**Supplementary Materials**

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*Parameter estimation*

Fitting of parameters to data was done in Matlab with the platform BYOM v.6.4 and the package DEBkiss v.2.3a (https://www.debtox.info/byom.html). BYOM uses a Nelder-Mead simplex search to optimize the parameters for a set of ordinary differential equations by minimizing negative log-likelihood (NLL). The DEBkiss package works under BYOM to estimate model parameters based on their effect on the DEBkiss equations and the auxiliary equations. The differential equations predict length, egg production, egg buffer mass, and survival over time with the differences from observations used to calculate NLL. Before estimating any parameters with the optimization described above, we ran simulations with fitting turned off using a set of recommended parameters (Jager, 2018) and parameters we calculated from data on *M. menidia*, as described in the main text (Section 2.3). We visually assessed fit and noted the NLL calculated from each simulation as we adjusted parameters to obtain a reasonable set of initial parameters before estimating any. Testing a range of parameters and obtaining realistic initial parameters helps avoid detecting local minima with the optimization. This also helped us reduce the number of parameters being estimated to avoid overfitting and so that there were not multiple correlated parameters free at once.

*Calculation of volume-specific maintenance costs*

By assuming all structural weight lost during starvation is used for maintenance, we can use data on dry weights during starvation to calculate mass-specific weight change over time. This can then be converted to volume-specific maintenance cost by multiplying it by the dry weight density. Because such data do not exist for *M. menidia*, we used dry weight data from the closely related *M. beryllina* from a study in which larvae were starved for 7 days starting at three ages (7, 14, and 21 days post-hatching) and at three different temperatures (21, 25, and 28°C; Letcher and Bengtson, 1993). We selected the data for the 7 day post-hatching fish at 25°C because it was closest to the temperature at which much of the data were collected, and because it had the greatest sample size (n=22). Based on the calculation used in Stevenson et al. (2023), we fit a function to the dry weights over time. While Stevenson et al. (2023) used an exponential function, we used a linear function because the dataset only reported dry weight at the beginning and end of the starvation period.

The mass-specific rate of change in mass (*kM0*, mg assimilates \* mg dry weight-1 \* d-1, assumed to be the mass-specific maintenance cost) is calculated as:

, (S1)

where *WV0* is the initial dry weight in mg, *WV* is the final dry weight in mg, and *t* is the duration of starvation in days. We then multiplied *kM0* by *dV* to obtain the volume-specific maintenance cost in mg mm-3 d-1. The values involved in the calculation are in Table S1.

|  |  |
| --- | --- |
| *WV0* | 0.160 mg |
| *WV* | 0.100 mg |
| *t* | 7 d |
| *kM0* | 0.0535 mg assimilates \* mg dry weight-1 \* d-1 |
| *dV* | 0.4 mg dry weight \* mm structural volume-3 |
| *JvM* | 0.0214 mg assimilates-1 \* mm structural volume-3 d-1 |

*Relating DEB processes to physiology*

Several genes controlling cell division and protein synthesis are regulated by hypoxia (Ton et al., 2003), such as insulin-like growth factor binding protein 1 (IGFBP-1), a protein controlled by hypoxia-inducible factor 1 (Hif-1) that has been shown to reduce growth and delay development in fish embryos exposed to hypoxia (Kajimura et al., 2005; Kajimura et al., 2006; Sun et al., 2011; Tian et al., 2014). This factor is thought to trade off growth for other oxygen-demanding processes and help fish tolerate hypoxia. By preventing insulin-like growth factors from binding to their receptors, IGFBP-1 inhibits signaling for cell division and differentiation and energy can be diverted to processes necessary for survival (Kajimura et al., 2005). In the DEBkiss model such forms of inhibition to the SU under hypoxia would be represented by reduced assimilation rates, though the link to survival is not represented explicitly.

The conversion efficiency of assimilates to structure determines growth and hatch timing because it represents the fraction of assimilates that are converted into structure rather than burned on overhead costs of growth (Jager, 2018). When oxygen is low enough that anaerobic metabolism must be used, this reduces conversion efficiency so that less growth results from the same amount of yolk or food (Thomas et al., 2019). Damage to the SU may also be responsible for reductions in conversion efficiency through lactate accumulation and consequential declines in internal pH. Even at oxygen levels above the critical level at which oxygen consumption declines, anaerobic glycolysis may increase (Nonnotte et al., 1993; Maxime et al., 2000; Wood et al., 2018). Although capability for anaerobic glycolysis in embryos and yolk sac larvae appears to vary widely across species (Wieser, 1995; Finn, 1995; Rombough, 1988), smaller fishes reach harmful levels of anaerobic end-products much faster than larger fishes due to their higher mass-specific metabolic rates (Nilsson and Östlund-Nilsson, 2008). We hypothesized that this contributed to a smaller hatch size and slower growth post-hatch.

Maintenance in DEBkiss is the energy allocated to any processes that support the integrity and functioning of the structural body (Jager, 2018), including homeostasis, damage repair, and activity. Demand for more protein turnover and cell repair can increase the volume-specific maintenance rate following damage (Bouma et al., 1994; Kooijman, 2010a) and indeed maintenance has been shown to increase with damage to structural proteins (Maury et al., 2019). In addition to damage repair, maintenance rate could be elevated by the activity required for some of the behavioral responses fish exhibit under hypoxia (Thomas et al., 2019). *M. menidia* exposed to hypoxia swim to the surface to use aquatic surface respiration, taking advantage of the diffusion of oxygen from the air (Miller et al., 2016). This behavior is impossible in embryos but has been observed in larvae (Cross et al., 2019). Fishes also expend energy on faster ventilation and heartbeat when ambient DO is low to increase oxygen uptake (Kramer, 1987; Maxime et al., 2000) and remove accumulated CO2 and lactate (Perry et al., 2009; Heath and Pritchard, 1965), but these capabilities may be limited until development has progressed further.

The maintenance flux in DEBkiss is represented in units of assimilated biomass required to meet the energy demand from maintenance. It therefore is only indirectly related to respiration rates measured as oxygen consumption. For example, an increase in the abstract maintenance parameter in the model could be caused by an increase in anaerobic processes without impacting oxygen consumption. The *measured* oxygen consumption rates of *M. menidia* early life stages did not significantly increase under experimental chronic hypoxia, but great variability in metabolic rates among individuals combined with the short respirometry periods used (<1 hour) may make small increases related to damage repair or activity difficult to detect (Schwemmer et al., 2020).

Although mortality is not a process directly represented by an SU, it could indirectly be impacted by hypoxia effects on SUs through failure to meet developmental milestones – particularly for hatching – or directly through increase in damage production or inhibition of damage repair rates. In the parameter estimation using data from normoxic conditions (Section 2.3), our estimated survival parameter for embryo mortality was greater than that of larvae (Table 1). If assimilation rate or conversion efficiency of *M. menidia* decreases under hypoxia, the resulting slower egg buffer depletion would delay hatching, extending individuals’ time in the stage with greater mortality and thus accounting for reduced hatch survival under hypoxia. We therefore hypothesized that if either assimilation rate or conversion efficiency is modified by the hypoxia-based correction factor, additionally modifying the embryo mortality parameter would consequently not be necessary to account for hypoxia effects on all four state variables. However, this would not be the case for the post-hatch mortality parameter because none of the processes in the DEBkiss model indirectly affect mortality after hatching, so changing either the assimilation or conversion efficiency parameter in combination with the post-hatch mortality parameter may be necessary to fully replicate the observed changes to growth, hatch timing, and survival under hypoxia.

Reduced food consumption or reduced conversion of food into utilizable compounds, and thus limitation of input of substrate to the SU, is a primary mechanism by which the fish energy budget is thought to be impacted by hypoxia (Chabot and Dutil, 1999; Thomas et al., 2019 with findings reinterpreted for DEBkiss). We did not test food consumption as a mechanism by which hypoxia affects the energy budget because effects on hatch timing and size, before feeding has begun, could not be explained by this mechanism.

References for Supplementary Methods

Supplementary Figure

A diagram of a curve

Description automatically generated with medium confidence

**Figure S1. Best fit of DEBkiss model to all experimental data from four DO levels.** The model was fitted to early life data (embryos, larvae, and juveniles) and the best fitting model was selected based on lowest AICc. (A) is total length (mm) over time (days), (B) is egg buffer mass (mg) over time (days), and (C) is survival over time (days).