Quantum Approaches to Sequence Alignment

Vivatsathorn Thitasirivit

2023/1 2110581 Bioinformatics I

Faculty of Engineering, Chulalongkorn University

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Outlines

- The Sequence Alignment Problem
- Classical Sequence Alignment and Parallelization

- Basics of Quantum Computing
- Quantum Algorithms for Sequence Alignment

- Experimentations and Results
- Challenges and Prospects
- Summary and Further Research

Disclaimers

- This project focuses on <u>experimentations</u> on a real quantum device compared to a simulator.

- Methods proposed in this project are plausible and <u>practical to run</u> on a real quantum device.

- The author has suggested many possibilities to address and solve the stated problems in <u>further research</u>.

The Sequence Alignment Problem (Pairwise)

- Aims to align 2 sequence with most similarity.
- Global and Local Alignment

- How similar is these two sequences?

AACGG

TGCGT

The Sequence Alignment Problem (Pairwise)

- Aims to align 2 sequence with most similarity.
- Global and Local Alignment

- How similar is these two sequences?

AACGG

TGCGT

```
AA--CGG-         AACGG
    **      or    **      or ... ?
--TGCG-T         TGCGT
```

Classical Sequence Alignment

- Dynamic Programming
- $O(n^2)$ in both time and space (score matrix + backtracking)

$$F(0,j) = dj$$
$$F(i,0) = di$$
$$F(i,j) = \max \begin{cases} F(i-1,j-1) + S(A_i, B_j) \\ F(i,j-1) + d \\ F(i-1,j) + d \end{cases}$$

$$S(a,b) = \begin{cases} c_1 & \text{if } a = b, \\ -c_2 & \text{if } a \neq b. \end{cases}$$

Classical Sequence Alignment

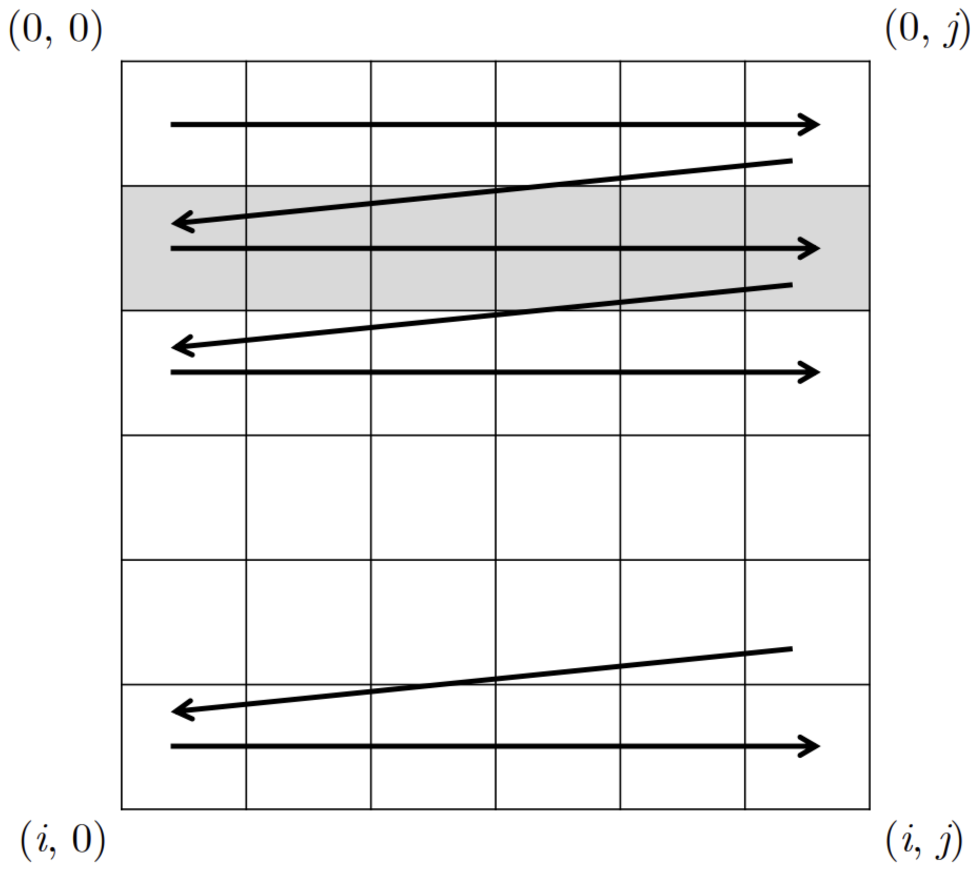
- Dynamic Programming
- $O(n^2)$ in both time and space (score matrix)

		T	G	C	G	T
	0	-2	-4	-6	-8	-10
A	-2					
A	-4					
C	-6					
G	-8					
G	-10					

Classical Sequence Alignment

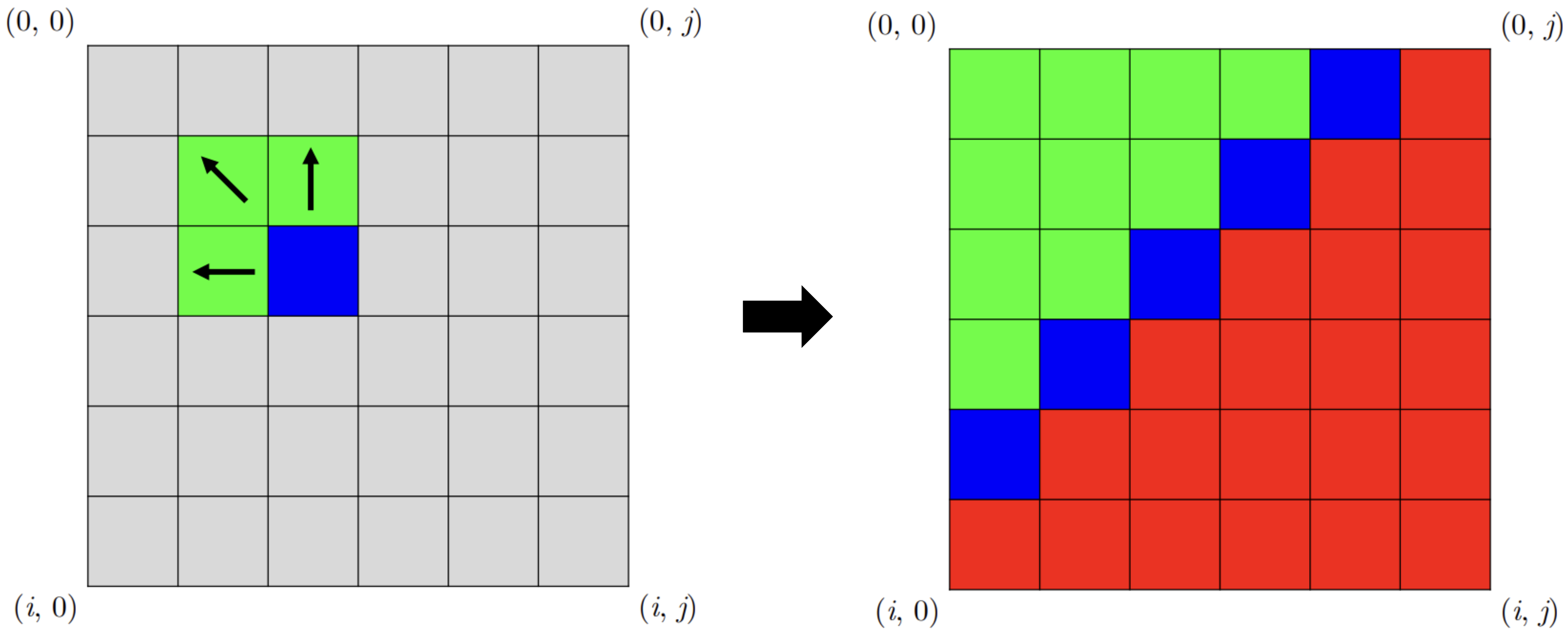
- Sequential Sweeping
- 2 nested for loops

- Can it be parallelized?
- What if the array is too large?



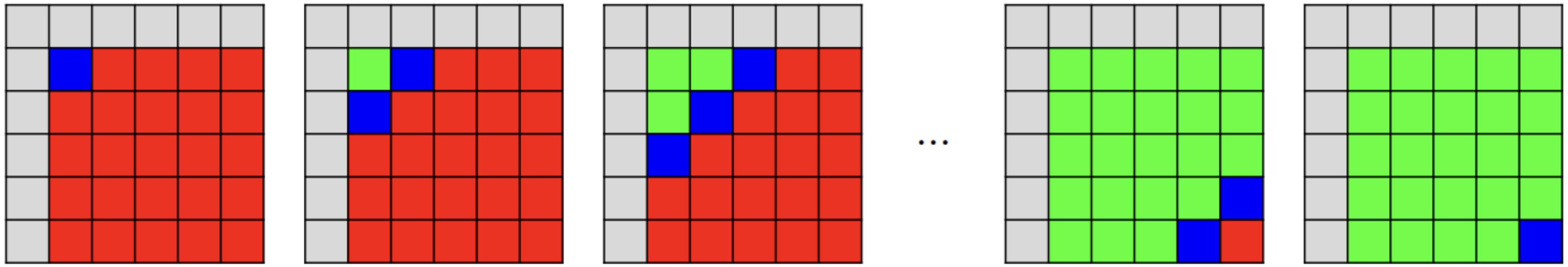
Classical Algorithms Parallelization

- Analyzing Cell's Dependencies



Classical Algorithms Parallelization

- Naïve Parallelization Method
- Doing each anti-diagonal wavefront in parallel
- Generally, slow access pattern for CPU
- Very slow in very large array that can't fit in CPU's cache (no spatial localization)
- Large threading overhead ratio.

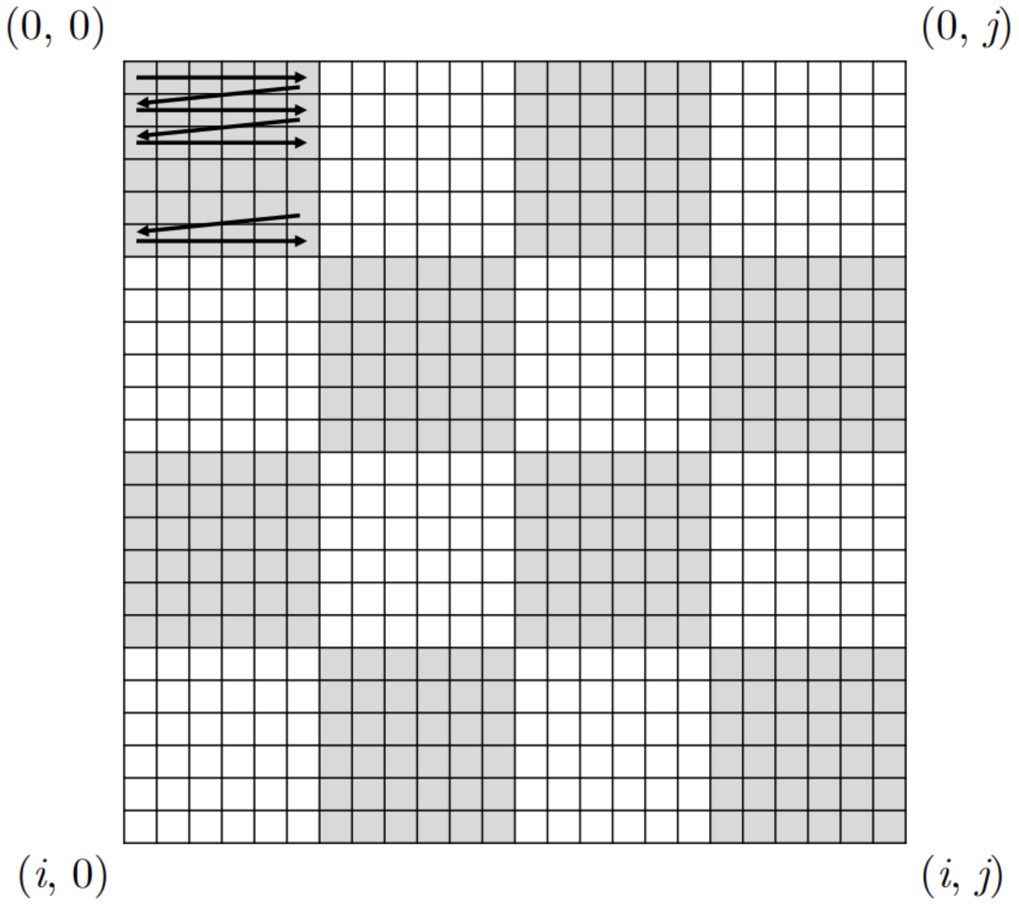


Iterations

Classical Algorithms Parallelization

- More thoughtful way:
  Split array into blocks conceptually

- Normal sweeping within each block

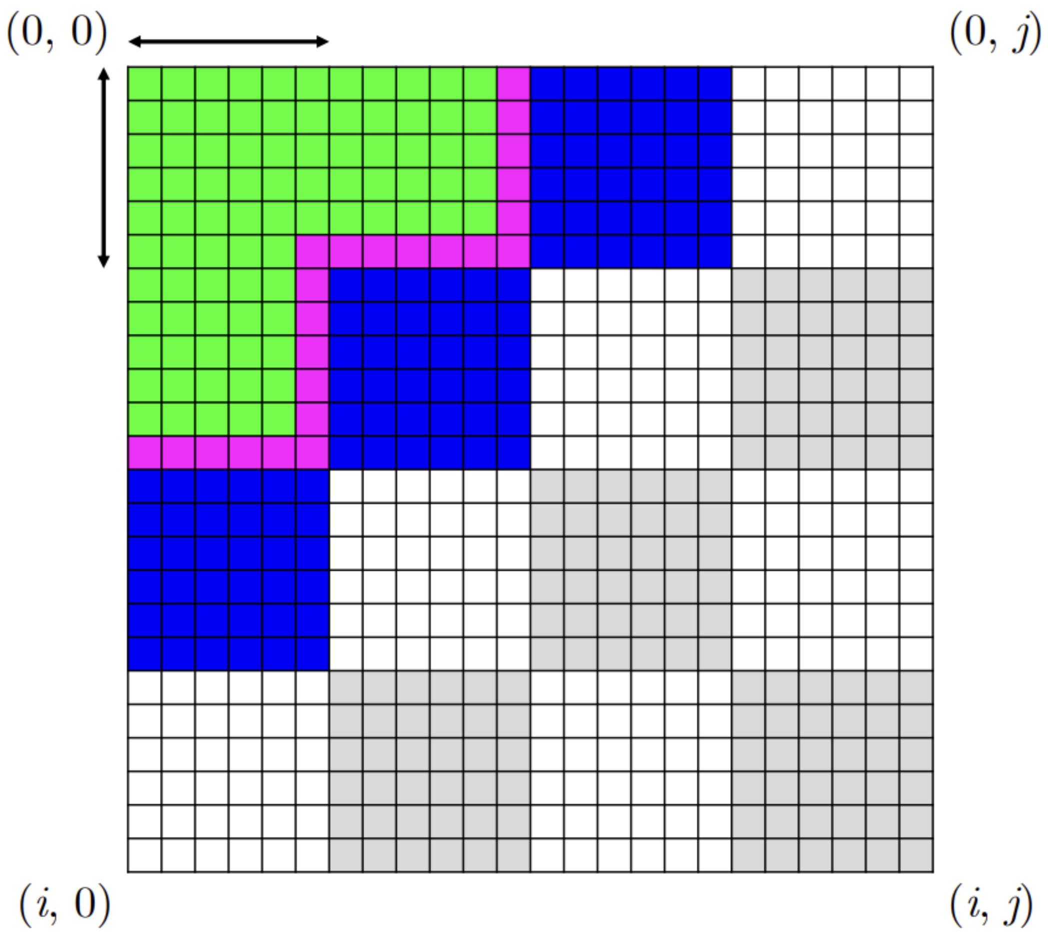


Classical Algorithms Parallelization

- Now, you can parallelize a wavefront in “blocks.”

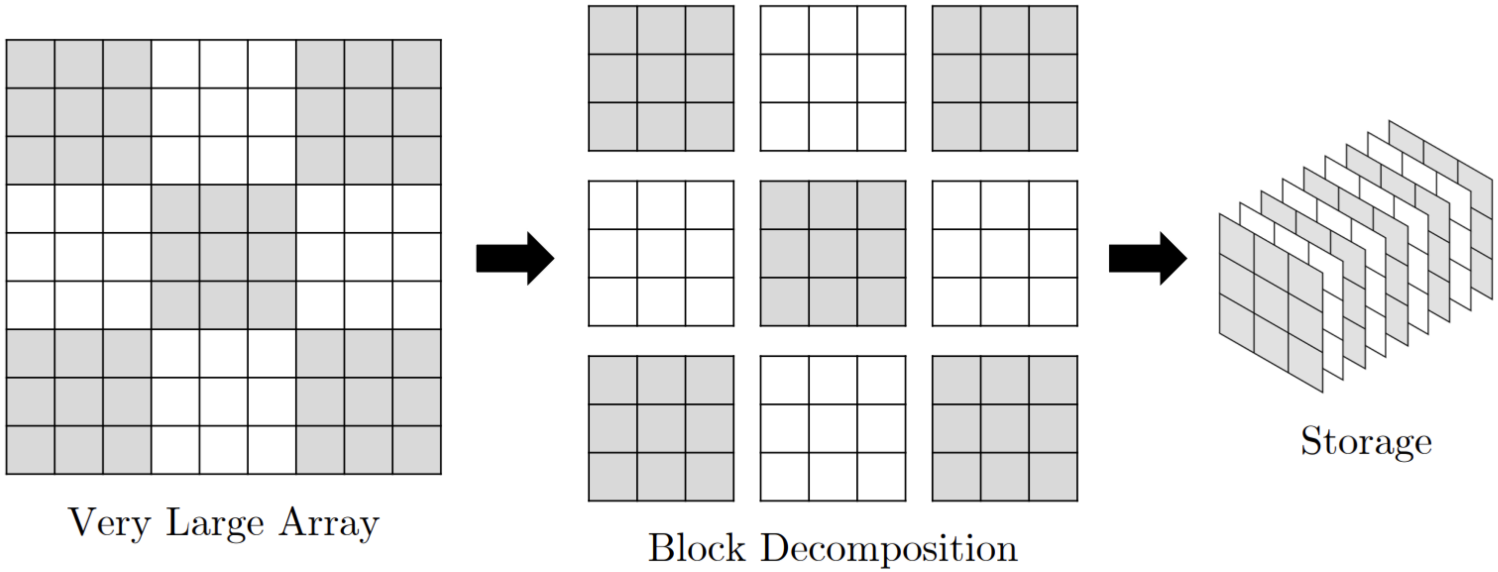
- Reduce threading overhead ratio
- Can fix localization problem
- Still taking very large memory

- How can we improve further?



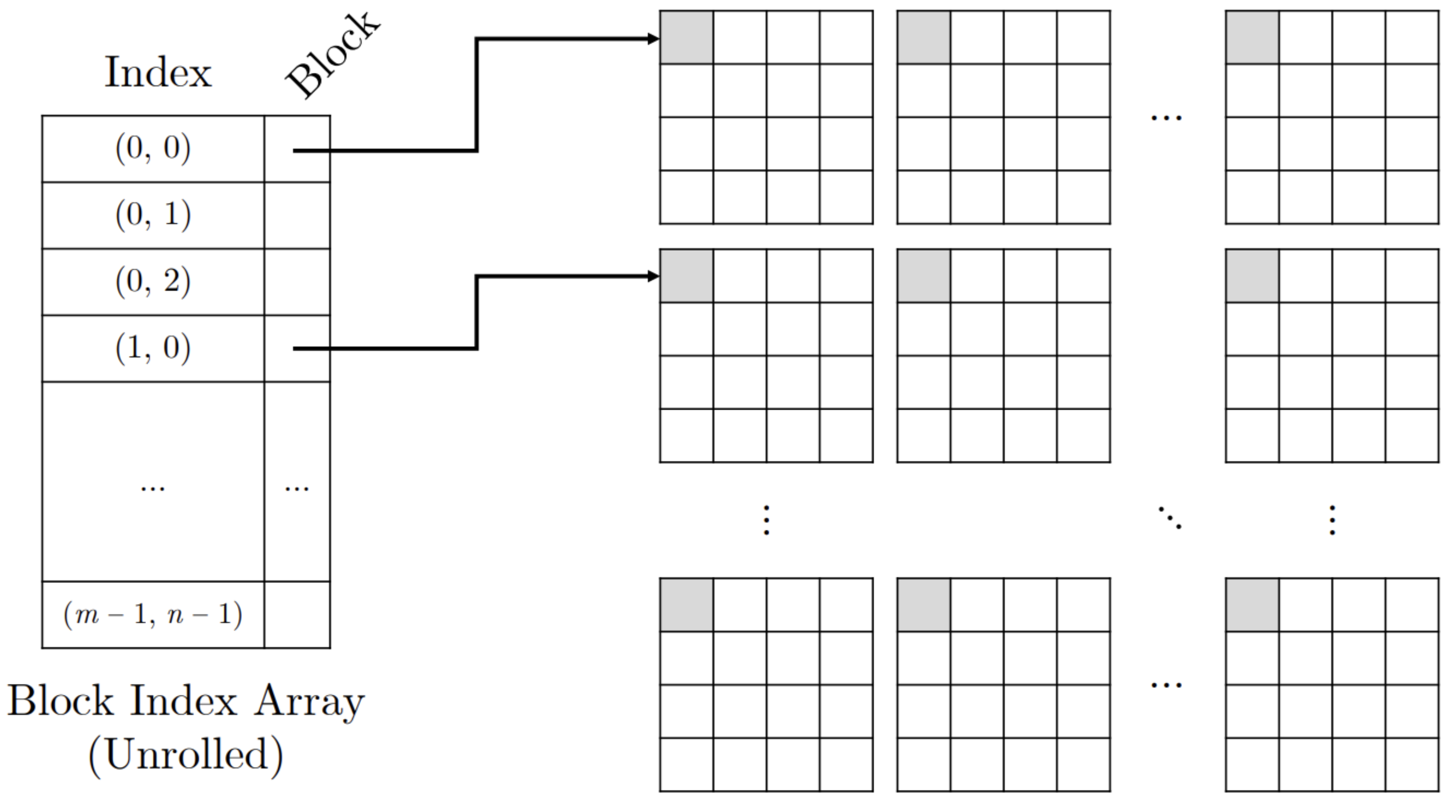
Classical Algorithms Parallelization

- Offloading and Lazy loading
- Load blocks currently in use at a time
- *Drawback: disk access is typically slower.*



Classical Algorithms Parallelization

- Block access referencing done in index array and lookup function.



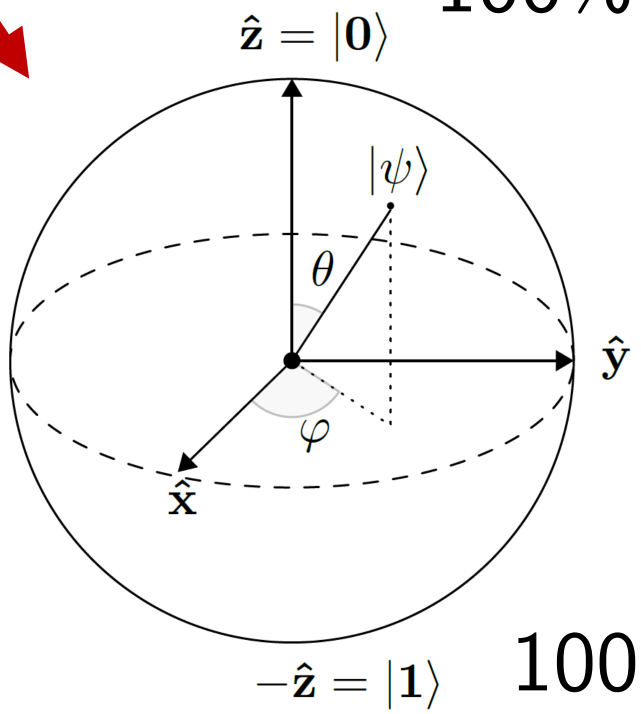
Qubits

Not real!

Either **0**

or **1**

Classical bit



100% be 0

somewhere in between

100% be 1

Qubit representation
(Bloch sphere)

Superposition → Parallelism & Searching

q1 q2 q3 q4 q5 q6

n qubits → Superposition of 2^n states.

e.g., $\underbrace{000000,\ 000001,\ \ldots\ ,\ 111110,\ 111111}_{\textit{6 qubits} \rightarrow \textit{Superposition of 64 } (2^6) \textit{ states.}}$

Basics of Quantum Computing

Decoherence

$$|\psi\rangle = \alpha\,|0\rangle + \beta\,|1\rangle$$

Quantum State

Measurement

Probability

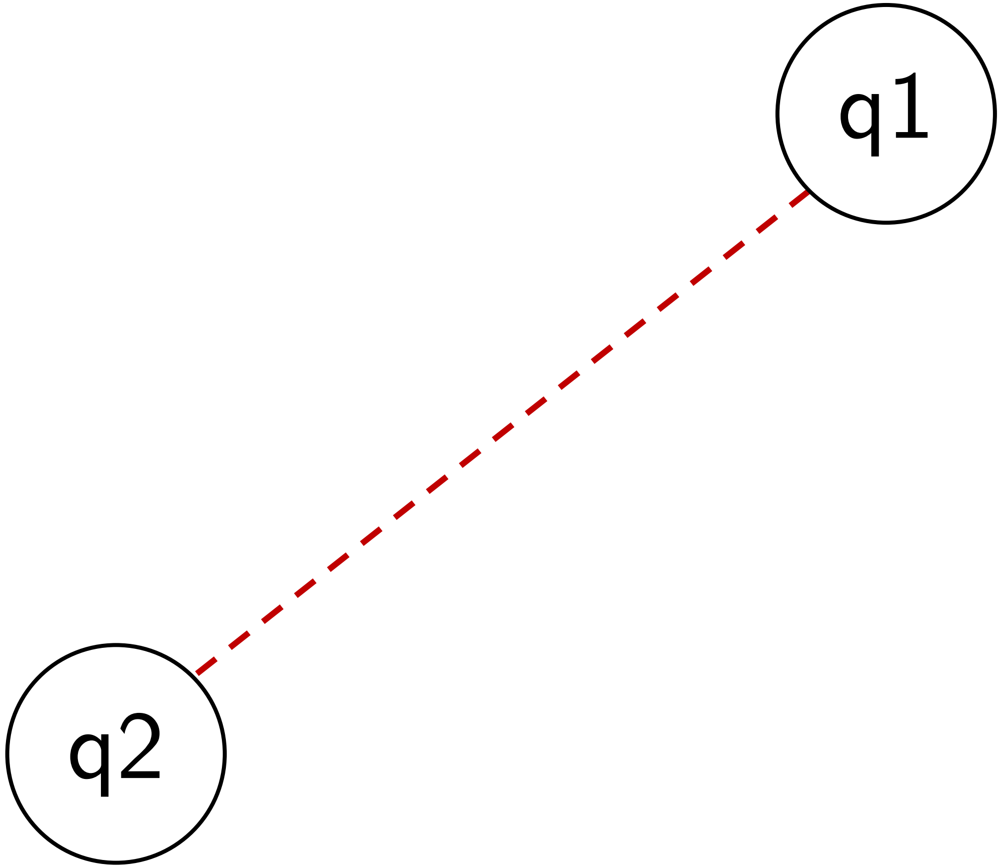
$\mathbf{0}$ $\qquad ||\alpha||^2$ %

$\mathbf{1}$ $\qquad ||\beta||^2$ %

Measured qubit

Basics of Quantum Computing

Quantum Entanglement



"Spooky action at a distance"

- Albert Einstein

Simplification

Any changes on q1 affects q2 instantly regardless of distance between them.

Quantum Entanglement: Example

Bell State

Bell basis [edit]

Four specific two-qubit states with the maximal value of
Bell states and they form a maximally entangled basis, k

$$|\Phi^+\rangle = \frac{1}{\sqrt{2}}(|0\rangle_A \otimes |0\rangle_B + |1\rangle_A \otimes |1\rangle_B) \quad (1)$$

$$|\Phi^-\rangle = \frac{1}{\sqrt{2}}(|0\rangle_A \otimes |0\rangle_B - |1\rangle_A \otimes |1\rangle_B) \quad (2)$$

$$|\Psi^+\rangle = \frac{1}{\sqrt{2}}(|0\rangle_A \otimes |1\rangle_B + |1\rangle_A \otimes |0\rangle_B) \quad (3)$$

$$|\Psi^-\rangle = \frac{1}{\sqrt{2}}(|0\rangle_A \otimes |1\rangle_B - |1\rangle_A \otimes |0\rangle_B) \quad (4)$$

Wikipedia

GHZ State

Definition [edit]

The GHZ state is an entangled quantum state for 3 qubits and its state is

$$|\mathrm{GHZ}\rangle = \frac{|000\rangle + |111\rangle}{\sqrt{2}}.$$

Generalization [edit]

The generalized GHZ state is an entangled quantum state of $M > 2$ subsystems. If each system has dimen
to $\mathbb{C}^d$, then the total Hilbert space of an M-partite system is $\mathcal{H}_{\mathrm{tot}} = (\mathbb{C}^d)^{\otimes M}$. This GHZ state is also calle
a tensor product is

$$|\mathrm{GHZ}\rangle = \frac{1}{\sqrt{d}} \sum_{i=0}^{d-1} |i\rangle \otimes \cdots \otimes |i\rangle = \frac{1}{\sqrt{d}}(|0\rangle \otimes \cdots \otimes |0\rangle + \cdots + |d-1\rangle \otimes \cdots \otimes |d-1\rangle).$$

In the case of each of the subsystems being two-dimensional, that is for a collection of *M* qubits, it reads

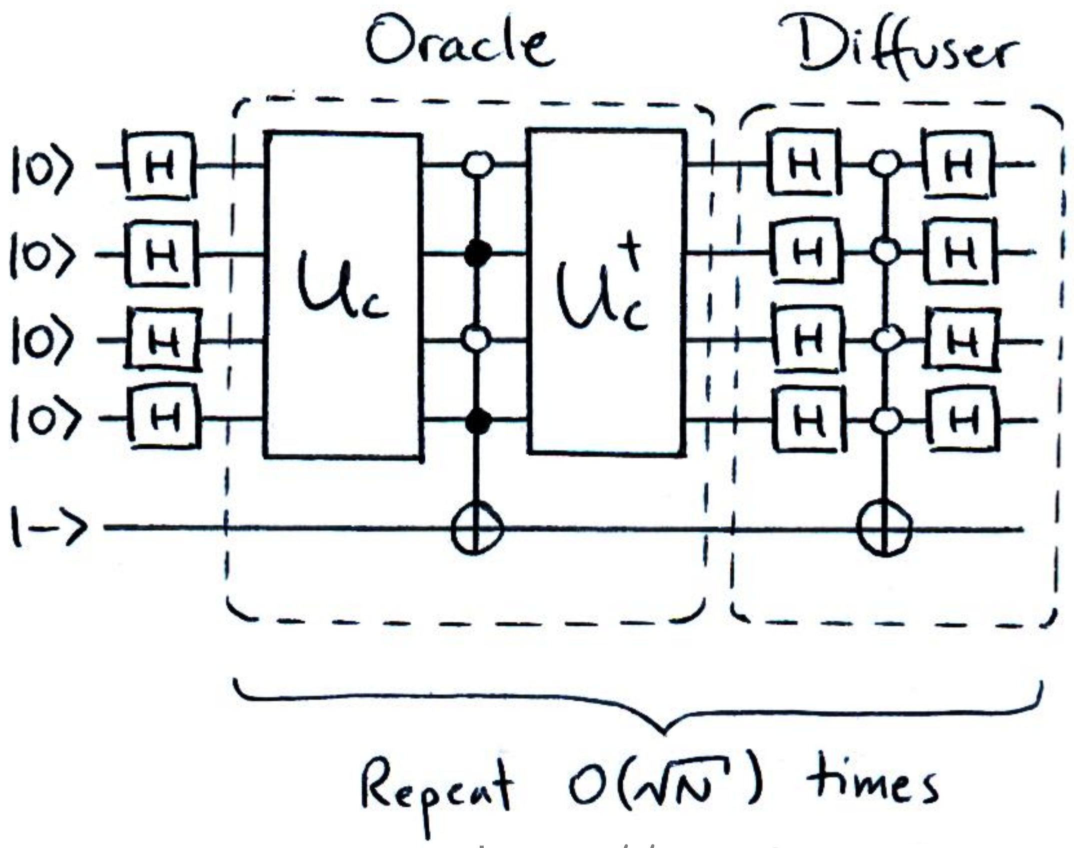
$$|\mathrm{GHZ}\rangle = \frac{|0\rangle^{\otimes M} + |1\rangle^{\otimes M}}{\sqrt{2}}.$$

Wikipedia

Quantum Algorithm Example

- Grover's Algorithm for searching database.
  - Focuses on unordered search
  - Query only $O(\sqrt{N})$ times.

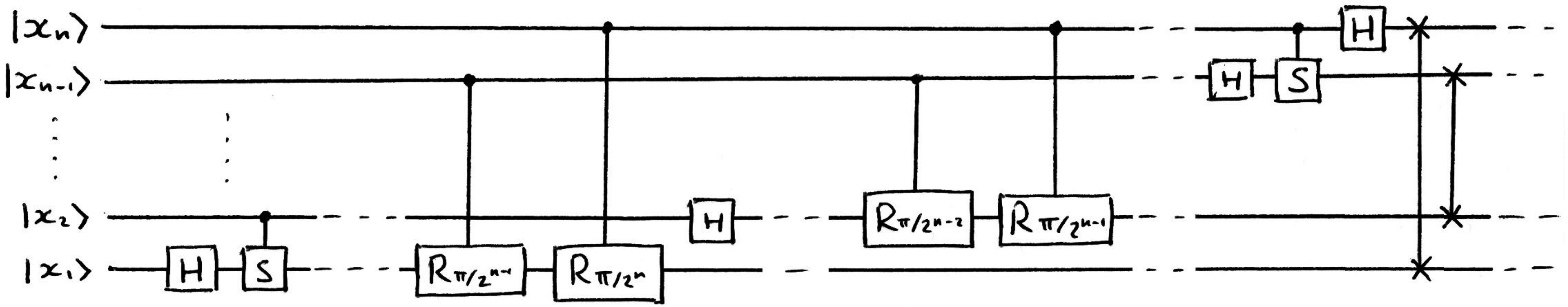
- **Oracle**: mark correct answer by applying negative phase.
- **Diffuser**: amplify correct answer back to original phase.



https://cnot.io

Quantum Algorithm Example

- Quantum Fourier Transform ⇔ Quantum version of DFT



https://cnot.io

Some Basic Quantum Gates

Single qubit gates

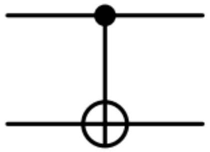
Hadamard	$-\boxed{H}-$	$\frac{1}{\sqrt{2}}\begin{pmatrix}1 & 1\\ 1 & -1\end{pmatrix}$
Pauli-X (Bit flip)	$-\boxed{X}-$	$\sigma_X = \begin{pmatrix}0 & 1\\ 1 & 0\end{pmatrix}$
Pauli-Z (Phase flip)	$-\boxed{Z}-$	$\sigma_Z = \begin{pmatrix}1 & 0\\ 0 & -1\end{pmatrix}$

Basics of Quantum Computing

Some Basic Quantum Gates

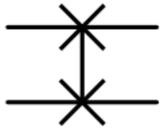
Two qubit gates

Controlled-NOT (CNOT, CX)



$$\begin{pmatrix} I & 0 \\ 0 & X \end{pmatrix}$$

SWAP



$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Quantum Algorithms for Sequence Alignment

- Hamming Edit Distance (Possible, Implementable)
- Levenshtein Edit Distance (Theoretical with qRAM)
- Needleman-Wunsch (Theoretical with qRAM)
- Smith-Waterman (Theoretical with qRAM)
- Cosine Similarity (Possible)
- Graph Edit Distance (Theoretical)
- Pattern Matching Approximation with QFT (Quantum DFT/FFT)
- BLAST Database Search Matching (Never proven as of now)
- Knuth-Morris-Pratt string search algorithm (Never proven as of now)

Quantum Algorithms for Sequence Alignment

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Quantum Algorithms for Sequence Alignment

- DNA Sequence string is represented by $\{\mathrm{A}, \mathrm{T}, \mathrm{C}, \mathrm{G}\}^n$
- Sequence Encoding
  - Minimal Encoding (2 bits): $\{00, 01, 10, 11\}$
  - One-hot Encoding (4 bits): $\{0001, 0010, 0100, 1000\}$
- #Qubits needed if:
  - 2 input quantum registers
  - 1 output quantum register
  - 1 output classical register (for measurement)
- $= 3 \times N_{\text{encode length}} \times N_{\text{string length}}$
- Example: 127-qubit system supports 42-bit string (21 characters) maximum.

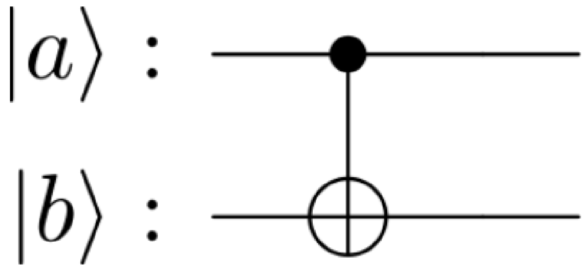
Quantum Algorithms for Sequence Alignment

- Concept: “Pairwise Comparison”

- In classical term, we would use XOR operation.
- In quantum system, we can use Controlled-NOT (CNOT, CX).

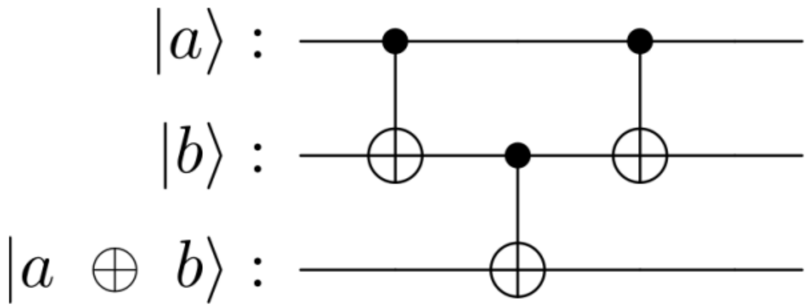
- Naïve approach turns $|b\rangle \rightarrow |a \oplus b\rangle$

- Input qubits are not conserved!



Quantum Algorithms for Sequence Alignment

- We can add an output quantum register.
- CNOT is its own inverse, so we can "sandwich" operations.

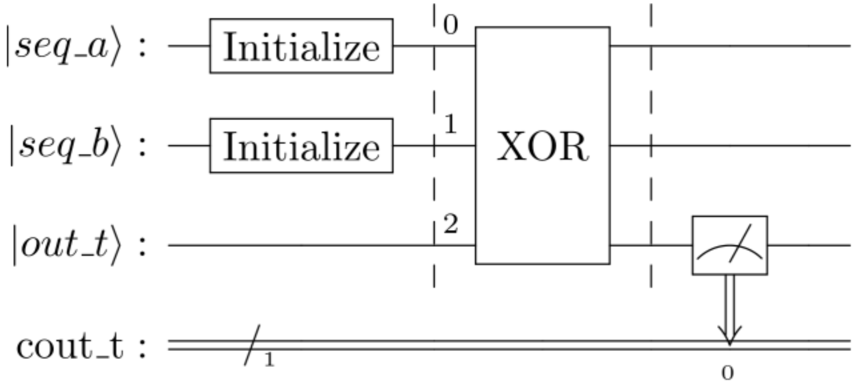


- Now, input qubits can conserve (if they are not entangled).

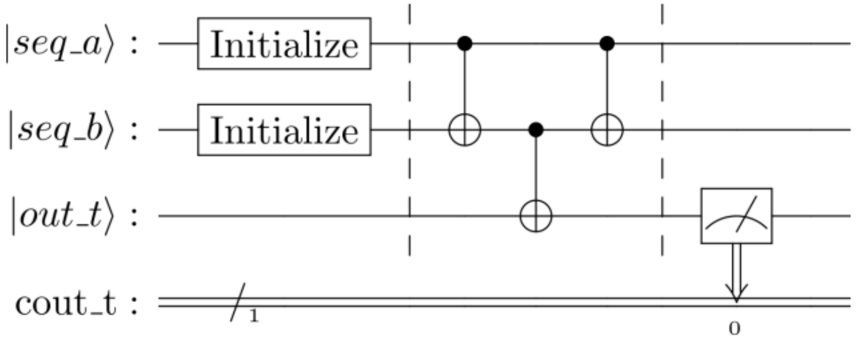
- *If input qubits are entangled, the output qubit will also be entangled with input qubits. Measurement will collapse the superposition.*

Quantum Algorithms for Sequence Alignment

- Method 1: Direct pairwise comparison using XOR



(a) Top-level block



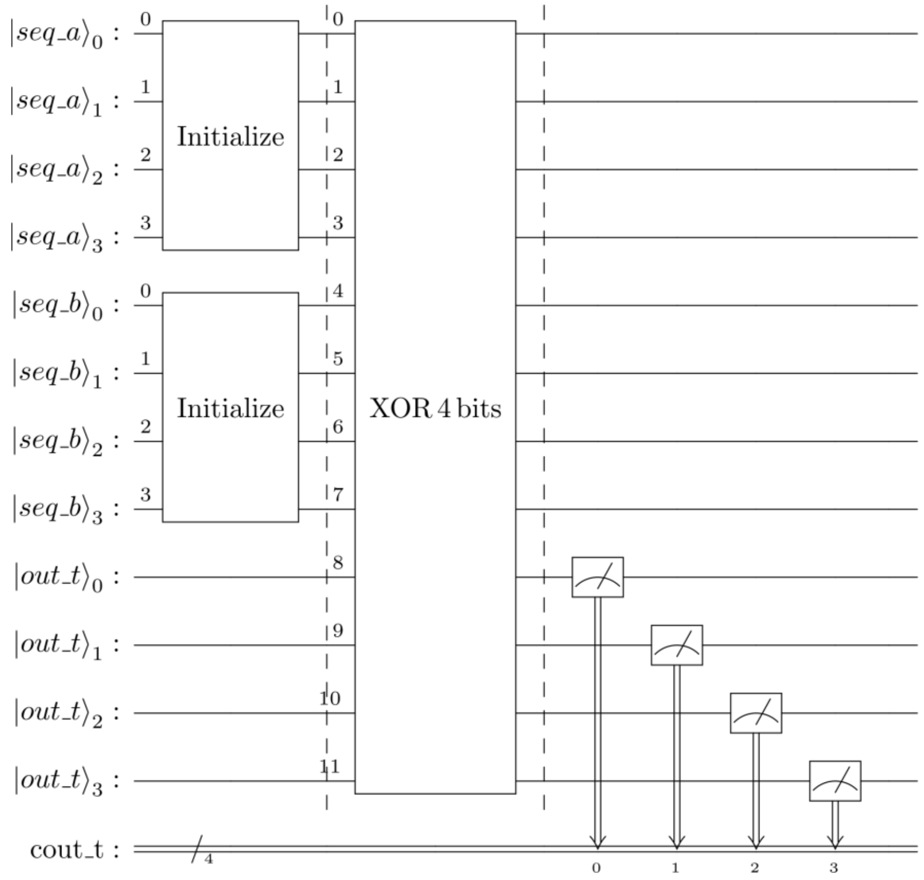
(b) Decomposed XOR

Quantum Algorithms for Sequence Alignment

- Method 1: Direct pairwise comparison using XOR

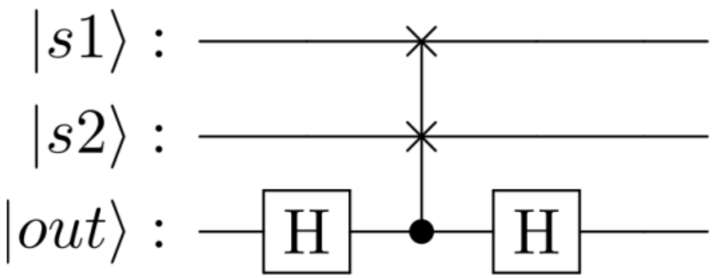
- Example:
  2-character (4-bit) input

- Potential improvements:
  - Implement quantum adder circuit
    - QFT Adder
    - Ripple Carry Adder
    - Adder using QPE



Quantum Algorithms for Sequence Alignment

- Method 2: Direct pairwise comparison using Swap Test



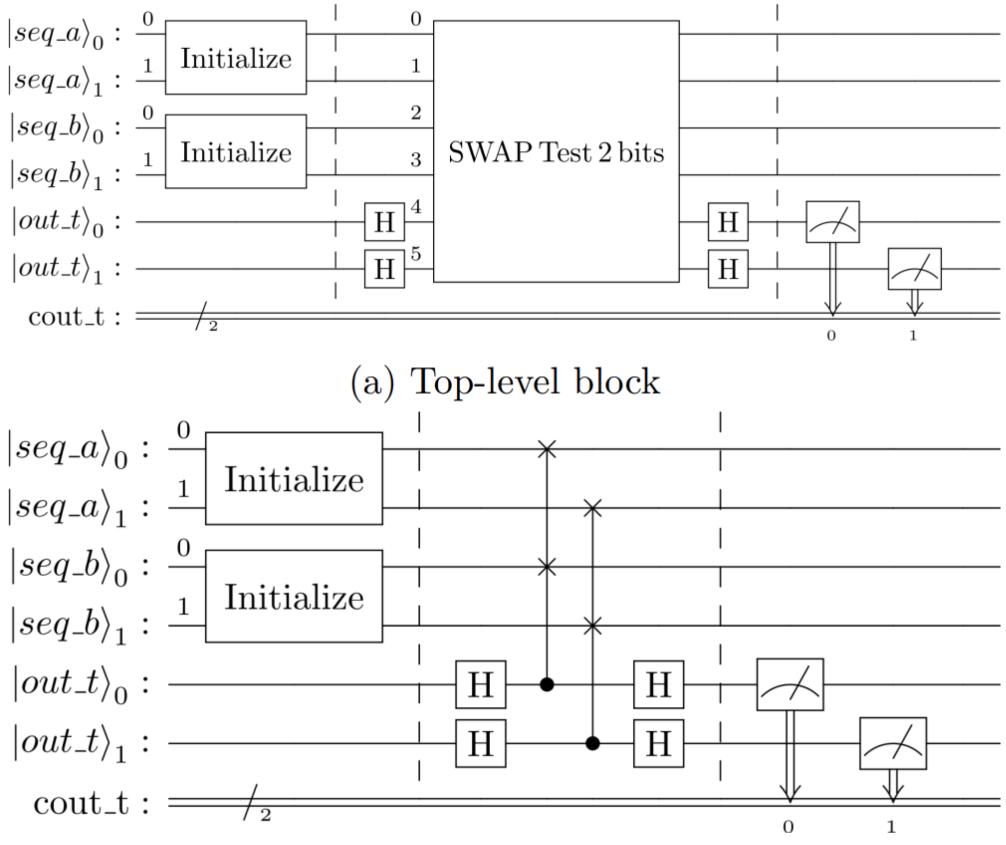
- This utilizes quantum properties of putting a control qubit in a superposition.
- This causes qubits entanglement.
- How do we determine the output?
  - If s1 equals s2, the output measurement is always 0.
  - Else, the output measurement is 0 for 50% and 1 for 50%.

Quantum Algorithms for Sequence Alignment

- Method 2: Direct pairwise comparison using Swap Test

- Example:
  1-character (2-bit) input

- What if we treated it as a signal?
  - Time-domain Comparison
  - Frequency-domain Comparison



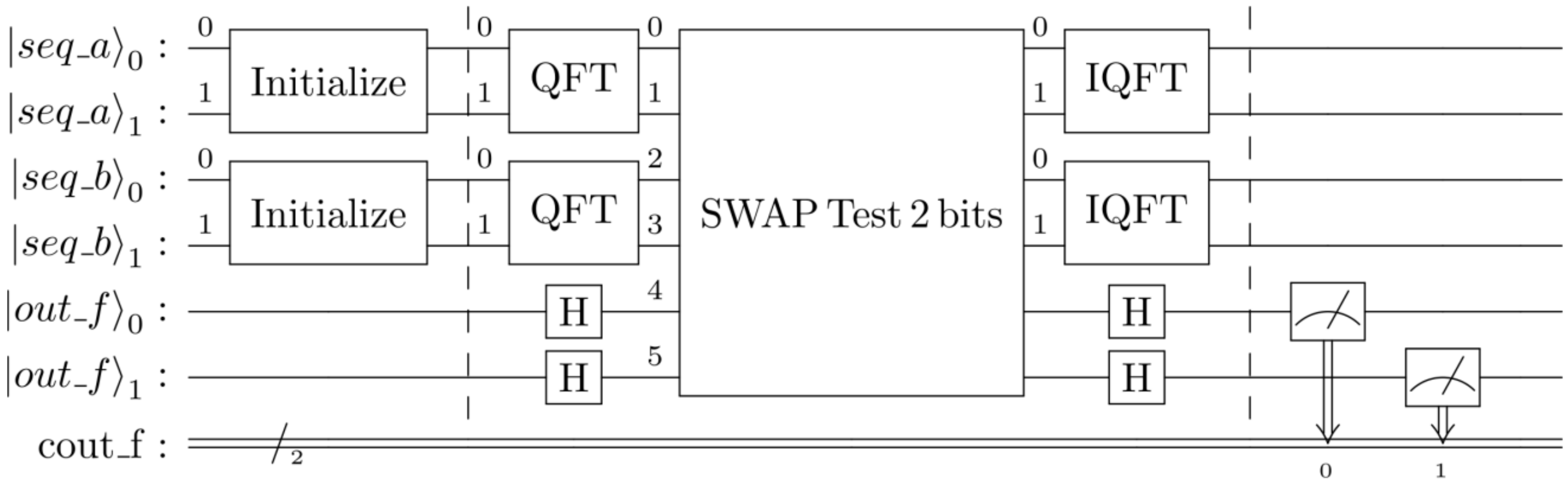
(a) Top-level block

(b) Decomposed Swap Test

Quantum Algorithms for Sequence Alignment

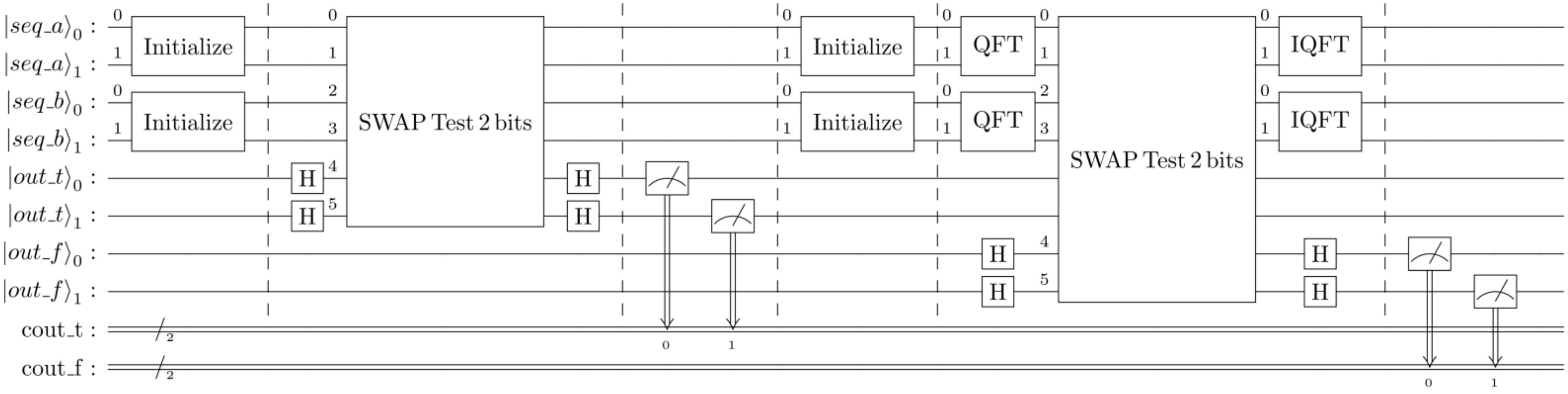
- Addition to Method 2: Compare in a Frequency Domain
- We can apply QFT and QFT^{-1} on both input quantum registers.
  - The state after initialization can be described as:

$$(\mathrm{H}\,|0\rangle)^{\otimes n} \otimes \mathrm{QFT}\,|s_1\rangle \otimes \mathrm{QFT}\,|s_2\rangle$$



Quantum Algorithms for Sequence Alignment

- Can we combine both domain in 1 circuit?
  - Yes, but it would be impractical: large circuit, potential noise, rigorous post-processing.
  - After the Swap Test and measurement, qubits are not reusable.
  - Must initialize qubits again.*



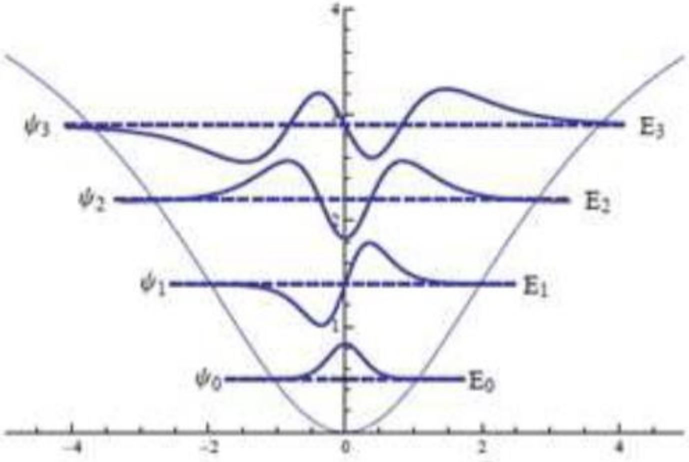
Quantum Algorithms for Sequence Alignment

- Further improvements:
  - I. Swap Test on every permutation of qubits.
    - From n to n^2

$$s_1\,\{0,1,...,n-1\}\;\times\;s_2\,\{0,1,...,n-1\}$$

  - II. Using QPE for frequency domain
  - III. Maybe go for a qudit (d-level quantum system)?

$$|\psi\rangle = \sum_{i=0}^{d-1} c_i\,|i\rangle \quad ; \quad \sum_{i=0}^{d-1} \|c_i\|^2 = 1$$



Non-linear oscillator

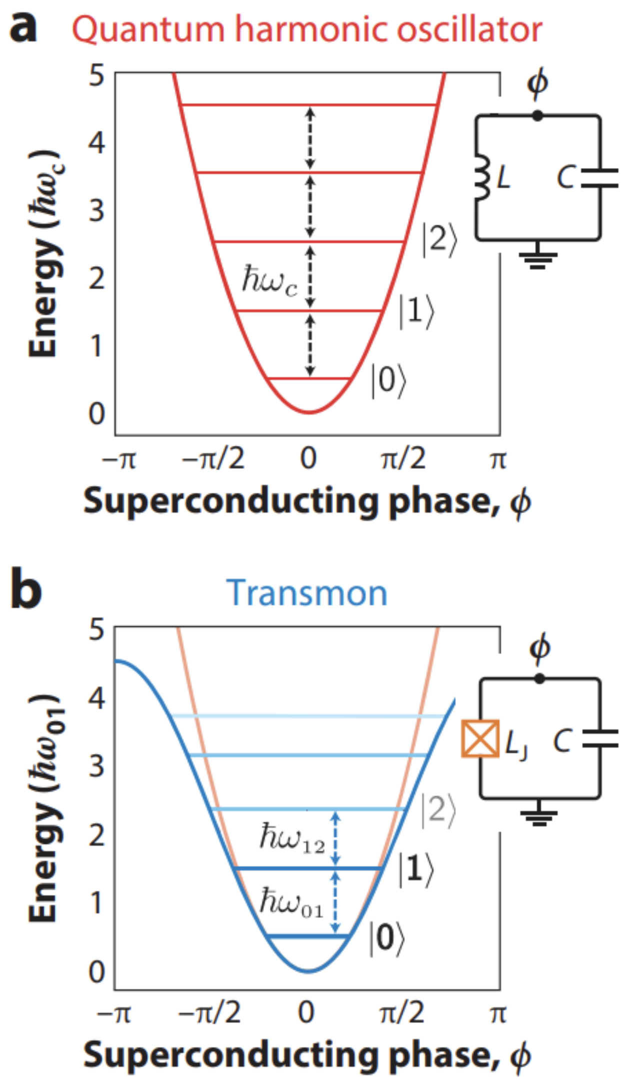
10.1063/1.4954283

A quantum computer

- There are many types of quantum computers!
- Analog Quantum Computer
  - Initializing a quantum state
  - Control the Hamiltonian to evolve the state directly
  - E.g., quantum annealing [D-Wave!] , adiabatic computation, quantum simulation
- Digital Quantum Computer
  - It is "gate-based" with universal set of gates
  - Typically, is a two-level quantum system.
  - Digital outcomes by measurement
  - Similar to classical computing.

A quantum computer

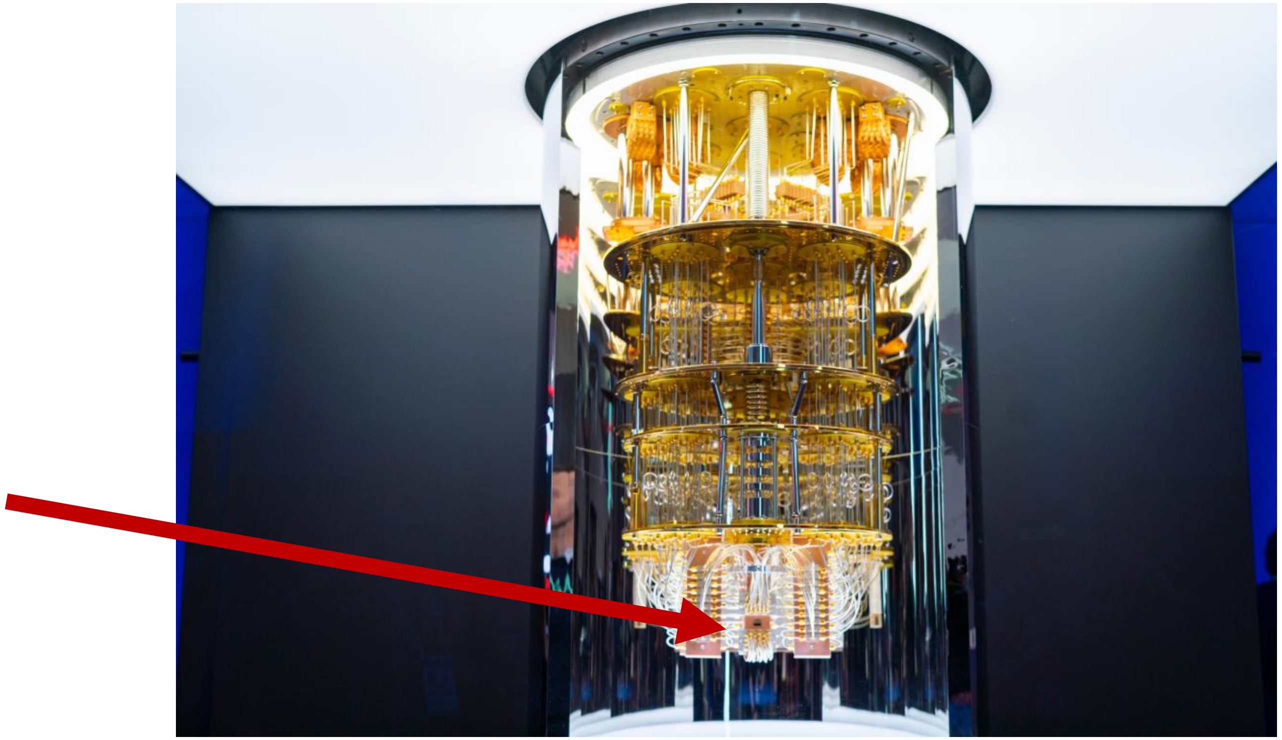
- There are also many qubit technologies used!
- Current technologies in NISQ era
  - Superconducting qubits
    - Transmon charge, nonlinear
  - Trapped ion
- Candidate technologies after NISQ
  - Photonic
  - Silicon-based
  - Topological



Superconducting Qubits: Current State of Play (annualreviews.org)

A quantum computer

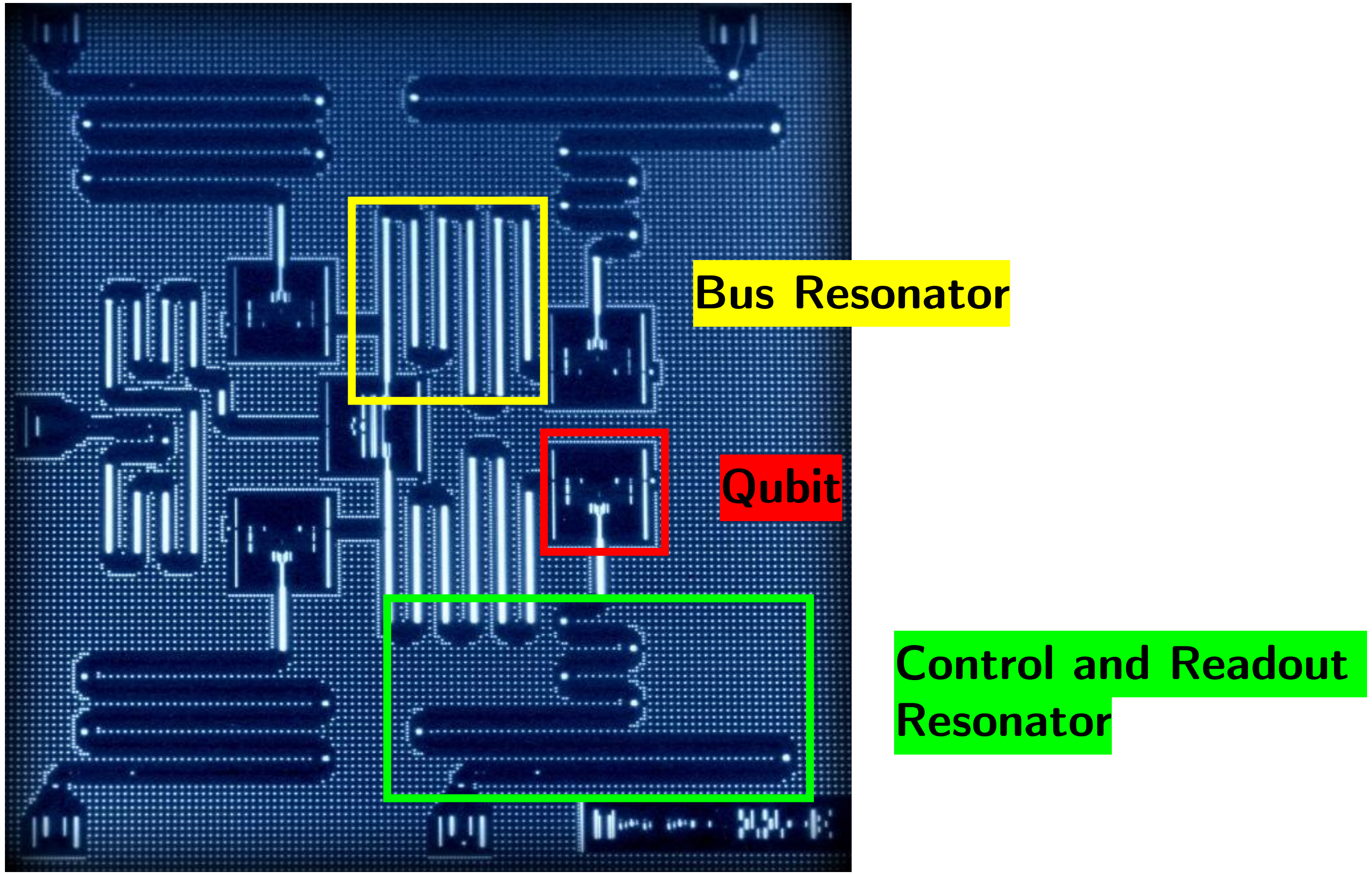
- This is IBM's 127 qubit quantum computer on which the circuit was run.

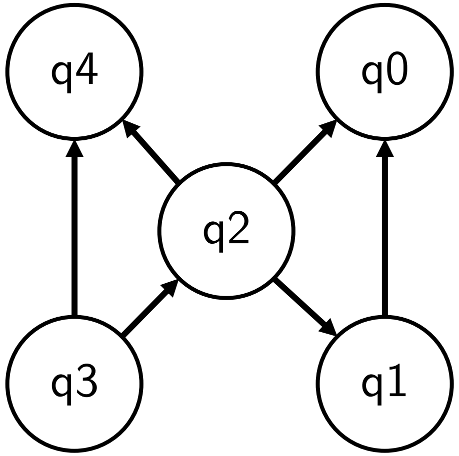


- Courtesy: IBM Quantum

A quantum computer

- Superconducting 5-qubit quantum processor (IBM).



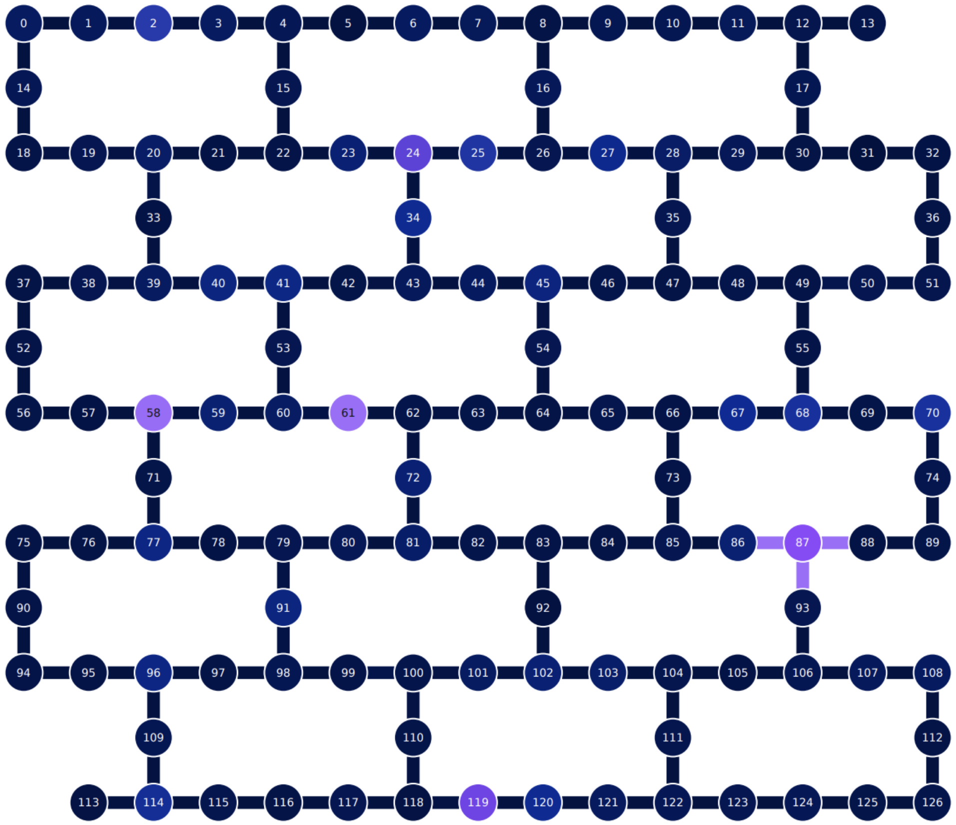


Qubit Diagram

Courtesy: IBM Quantum

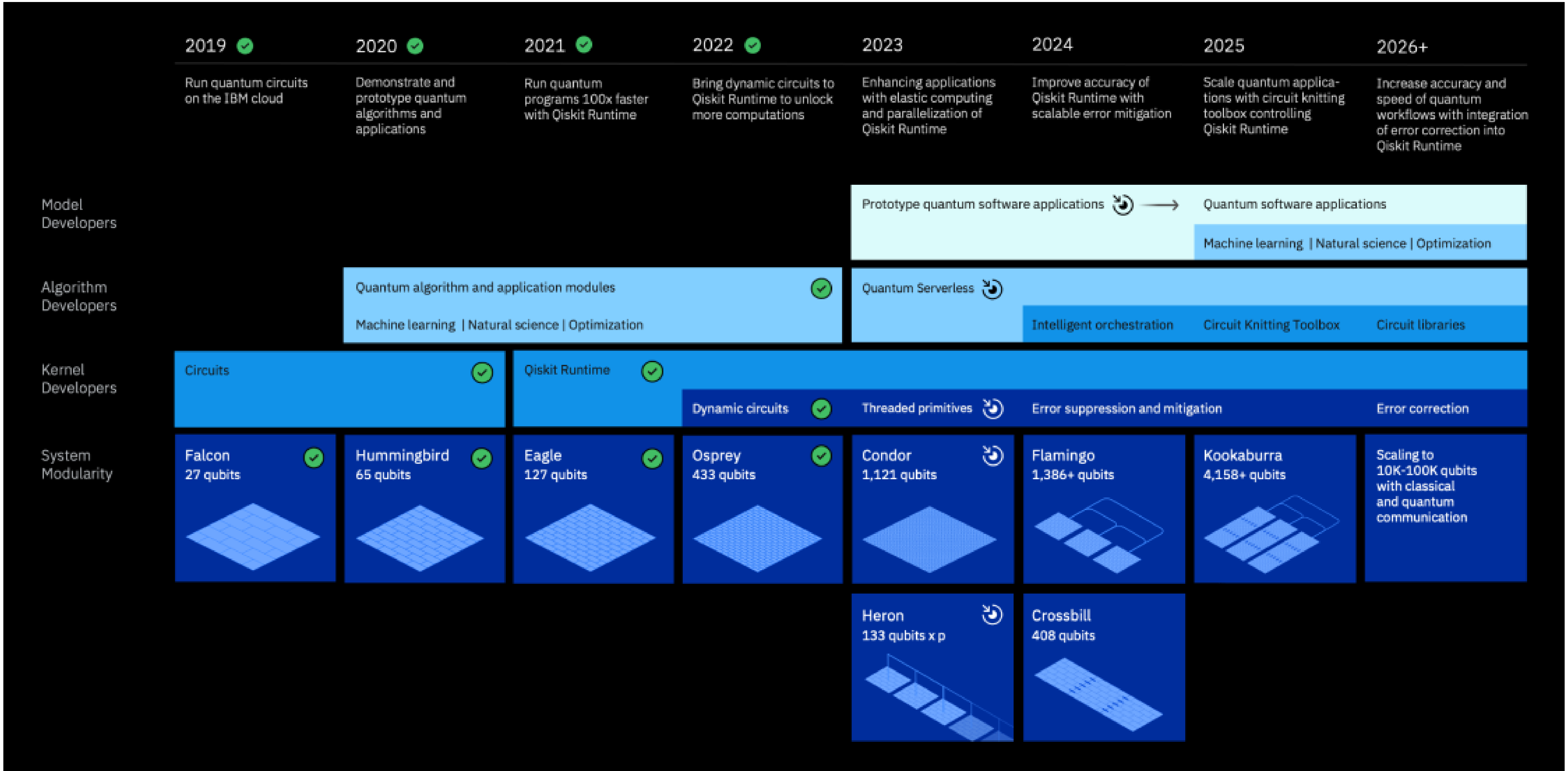
A quantum computer

- Superconducting 127-qubit quantum processor lattice (IBM).



Courtesy: IBM Quantum

A quantum computer: IBM Roadmap



Experimentation Setup

Translate + Compile

- Used IBM Qiskit framework (Python) to generate and transpile circuits.

- Experiment Setups:
  - Control: Running circuits on IBM's matrix product state (MPS) simulator
  - Independent: Running circuits on 127-qubit IBM Eagle r3 (ibm_brisbane)
  - Trials on 8-bit, 16-bit, 32-bit, 40-bit controlled encoded sequences.

- Circuits Tested:
  - Time-domain comparison with XOR (t dom XOR)
  - Time-domain comparison with Swap Test (t dom SWAP)
  - Frequency-domain comparison with Swap Test (f dom SWAP)

Initial Results: 8 bits

Sequences TTGC and TGCT are the test sample.

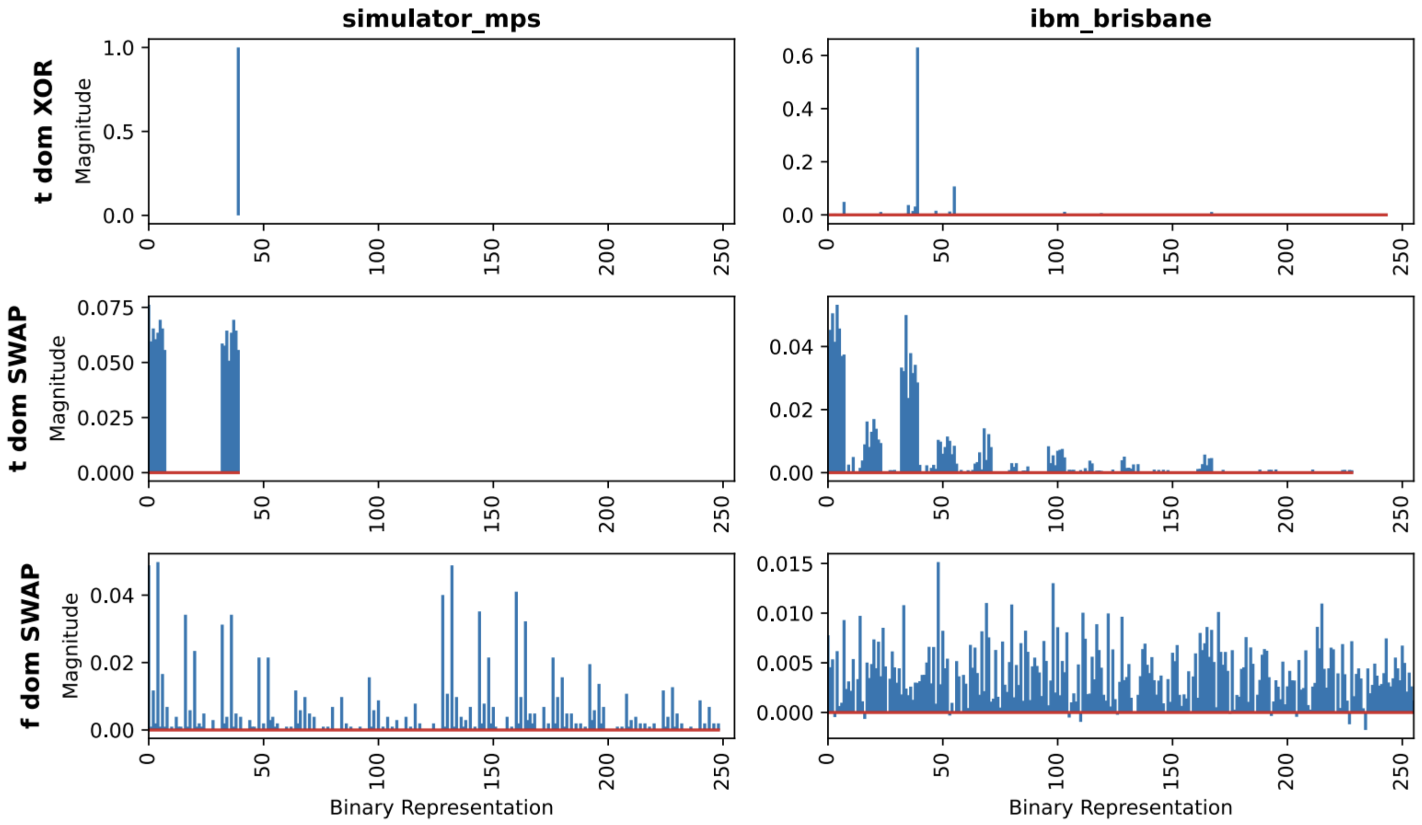


Figure 31: 8-bit String Running Results Comparison

Initial Results: 16 bits

Sequences `ATGCTTGC` and `TGCCTGCA` are the test sample.

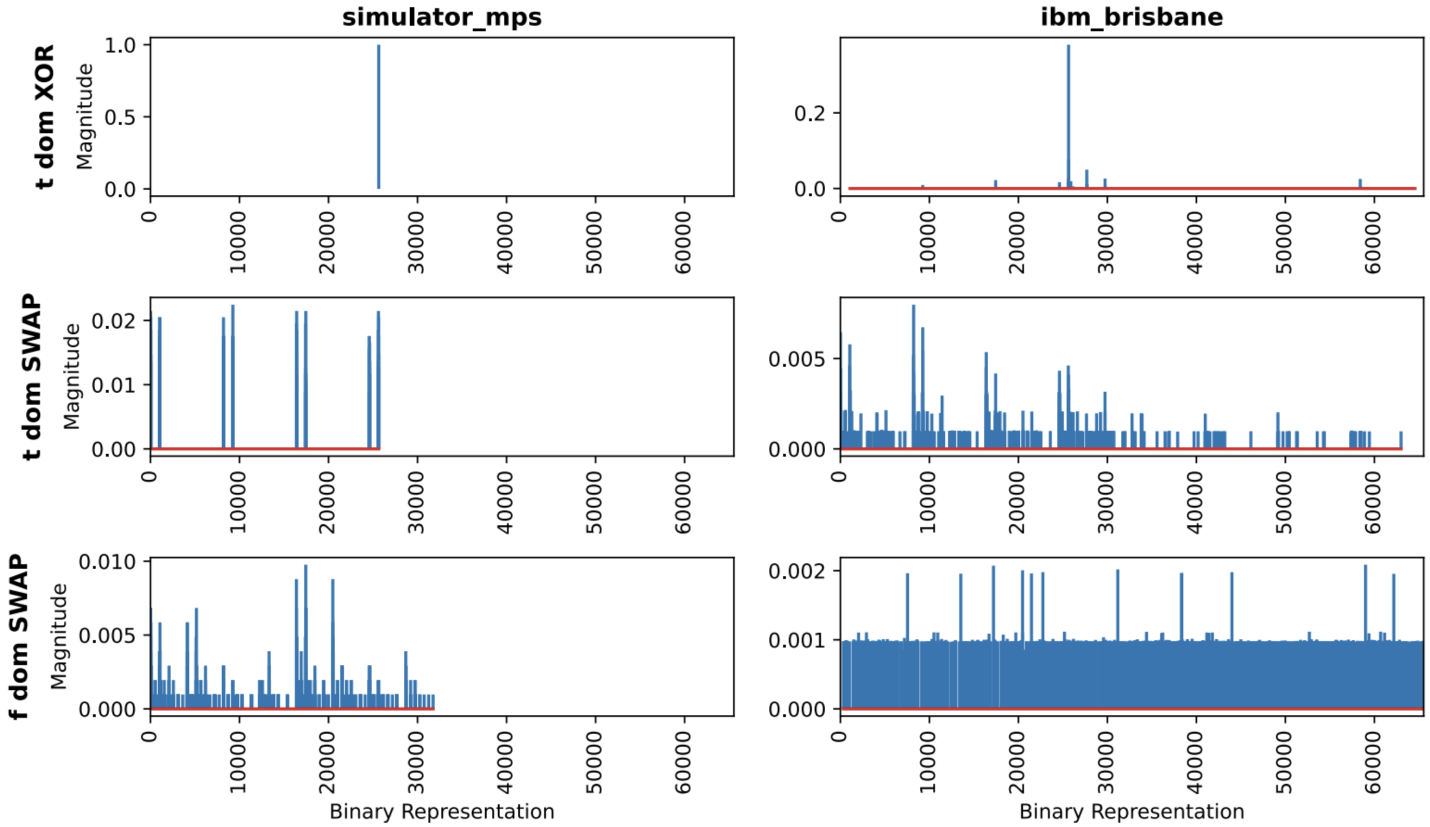


Figure 32: 16-bit String Running Results Comparison

Initial Results: 32 bits

Sequences `ATGCTTGCGGGGGGGG` and `TGCCTGCACGCGCGCA` are the test sample.

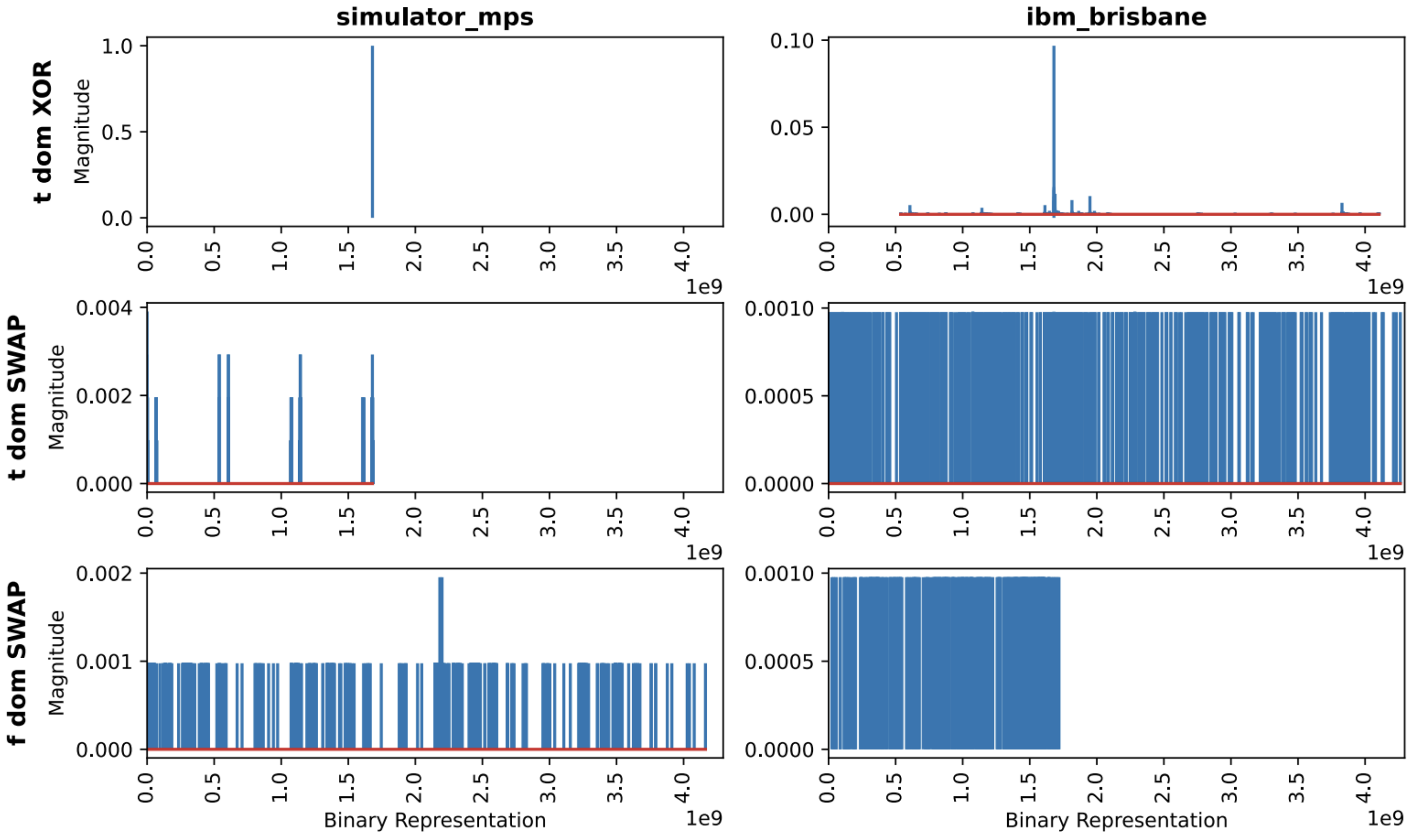


Figure 33: 32-bit String Running Results Comparison

Initial Results: 40 bits

Sequences `ATGCTTGCGGGGGGGACAG` and `TGCCTGCACGCGCGCATCAG` are the test sample.

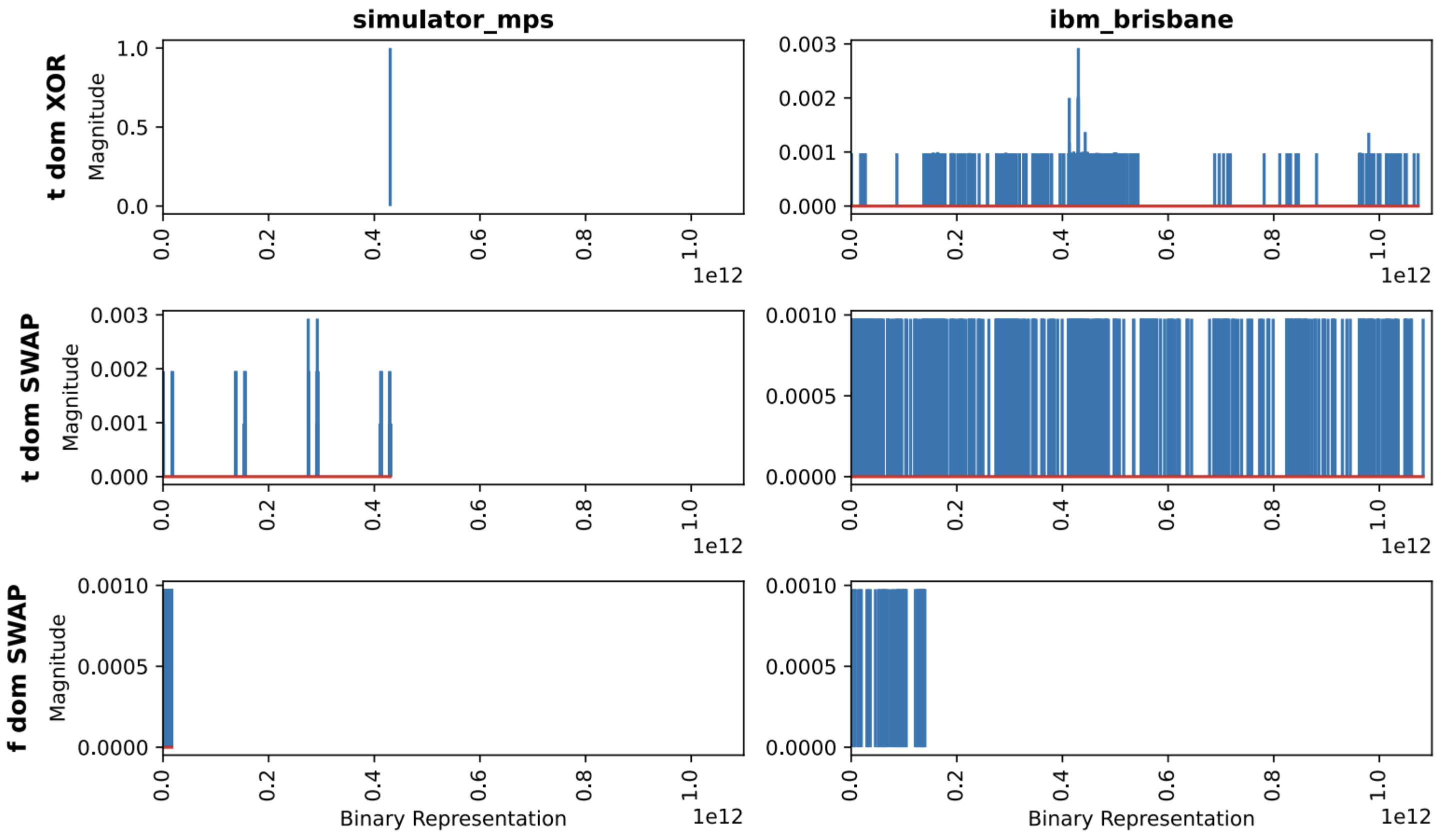


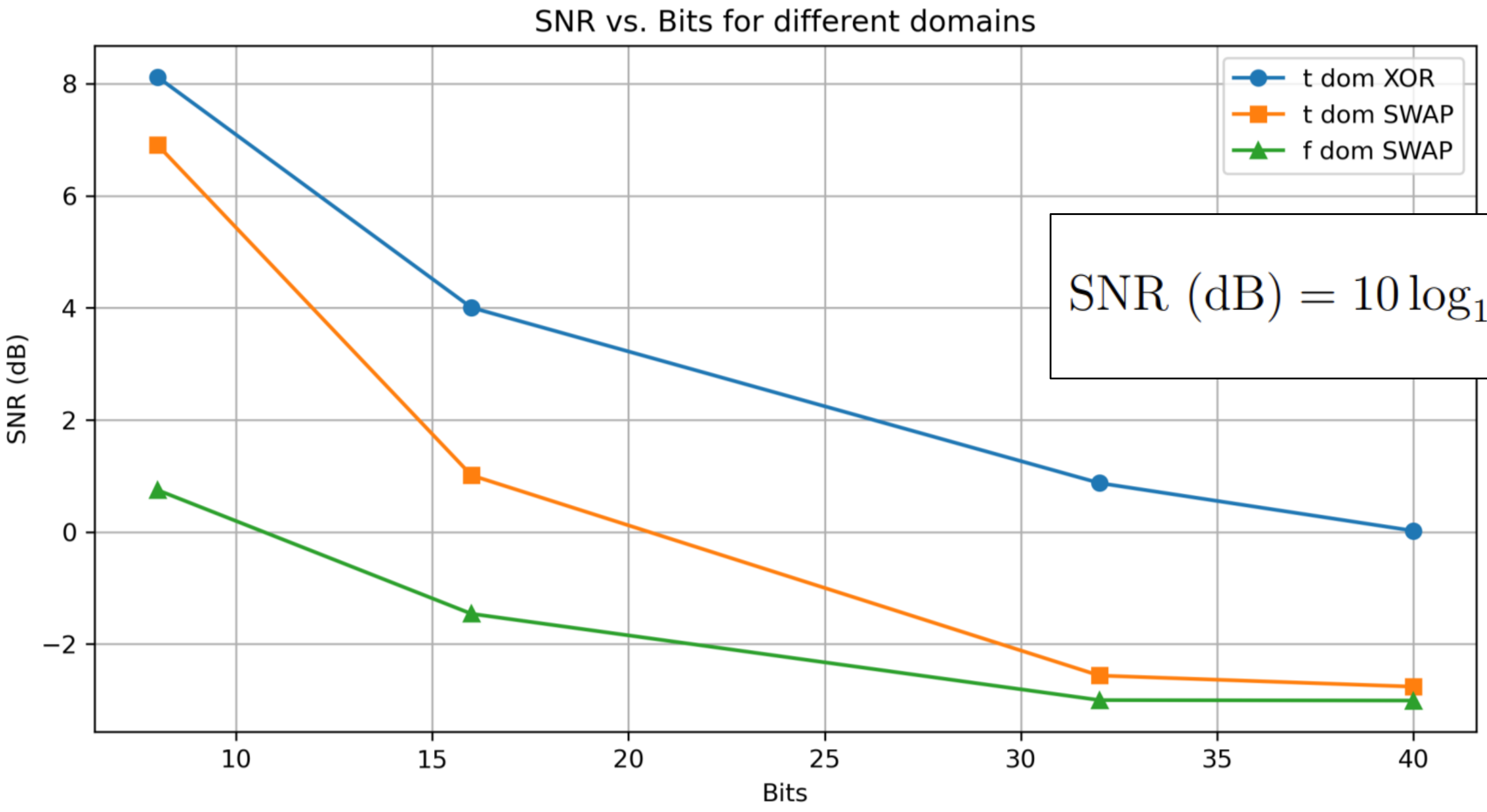
Figure 34: 40-bit String Running Results Comparison

Circuit Optimization

- Circuit & Transpilation Optimization:
  - Remove barrier separating each section entirely (except before measurement).
  - Increase optimization flag from 1 (default) to 3 (maximum).

- Sampler Primitive Improvement:
  - Increase sampling shot counts from 1,024 shots to 10,000 shots.

Noise Analysis



$$\text{SNR (dB)} = 10 \log_{10} \frac{\sum A_{\text{signal}}^2}{\sum A_{\text{noise}}^2}$$

Optimized Results: 8 bits

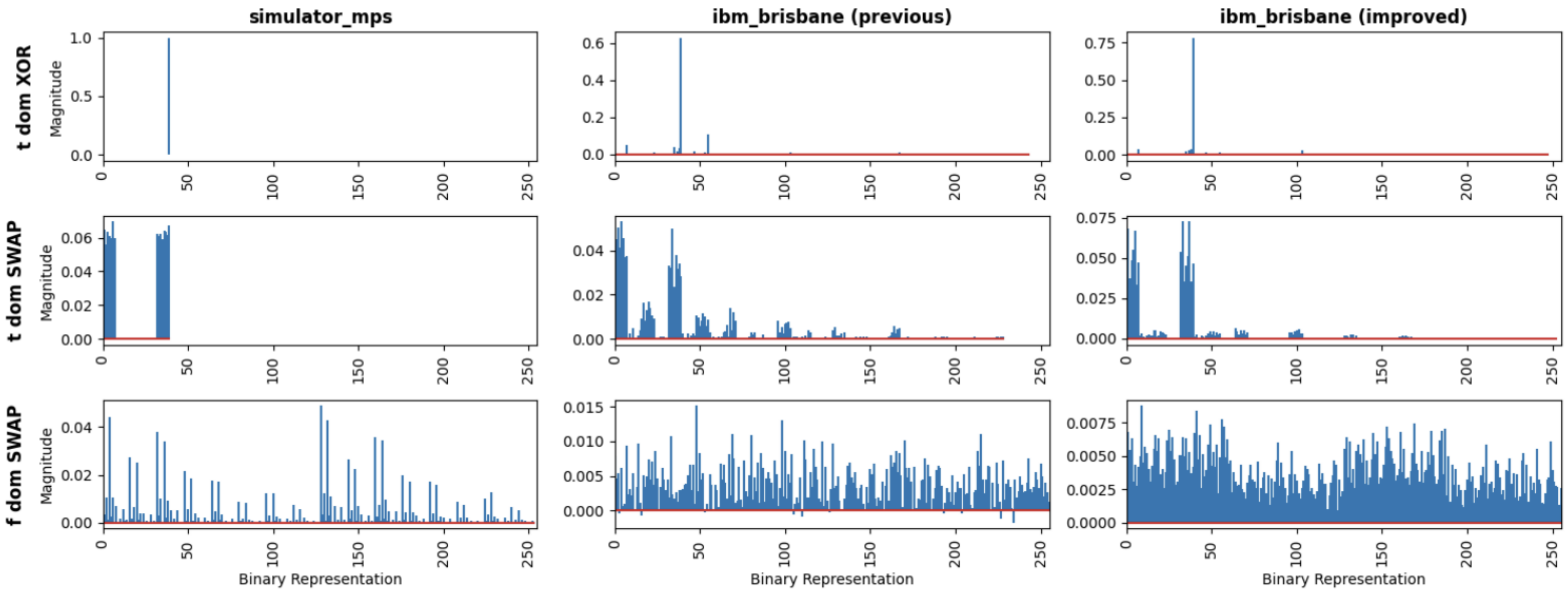


Figure 37: Quasiprobability Distribution Comparison (8 bits)

Optimized Results: 16 bits

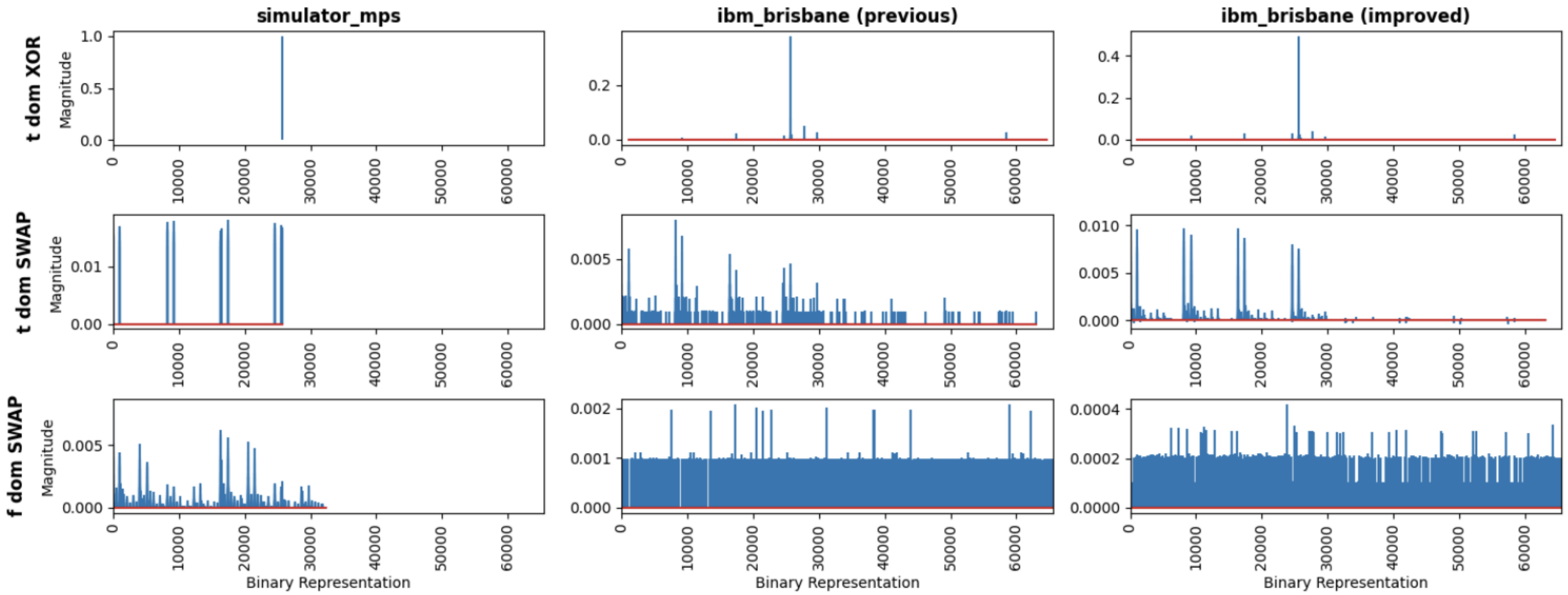


Figure 38: Quasiprobability Distribution Comparison (16 bits)

Optimized Results: 32 bits

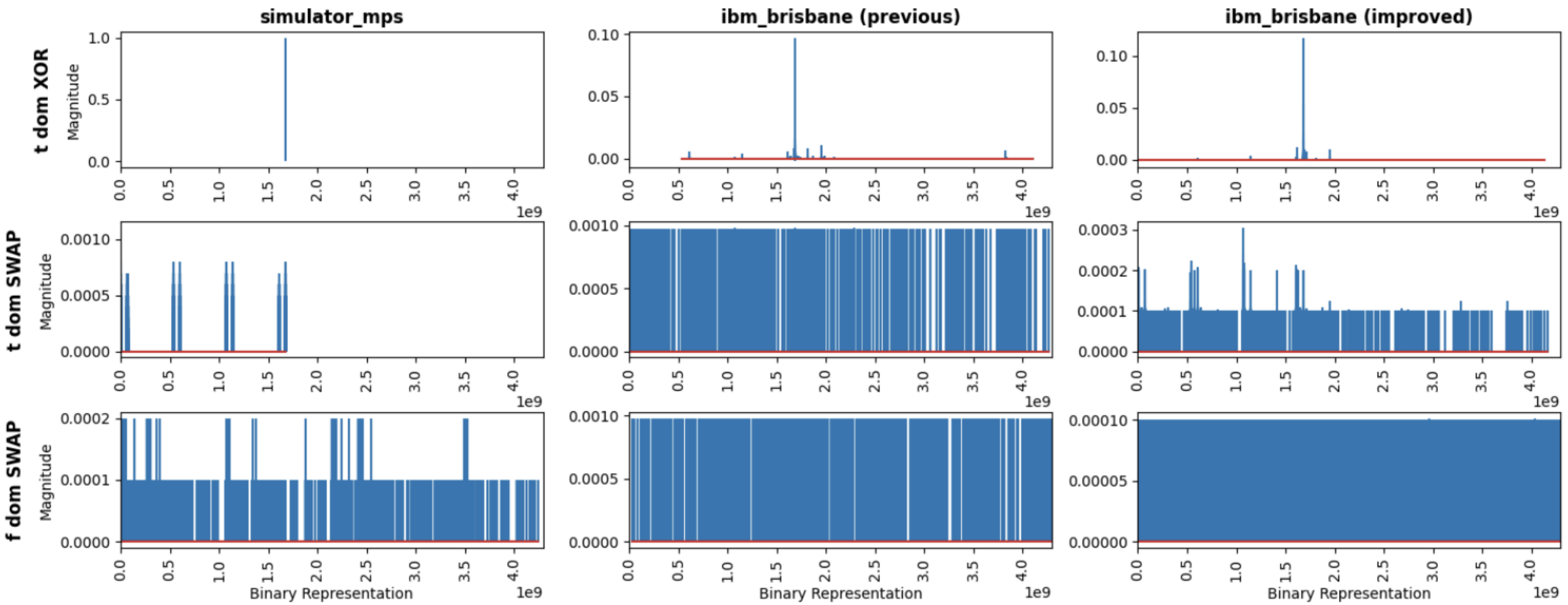


Figure 39: Quasiprobability Distribution Comparison (32 bits)

Optimized Results: 40 bits

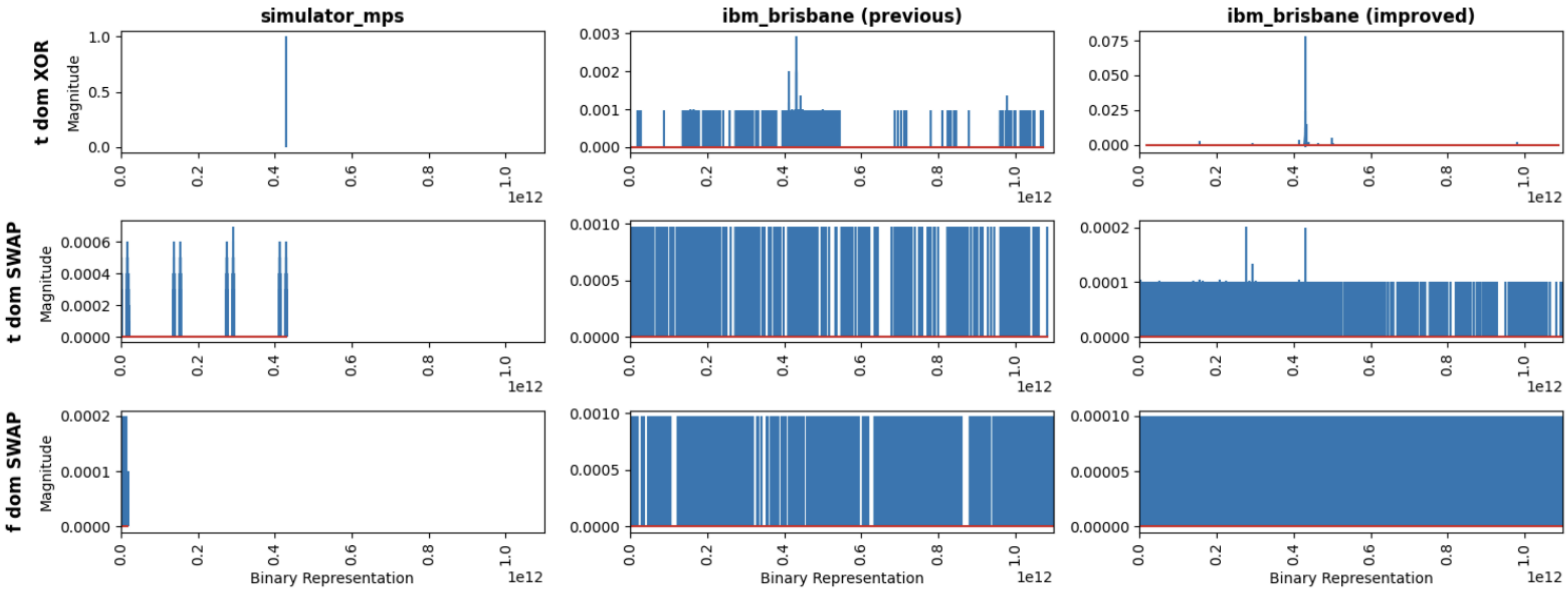


Figure 40: Quasiprobability Distribution Comparison (40 bits)

Summary

- Limited technology at this time.
  - Device noise, measurement error, etc.
  - Hope for future advancements

- Many potential alternatives in numerous research, this is only one of the approaches.

Further Research

- Mitigating Noise
- Interpreting QFT Result
- Alternative Problem Statements
  - Energy-Based Models
  - Graph-Theoretic Approaches
  - Quantum Machine Learning
- Quantum RNA Folding
- Motif Finding+
  - Algorithms proposed in this project may be more suitable for Motif finding problem.

References

- See the full report for more details.
- Visit **vt.in.th/quantum** for further readings, files and this slide.

vt.in.th/quantum

- More on quantum computing: Qiskit and other reading.