

*Correspondence***Comment: Remarks on the article 'Genetic code preferentially conserves long-range interactions among the amino acids' by V. Sitaramam**

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The author of the above paper [1] has claimed that "it is the long-range/solvent interactions and not the short-range/stereochemical properties which are preferentially conserved in the genetic code".

The origin of this surprising result can be found in the first sentence of the Methods of this paper, namely that the probabilities of 1, 2, 3 nucleotide substitutions are 1/9, 1/27, 1/27, respectively, and not 1/9, 1/81, 1/729, as stated. From a certain codon  $3 \times 3 = 9$  new codons can be generated by

one nucleotide replacement. Two replacements result in  $3 \times 3^2 = 27$  new codons and three replacements result in  $3^3 = 27$  new codons. Note that  $1 + 9 + 27 + 27 = 64$ , i.e. the total number of possible codons. From this point all correlation calculations are wrong.

## REFERENCE

[1] Sitaramam, V. (1989) FEBS Lett. 247, 46-50.

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**Reply to the comment by I. Simon and M. Cserző**

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We resort to the common definition of a mutation as a nucleotide substitution in the codons. The central assumptions relate to equal probability for substitution by any other nucleotide at any of the three sites of a codon. Thus, the probability of getting AAG from AAA is 1/9; we all agree at this step for a specific mutant by a single substitution.

By definition, the above probability is a product of 1/3 probability of place and 1/3 probability of the remaining three nucleotides. Now, the second mutation (considered sequentially for simplicity) again carries 1/3 for position and 1/3 for nucleotide substitution, i.e. 1/81 for two sequential mutations towards a specific mutant.

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