

11.000 Synonymous! But not so much...

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Abstract

Mutations that alter the amino acid sequence of a protein are known to be under natural selection while synonymous mutations are assumed to be neutral regarding protein function. Indeed, synonymous mutations have been used as a proxy for neutral alterations in genomes and as a reference against which potential selected mutations are being compared. However, it is becoming quite clear that at least a fraction of those synonymous mutations has deleterious effects. This work aims to create a method that correlates the influence of synonymous mutations, based on the genome codon bias over prokaryotes fitness. To perform such analysis was used data of the genome sequence of 12 E.coli populations sequenced 11 times over 50,000 generation (Tenaillon et al. 2016). To evaluate the putative impact of synonymous changes, we used the Relative Adaptiveness of a Codon (w) developed by Sharp (1987), in which every individual codon frequency is compared to an optimal codon frequency. Based on it, we proposed a w variation index (Δw) defined as w of mutation minus w of reference. A negative Δw would indicate that the new codon, resulting from the mutation, is less frequent in the genome of that species and likely associated to a less abundant tRNA. To evaluate whether synonymous mutations are randomly distributed regarding the Δw score, a 20,000 rounds Monte Carlo simulation was performed, in which the same number of real mutations was randomly created. As result, the pattern of Monte Carlo and real synonymous mutations set differs significantly and this discrepancy suggests that purifying selection is acting on synonymous mutations likely through tRNA abundance. Thus, the Δw seems to be an adequate index to evaluate the codon bias influence over microbial fitness and the results suggest a selection mechanism operating over synonymous mutations.

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