

CORRESPONDENCE

Origin of the Genetic Code

SIR,—I should like to make two points about the account of my talk to the British Biophysical Society which you published recently¹. I do not in fact believe that the idea of a stereochemical relationship between all amino-acids and their anticodons, as suggested by Dunnill², is likely. There is, in my opinion, suggestive evidence against it, but at the moment it is not enough to disprove the idea.

My second point concerns the main substance of my talk, which was an attempt to show that a plausible theory could be constructed without necessarily assuming any stereochemical interaction of amino-acids with either codons or anti-codons. I imagined the code to go through three phases:

1. The Primitive Code, in which a small number of amino-acids were coded by a small number of triplets.

2. The Intermediate Code, in which these primitive amino-acids took over most of the triplets of the code in order to reduce nonsense triplets to a minimum³. The codons produced by this process for any one amino-acid were likely to have been related.

Woese⁴ has pointed out that this state of affairs could also have been produced by reading only a single base of a triplet, or by considerable inaccuracy in the reading of a few triplets.

3. The Final Code, as we have it today.

The crucial idea, already mentioned by Jukes⁵, concerns the transition from 2 to 3, which I certainly do not think was "unlikely to have taken place"⁶. Evolutionary theory suggests that a new amino-acid was incorporated into the developing code only if its introduction at that time gave a selective advantage to the primitive organism. This implies that its introduction did not disturb too much the proteins then being produced, and in addition made a significant improvement to at least one of them. This would have happened most easily if

- (a) the new amino-acid was "related" to the one previously coded by the triplet(s) in question⁶;
- (b) the organism coded rather few proteins;
- (c) these proteins were rather primitive in their construction.

Eventually as the number of proteins coded became larger, and their design more sophisticated, no possible new amino-acid could, on balance, be an advantage and the code would be frozen.

Such a theory could thus explain in a general way the non-random nature of the present code, since "related" amino-acids might well have acquired related codons. It is quite distinct from theories⁷ which postulate that the code evolved as it did in order to minimize the damaging effects of present-day mutations on individual proteins.

F. H. C. CRICK

Medical Research Council,
Laboratory of Molecular Biology,
Hills Road, Cambridge.

¹ *Nature*, 212, 1397 (1966).

² Dunnill, P., *Nature*, 210, 1267 (1966).

³ Sonneborn, T. M., in *Evolving Genes and Proteins* (edit. by Bryson, Vernon, and Vogel, Henry J.) (Academic Press, New York and London, 1965).

⁴ Woese, C. R., *Proc. U.S. Nat. Acad. Sci.*, 54, 1546 (1965).

⁵ Jukes, T. H., *Molecules and Evolution*, 70 (Columbia University Press, 1966).

⁶ Epstein, C. J., *Nature*, 210, 25 (1966).

⁷ Goldberg, A. L., and Wittes, E. E., *Science*, 153, 420 (1966).