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ScFFold: Conditional Flow Matching for RNA Tertiary Structure Prediction

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RNA tertiary structure plays a critical role in its biological function. However, the intrinsic structural flexibility and conformational diversity of RNAs make accurate prediction highly challenging. We present ScFFold, an end-to-end conditional generative model for RNA folding based on flow matching. Rather than relying on multiple sequence alignments, ScFFold conditions on externally supplied base-pairing patterns, obtained from experiments or secondary-structure predictors, to generate diverse three-dimensional conformations that satisfy those constraints. This enables interactive structure exploration and the integration of heterogeneous priors when evolutionary information is weak or unavailable. On CASP15 natural RNA targets, ScFFold attains strong accuracy without using MSAs. At inference time, techniques such as classifier-free guidance further improve the fidelity–diversity trade-off. Together, these results highlight conditional generative modeling as a practical bridge between current data limitations and robust RNA tertiary structure prediction.