Selection on translation rate impacts genic base composition

Erik Quandt\(^1\), Charles Traverse\(^1\), Howard Ochman\(^1\)

\(^1\)Integrative Biology, The University of Texas at Austin, Austin, United States

Abstract: The maintenance of a G+C content that is higher than the mutational input to a genome supports the view that selection serves to increase G+C contents in many bacteria. Recent experimental evidence from *Escherichia coli* has demonstrated that selection for increasing G+C content operates at the level of translation, but the precise mechanism by which this occurs is unknown. To determine the substrate of selection, we asked whether selection on G+C content acts across all sites within a gene or was confined to particular nucleotide positions or genic regions. We systematically altered the G+C contents of the GFP gene and assayed the effects of each variant on cellular fitness. The fitness differences were attributable to the base compositional variation in the terminal portion of the gene: increasing G+C content produced more stable mRNA secondary structures, which, in turn, slowed translation rate and allowed proper protein folding. We show that purifying selection against A and T mutations results from their tendency to increase the rate of translation and perturb the dynamics of protein folding.

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