The Maintenance of the Accuracy of Protein Synthesis and Its Relevance to Ageing: A Correction

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An argument[1] purporting to show that the accuracy of protein synthesis would deteriorate in the absence of cellular selection, thus leading to an "error catastrophe," contains a hidden assumption that no longer seems justified. I supposed that the error frequency in protein synthesis could be approximated as the sum of a residual error frequency (applicable where the protein-synthetic apparatus contains no errors) and a term dependent linearly on the number of errors already present in the protein-synthetic apparatus. I deduced that the error frequency would increase exponentially.

To clarify the nature of the hidden assumption I now consider a simpler model in which successive generations of the protein-synthetic apparatus are discrete and distinguishable. Let c_n be the error frequency in the nth generation, R the residual error frequency, and α the proportionality constant between errors in the synthetic apparatus and errors in freshly synthesized protein. Then

$$c_{n+1} = R + \alpha c_n$$

and if $c_0 = 0$

$$c_n = R (1 + \alpha + \alpha^2 + \ldots + \alpha^{n-1}).$$

If $\alpha > 1$, c_n increases indefinitely and we get an error catastrophe; if $\alpha \gg 1$, the error frequency increases exponentially. Otherwise, a steady-state error frequency of $R/(1 - \alpha)$ will be reached.

Arguments concerning the value of α turn out to be more subtle than I appreciated and it is not clear that $\alpha > 1$ under all circumstances. Thus, while an error catastrophe can occur, and apparently does in certain *Neurospora* mutants,[2] it may not be inevitable even in the absence of cellular selection.

[1] Orgel, L. E., *Proc. Nat. Acad. Sci. USA*, **49**, 517 (1963).
[2] Lewis, C. M., and R. Holliday, *Nature*, in press.