chemostats with shorter generation time. Second, non-significant differences are taken to be zero in averaging in Table 2. Using all information (ignoring significance because zero differences in fitness are not really expected and 10 of 11 non-significant differences are ostensibly positive, as expected) gives mean fitness increments of 1.78 per 100 h for shorter-period chemostats and 1.18 for longer-period ones, using the last 300 h, and 2.33 and 0.55, respectively, using the last 200 h. Again, faster evolution with more rapid generations is suggested.

Third, in competition between the same strains grown in each of the two kinds of chemostats, interstrain selection coefficients in both conditions can be compared (their Fig. 2). The trend line summarizing the results seems, however, to be an ordinary regression rather than a co-regression[2], even though the two variables depend equally on each other and there is no asymmetrical prediction involved. A co-regression would be steeper and thus suggest that elimination of weaker strains is more rapid per unit time with short generations than with longer generations; even the regression given is significant in this direction at the 0.05 level. One might want to modify the statistics of their Table 2 by this result, but alternatively, it can itself be taken as another indication of faster change with faster turnover. I do not want to imply that the results suggest a proportionality between generation number and evolutionary rate, merely a positive relationship.

Conceptually, the experiment is interpreted (even in the title) as showing that a constant evolutionary rate per unit time can be caused by natural selection. However, even if the data gave clear support to the conclusions drawn (and I think they suggest the opposite), what would be shown is that generation time does not influence evolutionary rate even under strong selection pressure. The rates of change observed were far from constant even though (perhaps because only three time intervals are involved) not significantly more uneven than rates of molecular evolution. There is no evidence to suggest a long-term approximate constancy in mean rate, as there is for molecular evolution, and an independence of evolutionary rate and generation time has long been advocated[3] from palaeontological evidence. Such an independence, to the extent it exists, is easily explained if evolutionary rate is caused largely by changes in the total environment. A stochastically constant rate of evolution is a much more difficult phenomenon to explain. This gives it power in a genetically based view of evolution; only neutralism predicts it more or less adequately in that context. However, if we take ecology seriously with respect to evolutionary change, a natural (but still unproved) explanation

for the observed degree of constancy emerges[4]. It is quite consistent with the observed large short-term differences[5-7] in evolutionary rates, as neutralism may not be[7].

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DYKHUIZEN AND HARTL REPLY— Before discussing the particular points raised by Van Valen, we wish to emphasize that the molecular clock is sloppy[1], so exactitude should not be expected. It would be wonderful to carry out such experiments for 500 years (or, better yet, 500 Myr). In such a long time span, different results might very well be obtained. We have achieved only 500 h. Nevertheless, our data have remarkable internal consistency for experiments of this sort, and the formal congruence between the characteristics of our results and of the molecular clock are too striking to ignore. Also, we do not suggest that the environment is unimportant to the rate of evolution. The chemostat is a novel environment for *E. coli* K2, and it is likely that the large initial selection is due to this change of environment. It is also possible that the average rate of selection would decrease over time in the constant environment of the chemostat. Chemostats could be run for 2,500 h to see if this supposition is true. If true, it implies that environmental change is required to keep the selective clock wound.

Van Valen has questioned why we chose to analyse the last 300 h rather than the last 200 h. Most of our argument is actually based on the full 500 h as evidenced by the statement "The overall [that is, 500 h] average fitness increment per 100 h is 2.99 in the 2.5 h chemostat and 3.00 h in the 5.0 h chemostat"[2]. (Incidentally, if one treats all fitness differences as if they were significant, as Van Valen suggests, the corresponding averages are 3.28 and 3.05.) We presented the averages for the period 200–500 h only to show that we were not being misled by the large fitness increments that occur in the first 200 h. Van Valen points out that if only the last 200 h are taken for analysis, then it looks as if the 2.5 h strain is evolving faster. But this ignores more than half of the experimental measurements, and it contradicts the conclusion from the entire data set. By using a selected subset of any data, one can contradict any conclusion whatsoever.

There is, however, a better way to settle the issue, which is by direct competition between strains that have evolved for long periods at either a 2.5-h or a 5.0-h generation time. For strains that had evolved for the full 500 h, the largest fitness difference is observed when the experimental test is carried out in a 2.5-h chemostat; the 2.5-h strain is favoured, to be sure, but the fitness difference is a mere 5%. This amount of genetic divergence over 500 h is very small indeed. Moreover, when tests are carried out in a 5.0-h chemostat, selection actually favours the 5.0-h strain. These observations are difficult to reconcile with a presumed more rapid rate of evolution at a 2.5-h generation time[3].

The data in our[2] Fig. 2 are not relevant to the issue of rate of increase in fitness; they pertain to whether measured selection coefficients depend on the conditions of measurements. If the slope of the line in Fig. 2 is truly greater than 1.0, as Van Valen suggests, then we have actually overestimated the rate of increase in fitness in 2.5-h chemostats by about 25%, so our original conclusion receives additional support. Moreover, Van Valen's suggestion of co-regression is well taken. The co-regression line[4] has a slope of 1.5, which, if taken literally, calls for a correction of about 35%, so our original conclusion is more forcefully justified by Van Valen's own technique.

In short, our results indicate that the rate of increase in fitness is related to the amount of time spent in the chemostat rather than the number of generations. The issue is clearly an important one, and we hope that this exchange with Van Valen will encourage more of such experiments to be undertaken.

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