RiboBayes: Assessing the Transcriptome-Wide Expression of Ribosome Pause Sites in Ribosome Profiling Data With Bayesian Wavelet Thresholding

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The speed of ribosome movement along an mRNA transcript is a critical determinant of protein synthesis. Ribosome pause sites, or regions along an mRNA transcript where translating ribosomes halt, regulate an integral set of cellular processes, ranging from protein localization to translational repression. To analyze ribosome pausing, many studies utilize ribosome profiling (Ribo-seq) to obtain global profiles of ribosome occupancy with single nucleotide precision, enabling the identification of ribosome pause sites and their changes across conditions. Due to the rising utility of Ribo-seq in the study of protein synthesis, rigorous methods to identify these key regulatory sites from Ribo-seq data are critically necessary. However, current techniques used to identify ribosome pause sites exhibit both low specificity and inefficient computational runtime due to high levels of variation in Ribo-seq data, posing a major barrier to understanding the diverse roles of ribosome pause sites in translational regulation. Here, I develop RiboBayes, a computational workflow that couples a wavelet transform-based pause site detection algorithm with novel statistical models to rigorously evaluate the expression, distribution, and regulation of pause sites in Ribo-seq data. RiboBayes' peak detection capacities offer significantly enhanced specificity, biological consistency, and computational efficiency compared to leading pause site detection techniques. To demonstrate the detection and classification capabilities offered by RiboBayes, I further apply RiboBayes to reveal dynamic patterns in ribosome pausing in cells overexpressing or lacking major translational regulators, providing a high-resolution view of ribosome pause sites and their regulation across the transcriptome.

Awards Won:
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