Chemistry-informed Deep Generative Models for Catalytic RNA Design

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Ribozymes are RNA enzymes capable of accelerating chemical reactions. While they are relatively rare in extant life, they are central to hypotheses on the origin of life, where RNA is proposed to have functioned as both genetic material and catalyst [1]. Despite their fundamental and applied significance, rational design of catalytic RNAs is hindered by an incomplete understanding of the relationship between RNA sequence, structure, and catalytic activity. Compared to proteins, detailed experimental data on RNA active sites and atomic-level catalytic mechanisms remain limited, reducing the effectiveness of data-driven design approaches.

This project addresses these challenges by integrating molecular dynamics simulations [2], data-driven modeling, and high-throughput experimental measurements [3]. The approach combines generative deep learning methods with chemistry-based physical constraints to ensure that designed RNA sequences adopt structurally and catalytically viable conformations.

The goal is to enable the rational design of catalytic RNAs with enhanced activity and expanded sequence and structural diversity, followed by experimental validation. This work aims to improve our understanding of RNA catalysis and to support the development of RNA-based catalysts for applications in synthetic biology, therapeutics, and biotechnology.

Bibliography :

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