Docket #: S20-224

Algorithm for Maximizing mRNA Thermodynamic Stability

Stanford researchers have developed a stochastic algorithm *MC sampler* for designing mRNAs showing improved translation in vitro. It is known that degradation of RNA molecules at ambient conditions presents a major challenge for wide scale distribution of RNA-based vaccines. Recent studies have suggested that the translational efficiency of mRNA molecules is related to the degree of structure present in the molecule, but little is known about the optimal method to increase structure. The researchers developed a stochastic algorithm that samples nucleotides within synonymous codons to minimize the thermodynamic free energy of an mRNA molecule. A key innovation is that it selects nucleotides to mutate in proportion to their probability of being unpaired. This has been demonstrated to accelerate minimization by focusing sampling on regions lacking structure.

This technology is part of a portfolio of innovations aimed at fighting the COVID-19 pandemic.

Stage of Development
In vitro demonstration

Explore more RNA vaccine technologies and tools:

Stanford docket S20-183 - mRNA Vaccines: Methods of Synthesis and Stability Assessment
Stanford docket S20-258 - Additive Reduces Cost of Manufacturing mRNA

Applications

- mRNA design
- mRNA synthesis
- mRNA vaccine design

- COVID-19 mRNA vaccine design

Advantages

- Supports improved translation and stability of prospective mRNA vaccines

Publications

- Leppek et al. bioRxiv (2021) Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics

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