

Bayesian Approximation of RNA Folding Times

Dominik Scheuer^{1,*}, Frederic Runge^{1,*}, Jörg K.H. Franke¹, Michael T. Wolfinger^{2,3}, Christoph Flamm², Frank Hutter^{1,4}
¹University of Freiburg, Germany; ²University of Vienna, Austria; ³RNA Forecast e.U., Vienna, Austria; ⁴ELLIS Institute Tübingen, Germany; *Equal contributions



Summary

RNA folding kinetics describe the **probabilistic dynamics** of the RNA folding process.

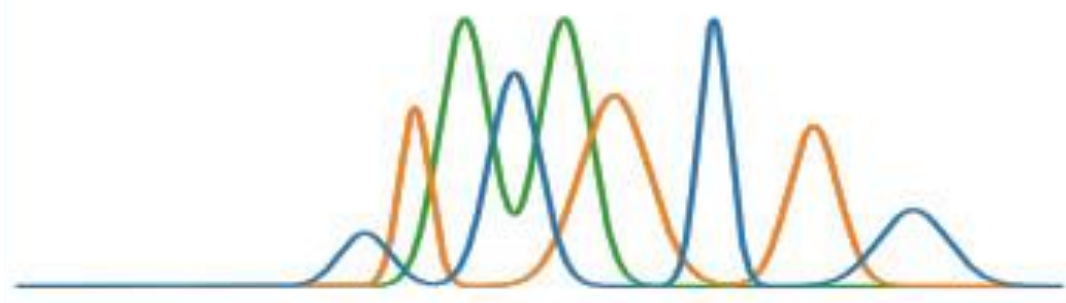
RNA folding times allow to analyse the **folding efficiency** with applications in **synthetic biology** and candidate selection for **drug discovery**.

Problem: Current **RNA kinetics simulators** are **costly** and **scale exponentially** with the RNA length.

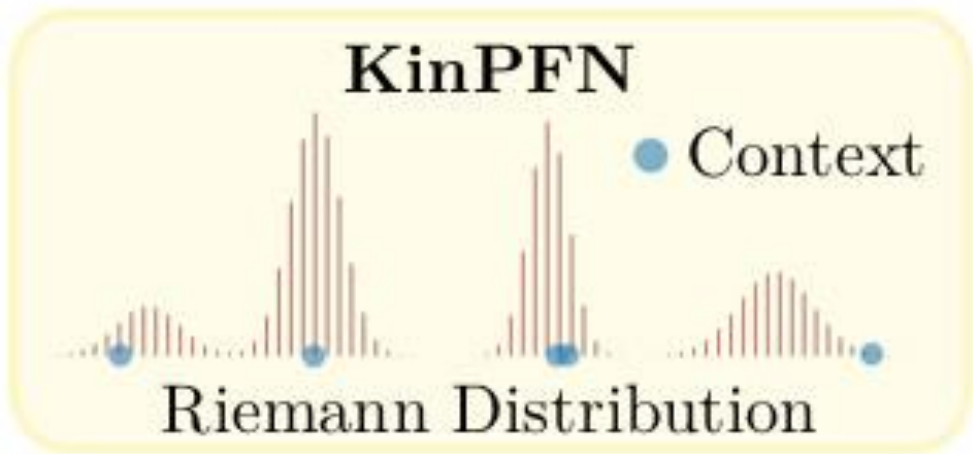
We present **KinPFN**, a novel approach for RNA folding kinetics based on **prior-data fitted networks (PFNs)**.

Trained on a **synthetic prior representing RNA folding times**, KinPFN achieves comparable results while **reducing simulator costs by $\geq 95\%$** .

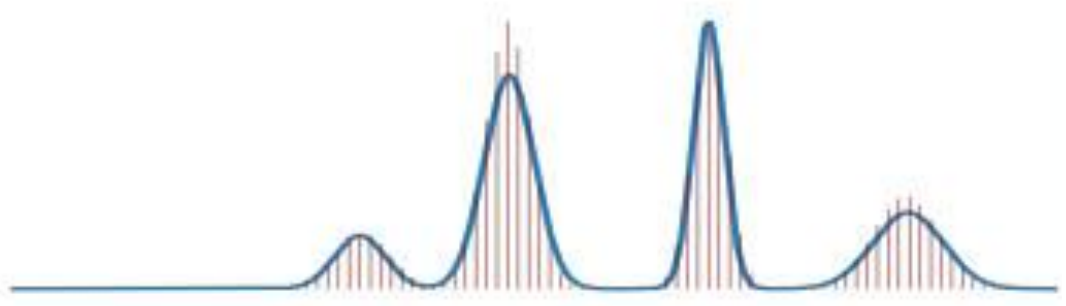
Training on a Synthetic Prior



Synthetic Datasets are drawn from multimodal Gaussians representing RNA folding times.



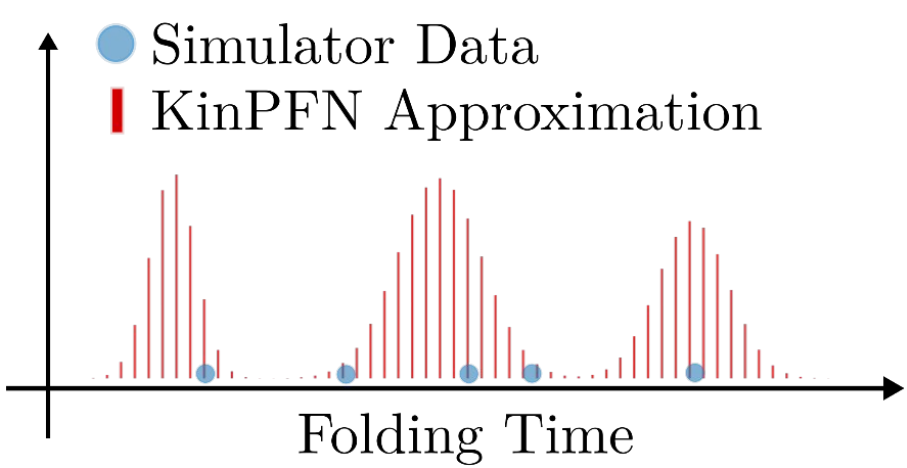
KinPFN approximates a given distribution from a few example “Times”.



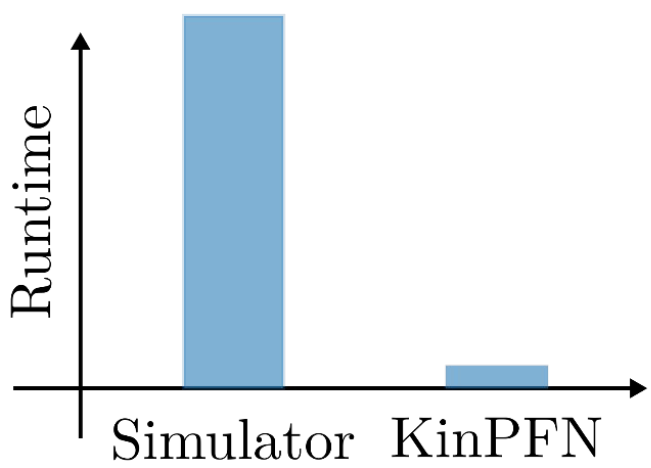
KinPFN is trained on ~5M distributions by minimizing the NLL.

Approximation via In-Context Learning

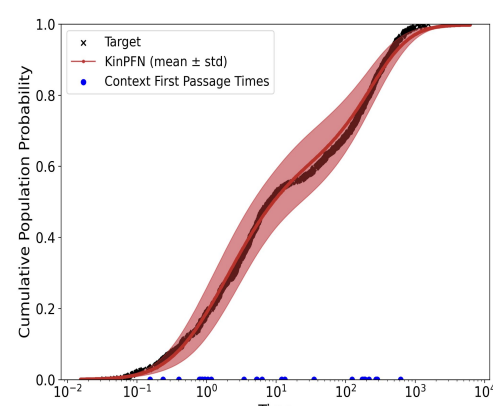
Use Kinetics Simulations data as Context to Approximate Folding Time Distributions



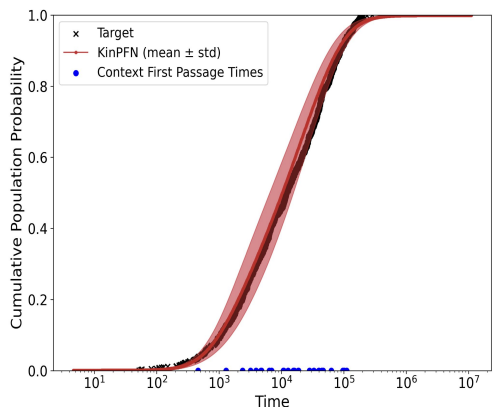
KinPFN Achieves Comparable Results While Reducing Simulator Costs by $\geq 95\%$



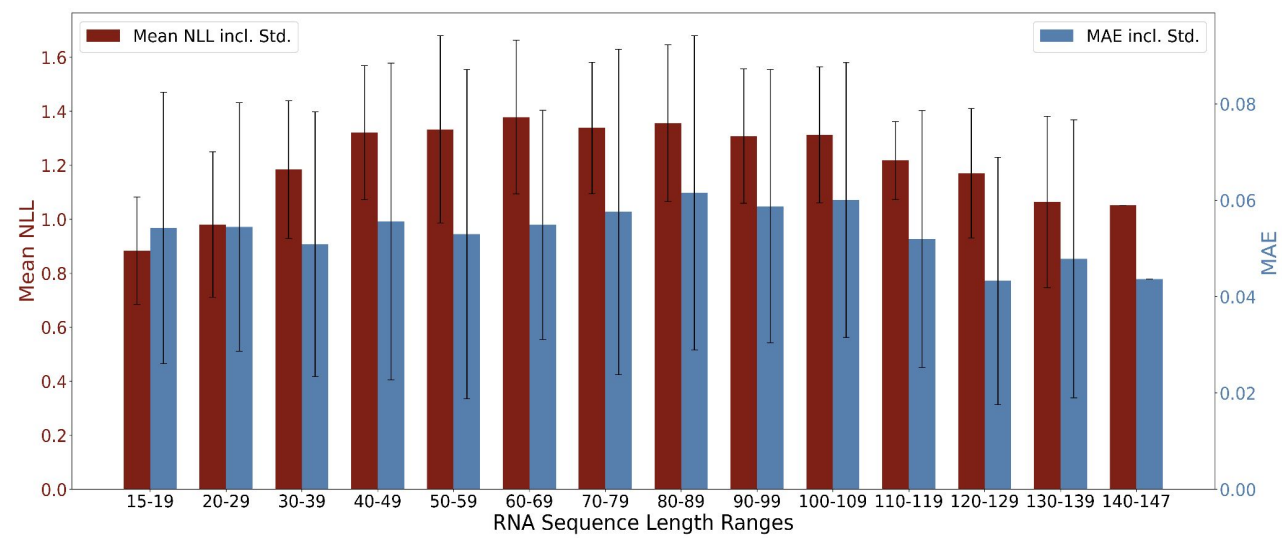
Feature and Simulator Independence



KinPFN approximation quality is independent of the choice of the simulator.



KinPFN approximation quality is independent of the start and stop structure.

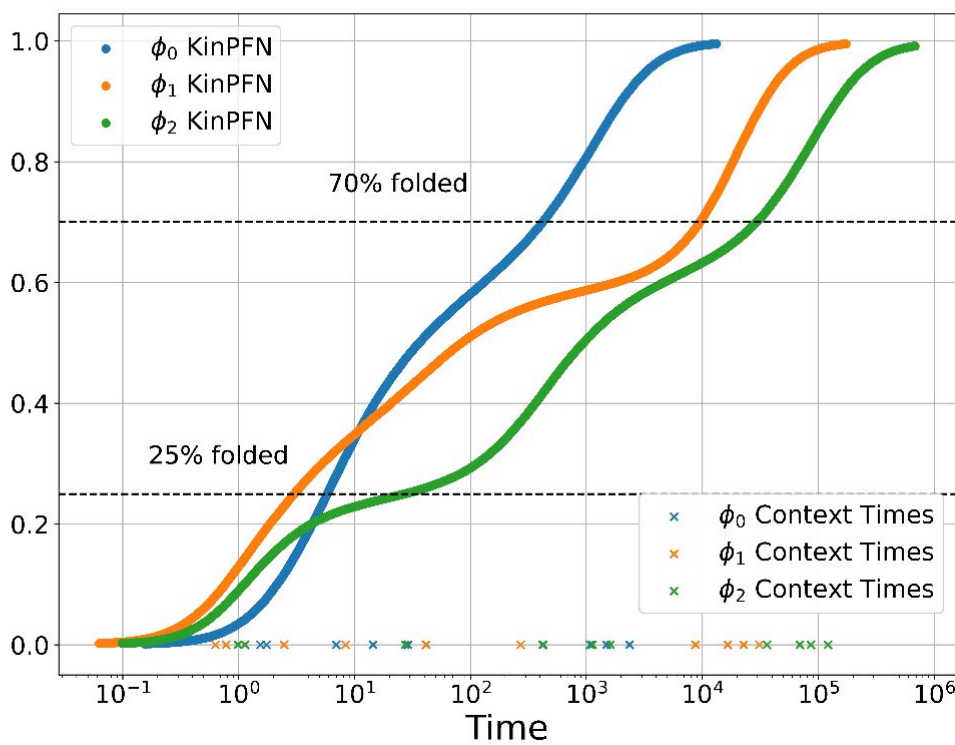
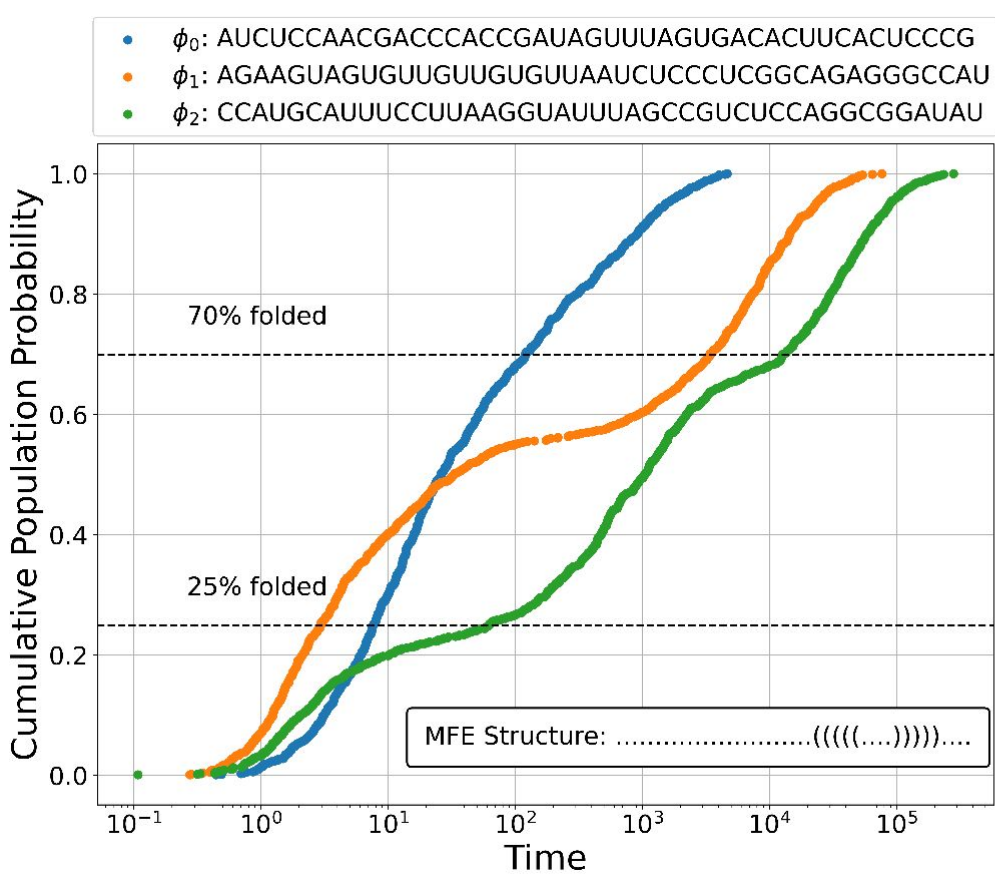


KinPFN prediction quality is independent of the RNA length.

Case Study: RNA Folding Efficiency

Setup: Compare the folding efficiency of three 43-nt RNAs (ϕ_0 , ϕ_1 , ϕ_2) with the same MFE structure using 10 example Times from kinetics simulations.

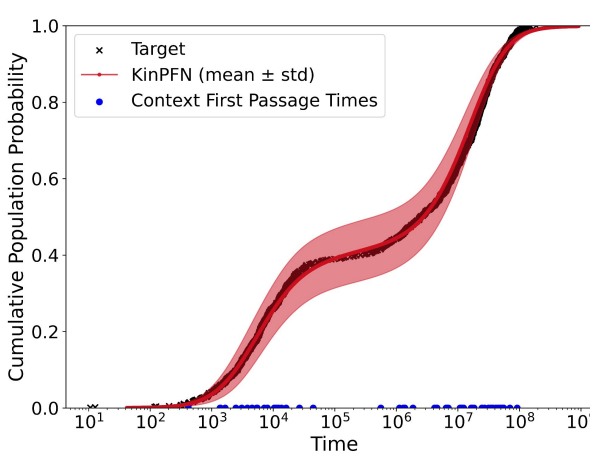
Results: 100× speed-up per RNA at comparable performance.



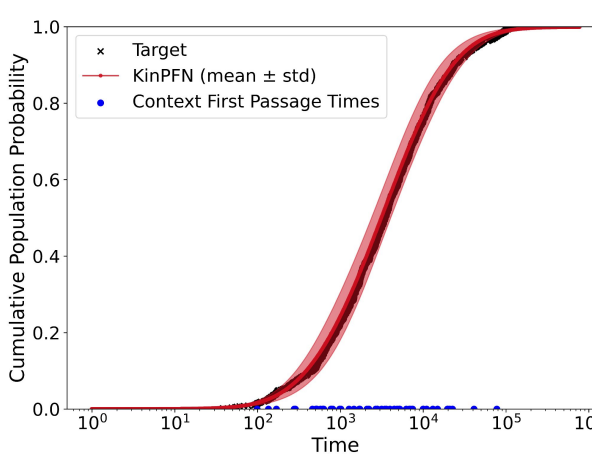
KinPFN requires only 1% of the compute per RNA!

Massive Speed-Ups for Natural RNAs

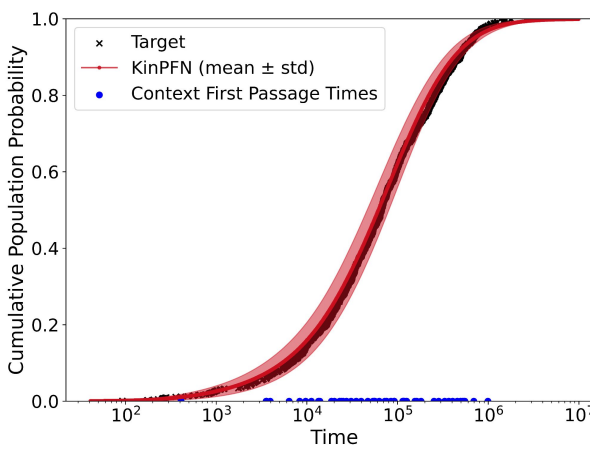
tRNA^{phe} (76nt)



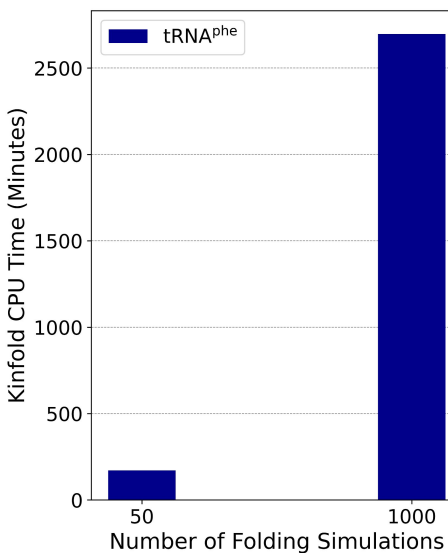
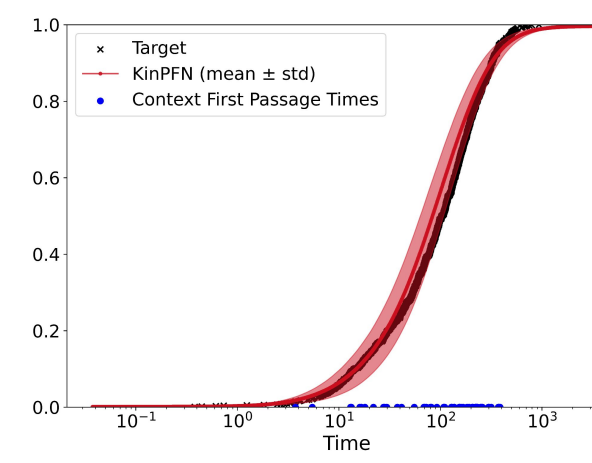
SAM Riboswitch (92nt)



5S rRNA (121nt)



hsa-miR-7107-3p (27nt)



95% runtime improvement
(~2 days → ~3 hours)
with minimal accuracy loss.

