RNA Modification and Degradation Patterns in Yeast Under Nutrient Stress Using Autoencoders, Clustering, and Random Forest

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Résumé

Regulation of RNA translation and abundance is a rapid adaptative mechanism in response to environmental stress. In yeast, cells adjust mRNA's production (transcription), degradation, and translation to cope with changes such as heat shock, oxidative stress, and osmotic alterations. However, the role of RNA modifications in this regulatory network, particularly under nutrient deprivation, remains poorly understood.
In this study, we investigated how nutrient deprivation affects RNA translation and modification. Using Direct RNA Sequencing, we compared yeast cells under two growth conditions: non-starved (NS) and 10-minute starved (S10). Our goal was to uncover relationships between translation rates, modification patterns in mRNA, and mRNA degradation rates.

First, we conducted an analysis to study missing values distribution across transcript features. To ensure the completeness of our dataset, we employed iterative imputation using machine learning models.

We used an autoencoder to reduce the dimensionality of over 60 transcript-level features measured on individual transcripts (n= 6791) into a two-dimensional latent space, where clustering was performed. These features included mRNA sequence characteristics (e.g., length and GC content), RNA modifications, and degradation rates, summarized across mRNA regions (5' UTR, CDS, 3' UTR).

Clustering within the latent space was carried out using the DBSCAN algorithm, and clusters were linked to a measure of stochastic translation efficiency (STE) obtained from previous analyses.
Within each cluster, we applied random forest regression models to explore the relationships between STE values and RNA modifications, sequence properties, and degradation rates. This allowed us to identify key variables that influence translation efficiency. We trained the model on the NS condition and applied it to the S10 dataset, revealing distinct clusters of genes that exhibit varied responses to nutrient deprivation. These gene clusters indicate potential shifts in RNA modification and degradation patterns, shedding light on how yeast cells adjust RNA processing mechanisms during starvation-induced stress.

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