for equations.

368

369**Results**

370The dDEB and stdDEB+ models are relatively parameter sparse. The dDEB

371model needed 21 parameters, of which 12 were estimated, to describe the

372patterns in the main data set by Gillies *et al.* (2016), including total body,

373ovaries, total body less ovaries and liver wet weight, mean follicle diameter

374and vitellogenin and estradiol plasma content. The stdDEB+ model required

375two more parameters, 23 in total, of which 11 could be estimated from the

376main data set. Thus, on average, less than two parameters were estimated

377from each data type.

378Despite this relative parameter sparseness, both models fit the trends in the

379main data set well (see Figure 2 and Table 2). The fits to the weight and

380follicle diameter data are virtually indistinguishable between the two models

381(see Figure 2A-E). The goodness-of-fit measures are also similar for the two

382models (see Table 2). In addition, the estimated values for the general

383reserve turnover rate k_E, the only free core DEB parameter, are statistically

384indistinguishable at the 95% level (see Table 2d), though the value implied

385by the parameters published in the DEB parameter database for rainbow

386trout (Kooijman *et al.* 2017) is about 10-20% lower (2.92 10^{-3} day^{-1} at 11°C).

387More divergence in model performance is seen in the predictions of plasma

388vitellogenin and estradiol contents, notably during the last third of the

389reproductive cycle (see Figure 2F-G). The peaks of those plasma contents in

390this period are substantially better described by dDEB than by stdDEB+, as

391the latter cannot capture the drop in plasma vitellogenin and estradiol levels

392near the end of the reproductive cycle. The goodness-of-fit measures for

393those plasma contents also favor dDEB over stdDEB+ (see Table 3). In

394addition, the overall goodness-of-fit measures point to dDEB as the superior

395model. The AIC criterion also points to dDEB as the preferable model, since

396the log likelihood of dDEB is 21.9 higher than that of stdDEB+, which is a

397large difference, especially given that dDEB has only one more free

398parameter than stdDEB+.

399Although cultivation conditions were roughly similar among the three

400experiments, the fish in the supplementary data sets SD1 and SD2 grew

401more vigorously than those in the main data set. This can be clearly seen in

402Fig. 3A, which shows that the model predictions by dDEB and stdDEB+ with

403the parameters estimated from the main data set (bottom two curves)

404underestimate growth of fish in set SD1. The predictions are greatly

405improved, however, by adjusting the general reserve turnover rate

406parameter. Increasing this value by 25% (dDEB) or 20% (stdDEB+) yields

407curves that are virtually indistinguishable and represent the growth data

408well. Similarly, with the value of the general reserve turnover rate parameter

409from the main data set, both models estimate the predictions of end weights

410in data set SD2 about 25-30% lower than actually observed. Also with this

411data set, satisfactory estimates of final body weights are obtained by

412increasing the value of the general reserve turnover rate parameter with

41335% (dDEB) or 20% (stdDEB+) (results not shown).

414The analysis of reproductive data from SD1 and SD2 comes with two

415caveats. First, the exact moment of spawning in these experiments is

416unknown. This hinders the comparison of model predictions of reproductive

417endpoints with observed values, as the former depend strongly on timing,

418given the relatively steep increase in ovary weight during the final weeks of

419the reproductive cycle (*cf.* Fig 2C). Second, the models predict the weight of

420ovaries, whereas the data report egg mass. With these caveats in mind, we

421take the census time to be 355 days into the reproductive cycle and assume

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422the final weight of the ovaries equals that of eggs. Then, with the reserve

423turnover rate from the main data set, the models overestimate the

424reproductive effort in data set SD1 by about a third (see Table 3). With the

425general reserve turnover rate adjusted (see above), this overestimation

426increases to 45-70%, though the gonadosomatic index (GSI) remains

427relatively unaffected as body masses are also predicted higher. Relative to

428data set SD2, the models underestimate reproduction 25-30%, assuming

429general reserve turnover rates estimated from the main data set. With those

430estimates adjusted as before, underestimates shrink to 2% and 20% for

431dDEB and stdDEB+, respectively, while predicted GSI values change

432relatively little. The models predict reproductive effort at day 355 as a

433function of total body mass about similarly, considering the scatter in the

434data (see Fig. 3B). With general reserve turnover rates adjusted, the

435measured mean mass and diameter of single eggs in data set SD2, 105.7

436(±14.5) mg and 5.54 (±0.36) mm, respectively, are close to the values

437predicted by dDEB (93.3 mg and 5.62 mm, respectively), whereas the

438predictions by stdDEB+ differ more (65.3 mg and 4.96 mm, respectively).

439

440**Discussion**

441We have formulated and evaluated two models of feedback control on the

442production of reproductive matter. The models provide a key to

443quantitatively connecting molecular level processes to organismal

444performance, a major challenge in biology. In particular, they describe

445growth and reproduction as processes subject to hormonal regulation, and

446thus provide a link between detailed physiologically-based models about the

447endocrine system (see e.g. Gillies *et al.* 2016) to the DEB modeling

448framework.

449Important strengths of DEB include its generality and relative simplicity. The

450core dynamics of the standard DEB model for a healthy animal consist of

451only three state equations and involve universal processes, such as feeding,

452maintenance, development, reproduction and growth, with similarly general

453formulae relating these processes to measurable rates, such as respiration,

454waste and heat production. The additional equations required for modeling

455particular species and context specific measurable quantities (e.g., Equations

4568-19 in Table 1) are somewhat narrower in applicability, but still have

457considerable generality. For example, we would expect these equations to be

458applicable to most fishes, albeit with species-specific values for their

459parameters.

460Our representation of demand-driven energy allocation to the production of

461reproductive matter focuses on a general dynamic mechanism, namely

462feedback control of gonads. We used this mechanism to develop two

463extensions of the standard DEB model, stdDEB+ and dDEB (see Figure 1).

464These extensions share the feature that, depending on the nutritional state

465of an adult, growth may occur concurrently with the accumulation of

466reproductive matter; this contrasts with other simple models, often used in

467optimality arguments, in which an adult commits either resources to growth

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468or to reproduction at any given time (see e.g. Cohen 1971; Quince *et al.*
4692008). However, a dDEB organism may cease to grow, and may even shrink,
470while it continues to allocate resources to reproduction (see below). We
471evaluated these extensions in depth with data on a single fish species, i.e.,
472rainbow trout, due to the availability of extensive, time-resolved information
473on whole organism performance as well as on suborganismal processes
474related to the endocrine system.

475Our models describe the production of biomass and reproductive matter in
476female rainbow trout in the three data sets analyzed here about equally well
477(see Fig. 2A-D, 3 and Table 3). Values of the core DEB parameter quantifying
478the rate of general reserve turnover estimated from these data sets differ
47920-35% from each other, and they are 10-55% higher than the value
480published in the DEB parameter database (Kooijman *et al.* 2017), though are
481rather similar in dDEB and stdDEB+ (see Table 2d). Rainbow trout are a
482remarkably adaptable species with a long history of domestication and wide
483geographic distribution, existing as both anadromous and land locked
484varieties and have a relatively high level of genetic variation among different
485populations (Maccrimmon 1971; Hershberger 1992). Thus, it is not surprising
486that the general reserve turnover rate parameter varies among strains. The
487dDEB variant performs better in describing the dynamics of plasma estradiol
488and vitellogenin contents as well as the development of individual eggs (see
489Fig. 2E-G), and overall dDEB fits the main data set significantly better than
490stdDEB+, as judged from likelihood values (see Table 3). While the types of

491data best described by dDEB are of relatively minor importance to whole 492organism performance, their consideration reflects conceptual differences 493between model variants with important implications.

494The major conceptual difference between dDEB and stdDEB+ lies in the 495timing of (somatic) reserve allocation to reproduction. In stdDEB+, a well-fed 496adult allocates a constant fraction of mobilized reserves to reproduction plus 497maturity maintenance throughout the reproductive cycle and grows at a rate 498that is independent of the size of the reproductive buffer. This contrasts with 499the dynamic allocation of reserves in dDEB, in which the allocation is under 500the control of the size of the reproductive buffer relative to that of the 501animal. Consequently, this allocation can vary a great deal over a 502reproductive cycle (see Fig. S1 in the Supporting Information). Concurrently, 503growth follows an opposite trend. In a constant environment, dDEB predicts 504that most of the growth of a species with a seasonal reproduction pattern 505occurs before the gonads start developing substantially, whereas growth in 506stdDEB+ is of the von Bertalanffy type. Consequently, size data could 507discriminate between the two models. Unfortunately, the total body weight 508measurements analyzed in this study contain too much scatter to be of much 509help. Length measures typically are relatively precise and could therefore be 510used to evaluate the merits of dDEB and stdDEB+. It should be noted, 511though, that dDEB reduces to stdDEB in a hypothetical adult animal that 512releases gametes nearly continuously, as the density of the reproductive 513buffer would be almost constant.

514Both dDEB and stdDEB+ predict the growth of the gonads occurs primarily 515during the later parts of the reproductive cycle, which is a common 516observation for synchronous annually spawning fishes like rainbow trout 517(Tyler & Sumpter 1996) as well as many marine invertebrates, 518notwithstanding the time-invariant fraction of reserves being allocated to 519reproduction in the latter model variant. In stdDEB+, this is made possible by 520separating the reproductive buffer into two sequential pools, of which the 521first, reproductive reserves, receives somatic reserves according to the 522kappa rule of standard DEB, whereas the second containing actual 523reproductive matter (e.g., eggs) exerts positive and negative feedback 524control on the rate at which it is being filled with reserves from the first pool 525(see Equations 10-11 and Fig. 1). A potentially unrealistic consequence of 526separating the reproductive buffer into two pools is that although the gonad 527pool may be completely emptied during spawning, an animal following 528stdDEB+ may be left with a substantial amount of reproductive reserves at 529the time of spawning. Indeed, in stdDEB+ parameterized with the main data 530set, a three year old female rainbow trout releases only a little over 50% of 531the total amount of somatic reserves allocated to reproduction at spawning, 532despite its negligible reproductive buffer at the beginning of the reproductive 533cycle (see Figure S2 in the Supporting Information). In addition, stdDEB+ 534recognizes two reserve pools, reproductive and somatic, with different 535dynamics; this begs the question how an animal following stdDEB+ would be

536able to tell apart those reserve pools, given their likely large overlap in

537chemical nature and storage location.

538A particular characteristic of dDEB is that reproduction can induce starvation

539symptoms, even when environmental resources are abundant. Due to the

540demand driven positive feedback of the reproductive buffer on reserve

541allocation in dDEB, the energy flow to the somatic branch may become

542insufficient to meet somatic maintenance demands. At that point, an

543organism has several options (Kooijman 2010). For instance, it could

544increase the reserve mobilization rate, give maintenance requirements

545priority over reproduction, reabsorb reproductive matter, skimp on

546maintenance, or use structural biomass as an energy source to meet

547maintenance, i.e., shrink. All these options may be realistic, depending on

548the life history strategy of the organism. For instance, reabsorption of

549gonads under stress conditions occurs in parasitoid wasps (Richard & Casas

5502009; Richard & Casas 2012), bivalves (Gosling 2003) and fishes (Schreck,

551Contreras-Sanchez & Fitzpatrick 2001), among other groups. Here we

552allowed structural biomass to be recycled for maintenance purposes, but did

553so in a provisional manner (the thermodynamic implications of shrinking are

554rather intricate and fall beyond the scope of this paper). This mechanism of

555structure recycling may be of use to describe the degeneration of structures

556and the loss in vitality before and after spawning in semelparous fishes, such

557as species of eel and salmon.

558In addition, this recycling mechanism is relevant for species with marked

559biomass turnover processes, such as holometabolous insects and annual

560plants. In the pupa stage, holometabolous insects degrade most tissues and

561build new structures. Without demand-driven feedback mechanisms and

562implied recycling mechanisms for structural biomass, such as in dDEB, the

563modeling of holometabolous insects within a DEB context is cumbersome

564(Llandres *et al.* 2015). Many annual plants feature strategies in which

565vegetative structures wither while seed mass is still increasing. The common

566bean, *P. vulgaris*, for instance, clearly displays this pattern (see e.g. Lima *et*

567*al.* 2005). In order to illustrate the ability of dDEB to capture this pattern, we

568used a stripped-down dDEB model without reserves, added an empirical

569relationship describing the dynamics of relative leaf cover (see Figure 4A)

570and a simple standard model describing photosynthesis as a function of leaf

571cover (see Supplemental Information for a full description of the model). This

572modified dDEB model describes the dynamic allocation of resources to above

573ground vegetative biomass and reproductive matter in this particular data

574set quite well (see Fig. 4B). It should be noted that the apparent relocation of

575structural biomass to seeds is due to an indirect mechanism: structural

576biomass is metabolized to meet the maintenance demands of the remaining

577structure, while an increasing fraction of photosynthate is invested in seed

578production.

579Our models are designed to serve as pivots connecting Adverse Outcome

580Pathways (AOP) for endocrine disruptors to processes at ecological levels of

581organization. AOPs conceptualize the transfer of information from molecular

582to organismal levels of organization as the first step in scaling up to inform

583ecological risk assessment (Ankley *et al.* 2010). Starting with one or more

584molecular initiating events, i.e., perturbations caused by a chemical stressor,

585AOP models quantify the impacts of that stressor on molecular, cellular

586and/or organ-level processes. However, these models currently lack the

587ability to further these impacts to projections of those adverse effects on

588individual growth, reproduction, and survival, which are in the realm of the

589DEB modeling framework. Thus, the AOP framework could provide the

590mechanistic basis for modeling toxic effects within the DEB modeling

591framework, and thereby opening the door to process-based risk assessments

592in ecotoxicology (Murphy *et al.* 2018).

593In conclusion, by including gonadal feedback control on energy allocation to

594reproduction and somatic processes we obtain three major benefits. Firstly,

595through this mechanism, the formation of reproductive matter can take on a

596marked seasonal, semelparous or batch-mode pattern with a minimum of

597mathematical complexity. Secondly, it facilitates the modeling of growth and

598reproduction as processes subjected to endocrine regulation, that is, it

599enables a connection between organismal and suborganismal level

600processes. Thirdly, since the control variable, i.e., the density of reproductive

601matter, has a generic form, species and sex specific attributes of endocrine

602regulation can be added without changing the core of the model. We

603anticipate that this mechanism, and our two model extensions that follow

28

604from it, will provide a gateway for incorporating molecular-level mechanisms
605of endocrine disruption into organismal-level models of individual
606performance, such as those in the DEB framework.

607

608Authors' contributions

609All authors conceived the ideas. EM, KL and RN developed the models. IS
610collected the data. EM analyzed models and data and led the writing of the
611manuscript. All authors contributed critically to the drafts and gave final
612approval for publication.

613Data accessibility

614Data available from the Dryad Digital Repository:
615https://doi.org/10.5061/dryad.58j9r88 (Muller *et al.* 2018).

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632**References**

633AmP (2018) Online database of DEB parameters, implied properties and
634   referenced underlying data. Accessed 2018/09/11.
635   http://www.bio.vu.nl/thb/deb/deblab/add_my_pet/.
636Ankley, G.T., Bennett, R.S., Erickson, R.J., Hoff, D.J., Hornung, M.W., Johnson,
637   R.D., Mount, D.R., Nichols, J.W., Russom, C.L., Schmieder, P.K.,
638   Serrrano, J.A., Tietge, J.E. & Villeneuve, D.L. (2010) Adverse outcome
639   pathways: a conceptual framework to support ecotoxicology research
640   and risk assessment. *Environmental Toxicology and Chemistry,* **29,**
641   730-741.
642Augustine, S., Gagnaire, B., Adam-Guillermin, C. & Kooijman, S. (2012)
643   Effects of uranium on the metabolism of zebrafish, Danio rerio. *Aquatic*
644   *Toxicology,* **118,** 9-26.
645Brill, R.W., Cousins, K.L., Jones, D.R., Bushnell, P.G. & Steffensen, J.F. (1998)
646   Blood volume, plasma volume and circulation time in a high-energy-
647   demand teleost, the yellowfin tuna (Thunnus albacares). *Journal of*
648   *Experimental Biology,* **201,** 647-654.
649Cohen, D. (1971) Maximizing final yield when growth is limited by time or by
650   limiting resources. . *Journal of Theoretical Biology,* **33,** 299-307.
651Einarsson, B., Birnir, B. & Sigurosson, S. (2011) A dynamic energy budget
652   (DEB) model for the energy usage and reproduction of the Icelandic
653   capelin (Mallotus villosus). *Journal of Theoretical Biology,* **281,** 1-8.
654Gergs, A. & Jager, T. (2014) Body size-mediated starvation resistance in an
655   insect predator. *Journal of Animal Ecology,* **83,** 758-768.
656Gergs, A., Preuss, T.G. & Palmqvist, A. (2014) Double Trouble at High
657   Density: Cross-Level Test of Resource-Related Adaptive Plasticity and
658   Crowding-Related Fitness. *Plos One,* **9**.

659 Gillies, K., Krone, S.M., Nagler, J.J. & Schultz, I.R. (2016) A Computational
660   Model of the Rainbow Trout Hypothalamus-Pituitary-Ovary-Liver Axis.
661   *Plos Computational Biology,* **12**.

662 Gosling, E. (2003) *Bivalve molluscs: biology, ecology and culture*. Blackwell.

663 Hershberger, W.K. (1992) Genetic-variability in rainbow-trout populations.
664   *Aquaculture,* **100,** 51-71.

665 Jager, T., Barsi, A., Hamda, N.T., Martin, B.T., Zimmer, E.I. & Ducrot, V.
666   (2014) Dynamic energy budgets in population ecotoxicology:
667   Applications and outlook. *Ecological Modelling,* **280,** 140-147.

668 Jager, T., Ravagnan, E. & Dupont, S. (2016) Near-future ocean acidification
669   impacts maintenance costs in sea-urchin larvae: Identification of stress
670   factors and tipping points using a DEB modelling approach. *Journal of*
671   *Experimental Marine Biology and Ecology,* **474,** 11-17.

672 Jusup, M., Sousa, T., Domingos, T., Labinac, V., Marn, N., Wang, Z. &
673   Klanjscek, T. (2017) Physics of metabolic organization. *Physics of Life*
674   *Reviews,* **20,** 1-39.

675 Kooijman, S.A.L.M. (1986) Energy Budgets Can Explain Body Size Relations.
676   *Journal of Theoretical Biology,* **121,** 269-282.

677 Kooijman, S.A.L.M. (2010) *Dynamic energy and mass budgets in biological*
678   *systems,* 3rd edn. Cambridge University Press, Cambridge.

679 Kooijman, S.A.L.M., Augustine, S., Sadoul, B. & Zimmer, E.I. (2017) *AmP*
680   Oncorhynchus mykiss, version 2017/05/27. Online database of DEB
681   parameters, implied properties and referenced underlying data,
682   http://www.bio.vu.nl/thb/deb/deblab/add_my_pet/.

683 Kooijman, S.A.L.M. & Bedaux, J.J.M. (1996) Analysis of toxicity tests on
684   Daphnia survival and reproduction. *Water Research,* **30,** 1711-1723.

685 Kooijman, S.A.L.M. & Troost, T.A. (2007) Quantitative steps in the evolution
686   of metabolic organisation as specified by the Dynamic Energy Budget
687   theory. *Biological Reviews,* **82,** 113-142.

688 Lima, E.R., Santiago, A.S., Araujo, A.P. & Teixeira, M.G. (2005) Effects of the
689   size of sown seed on growth and yield of common bean cultivars of
690   different seed sizes. *Brazilian Journal of Plant Physiology,* **17,** 273-281.

691 Llandres, A.L., Marques, G.M., Maino, J.L., Kooijman, S., Kearney, M.R. &
692   Casas, J. (2015) A dynamic energy budget for the whole life-cycle of
693   holometabolous insects. *Ecological Monographs,* **85,** 353-371.

694 Maccrimmon, H.R. (1971) World distribution of rainbow trout (*Salmo*
695   *gairdneri) Journal of the Fisheries Research Board of Canada,* **28,** 663-
696   +.

697 Muller, E.B., Hanna, S.K., Lenihan, H.S., Miller, R. & Nisbet, R.M. (2014)
698   Impact of engineered zinc oxide nanoparticles on the energy budgets
699   of Mytilus galloprovincialis. *Journal of Sea Research,* **94,** 29-36.

700 Muller, E.B., Lika, K., Nisbet, R.M., Schultz, I.R., Casas, J., Gergs, A., Murphy,
701   C.A., Nacci, D. & Watanabe, K.H. (2018) Data from: Regulation of
702   reproductive processes with dynamic energy budgets. *Dryad Digital*
703   *Repository,* https://doi.org/10.5061/dryad.58j9r88.

704 Muller, E.B. & Nisbet, R.M. (2014) Dynamic energy budget modeling reveals
705　　the potential of future growth and calcification for the coccolithophore
706　　Emiliania huxleyi in an acidified ocean. *Global Change Biology,* **20,**
707　　2031-2038.

708 Murphy, C.A., Nisbet, R.M., Antczak, P., Garcia-Reyero, N., Gergs, A., Lika, K.,
709　　Mathews, T., Muller, E.B., Nacci, D., Peace, A., Remien, C.H., Schultz,
710　　I.R., Stevenson, L.M. & Watanabe, K.H. (2018) Incorporating
711　　Suborganismal Processes into Dynamic Energy Budget Models for
712　　Ecological Risk Assessment. *Integrated Environmental Assessment and*
713　　*Management,* **14,** 615-624.

714 Nagler, J.J., Cavileer, T.D., Verducci, J.S., Schultz, I.R., Hook, S.E. & Hayton,
715　　W.L. (2012) Estrogen receptor mRNA expression patterns in the liver
716　　and ovary of female rainbow trout over a complete reproductive cycle.
717　　*General and Comparative Endocrinology,* **178,** 556-561.

718 Nisbet, R.M., Muller, E.B., Lika, K. & Kooijman, S. (2000) From molecules to
719　　ecosystems through dynamic energy budget models. *Journal of Animal*
720　　*Ecology,* **69,** 913-926.

721 Pecquerie, L., Petitgas, P. & Kooijman, S. (2009) Modeling fish growth and
722　　reproduction in the context of the Dynamic Energy Budget theory to
723　　predict environmental impact on anchovy spawning duration. *Journal*
724　　*of Sea Research,* **62,** 93-105.

725 Quince, C., Abrams, P.A., Shuter, B.J. & Lester, N.P. (2008) Biphasic growth in
726　　fish I: Theoretical foundations. *Journal of Theoretical Biology,* **254,** 197-
727　　206.

728 Richard, R. & Casas, J. (2009) Stochasticity and controllability of nutrient
729　　sources in foraging: host-feeding and egg resorption in parasitoids.
730　　*Ecological Monographs,* **79,** 465-483.

731 Richard, R. & Casas, J. (2012) A quantitative framework for ovarian
732　　dynamics. *Functional Ecology,* **26,** 1399-1408.

733 Sale, P.J.M. (1975) Productivity of Vegetable Crops in a Region of High Solar
734　　Input. IV. Field Chamber Measurements on French Beans (Phaseolus
735　　vulgaris L.) And Cabbages (Brassica oleracea L.). *Australian Journal of*
736　　*Plant Physiology,* **2,** 461-470.

737 Schreck, C.B., Contreras-Sanchez, W. & Fitzpatrick, M.S. (2001) Effects of
738　　stress on fish reproduction, gamete quality, and progeny. *Aquaculture,*
739　　**197,** 3-24.

740 Schultz, I.R., Nagler, J.J., Swanson, P., Wunschel, D., Skillman, A.D., Burnett,
741　　V., Smith, D. & Barry, R. (2013) Toxicokinetic, Toxicodynamic, and
742　　Toxicoproteomic Aspects of Short-term Exposure to Trenbolone in
743　　Female Fish. *Toxicological Sciences,* **136,** 413-429.

744 Shcherbakov, M.V., Shcherbakova, N.L., Janovsky, T.A. & Kamaev, V.A.
745　　(2013) A survey of forecast measures. *World Applied Sciences Journal,*
746　　**24,** 171-176.

747 Sousa, T., Domingos, T. & Kooijman, S.A.L.M. (2008) From empirical patterns
748　　to theory: a formal metabolic theory of life. *Philosophical Transactions*
749　　*of the Royal Society B-Biological Sciences,* **363,** 2453-2464.

750 Sousa, T., Domingos, T., Poggiale, J.C. & Kooijman, S. (2010) Dynamic energy
751   budget theory restores coherence in biology Introduction. *Philosophical*
752   *Transactions of the Royal Society B-Biological Sciences,* **365,** 3413-
753   3428.
754 Stearns, S.C. (1992) *The evolution of life histories*. Oxford University Press,
755   New York.
756 Tyler, C.R. & Sumpter, J.P. (1996) Oocyte growth and development in
757   teleosts. *Reviews in Fish Biology and Fisheries,* **6,** 287-318.

758

Table 1. Equations.

DEB Model Expressions

General reserve density (constant food), m_E

All variants $f m_{Em}$ (1)

Fraction mobilized general reserves to reproduction and maturity maintenance, λ

stdDEB+, stdDEB $1 - \kappa$ (2)

dDEB $4 \lambda_m m_E \left(m_{Em} - m_E \right) m_{Em}^{-2}$ (3)

Growth rate, $dM_V / dt = j_V M_V$

All variants $\left((1 - \lambda) k_E S m_E - j_M \right) M_V \left((1 - \lambda) m_E + y_V^{-1} \right)^{-1}$ (4)

Dynamics of the density of reproductive buffer in between spawning events, dm_F / dt

dDEB, stdDEB $y_F \left(\lambda m_E \left(k_E S - j_V \right) - k_J M_{HD} M_V^{-1} \right) - j_V m_F$ (5)

Dynamics of the density of reproductive reserves, dm_{RE} / dt

stdDEB+ $y_{RE} \left((1 - \kappa)(k_E S - j_V) m_E - k_J M_{HD} M_V^{-1} \right) - m_{RE} \left(j_V + k_F m_G (m_{Gm} - m_G) \right)$ (6)

Dynamics of the density of reproductive matter in between spawning events, dm_G / dt

stdDEB+ $y_G k_{RE} m_{RE} m_G (m_{Gm} - m_G) - j_V m_G$ (7)

Equations Linking Trout Data to DEB quantities

Total body wet weight, W_B

dDEB $(1 + m_E + m_F) d_M M_V / d_W$ (8)

stdDEB+ $(1 + m_E + m_F + m_G) d_M M_V / d_W$ (9)

Ovary wet weight, W_O

dDEB $\kappa_{OV} m_F d_M M_V / d_W$ (10)

stdDEB+ $\kappa_{OV} m_G d_M M_V / d_W$ (11)

Liver wet weight, W_L

dDEB $(p + m_F)(1 - \kappa_{OV}) d_M M_V / d_W$ (12)

stdDEB+ $(p + m_G)(1 - \kappa_{OV}) d_M M_V / d_W$ (13)

Mean follicle diameter, L_F

dDEB	$\left(6\kappa_{OV}d_M M_V m_F/\pi n d_W\right)^{1/3}$	(14)
stdDEB+	$\left(6\kappa_{OV}d_M M_V m_G/\pi n d_W\right)^{1/3}$	(15)

Plasma estradiol concentration, $E2$

dDEB	$q_1\lambda$	(16)
stdDEB+	$q_2 m_G\left(m_{Gm}-m_G\right)$	(17)

Plasma vitellogenin concentration, V_T

dDEB	$d_T y_F\left(\lambda m_E\left(k_E S - j_V\right)-k_J M_{HD}M_V^{-1}\right)-\left(k_T+j_V\right)V_T$	(18)
stdDEB+	$d_T k_{RE}m_{RE}m_G\left(m_{Gm}-m_G\right)-\left(k_T+j_V\right)V_T$	(19)

760

761

762 **Table 2.** Parameters and variables used in the analysis of the main set of
763 rainbow trout data. (a) Dynamic model quantities; (b) Experimental
764 variables; (c) fixed parameters; (d) estimated parameters.

765 (a) Dynamic model quantities

	Interpretation	Units
j_V	Specific growth rate	day^{-1}
m_E	Density of general reserves	-
m_F	Density of reproductive buffer (dDEB)	-
m_G	Density of reproductive matter (stdDEB+)	-
m_{RE}	Density of reproductive reserves (stdDEB+)	-
M_V	Amount of structural biomass	C-mole
S	Surface correction function, $\left(M_{Vm}/M_V\right)^{1/3}$	-
λ	Fraction of reserves allocated to reproduction (dDEB)	-

766
767 (b) Experimental variables

	Interpretation	Units
$E2$	Plasma estradiol content	ng ml^{-1}
L_F	Follicle diameter	mm

W_B	Wet weight total body		kg
W_L	Wet weight liver		g
W_O	Wet weight ovaries		kg
V_T	Plasma vitellogenin content		mg ml^{-1}

768

769 (c) Fixed parameters (T=11°C)

	Interpretation	Value	Source
d_M	C-mole to dry weight conversion	24.6 g C-	AmP[*]
d_W	Wet weight to dry weight conversion	0.2	AmP
f	Scaled food density	0.9	See text[**]
j_M	Specific maintenance rate	0.025 day^{-1}	AmP
k_J	Maturity maintenance coefficient	0 day^{-1}	See text
m_{F0}	Initial density of reproductive matter (stdDEB+)	0[***]	See text
m_{Gm}	Maximum density of reproductive matter (stdDEB+)	6.60	See text
M_{Vm}	Maximum structural biomass	1.12 C-mole	AmP
y_F	Conversion efficiency general reserve to reproductive buffer	0.95	AmP
y_G	Conversion efficiency reproductive reserve to gonads (stdDEB+)	1	See text
y_{RE}	Conversion efficiency general to reproductive reserve	0.95	AmP
y_V	Conversion efficiency general reserve to structure	0.88	AmP
κ	Fraction reserves allocated to soma (stdDEB+)	0.56	AmP

770 [*] 'Add my Pet' DEB parameter data base (Kooijman *et al.* 2017)

771 [**] Parameterization section in Materials and Methods

772 [***] Free parameter in dDEB – see Table 2d

773

774(d) Estimated parameters

	Interpretation	dDEB		stdDEB+		Units
		Value	95% CI	Value	95% CI	
d_T	Vitellogenin conversion factor	131.6	71.5-339.3	102.2	56.4-404.7	mg day^{-1}
k_E	General reserve turn-over rate	3.37	2.99-3.71	3.63	3.25-3.99	x 10^{-3} day^{-1}
k_{RE}	Reproductive reserve turn-over rate	NA	NA	1.11	1.00-1.24	x 10^{-3} day^{-1}
k_T	Vitellogenin clearance rate	0.044	0.016-0.142	0.032	0.012-0.166	day^{-1}
m_{F0}	Initial density of reproductive buffer	1.67	0.66-3.64	NA*	NA*	x 10^{-3}
m_{Fm}	Maximum density of reproductive buffer	3.67	3.20-4.21	NA	NA	-
m_{G0}	Initial density of reproductive matter	NA	NA	9.28	4.60-17.5	x 10^{-3}
M_{V0}	Initial amount of structural biomass	0.846	0.787-0.915	0.827	0.770-0.890	C-mole
n	Number of eggs	4.43	3.57-5.48	5.15	4.10-6.52	x 10^3 #
p	Compound parameter, $(\kappa_{VL}+\kappa_{EL}m_E)/(1-\kappa_{OV})$	5.50	3.52-10.89	5.76	3.63-11.6	-
q_1	Estradiol conversion factor	56.0	44.6-66.9	NA	NA	ng ml^{-1}
q_2	Estradiol conversion factor	NA	NA	3.40	2.58-4.24	ng ml^{-1}
V_{T0}	Initial plasma vitellogenin content	102.3	66.1-142.6	96.7	57.2-144.9	mg ml^{-1}
κ_{OV}	Fraction of reproductive matter in ovaries	0.971	0.957-0.984	0.967	0.951-0.982	-
λ_m	Maximum fraction of reserves to reproduction	0.761	0.684-0.839	NA	NA	-

775

776 * Fixed parameter in stdDEB+ - see Table 2c.

777

Table 3. Statistics of model fits to Main data set[1].

Data type	Figure	dDEB	$\ln\mathcal{L}=-1551.2$		stdDEB+	$\ln\mathcal{L}=-1573.1$	
		σ	*SMScE*	*ME*	σ	*SMScE*	*ME*
E2	2G	11.8 ng. ml^{-1}	0.592	0.556	14.2 ng ml^{-1}	0.724	0.363
L_F	2E	0.445 mm	0.162	0.906	0.491 mm	0.298	0.885
W_B	2A	170 g	0.077	0.811	157 g	0.071	0.838
W_L	2D	5.66 g	0.176	0.449	5.70 g	0.175	0.439
W_O	2B	44.7 g	0.304	0.871	47.7 g	0.298	0.853
W_B - W_O	2C	305 g	0.109	0.071	299 g	0.107	0.110
V_T	2F	35.2 mg ml^{-1}	0.542	0.644	40.3 mg ml^{-1}	0.635	0.534
Overall	2		0.280	0.615		0.309	0.575

779 [1]A perfect fit implies *SMScE* $=0$ and *ME* $=1$.

780

781**Table 3.** Measured and predicted body and egg masses supplementary data
782sets on day 355.

Set		Body mass	Egg mass	GSI
SD1	Data	2608	274 (±84)	0.105
	dDEB, k_E from main	2096	373 (±34)	0.178
	dDEB, k_E 25% higher	2660	470 (±40)	0.177
	stdDEB, k_E from main	2177	370 (±42)	0.170
	stdDEB, k_E 20%	2629	400 (±46)	0.152
SD2	Data	2483	419 (±161)	0.169
	dDEB, k_E from main	1732	296 (±35)	0.171
	dDEB, k_E 35% higher	2428	412 (±43)	0.170

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stdDEB, k_E from main	1849 (±213)	308 (±67)	0.167
stdDEB, k_E 20%	2263 (±346)	336 (±80)	0.149
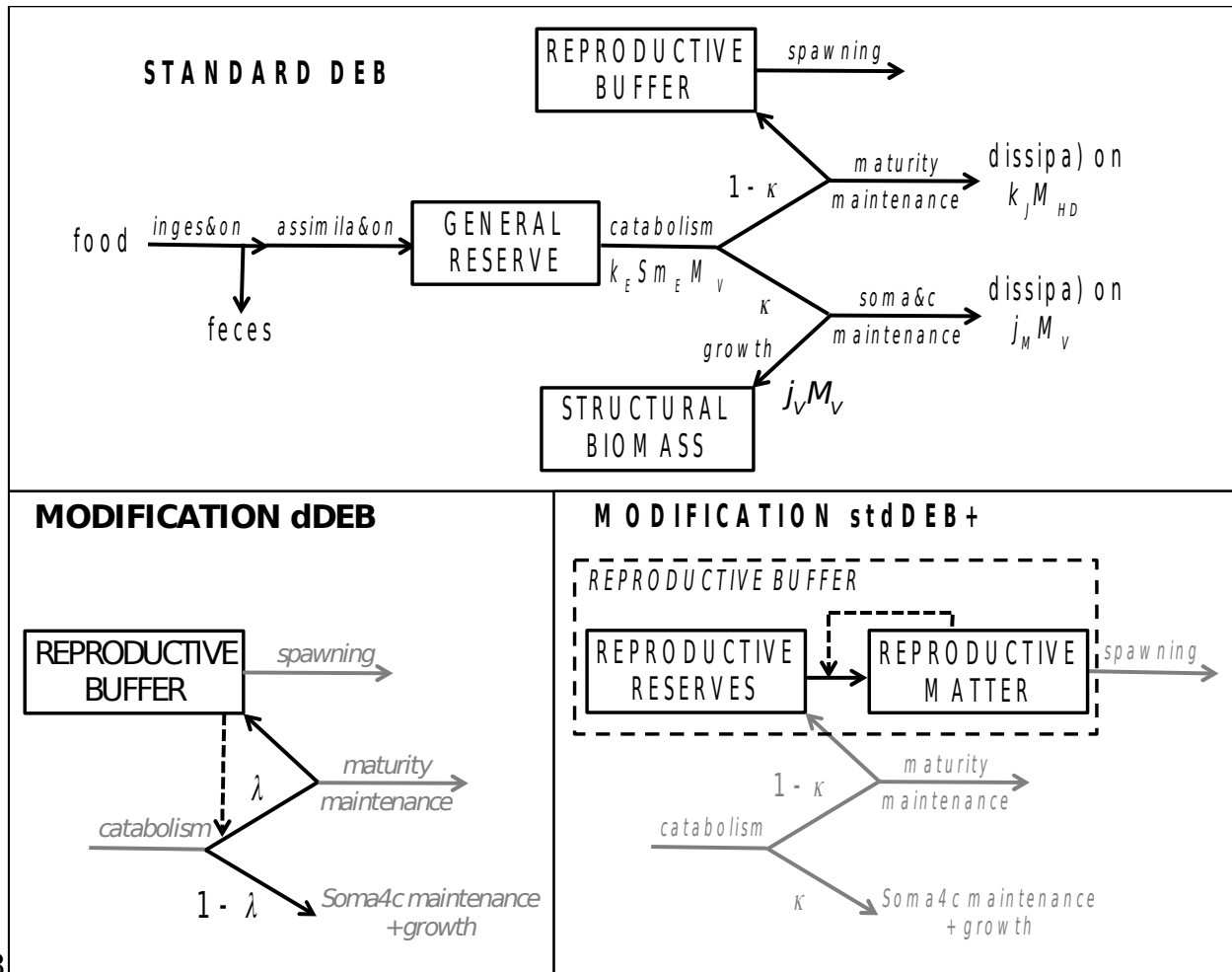
Figure 1. Conceptual representations of the standard DEB (stdDEB) model for healthy adults and of two types of modifications, dDEB and stdDEB+. stdDEB (Nisbet *et al.* 2000; Kooijman 2010; Jusup *et al.* 2017) describes the rates at which an adult animal acquires food, assimilates the energy and nutrients therein into general reserves, and allocates those reserves to somatic and maturity maintenance, growth and reproduction; this allocation is defined as catabolism. A fixed fraction κ of the catabolic flux is allocated to somatic maintenance and growth. Somatic and maturity maintenance are demand-driven processes and take priority over growth and reproduction; all other processes in stdDEB are supply-driven. In dDEB, stdDEB is modified to include positive and negative feedback of the reproductive buffer on the allocation of the catabolic flux. Thus, in dDEB, reproduction is a demand-

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797driven process with a variable fraction λ of the catabolic flux allocated to 798maturity maintenance and reproduction. stdDEB+ separates the 799reproductive buffer in two pools: reproductive reserves and actual 800reproductive matter (gonads). The rate at which reproductive reserves are 801converted into reproductive matter depends on the densities of reproductive 802reserve and reproductive matter, implying that gonad loading is a demand-803driven process. Solid arrows represent energy and material fluxes; broken 804arrows represent feedback mechanisms; boxes represent state variables; 805modifications of dDEB and stdDEB+ relative to stdDEB are presented in black 806while communalities are shown in grey. Note that DEB processes and 807quantities are abstractions; auxiliary rules are required to relate them to 808experimental quantities – see Table 1.
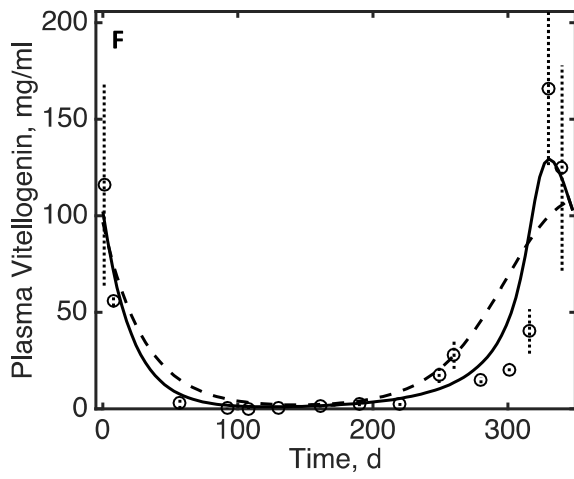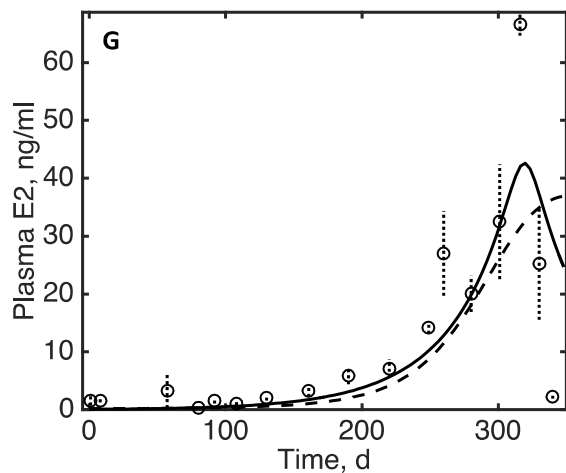
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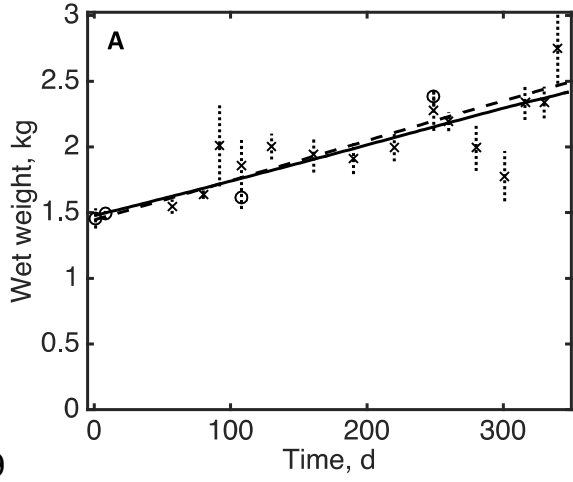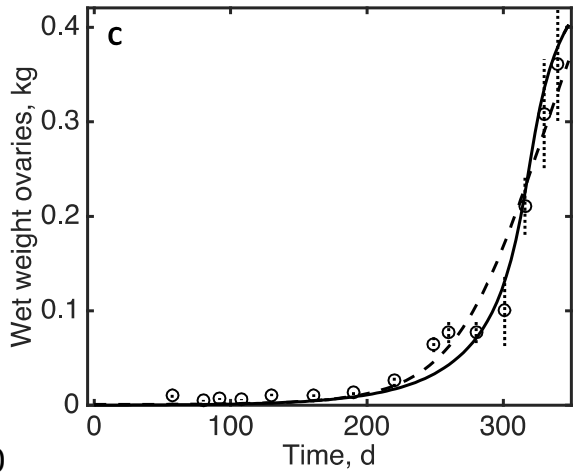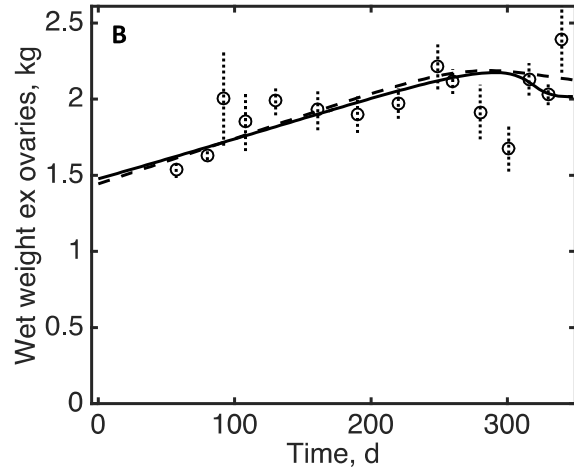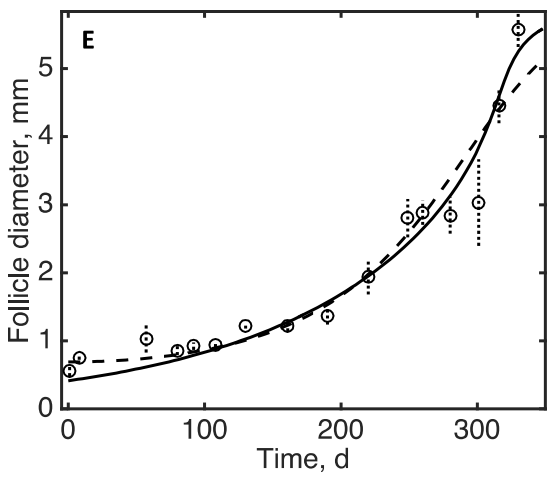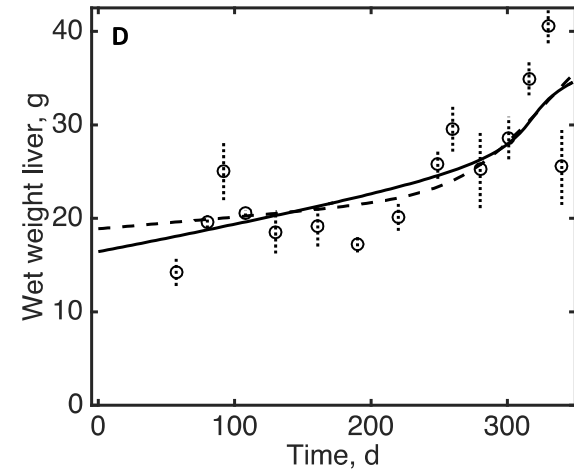
Figure 2. Model fits of dDEB (solid line) and stdDEB+ (dashed line) to main data set with rainbow trout (symbols), including (A) total body wet weight; (B) total body wet weight less wet weight of ovaries; (C) wet weight of ovaries; (D) wet weight of liver; (E) mean diameter of maturing follicles (mean per fish); (F) plasma vitellogenin content; and (G) plasma estradiol content. Measurements denoted 'x' in Panel A were used to calculate corresponding data in Panel B and were therefore omitted in the fitting procedure. Error bars denote standard deviations (n = 3 or 4). Parameter estimates are given in Table 1d and goodness-of-fit measures in Table 2. Data from Nagler *et al.* (2012) and Gillies *et al.* (2016).

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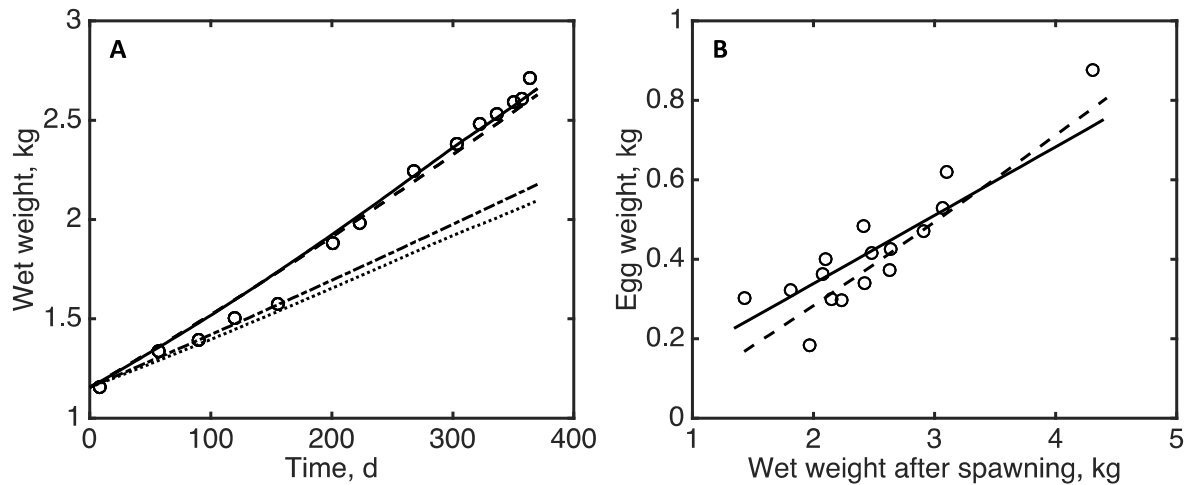
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825**Figure 3.** The ability of dDEB and stdDEB+ parameterized with values
826estimated from the main data set (see Fig. 2 and Table 1d) to predict
827production in rainbow trout was evaluated with supplementary data set SD1
828(A) and set SD2 (B). (A) With the estimated parameter values, both dDEB
829(dotted curve) and stdDEB+ (dot-dashed curve) underestimated the gain in
830weight in set SD1 (circles). Predictions are greatly improved by increasing
831the reserve turnover rate by 25% (dDEB, solid curve) or 20% (stdDEB+,
832broken curve) relative to the value estimated from the main data set. (B)
833dDEB (solid curve, reserve turnover rate 35% higher than the one in the
834main data set) and stdDEB+ (broken curve, reserve turnover rate 20%
835higher than the one in the main set) predict measured total egg mass versus
836body weight (symbols) from data set SD2 about equally well.
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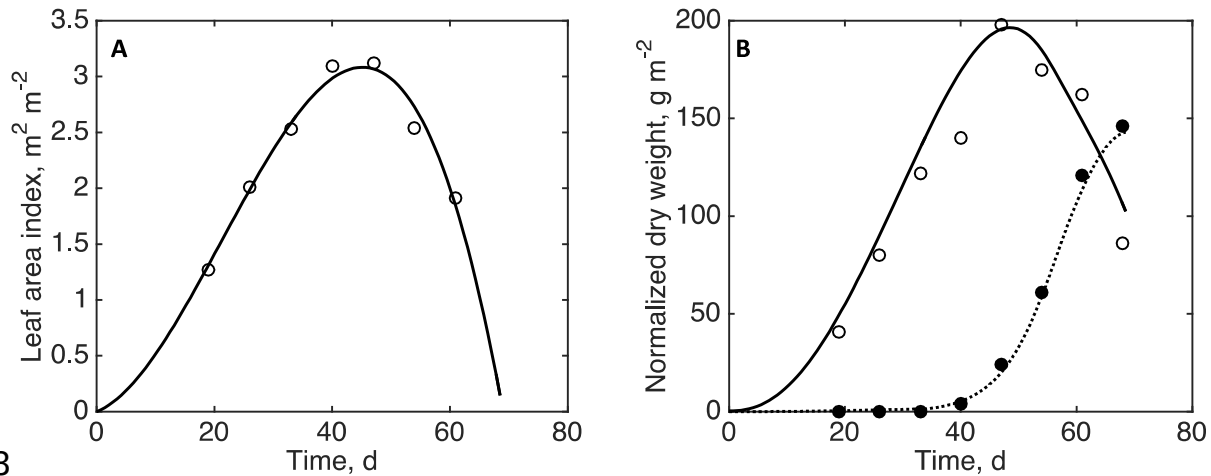
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840**Figure 4.** Application of a simplified version of dDEB to production in the 841common bean, *Phaseolis vulgaris*. (A) An empirical third degree polynomial 842describes the dynamics of the leaf area index, defined as the total green leaf 843surface are per unit area ground cover, an important determinant of the

844photosynthetic capacity ($p_1 = 30.5 \, \text{min}^{-1}$, $p_2 = 5.2 \, \text{min}^{-2}$, $p_3 = -0.08 \, \text{min}^{-3}$). (B) The 845simplified dDEB model fits above ground vegetative biomass (open circles, 846solid curve) and pod mass (closed circles, dotted curve) with mean bean 847mass as the initial amount of structural biomass, observed mean time of first 848flowering (34 d) as starting point of photosynthate allocation to reproduction,

849$m_F = 0.01$ and negligible losses in converting photosynthate into vegetative 850and reproductive biomass. Parameter estimates (with 95% confidence 851intervals) are $\lambda_m =$ 0.52 (0.30-0.87), $m_{Fm} =$ 1.09 (0.95-1.24), $j_M =$ 0.08 (0.03-

8520.16) d^{-1} and $c =$ 0.12 (0.08-0.17); $J_{Pm}^{\circ} =$ 65.2 g dry weight m^{-2} d^{-1} based on 853the net photosynthesis rate estimated by Sale (1975). Data are from Lima *et* 854*al.* (2005) and represent the means of four replicates of six cultivars grown 855from large seeds. See Supplemental Information for model description.