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Letter to the Editor

Stress resistance, heterogeneity and mortality plateaus: response by the authors

Service has focussed on one model of environmental heterogeneity in discussing the results of our paper, which we call the variance-in- A model. In this model, individuals vary in frailty due to environmental effects. The mortality rate of individuals aged- x in such a population is given by,

$$\bar{\mu}(x) = \frac{A \exp(bx)}{1 + \sigma^2 \frac{A}{b} (\exp(bx) - 1)} \quad (1)$$

where σ^2 is the variance in frailty among individuals, and A and b are the age-independent and age-dependent parameters of the Gompertz equation, respectively. The height of the asymptotic age-specific mortality does not depend on A and will increase with decreasing variance and increasing b . However, another property of Eq. (1) is its inflection point, which equals,

$$\frac{\ln \left[\frac{b}{\sigma^2 A} - 1 \right]}{b}.$$

As A gets larger the inflection point (when it exists) gets smaller. The parameter we (Drapeau et al., 2000) call a “breakpoint” is the day at which a Gompertz equation plus a flat line fits the data better than the Gompertz alone. The actual values of the breakday occur before the data have settled down to a flat line. This happens because well before an asymptote is reached the rate of increase in mortality rates slows and the observed mortality rates start to depart from the Gompertz predictions. Consequently, we would expect that the parameter breakday would be highly correlated with the inflection point. If the more robust lines have lower values of A then they should have greater breakdays, which they do not.

Eq. (1) can be used to estimate the parameters of A , b , and σ^2 for the variance-in- A model. When this is done for large cohorts the resulting model predicts the timing of mortality fairly well except for a prediction of a small class of very old individuals that are not observed (Rose and Mueller, 2000). The difference between the observed number of very old individuals and the expected is large enough to reject the variance-in- A model.

If the variance-in- A model described by Service is to be taken seriously then there should be some empirical support for its underlying mechanisms. Eq. (1) can be used to derive estimates of σ^2 directly. For many *Drosophila* populations, we typically get estimates in the range of 1. If we assume the variance of frailty is 1 and has a gamma

distribution with a mean of 1 then a 95% confidence interval on frailty is (0.025,3.7). Since frailty is assumed to be due to differences in A (of the Gompertz equation) this confidence interval suggests that micro-environmental variation can cause some individuals to have values of A that are less than the population mean by a factor of 40. Experiments that have deliberately altered the environment by changing the food level or adding urea, dramatically alter longevity but the estimated values of A change only by a factor of 4 at most (Joshi et al., 1996; Nusbaum et al., 1996). Even though these estimates are for the mean of all individuals it is difficult to imagine that a single population in a homogeneous environment will have individuals whose A values vary by a factor of 160. This criticism applies to just one heterogeneity model, and many other such models are conceivable.

For example, if individuals vary in their b -values, rather than A , and the more robust lines have reduced values of b then the plateau heights and breakdays can differ between more and less robust lines. Although we do not have analytic results for this variance-in- b heterogeneity model, it is easy to generate from simulations mean mortality rates with different values of b and variance in b only. Our simulation results (not shown) suggest that, when b decreases, the initial height of the plateau decreases and the breakday increases. We use the term initial height, since it appears that with the variance-in- b model, the mortality rates can actually decrease at old ages. In Nusbaum et al. (1996) it appeared that the starvation selected lines had reduced b relative to their controls. Thus, a plausible expectation of a b -heterogeneity theory would be fly populations with different values of b and thus different plateau height and breakdays, which were not seen in the study of Drapeau et al. (2000).

In fact, an interesting test of the variance-in- b model would be to find populations that show real declines in mortality at old ages. This behavior does not follow from variance-in- A models or from evolutionary models.

A more general point that this exchange raises is the scientific value of heterogeneity theories as a group, because they are not based on a single well-defined model. Service's comments illustrate a general problem, which is that there will usually be some type of heterogeneity model that can explain any reasonable mortality rate pattern post hoc. Even cursory consideration of this problem suggests that it makes it very difficult to test the heterogeneity theory empirically. Heterogeneity theory appears to teeter on the edge of scientific testability, unless an experimenter is willing to test just one model variant at a time, and then face the type of criticism that Service offers.

By contrast, the evolutionary models of Mueller and Rose (1996) lead to some very general predictions that can be tested critically. For example, the evolutionary models imply a positive evolutionary correlation between plateau breakday and the last age of reproduction, two easily measured variables. Another interesting feature of this evolutionary theory is that it generates Gompertz adult mortality patterns, in the period before the mortality-rate plateau, from first principles. The heterogeneity theory has to assume such mortality patterns on an ad hoc basis. Indeed, all the components of heterogeneity theory are ad hoc or post hoc. This deficiency, together with its modest testability suggest that heterogeneity theory does not have the hallmarks of useful scientific theory.

References

- Drapeau, M.D., Gass, E.K., Simison, M.D., Mueller, L.D., Rose, M.R., 2000. Testing the heterogeneity theory of late-life mortality plateaus by using cohorts of *Drosophila melanogaster*. *Exp. Gerontol.* 35, 71–84.
- Joshi, A., Shiotsugu, J., Mueller, L.D., 1996. Phenotypic enhancement of longevity by environmental urea in *Drosophila melanogaster*. *Exp. Gerontol.* 31, 533–544.
- Mueller, L.D., Rose, M.R., 1996. Evolutionary theory predicts late-life mortality plateaus. *Proc. Natl. Acad. Sci. USA* 93, 15 249–15 253.
- Nusbaum, T.J., Mueller, L.D., Rose, M.R., 1996. Evolutionary patterns among measures of aging. *Exp. Gerontol.* 31, 507–516.
- Rose, M.R., Mueller, L.D., 2000. Ageing and immortality. *Philos. Trans. R. Soc.* (in press).

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