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Increasing protein production rates can decrease the rate at which functional protein is produced AJEET SHARMA, EDWARD O'BRIEN, Department of Chemistry, Pennsylvania State University — The rate at which soluble, functional protein is produced by the ribosome has recently been found to vary in complex and unexplained ways as various translation-associated rates are altered through synonymous codon substitutions. We combine a well-established ribosome-traffic model with a master-equation model of co-translational domain folding to explore the scenarios that are possible for the protein production rate, $\boldsymbol{J}$, and the functional-nascent protein production rate, $\boldsymbol{F}$, as the rates associated with translation are altered. We find that while $\boldsymbol{J}$ monotonically increases as the rates of translation-initiation, -elongation and -termination increase, $\boldsymbol{F}$ can either increase or decrease. $\boldsymbol{F}$ exhibits non-monotonic behavior because increasing these rates can cause a protein to be synthesized more rapidly but provide less time for nascent-protein domains to co-translationally fold thereby producing less functional nascent protein immediately after synthesis. We further demonstrate that these non-monotonic changes in $\boldsymbol{F}$ affect the post-translational, steady-state levels of functional protein in a similar manner. Our results provide a possible explanation for recent experimental observations that the specific activity of enzymatic proteins can decrease with increased synthesis rates and can in principle be used to rationally-design transcripts to maximize the production of functional nascent protein.

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