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# Is lifespan linked with developmental viability in *Drosophila melanogaster*?

**Eric Le Bourg**

E. Le Bourg (O) Centre de Recherches sur la Cognition Animale (CRCA), Centre de Biologie  
Intégrative (CBI Toulouse), Université de Toulouse, CNRS, UPS, Toulouse, France

e-mail address: [eric.le-bourg@univ-tlse3.fr](mailto:eric.le-bourg@univ-tlse3.fr)

Orcid iD: <https://orcid.org/0000-0001-5578-025X>

## **Abstract**

Long-lived lines of flies have been selected by reproduction at older ages and correlated responses observed, and particularly whether development of flies was modified. Using these selected lines or flies subjected to larval crowding or food restriction during development, two studies have computed, among lines, a correlation between viability of eggs and larvae and mean lifespan of adults: mean lifespan was longer when the viability was lower, showing a selection of fittest flies. The present study correlates viability and mean lifespan observed during three decades in a single wild-type strain. Contrary to the previous studies, a slight but not significant positive correlation is observed, showing that lifespan can hardly increase when viability increases. Therefore, it is not clear whether development and lifespan are linked, as hypothesised by some authors.

## **Key-words**

*Drosophila melanogaster* – lifespan – viability

## Introduction

Three centuries ago, Buffon (1749) wrote that, among species, duration of development is linked with lifespan. This idea has been confirmed by showing that species are spread on a continuum (Stearns, 1983) with, on one side, short-lived species with a small body size, a short gestation, maturing quickly, and giving birth at short intervals to many offspring (e.g. mice and rats), and, on the other side, species with the opposite life-history strategy (e.g. elephants or primates).

Regarding, within a species, the relationship between development and ageing, Lints (1988) reviewed the developmental theory of ageing stating that “some genes affect both traits pleiotropically, or that genes affecting both characters are closely linked”. Studies of Lints and Lints (1971) making to vary environmental conditions during development of *Drosophila melanogaster* flies seemed to confirm this statement, showing a negative relationship between growth rate of larvae and lifespan, but Lints (1988) concluded that Economos and Lints (1984, 1986) eventually showed that there was “an optimal growth rate on both sides of which lifespan decreased”.

In addition, many studies have selected long-lived lines of flies by reproduction at older ages and observed correlated responses and particularly whether development was modified. Reviewing studies measuring in long-lived and control lines developmental time and viability of flies, i.e. the percentage of eggs reaching adulthood, Wit et al. (2013) reported that any outcome could be observed. These results could allow to conclude that there is no clear link between development and mean lifespan of flies, but the only study (Buck et al., 2000) that computed a correlation between the viability and mean lifespan of selected lines seemed to point in another direction (Fig. 1). Buck et al. (2000) reported that mean lifespan decreased when viability increased in the 65-90% range, but did not indicate whether they used the longevity of males, females, or of both sexes combined. In flies subjected to larval crowding or food restriction during development, Zwaan et al. (1991) also reported a lower mean lifespan, in each sex, when viability increased in the 60-90% range. A high viability means that most of larvae, even the poorly fit ones, reach the adult stage. These flies could have a low lifespan and this could explain the negative relationship between viability and mean lifespan of the lines. As emphasised by Zwaan et al. (1991), one can hypothesise that, “if viability is decreased, only the fittest individuals survive to adults (viability selection) and this increase in mean fitness becomes evident in increased adult longevity”.

Obviously, these studies do not show that, at the individual level, there is a link between viability and lifespan because viability is measured in groups and not at the individual level. In human beings, the developmental origins of adult health and disease (DOHaD) theory explains that early life events, including in utero, can have major consequences in the adult and even at old age

60 (reviews in Vaiserman 2019).

61 The purpose of this paper is to confirm or not the results of Buck et al. (2000) and Zwaan et  
62 al. (1991) by correlating viability and mean lifespan. The same wild-type strain was used during  
63 three decades and viability was observed for the very rearing groups used to observe lifespan in  
64 various experiments, all these groups living in very similar conditions, **by controlling the age of**  
65 **parents and larval crowding. Eggs were transferred into vials, making possible to know the**  
66 **viability, developmental duration of flies, and the sex-ratio. In addition, larvae developed without**  
67 **larval crowding on a fresh medium, not used by other flies, and thus with no wastes of previous**  
68 **larvae or flies. For instance, urea, a toxic waste of larvae, which decreases viability and increases**  
69 **development duration (Botella et al. 1985), increases in crowded cultures (Henry et al. 2018). It has**  
70 **been shown that males and females developing in larval crowding conditions that emerged 3 days**  
71 **after the first ones had a lower weight and lifespan, and females had a lower fecundity measured**  
72 **once at young age (Lushchak et al., 2019): in all experiments reported below flies emerged 9-10**  
73 **days after egg-laying.**

74

## 75 **Material and methods**

76 The viability of the wild-type strain Meyzieu, caught at the end of the 1970s near the city of  
77 Lyon (France) was observed from 1988 to 2016 at 25°C in nearly 800 weeks (see the whole results  
78 in Le Bourg, 2021a). Groups with a very low viability (see Fig. 1 in Le Bourg, 2021a) were  
79 however not used to observe lifespan. Flies used in the present article were the control groups of  
80 several articles observing the effect of various factors on lifespan (Le Bourg, 2007, 2010, 2011,  
81 2012, 2021b; Le Bourg and Lints, 1989; Le Bourg and Médioni, 1991; Le Bourg et al., 2000, 2002,  
82 2015; Le Rohellec and Le Bourg, 2009), and were subjected to the very same rearing conditions  
83 (see below). The mean viability in the present study was 74.42% (26 groups, range: 41.37-87.09%).  
84 The mean lifespan of males was  $46.09 \pm 1.02$  days (26 groups, range of means: 35.24-53.76 days),  
85 and that of females  $52.37 \pm 1.27$  days (only 25 groups, females being not used in one experiment,  
86 range of means: 38.39-65.22 days). The number of harvested eggs in each group was in the 700–  
87 2975 range. The number of flies in the longevity experiments was in the 40-130 range, depending  
88 on experiments.

89 In order to obtain the parents of the experimental flies, flies were allowed to lay eggs for one  
90 night in a bottle containing the medium (agar, sugar, corn meal and killed yeast) containing a mould  
91 inhibitor (para-hydroxymethyl-benzoic acid) and enriched with live yeast at the surface of the  
92 medium. This medium was used in all experiments. Flies emerging 9–10 days after egg-laying were

transferred to fresh bottles: they are the parents of the experimental flies. Experimental flies were obtained as follows: eggs laid by ca. 5 day-old parents during one night on a Petri dish containing the medium coloured with charcoal were transferred by batches of 25 into 80 ml glass vials. At emergence, flies were transferred in groups of 15 virgin flies of the same sex into 20 ml polystyrene vials. Flies lived at 25°C (LD: 12-12) at the Earth gravity level (1 g) and were transferred twice a week to new vials. To sum up, all groups of flies of the strain used in this article were subjected to the very same conditions. In such conditions, one can expect that viability and lifespan can vary among groups of flies because of random variations, showing a relationship between these traits if it indeed exists. However, a caveat is that, obviously, changes did occur between 1988 and 2016. The stocks of agar, sugar, corn meal, killed yeast were renewed when they were exhausted, and new live yeast was bought very often, as it cannot be used for a long time, even if kept at 4°C. In addition, even if the temperature was always the same, different incubators could be used. Therefore, “very same conditions” should not be understood as meaning that all things were equal for three decades, but simply that care was taken to use similar rearing conditions: temperature, larval density, age of parents of experimental flies, transfers to new vials.

## Results and discussion

Figure 2 shows the relationship between viability and lifespan. In each sex, the correlation is positive but not significant ( $r = 0.371$ ,  $n = 26$  in males, and  $r = 0.282$ ,  $n = 25$  in females). Pooling the two sexes, as Zwaan et al. (1991) did, made it become just significant ( $r = 0.283$ ,  $p = 0.0440$ ,  $n = 51$ ). These results thus show hardly a positive correlation between viability and mean lifespan, but in no case that longevity increased when viability decreased, contrary to the results of Buck et al. (2000) and Zwaan et al. (1991). However, a significant correlation was observed in this last study only if both sexes were pooled, the effect being marginally significant in each sex (Fig. 1). The present results show that viability does not help to predict lifespan of flies able to reach the adult stage. Observing individual durations of development and lifespans could allow to know whether development is linked to lifespan at the individual level, but a previous study of Mayer and Baker (1984) only showed a negligible relationship between these traits in both sexes, if any.

One of the strengths of the present study is that viability and lifespan were observed on the same groups and that the rearing conditions were the same for all groups during nearly three decades. One could thus expect that variation of viability and lifespan is linked to random environmental variation and possibly to genetic drift. For instance, larval crowding is not controlled in the stocks of flies kept in bottles for years, if not decades, and this could have an effect on

lifespan. Lints et al. (1989) showed lifespan variations during a 4-year period in a single strain and were unable to explain them. Could the discrepancy between the present results and those of Buck et al. (2000) and Zwaan et al. (1991) be explained by the fact that these authors manipulated developmental conditions, by modifying larval density or food quantity (Zwaan et al., 1991), or age at reproduction (Buck et al., 2000)? Indeed, the procedure of the present article is similar to that of Mayer and Baker (1984) who, “instead of perturbing the systems of development and aging, ... attempted to observe them in a "free running" state by minimizing stresses known to influence the duration of development or the length of imaginal life span”.

For the time being, it seems possible to conclude that, when flies develop in controlled conditions, there is no clear relationship between viability and mean lifespan, but these results do not allow concluding that there is not any link between development and ageing, particularly in human beings.

In humans, one of the first studies showing the importance of early-life events was that of Barker and Osmond (1986) who reported that the 1968-1978 ischaemic heart disease prevalence in various sites of UK, differing by their wealth, was strongly linked to infant mortality in 1921-1925 in the same sites. Because both infant mortality in 1921-1925 and ischaemic heart disease prevalence in the 1970s were higher in lower socio-economic groups, the authors suggested that “the geographical distribution of ischaemic heart disease in England and Wales reflects variations in nutrition in early life”. In a subsequent study, Osmond et al. (1993) showed that low birth weight is linked to death from cardiovascular disease in both sexes. It is thus not surprising that women suffering from the 1944 Dutch winter famine during their mid-to late gestation gave birth to low-weight babies, and, in addition, that famine during early gestation, even if birth weight was normal, was also associated with cardio-vascular disease at middle age (review in Preston et al., 2018) and death rate in women, but not in men (van Abeelen et al., 2012). On the whole, early-life events, and particularly foetal nutrition, can have long-lasting adverse consequences in humans (review in Vaiserman et al., 2018) and results in animal models are not at variance (Tarry-Adkins and Ozanne 2017).

153

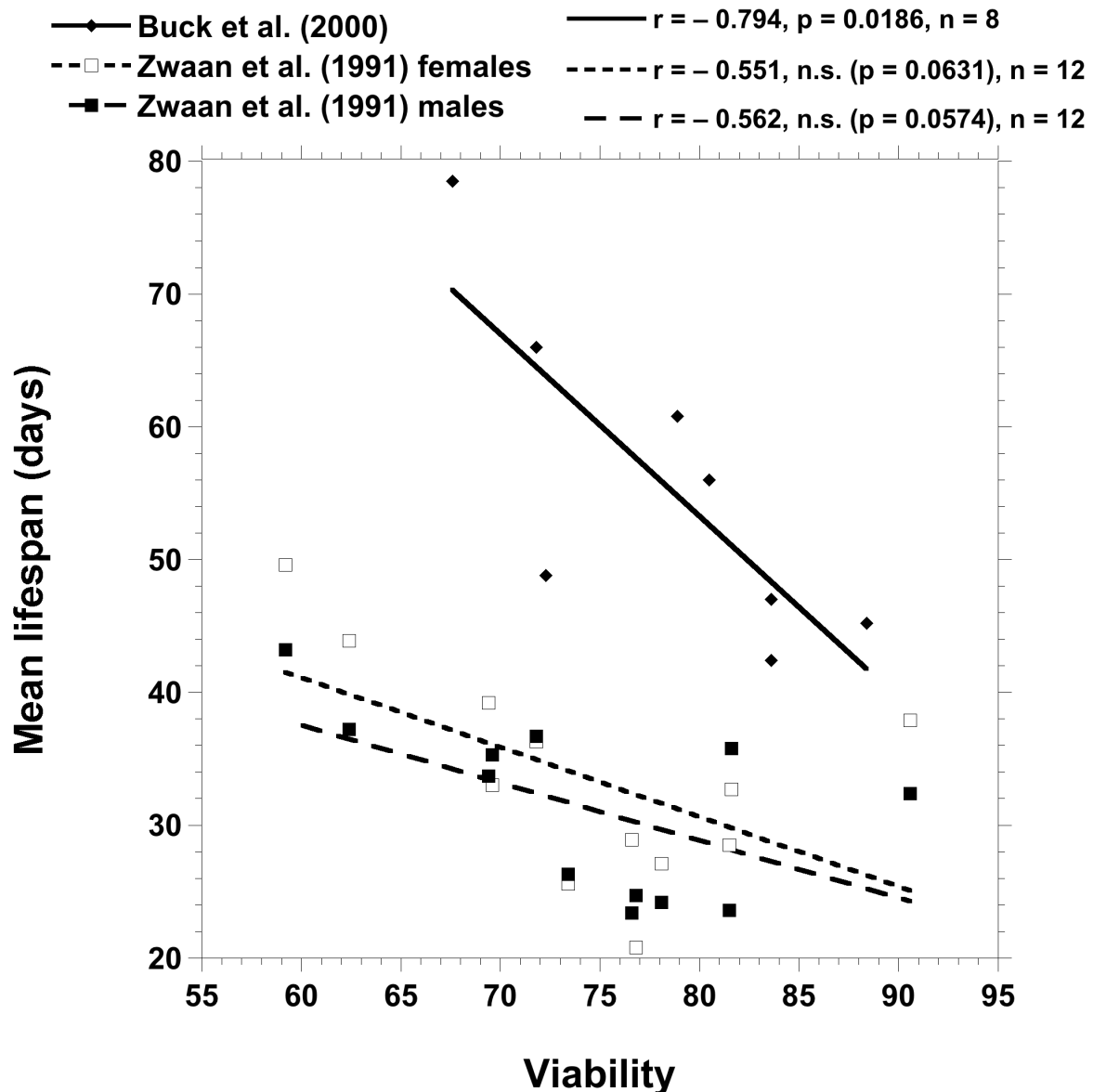
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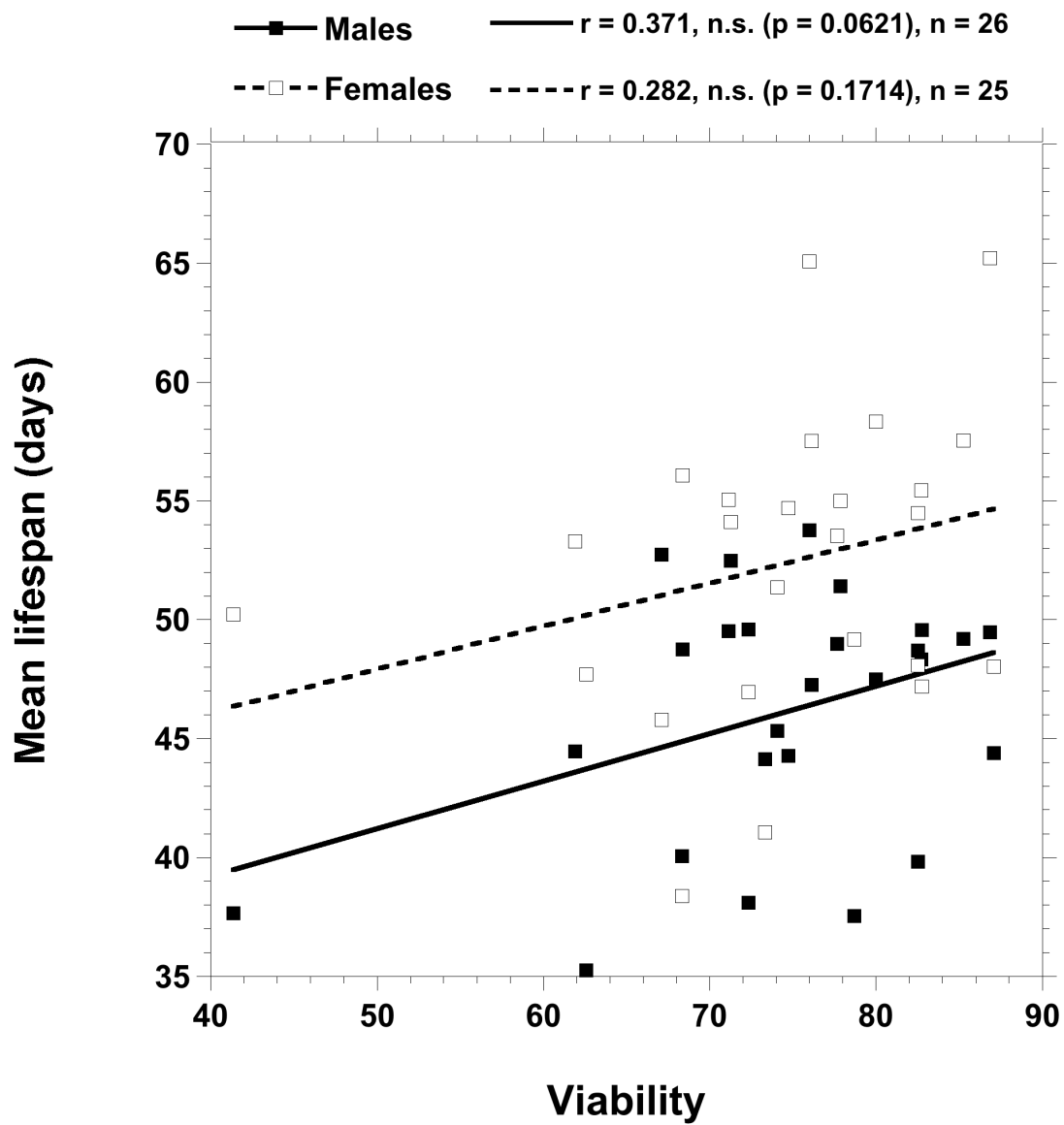
#### 156 **Disclosure statement**

157 No conflict of interest.

158 Figure 1. Relationship between viability and mean lifespan in Buck et al. (2000) and Zwaan et  
 159 al. (1991). Lifespan is observed, respectively at 25 and 29°C, but the development is done at 25°C  
 160 in both studies. For the Buck et al.'s (2000) study, lifespan data were determined from Figure 5 and  
 161 viability ones were extracted from Table 2. For the Zwaan et al.'s (1991) study, data were extracted  
 162 from Tables 3, 4, 5, 7. The correlation is not significant in Zwaan et al. (1991) if sexes are analysed  
 163 separately, but the authors pooled sexes, which made the correlation being significant (in the figure:  
 164  $r = -0.546$ ,  $p = 0.0057$ ,  $n = 24$ ; in Zwaan et al. (1991):  $r = -0.59$ ,  $p < 0.01$ ). The correlation  
 165 reported by Buck et al. (2000) is  $r = -0.791$  ( $r = -0.794$  in the figure).



166 Figure 2. Relationship between viability and mean lifespan in the Meyzieu wild-type strain in  
167 flies observed during three decades.





## References

- 168 van Abeelen, A.F., Veenendaal, M.V., Painter, R.C., De Rooij, S.R., Dijkgraaf, M.G., Bossuyt,  
169 P.M., Elias, S.G., Grobbee, D.E., Uiterwaal, C.S., Roseboom, T.J., 2012. Survival effects of  
170 prenatal famine exposure. *Am. J. Clin. Nutr.* 95, 179–183.  
171 <https://doi.org/10.3945/ajcn.111.022038>  
172 Barker, D.J.P., Osmond, C., 1986. Infant mortality, childhood nutrition, and ischaemic heart disease  
173 in England and Wales. *Lancet* 327, 1077–1081. [https://doi.org/10.1016/S0140-](https://doi.org/10.1016/S0140-6736(86)91340-1)  
174 [6736\(86\)91340-1](https://doi.org/10.1016/S0140-6736(86)91340-1)  
175 Botella, L.M., Moya, A., Gonzalez, M.C., Ménsua, J.L., 1985. Larval stop, delayed development  
176 and survival in overcrowded cultures of *Drosophila melanogaster*: effect of urea and uric  
177 acid. *J. Insect Physiol.* 31, 179–185. [https://doi.org/10.1016/0022-1910\(85\)90118-0](https://doi.org/10.1016/0022-1910(85)90118-0)  
178 Buck, S., Vettraino, J., Force, A.G., Arking, R., 2000. Extended longevity in *Drosophila* is  
179 consistently associated with a decrease in developmental viability. *J. Geront. Biol. Sci.* 55A,  
180 B292–B301. <https://doi.org/10.1093/gerona/55.6.B292>  
181 Buffon, G.L., 1749. *Histoire naturelle de l'Homme* (Natural history of Man). Imprimerie royale,  
182 Paris (English translation: Natural history, general and particular, Strahan W and Cadell T,  
183 London, 1785). <https://gallica.bnf.fr/ark:/12148/bpt6k1067226x>  
184 Economos, A.C., Lints, F.A., 1984. Growth rate and life span in *Drosophila*. II. A biphasic  
185 relationship between growth rate and life span. *Mech. Ageing Dev.* 27, 143–151.  
186 [https://doi.org/10.1016/0047-6374\(84\)90039-3](https://doi.org/10.1016/0047-6374(84)90039-3)  
187 Economos, A.C., Lints, F.A., 1986. Developmental temperature and life span in *Drosophila*  
188 *melanogaster* I. Constant developmental temperature: evidence for physiological adaptation  
189 in a wide temperature range. *Gerontology* 32, 18–27. <https://doi.org/10.1159/000212761>  
190 Henry, Y., Renault, D., Colinet, H., 2018. Hormesis-like effect of mild larval crowding on  
191 thermotolerance in *Drosophila* flies. *J. Exp. Biol.* 221pii:jeb169342.  
192 <https://doi.org/10.1242/jeb.169342>  
193 Le Bourg, E., 2007. Hormetic effects of repeated exposures to cold at young age on longevity,  
194 aging and resistance to heat or cold shocks in *Drosophila melanogaster*. *Biogerontology* 8,  
195 431–444. <https://doi.org/10.1007/s10522-007-9086-6>  
196 Le Bourg, E., 2010. Combined effects of suppressing live yeast and of a cold pretreatment on  
197 longevity, aging and resistance to several stresses in *Drosophila melanogaster*.  
198 *Biogerontology* 11, 245–254. <https://doi.org/10.1007/s10522-009-9250-2>  
199 Le Bourg, E., 2011. A cold stress applied at various ages can increase resistance to heat and fungal  
200 infection in aged *Drosophila melanogaster* flies. *Biogerontology* 12, 185–193.  
201

- 202 <https://doi.org/10.1007/s10522-010-9309-0>
- 203 Le Bourg, E., 2012. Combined effects of two mild stresses (cold and hypergravity) on longevity,  
204 behavioral aging, and resistance to severe stresses in *Drosophila melanogaster*.  
205 Biogerontology 13, 313–328. <https://doi.org/10.1007/s10522-012-9377-4>
- 206 Le Bourg, E., 2021a. Neglecting larval rearing conditions in *Drosophila melanogaster* can  
207 negatively impact research on ageing. Biogerontology 22, 369–373.  
208 <https://doi.org/10.1007/s10522-021-09917-y>
- 209 Le Bourg, E., 2021b. A mild heat stress increases resistance to heat of *dFOXO Drosophila*  
210 *melanogaster* mutants but less in wild-type flies. Biogerontology 22, 237–251.  
211 <https://doi.org/10.1007/s10522-021-09914-1>
- 212 Le Bourg, E., Gauthier, T., Colinet, H., 2015. Feeding on frozen live yeast has some deleterious  
213 effects in *Drosophila melanogaster*. Exp. Geront. 69, 202–210.  
214 <http://dx.doi.org/10.1016/j.exger.2015.06.019>
- 215 Le Bourg, E., Lints, F.A., 1989. Hypergravity and ageing in *Drosophila melanogaster*. 2.  
216 Longevity. Gerontology 35, 244–252. <https://doi.org/10.1159/000213033>
- 217 Le Bourg, E., Médioni, J., 1991. Food restriction and longevity in *Drosophila melanogaster*. Age  
218 Nutr. 2, 90–94.
- 219 Le Bourg, E., Minois, N., Bullens, P., Baret P., 2000. A mild stress due to hypergravity exposure at  
220 youngage increases longevity in *Drosophila melanogaster* males. Biogerontology 1, 145–155.  
221 <https://doi.org/10.1023/A:1010043914016>
- 222 Le Bourg, E., Valenti, P., Payre, F., 2002. Lack of hypergravity-associated longevity extension in  
223 *Drosophila melanogaster* flies overexpressing *hsp70*. Biogerontology 3, 355–364.  
224 <https://doi.org/10.1023/A:1021367800170>
- 225 Le Rohellec, M., Le Bourg, E., 2009. Contrasted effects of suppressing live yeast from food on  
226 longevity, aging and resistance to several stresses in *Drosophila melanogaster*. Exp. Geront.  
227 44, 695–707. <https://doi.org/10.1016/j.exger.2009.08.001>
- 228 Lints, F.A., 1988. Genetics, in: Lints, F.A., Soliman, M.H. (Eds.) *Drosophila as a model organism*  
229 for ageing studies. Blackie, Glasgow, pp. 99–118. <https://doi.org/10.1007/978-1-4899-2683-8>
- 230 Lints, F.A., Lints, C.V., 1971. Influence of preimaginal environment on fecundity and ageing in  
231 *Drosophila melanogaster* hybrids — III. Developmental speed and life-span. Exp. Geront. 6,  
232 427–445. [https://doi.org/10.1016/0531-5565\(71\)90022-2](https://doi.org/10.1016/0531-5565(71)90022-2)
- 233 Lints, F.A., Lints, C.V., Bullens, P., Bourgois, M., Delincé, J., 1989. Unexplained variations in life  
234 span of the Oregon-R strain of *Drosophila melanogaster* over a four-year period. Exp.  
235 Geront. 24, 265–271. [https://doi.org/10.1016/0531-5565\(89\)90017-X](https://doi.org/10.1016/0531-5565(89)90017-X)

- 236 Lushchak, O.V., Karaman, H.S., Kozeretska, I.A., Koliada, A.K., Zabuga, O.G., Pisaruk, A.V.,  
237 Koshel, N.M., Mechova, L.V., Inomistova, M.V., Khranovska, N.M., Vaiserman, A.M., 2019.  
238 Larval crowding results in hormesis-like effects on longevity in *Drosophila*: timing of  
239 eclosion as a model. *Biogerontology* 20, 191–201. <https://doi.org/10.1007/s10522-018-9786-0>
- 240 Mayer, P.J., Baker, G.T., III, 1984. Developmental time and adult longevity in two strains of  
241 *Drosophila melanogaster* in a constant low-stress environment. *Mech. Ageing Dev.* 26, 283–  
242 298. [https://doi.org/10.1016/0047-6374\(84\)90101-5](https://doi.org/10.1016/0047-6374(84)90101-5)
- 243 Osmond, C., Barker, D.J.P., Winter, P.D., Fall, C.H.D., Simmonds, S.J., 1993. Early growth and  
244 death from cardiovascular disease in women. *Brit. Med. J.* 307, 1519–1524.  
245 <https://doi.org/10.1136/bmj.307.6918.1519>
- 246 Preston, J.D., Reynolds, L.J., Pearson, K.J., 2018. Developmental origins of health span and life  
247 span: a mini-review. *Gerontology* 64, 237–245. <https://doi.org/10.1159/000485506>
- 248 Stearns, S.C., 1983. The influence of size and phylogeny on patterns of covariation among life-  
249 history traits in the mammals. *Oikos* 41, 173–187. <https://doi.org/10.2307/3544261>
- 250 Tarry-Adkins, J.L., Ozanne, S.E., 2017. Nutrition in early life and age-associated diseases. *Ageing*  
251 *Res. Rev.* 39, 96–105. <https://doi.org/10.1016/j.arr.2016.08.003>
- 252 Vaiserman, A., (Ed.) 2019. Early life origins of ageing and longevity. Springer, Dordrecht, 310 pp.  
253 <https://doi.org/10.1007/978-3-030-24958-8>
- 254 Vaiserman, A., Koliada, A., Lushchak, O. 2018. Developmental programming of aging trajectory.  
255 *Ageing Res. Rev.* 47, 105–122. <https://doi.org/10.1016/j.arr.2018.07.007>
- 256 Wit, J., Sarup, P., Lupsa, N., Malte, H., Frydenberg, J., Loeschcke, V., 2013. Longevity for free?  
257 Increased reproduction with limited trade-offs in *Drosophila melanogaster* selected for  
258 increased life span. *Exp. Geront.* 48, 349–357. <https://doi.org/10.1016/j.exger.2013.01.008>
- 259 Zwaan, B.J., Bijlsma, R., Hoekstra, R.F., 1991. On the developmental theory of ageing. I.  
260 Starvation resistance and longevity in *Drosophila melanogaster* in relation to pre-adult  
261 breeding conditions. *Heredity* 66, 29–39. <https://doi.org/10.1038/hdy.1991.4>