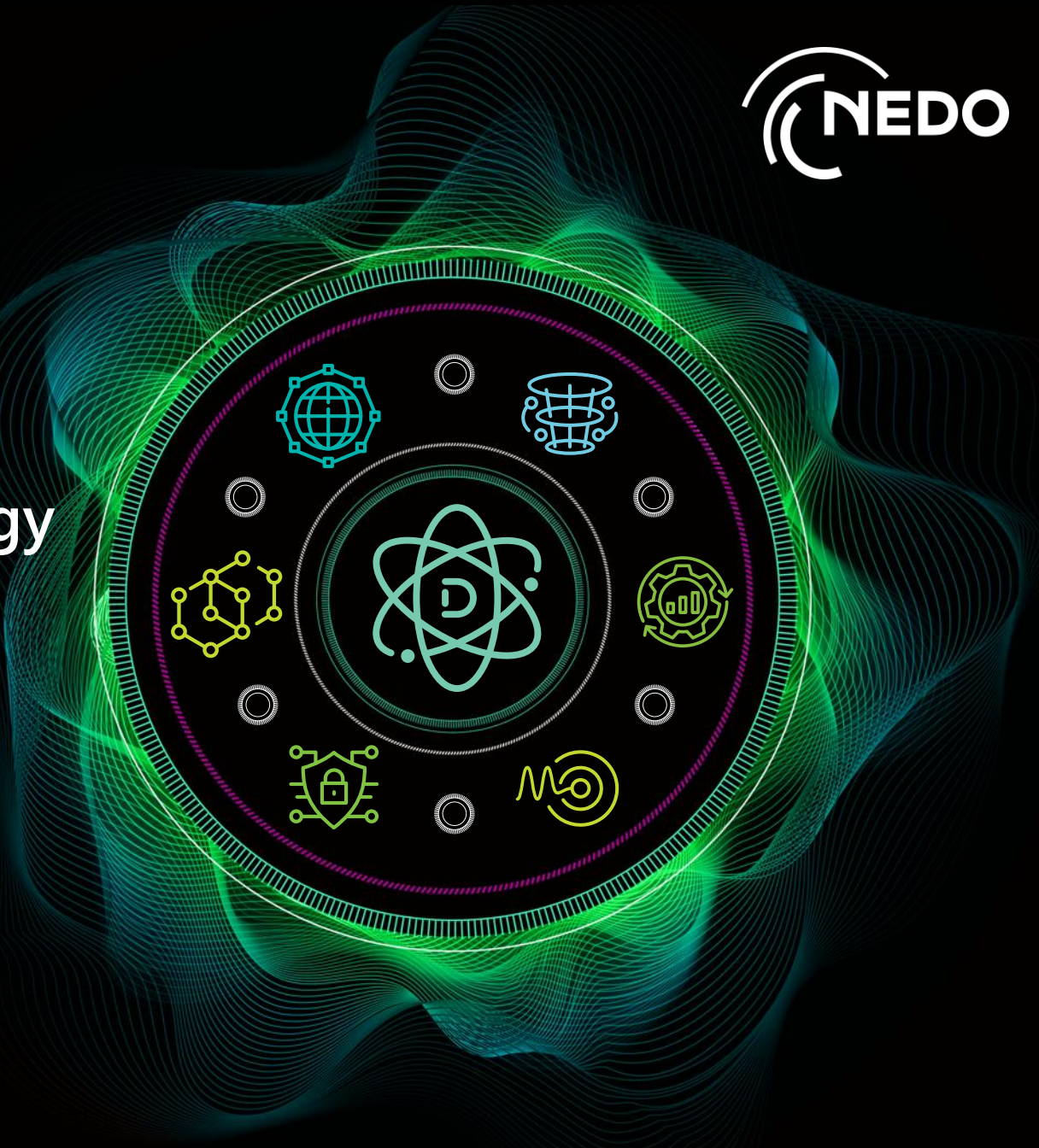
Quantum Computing Use Cases

Development of Large-Scale Molecular Computation Technology through Quantum–Classical Integration

IBM × RIKEN × Cleveland Clinic



New Energy and Industrial Technology Development Organization (NEDO)

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Validation

Industry	Drug Discovery and Healthcare
Process	lead search and optimization
Method	Simulation
Category	Gate*

Background

- Drug discovery faces the challenge of requiring substantial time and cost. In this context, **if combinations of proteins and drug candidates can be evaluated computationally and binding strength can be predicted, this may help reduce the time and cost of experiments**
- However, **this requires both accuracy close to experimental values and computational scalability to handle large molecular systems with thousands of atoms**
- Conventional computational methods have **faced a trade-off between methods that can handle relatively large systems but have limited accuracy, and methods that offer high accuracy but are too computationally demanding.** To address this, an approach was considered in which molecules are divided into smaller fragments and computed using a combination of quantum computers and classical supercomputers

Issues and motivation to be solved

- The aim of this study **is to enable the computation of large biomolecules within practical time by combining quantum computers and supercomputers**
- This **required maintaining sufficient accuracy after dividing molecules into smaller parts while reducing computational cost, as well as an efficient way to execute complex processing across quantum and classical computing resources**
- In this study, **these key challenges were addressed through lower-scaling EWF fragment construction, improved accuracy with TrimSQD, GPU-accelerated Selected-Basis Diagonalization, and an automated workflow**

References: News release on Cleveland Clinic, RIKEN, and IBM being selected as finalists for the 2026 ACM Gordon Bell Prize(https://jp.newsroom.ibm.com/2026-09-09-cleveland-clinic,-riken-and-ibm-team-advance-to-finals-for-2026-acm-gordon-bell-prize)

*Gate（gate-based）: A computing approach in which operations are applied sequentially to qubits to perform calculations. Similar in concept to logic circuits in classical computers, it can address a wide range of problems.

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Problem setting as a quantum computer

- In this study, **the quantum computer does not solve the entire molecule on its own. Instead, the molecule is first divided into multiple smaller parts, and the quantum computer samples the information needed for calculation for the parts where quantum treatment is particularly important**
- **The results obtained are then combined with calculations on the supercomputer side to evaluate the total energy and binding strength of the system**
- In other words, **the quantum computer is used not as a replacement for CPUs or GPUs, but as a complementary computational resource responsible for part of the overall workflow**
  - ✓ Specifically, the molecule is decomposed into fragments using EWF, quantum circuits are constructed for each fragment, and repeated measurements are performed on the QPU to sample electronic configurations
  - ✓ For the resulting samples, error mitigation, subspace diagonalization, and subspace expansion are performed on the classical side to obtain fragment energies and 2-RDMs. These are then recombined to determine the total-system energy and binding energy
- In the experiments, **two 156-qubit QPUs were used, with up to 94 qubits employed. A total of 21,006 circuits were executed over more than 239 hours, and 3.0 × 10^9 measurement outcomes were collected**

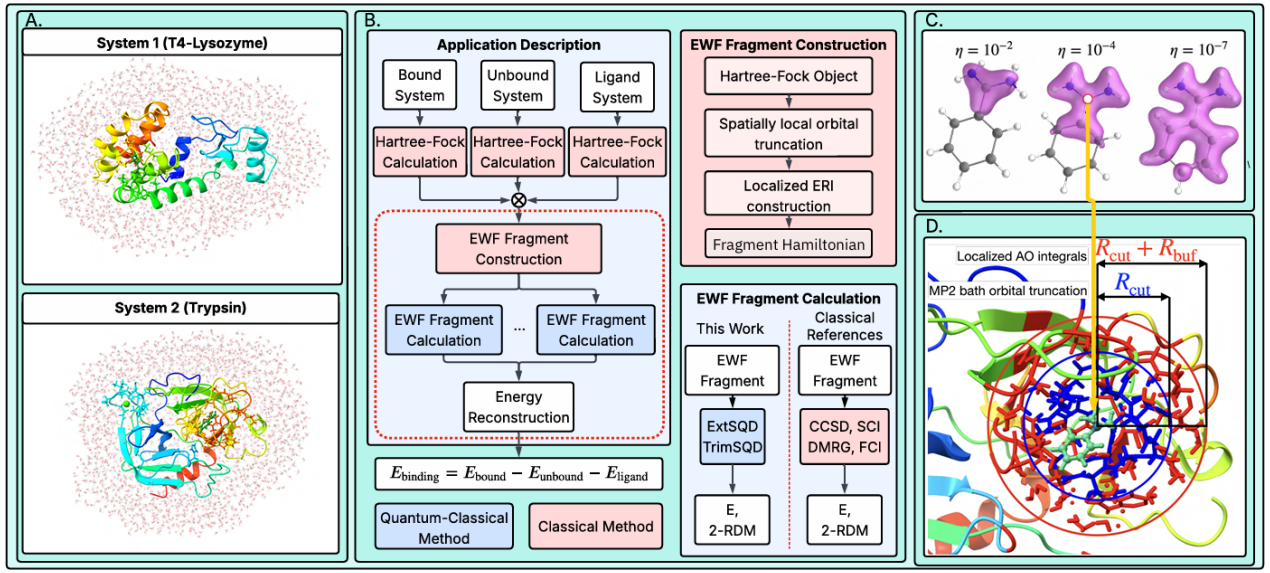


Figure: Overall flow of quantum–classical computation for large-scale protein–ligand systems
A shows the two protein–ligand complexes studied. B shows the overall computational flow through binding energy evaluation. C shows fragment representations according to the bath truncation threshold. D shows lower-scaling fragment construction using localized orbitals and localized ERIs. The red dashed frame indicates the scope covered by the automated workflow

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Expected business benefits

- This study presents **a computational foundation for advancing the evaluation of binding between proteins and drug candidates in drug discovery with higher accuracy and at larger scale**
  - ✓ **HQC calculations were carried out for protein–ligand complexes containing 11,608 and 12,635 atoms, representing an expansion of more than 40 times in system size compared with the prior 303-atom Trp-cage example**
  - ✓ In addition, **the energy difference between HQC and the reference classical calculation for the largest fragment improved from 21 mHa for Trp-cage to 0.10 mHa for trypsin, corresponding to up to 210 times higher accuracy**
  - ✓ Furthermore, the automated workflow established an end-to-end framework covering computation, monitoring, rerun, and fault recovery across QPU, CPU, and GPU resources. For the mixed-basis calculation of the T4-Lysozyme system, an end-to-end execution time of 62.4 hours was reported
- This may **strengthen the ability to computationally assess interactions between drug candidates and target proteins in advance and contribute to more efficient drug discovery research**
- In addition, by automating processing across quantum computers and supercomputers, the study also showed a foundation for moving beyond one-off demonstrations toward more continuous research operations

Method	Benchmark system	Atoms	Active space	Embedding (largest HQC)	Features	HQC error‡ (largest HQC)
SQD	[4Fe-4S]	28	$(54e, 36o)$	N/A	1. ansatz-based circuit 2. closed-loop parametrization 3. configuration carryover 4. Selected basis diagonalization	250 mHa*
ExtSQDrift	$C_{13}Cl_{12}$	15	$(46e, 50o)$	N/A	1. random time-evolution circuits 2. ExtSQD	75 mHa
EWF-ExtSQD	Trp-cage	303	$(1, 158e, 919o)$	EWF $(34e, 33o)$	1. ansatz-based circuit 2. classical parametrization 3. configuration carryover 4. ExtSQD	21 mHa†
EWF-TrimSQD STO-3G basis	trypsin benzamidine	12,635	(43,858e, 31,795o)	EWF + Sec. IV $(66e, 45o)$	Sec. IV	0.10 mHa†
EWF-TrimSQD STO-3G basis	T4-Lysozyme *n*-butyl-benzene	11,608	$(39, 880e, 28, 844o)$	EWF + Sec. IV $(36e, 35o)$	Sec. IV	0.16 mHa†
EWF-TrimSQD mixed basis§	T4-Lysozyme *n*-butyl-benzene	11,608	$(39, 880e, 29, 455o)$	EWF + Sec. IV $(34e, 42o)$	Sec. IV	2.23 mHa†

Table: Comparison with prior HQC methods in terms of application scale and maximum fragment error

This table shows that, compared with prior HQC methods, this study was applied to larger protein–ligand systems and achieved smaller error in the largest fragment. It organizes the change from 303 atoms to 12,635 atoms and from 21 mHa to 0.10 mHa as an expansion of more than 40 times in system size and up to 210 times improvement in accuracy

References: News release on Cleveland Clinic, RIKEN, and IBM being selected as finalists for the 2026 ACM Gordon Bell Prize(https://jp.newsroom.ibm.com/2026-09-09-cleveland-clinic,-riken-and-ibm-team-advance-to-finals-for-2026-acm-gordon-bell-prize)

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More use cases are available on our website. We invite you to explore them.
https://www.quantum-computing-use-cases.nedo.go.jp/english/

More Use Cases

New Energy and Industrial Technology Development Organization (NEDO)
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This collection of use cases was obtained as a result of the work commissioned by the New Energy and Industrial Technology Development Organization (NEDO) "Cyber-Physical Development Business of Quantum/Classical Hybrid Technology/Study of Use Case of Quantum Technology" and the “Post-5G Information and Communications System Infrastructure Reinforcement R & D Project (Quantum Industrialization)/Comprehensive Study for Promoting the Industrialization of Quantum Computers”.