

Notes

Experimental evidence on the frequency of neutral mutations

J. ANTONOVICS AND M. C. GRANT

RESOLUTION of the recent controversy regarding the role of neutral mutations in evolution^{1,2,5-8,12} has been partially hampered by a lack of information on the frequency of mutational events in terms of their phenotypic effect. Spontaneous mutation rates of quantitative characters appear surprisingly high⁹⁻¹¹, but these are difficult to translate into rates per gene or magnitude of individual mutational events since they are considered in a cumulative fashion. Data that bear on this problem, however, are provided by Gregory⁴. We present a brief reanalysis of these data in the light of neutral mutation theory⁵, and point to a method that could be used to quantify the frequency of neutral and nearly neutral mutations.

Gregory⁴ studied the magnitude of changes in an M₂ population (F₂ produced by selfing irradiated parental seed) of peanuts (*Arachis hypogaea* L.) following irradiation with 18,500 r of X-rays. Variation of plants from controls was recorded independently by three observers for each character on an arbitrary scale that, when combined additively, yielded an overall estimate of the phenotypically observed mutational magnitude with low scores for controls and high scores for increasing mutant severity. Gregory⁴ writes, "The daily observations of the plants and the synchronizing discussions among the observers . . . led to a unanimity of understanding and a power of subjective estimation of unparalleled consistency which was tested repeatedly. . . ." Four groups of M₂ plants were studied independently to give a total of 83,793 M₂ plants in the overall investigation.

The resultant plot of magnitude of mutational changes

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(x) against the frequency of plants with that particular magnitude of change showed a negative exponential distribution of the form

$$y = be^{-ax}$$

The unconstrained least-squares fit of these data yielded values for *b* of 0.52 and for *a* of 0.45. Gregory's⁴ results are replotted on a semilog scale in Figure 1 for the four M₂ groups up to magnitudes of change where *x* = 10. Frequencies of plants with effects greater than 10 were very low, variable, and of lesser reliability. Using these estimates for *a* and *b*, we can calculate the frequency of plants showing a magnitude of mutational effect equal to or less than some specified *x* by evaluating the integral

$$\int_0^x be^{-ax} dx = -\frac{b}{a}(1 - e^{-ax}).$$

(Evaluation of this integral over the interval $0 \leq x \leq \infty$ yields an area = 1.1, which is sufficiently close to 1 to consider it normalized.)

We can extend these results to calculate the frequency of neutral, harmful, and beneficial mutations if we make certain assumptions: a) that we can validly extrapolate the curve back to *x* = 0, i.e., that neutral (invisible) mutations do not occur at a rate several orders of magnitude greater than non-neutral ones. This seems a valid assumption in the absence of any evidence to the contrary, and because it is difficult to see either how the genetic code could provide a basis for predicting which changes (other than silent mutations to synonymous codons) would have a certain phenotypic effect, or, given such informational content, how this could be recognized by a mutagen such as X-rays. From a purely statistical viewpoint, it can be seen (Figure 1) that the distance over which the curve is extrapolated is short, and that there is excellent agreement between the four groups of M₂ plants. b) We must assume that each mutational effect is the result of a similar number of mutations. It is clear that magnitude of mutational change need not be directly proportional to number of mutations. It would be very desirable in this context to

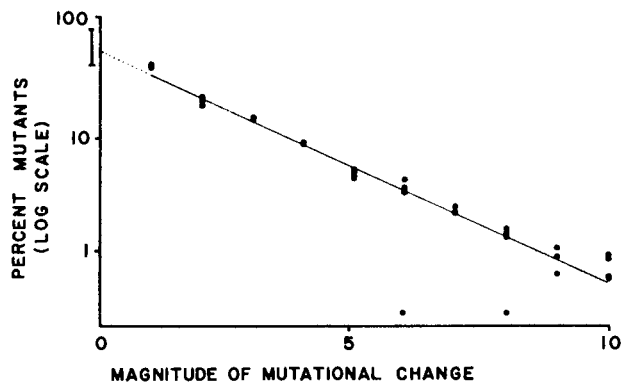


FIGURE 1—The relationship between mutant frequency and magnitude of mutational effect for four different mutant groups (from Gregory⁴). Extrapolated portion shown as dotted line, and standard error of intercept indicated at top left.

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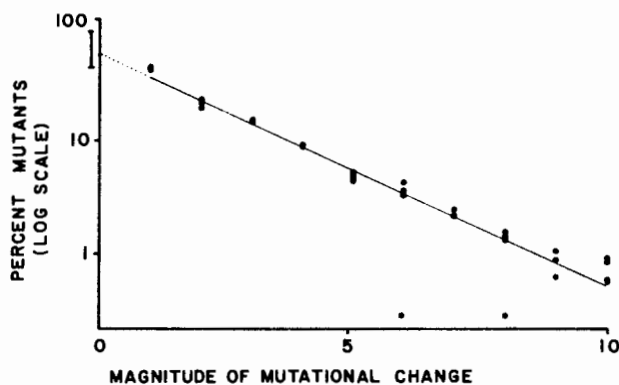


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