Transforming mRNA therapeutics with quantum computing

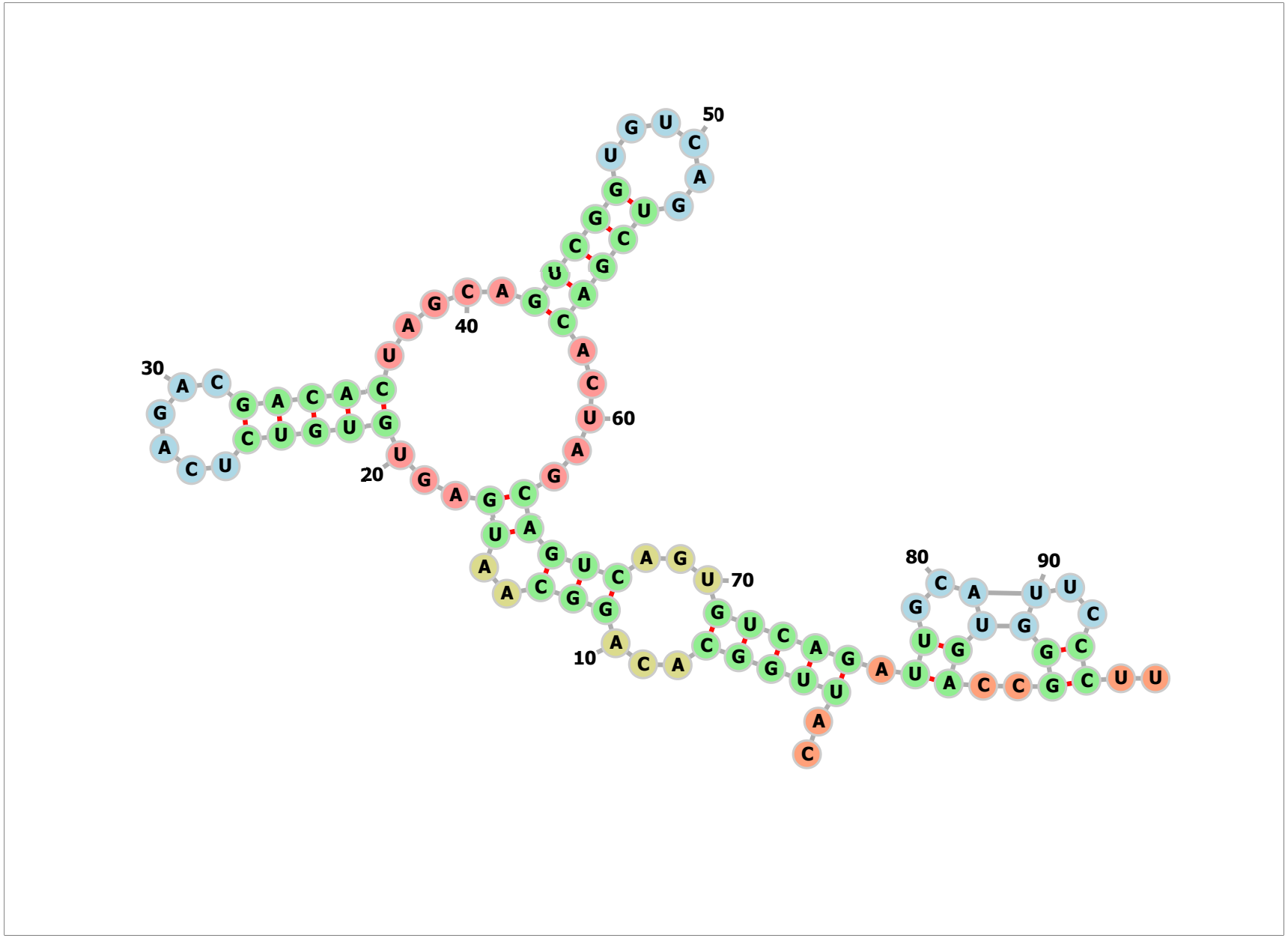
Alexey Galda



moderna

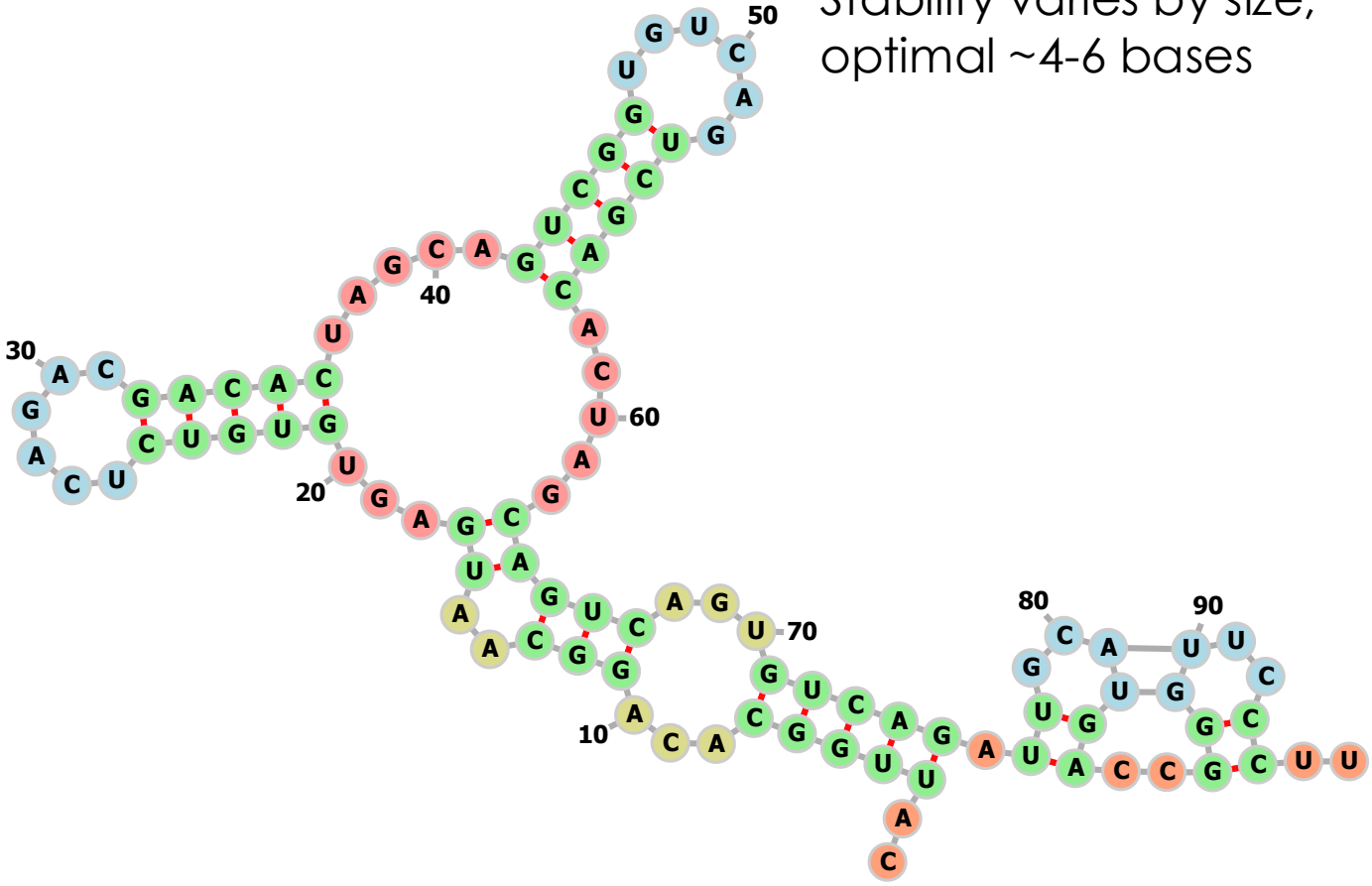
- WHAT IF WE COULD **REVOLUTIONIZE DRUG DESIGN** THROUGH **COMPUTING?**
- **Explore how Quantum Computing technology can unlock the potential of mRNA therapeutics, Transforming the Future of Medicine and Biotechnology.**

- **Quantum Leap into a New Era of RNA Therapeutics Harnessing Quantum Computing to Transform the Future of Medicine and Biotechnology.**



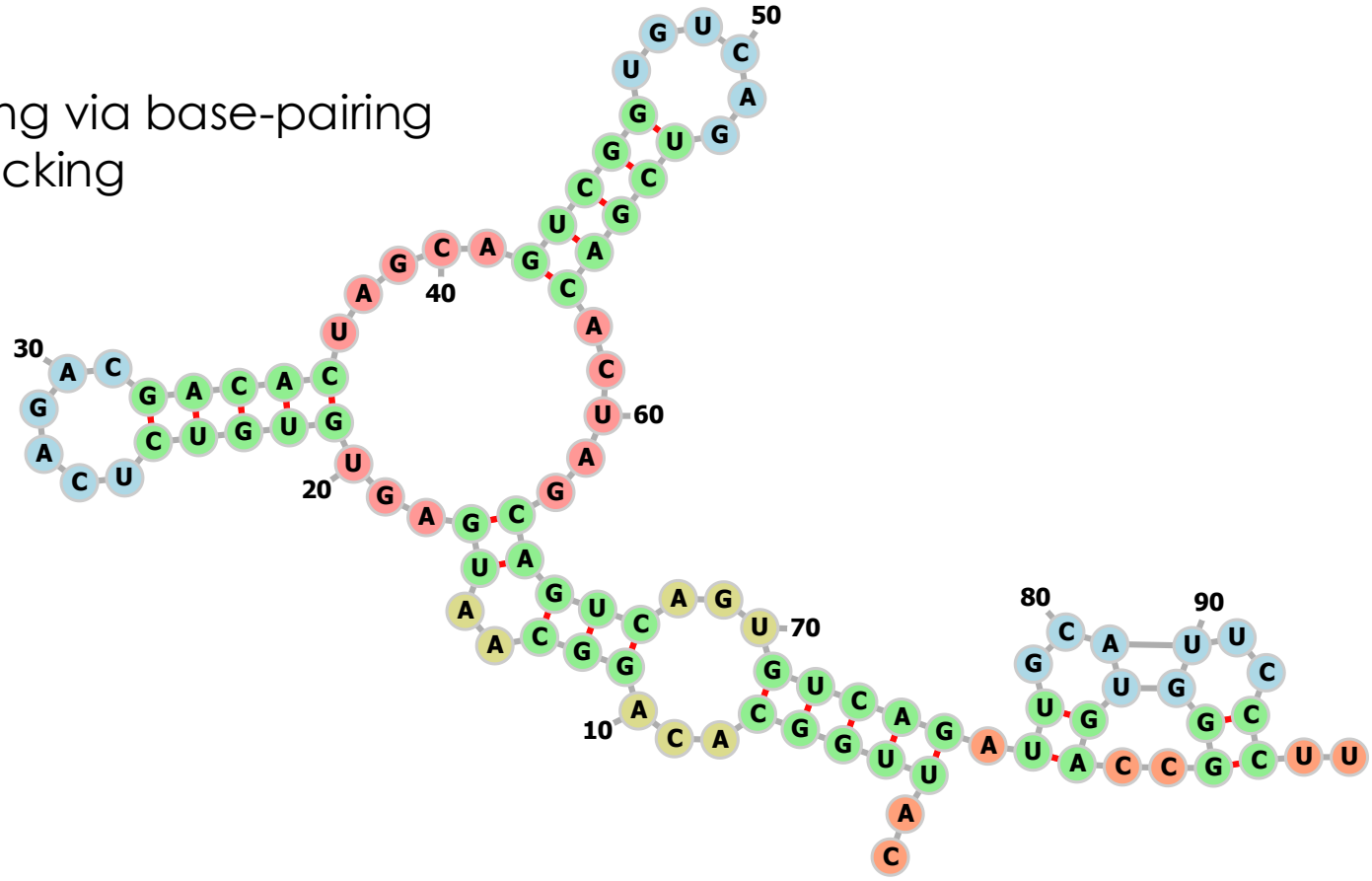
Hairpin

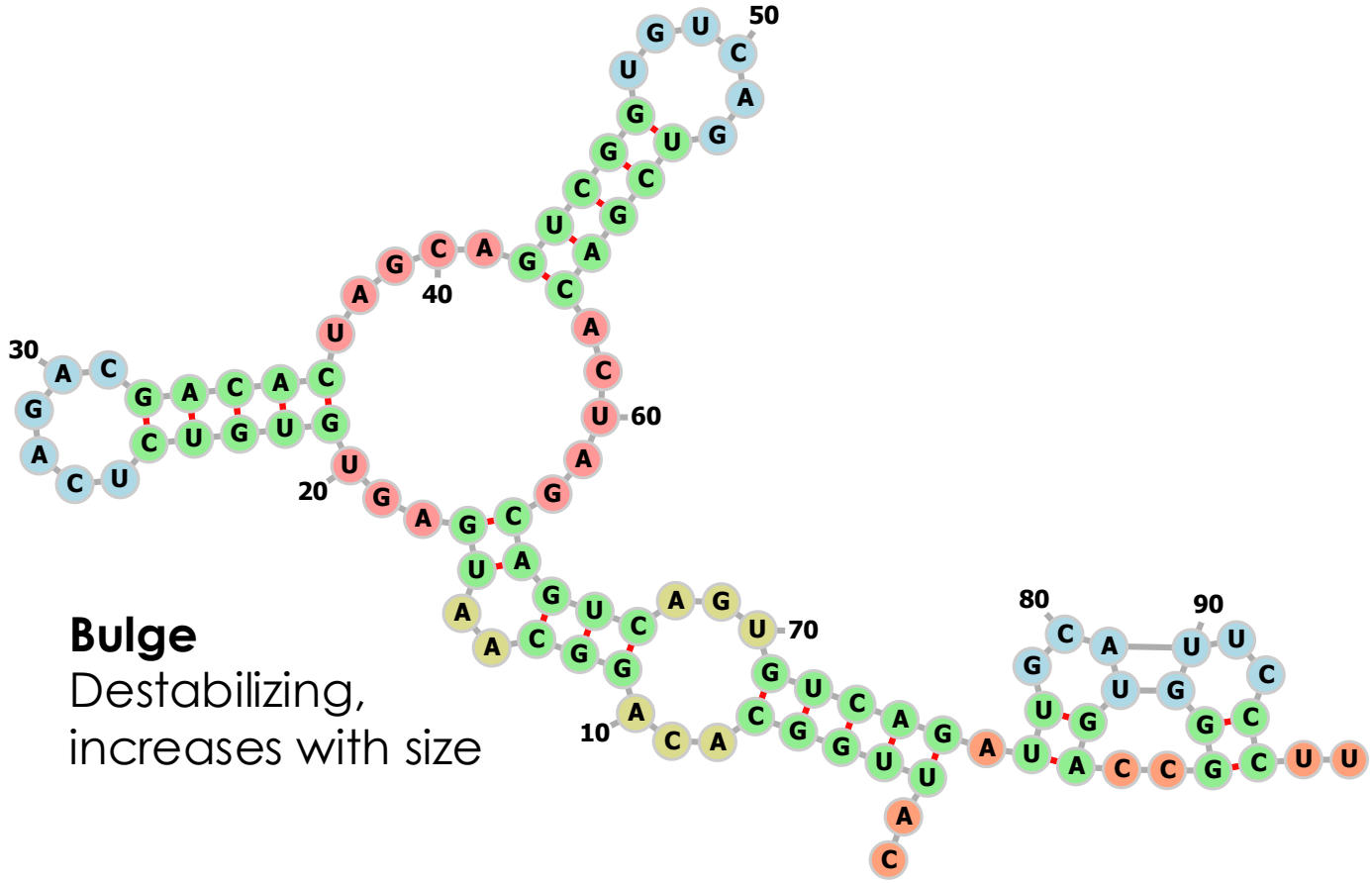
Stability varies by size, optimal ~4-6 bases



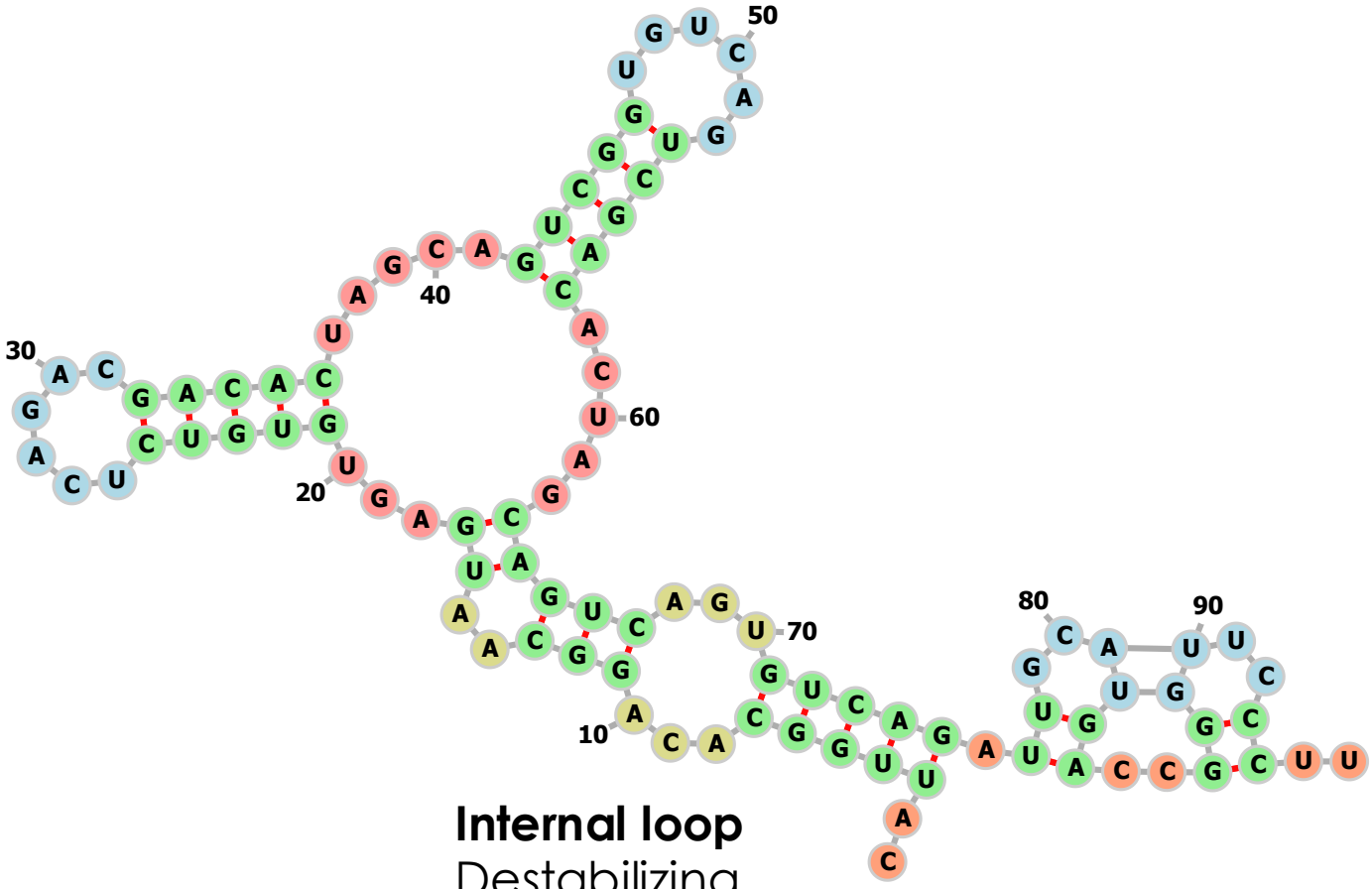
moderna

Helices
Stabilizing via base-pairing and stacking





Bulge
Destabilizing,
increases with size

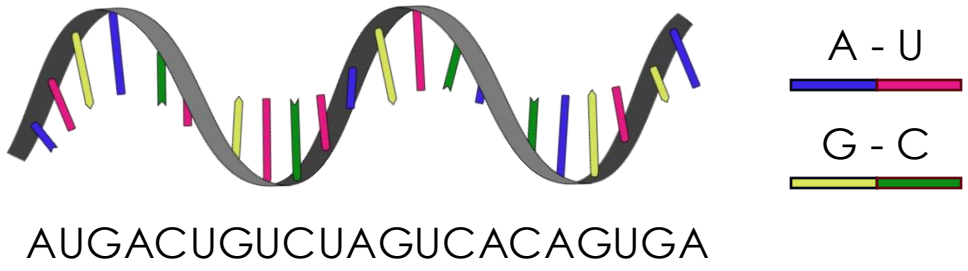


Internal loop
Destabilizing,
worse for asymmetry

Introduction

Rules:

1. Canonical Watson-Crick base pairing



2. No kinks or sharp bends in the folded molecule
3. Free energy is calculated based on the nearest neighbor rule database [Turner, Mathews (2009)]
4. To achieve thermodynamic stability (minimum free energy), the number of allowed base pairs is maximized, and stacking is rewarded
5. Terminal AU base pairs receive a penalty
6. …

Can Quantum Computing accelerate the design of more stable, effective mRNA therapeutics?

Structure defines success

Explore more, discover better

More diversity, better outcomes

- The complex task of mRNA structure prediction ensures optimal folding for stability and function
- It is an NP-complete combinatorial optimization problem

moderna

Can Quantum Computing accelerate the design of more stable, effective mRNA therapeutics?

Structure defines success

Explore more, discover better

More diversity, better outcomes

- Efficiently exploring vast sequence spaces enables unveiling novel, stable mRNA designs
- Quantum speedup will accelerate mRNA drug discovery

Can Quantum Computing accelerate the design of more stable, effective mRNA therapeutics?

Structure defines success

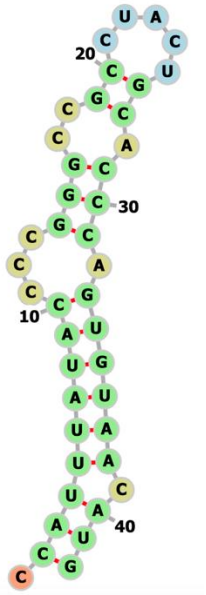
Explore more, discover better

More diversity, better outcomes

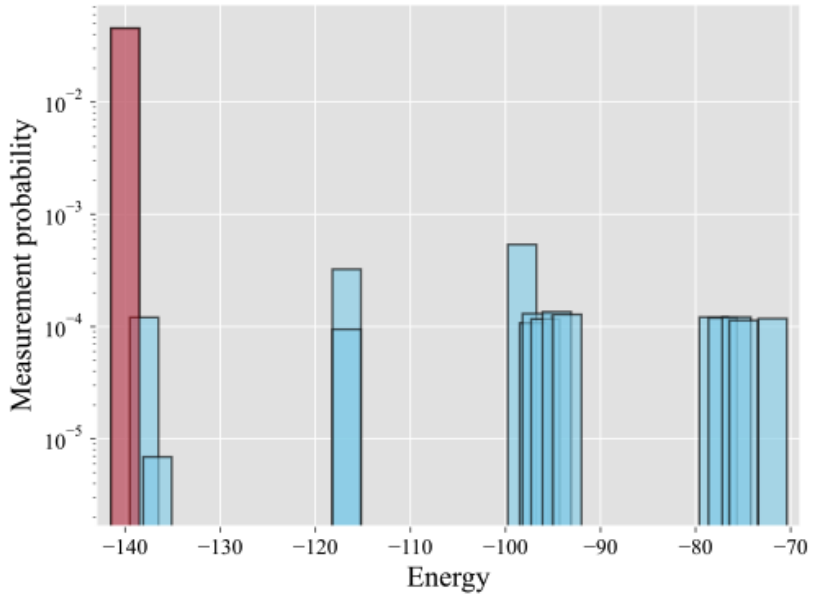
- Broader diversity of mRNA designs leads to higher-quality therapeutics
- Quantum computing for speed to diversity

Current progress

- Verified feasibility of mRNA secondary structure prediction on a quantum computer
- Validated utility of 100-qubit devices for practical use cases
- Approaching problem sizes required for commercial applications



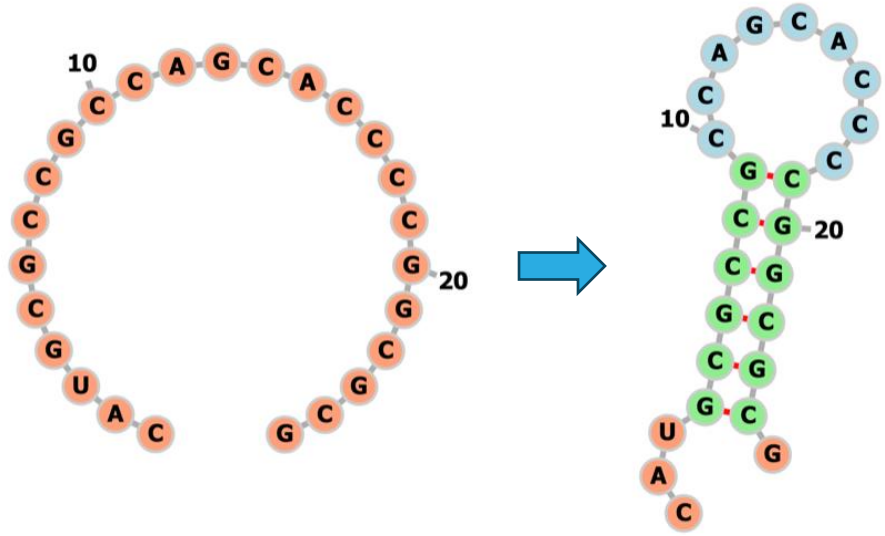
80 qubits, 42 nucleotides



arXiv: 2405.20328, accepted in 2024 IEEE QCE

Motivation

- mRNA secondary structure prediction is an NP-complete combinatorial optimization problem
- Its classical hardness positions it as a compelling application for quantum computing
- mRNA therapeutics are rapidly transforming medicine



Problem definition

Approach:

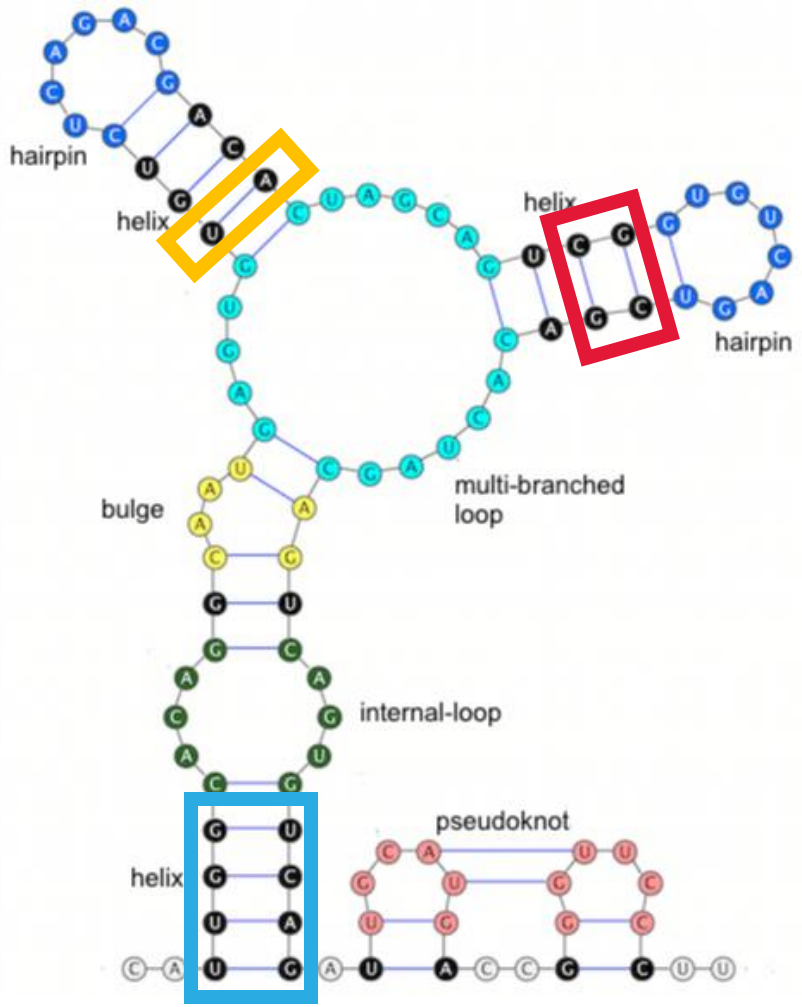
- Account for hairpins and helices but not bulges or internal loops
- Use quartets (two consecutive base pairs) as binary variables

$$x(i,j,i+1,j-1) = \begin{cases} 1 & \text{if } (i,j),\ (i+1,j-1) \text{ are made} \\ 0 & \text{otherwise} \end{cases}$$

- Formulated the problem as QUBO
- Used the classical solver CPLEX as a baseline

Data set:

- 10,000 random mRNA sequences, between 15 and 60 nucleotides
- 64% solutions matched the ground truth
- Time to solution grows exponentially with sequence length



Mamuye, Merelli,Tesei, arXiv:1612.01639

Problem definition

Approach:

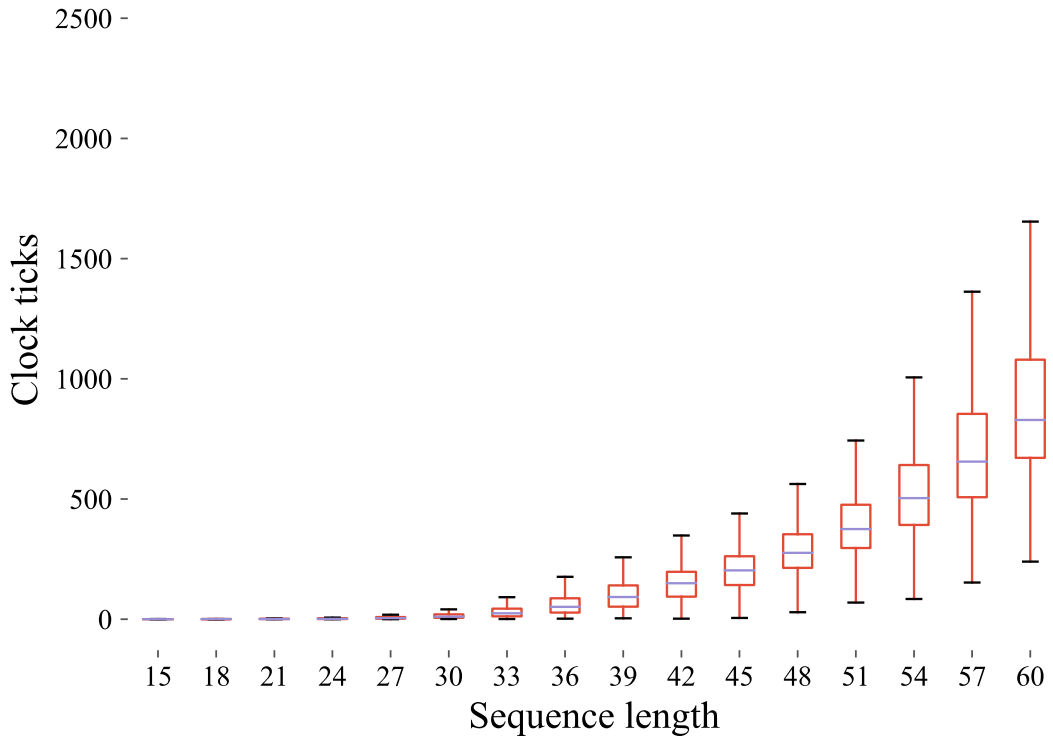
- Account for hairpins and helices but not bulges or internal loops
- Use quartets (two consecutive base pairs) as binary variables

$$x(i,j,i+1,j-1) = \begin{cases} 1 & \text{if } (i,j),\ (i+1,j-1) \text{ are made} \\ 0 & \text{otherwise} \end{cases}$$

- Formulated the problem as QUBO
- Used the classical solver CPLEX as a baseline

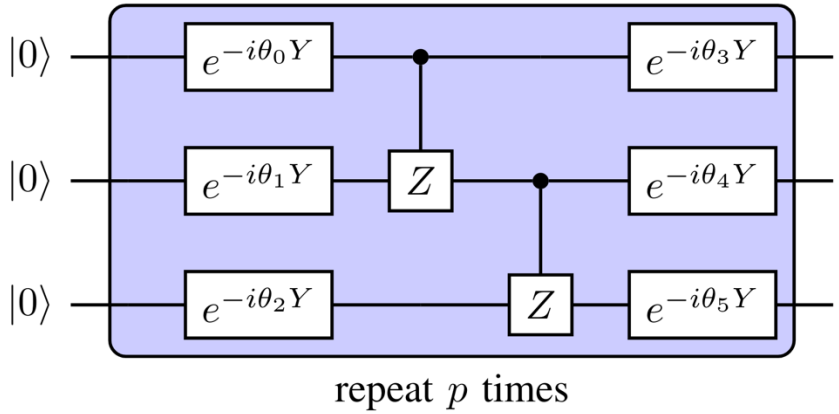
Data set:

- 10,000 random mRNA sequences, between 15 and 60 nucleotides
- 64% solutions matched the ground truth
- Time to solution grows exponentially with sequence length



Quantum approach

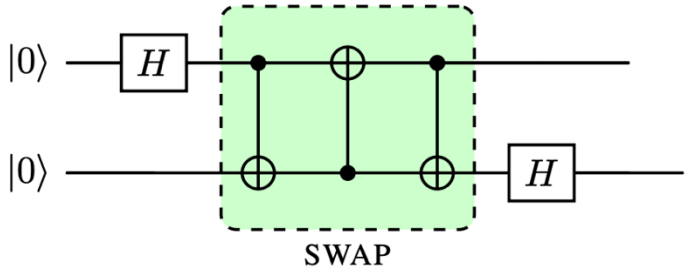
- **CVaR VQE** – optimizes the tail of a distribution of the objective function for better convergence and robustness to noise
- **NFT classical optimizer** – gradient-free with good convergence
- **Two-local ansatz** – shallow quantum circuits
- **Error suppression/mitigation** – Dynamical Decoupling (DD) and Matrix-free Measurement Mitigation (M3)



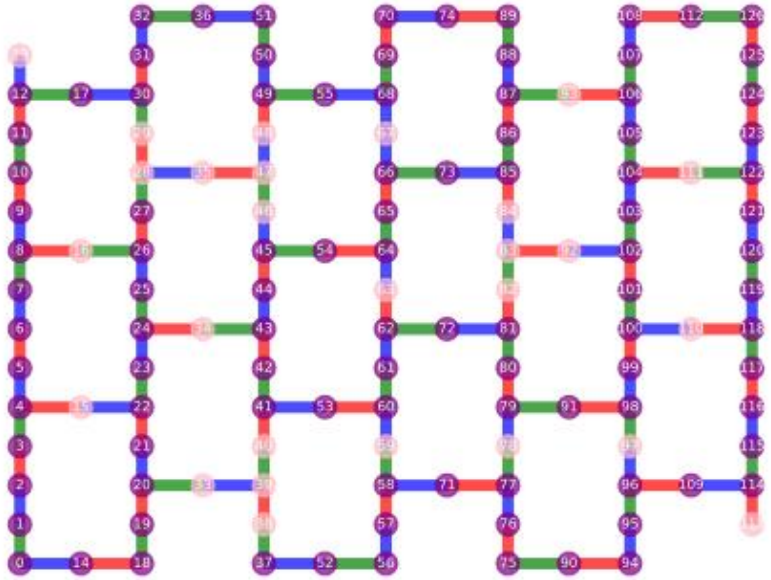
Two-local ansatz for a three-qubit case

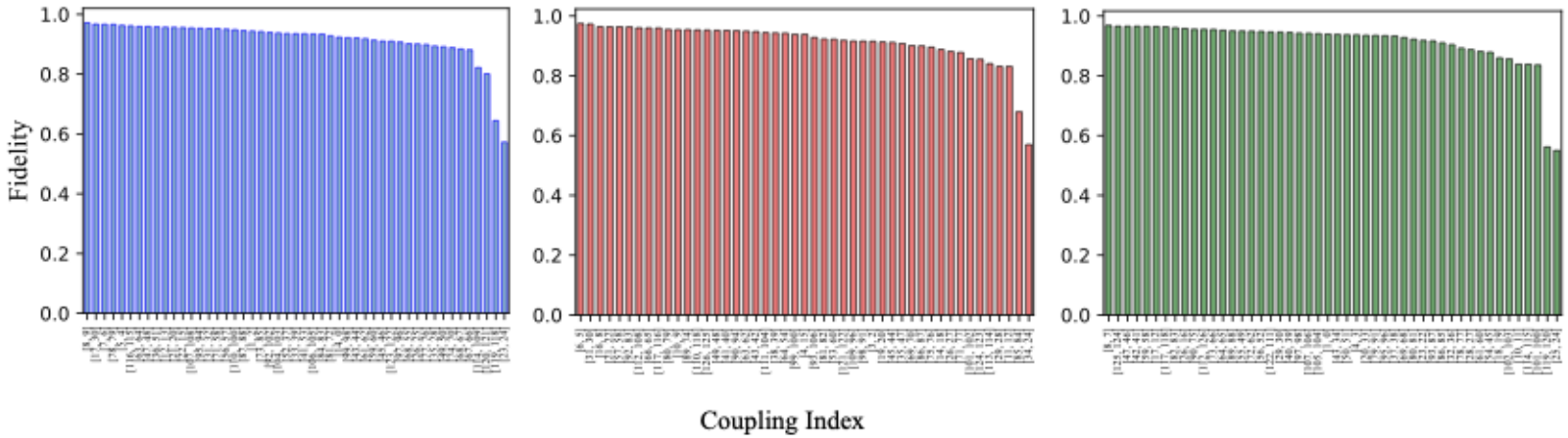
Quantum approach

- **Qubit selection** – optimal chain of qubits
- **Two-qubit fidelity characterization**



ibm_brisbane

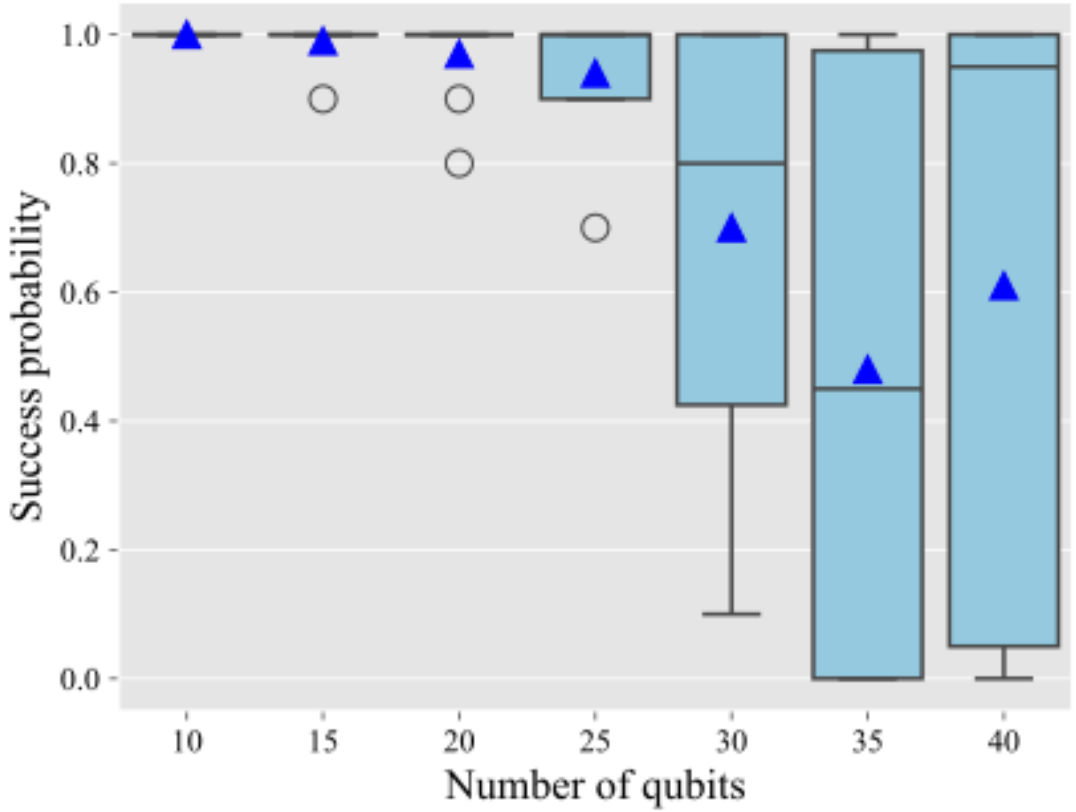




Results

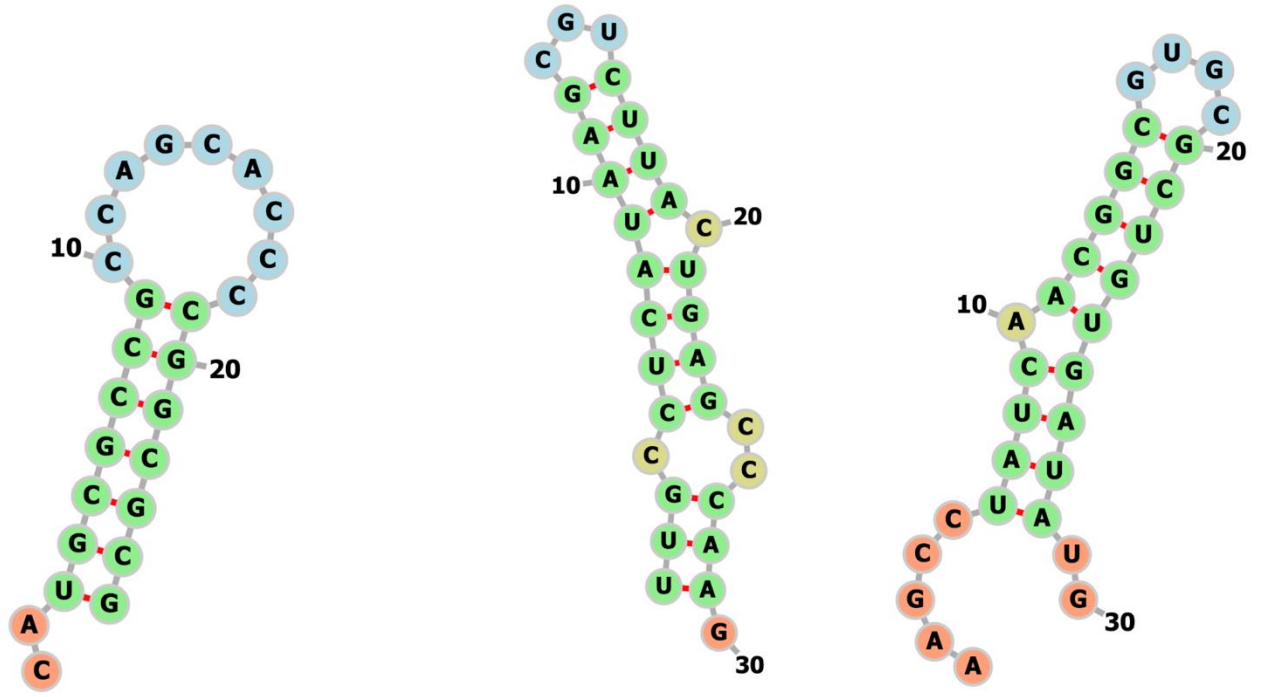
Simulation runs

- Noise-free using MPS simulator
- 2 layers of the two-local ansatz ($p = 2$)
- $\alpha = 0.1$ (CVaR parameter)
- Convergence after ~100-200 iterations
- Examined 10 different RNA sequences for each number of qubits

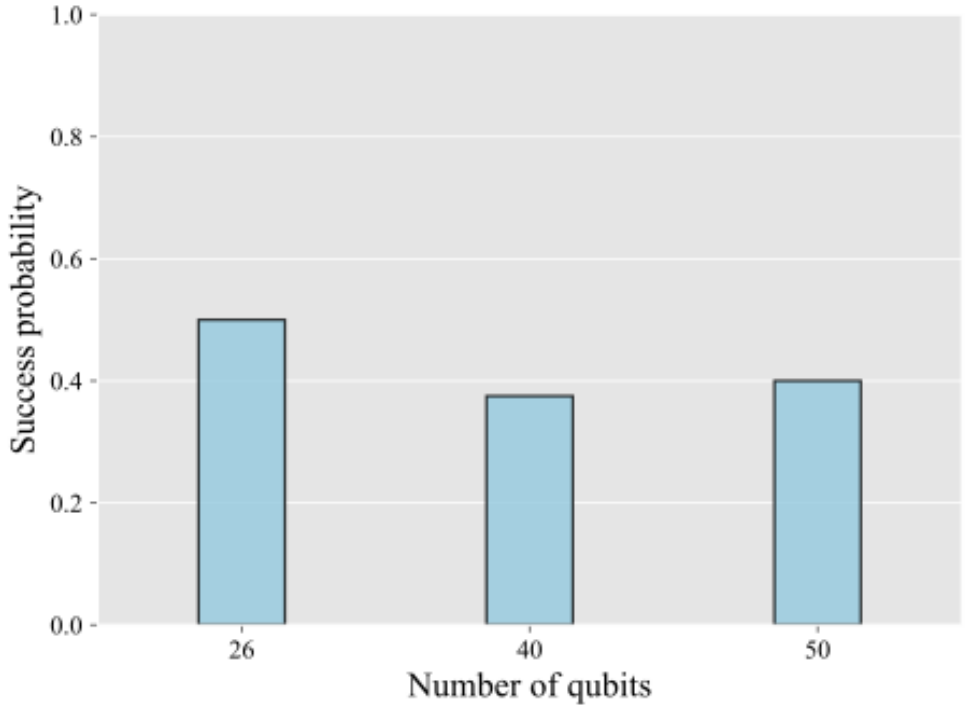


Hardware runs (26-50 qubits)

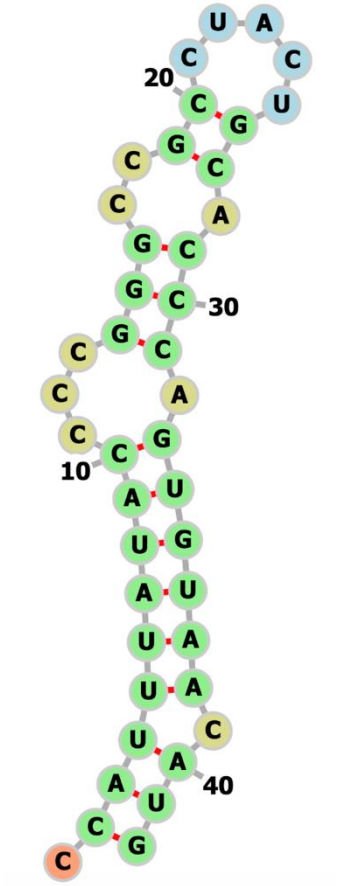
	ibm_brisbane, ibm_osaka (Eagle)			ibm_torino (Heron)
Qubits	26	40	50	80
Circuit Depth	18	20	20	17
ECR \ CZ gate count	25	39	49	158



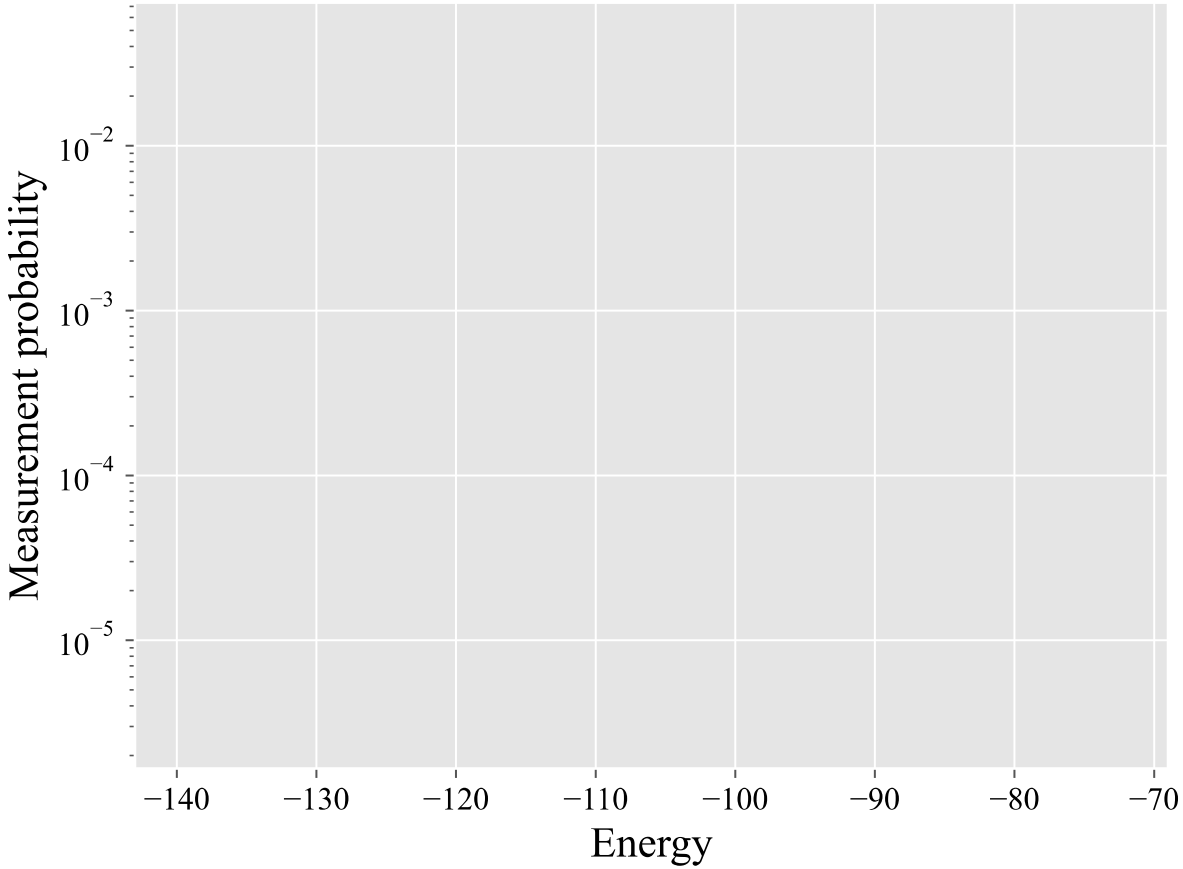
(a) 26 qubits, 25 nucleotides (b) 40 qubits, 30 nucleotides (c) 50 qubits, 30 nucleotides



Hardware runs (80 qubits)



80 qubits, 42 nucleotides



Conclusions and Outlook

- Verified feasibility of mRNA secondary structure prediction on a quantum computer
- Successful utility-scale proof-of-concept implementation of the algorithm on NISQ hardware
- It is essential to address numerous technical and algorithmic hurdles to scale up beyond 100 qubits and approach the problem sizes required for commercial applications.

moderna