RandomRibo: A Novel Tool for Transcript-Level Ribosome Velocity Determinant Identification With Single Codon Resolution

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Cells have evolved the process of translational regulation to rapidly fine-tune protein expression to suit intracellular needs. Ribosome velocity during translation elongation is a key contributor to typical protein expression, as abnormal regulation of it can give rise to disease states. Ribosomes travel along mRNA transcripts with varying speeds, with regions of high movement to increase efficiency as well as pause site regions to allow for processes such as co-translational folding. Having a comprehensive understanding of why ribosomal movement undergoes such positional fluctuation gives researchers critical, molecular-level insight into disease states. However, previous methods cannot offer precise information at the single transcript level due to the high amounts of noise present in Ribo-seq data and simple measures of determinants, rendering them unable to analyze a variety of disease states affecting the translation of specific genes. In this study, I present the software RandomRibo, the first computational tool to identify translation velocity determinants for individual transcripts by incorporating (1) Bayesian wavelet thresholding with double exponential priors to denoise ribosome profiling data, (2) nascent chain alpha helix propensity and electrostatic force algorithms to better model interactions with the ribosome exit tunnel, and (3) Random Forest Regression models to capture the non-linear relationships between translation velocity and its determinants. I demonstrate RandomRibo's capabilities by applying its algorithms to different cell lines and cellular states to corroborate previous observations and establish novel hypotheses regarding the mechanisms of SARS-CoV-2 Nonstructural protein 1 (Nsp1).

Awards Won:
Second Award of $2,000