**Inhibition and Damage in DEBkiss. RMN-10/31/23**

Teresa’s notes entitled “Summary of approaches to modeling hypoxia in M. menidia DEB” cited data offering two possible hints on the processes impacted by hypoxia in embryos and larvae. These were up-regulation of IGFBP-1 expression and lactate accumulation or LDH activity. Here I tentatively suggest that changes in IGFBP-1 can be represented as inhibition and lactate accumulation as damage in a DEB model.

I think of inhibition as slowing some process and damage as destroying something. Muller et al. (2019) formalize this for processes that involve a SU:

**Inhibition**: *Inhibition is the process by which a compound reversibly binds to an enzyme and thereby impedes its activity; enzymatic activity is fully restored upon dissociation of the inhibitor.*

**Damage**: *Damage is* *the process by which a detrimental agent irreversibly destroys the functionality of an SU, which then either needs to be replaced through de novo synthesis or requires restoration through a repair process*.

In DEBkiss, all biosynthesis processes have rates proportional to the assimilation rate. The loss rate of egg buffer is equal to  and the material available to growth is . Thus, with the Muller et al definition, **inhibition would correspond to a reduction in the assimilation parameterbut NOT a change in any yield coefficients.** As noted by Teresa, this can explain reduced size at hatching and delayed hatching. It also explains reduced embryo survival because of the extended embryonic duration. Strictly speaking it is possible for inhibition to indirectly lead to loss of material depending on assumptions about recycling, but perhaps we can neglect this for now

By contrast, **damage can** (directly or indirectly) **impact any of the model parameters**, but the most obvious expression is via **yield coefficients**.

The papers cited in Teresa’s notes point to **correlations** between Hif or lactate and changes in growth and/or development. Absent details on mechanisms I see little value in creating a damage module. The decision regarding inhibition is less clear and given that the paper is targeted at a DEB special issue, we might consider deriving a correction factor from the SU formalism. However, I’m unconvinced that this would be of value. I’m therefore comfortable continuing with the ad hoc correction factor from the dissertation.

More notes on Muller paper

* “Inhibitors act reversibly” this is true of IGFBP-1, and they even can compensate for growth after.