Predictive design of mRNA translation initiation region to control prokaryotic translation efficiency

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Precise prediction of prokaryotic translation efficiency can provide valuable information for optimizing bacterial host for the production of biochemical compounds or recombinant proteins. However, dynamic changes in mRNA folding throughout translation make it difficult to assess translation efficiency. Here, we systematically determined the universal folding regions that affect the efficiency of translation arising via two different initiation mechanisms in *Escherichia coli*. By assessing the exquisite regions for mRNA folding, we could construct a predictive design method, UTR Designer, and demonstrate that proper codon optimization around the 5'-proximal coding sequence is necessary to achieve a broad range of expression levels. Finally, we applied our method to control the threshold value of input signals switching on a genetic circuit. This should increase our understanding of the processes underlying gene expression and provide an efficient design principle for optimizing various biological systems, thereby facilitating future efforts in metabolic engineering and synthetic biology.