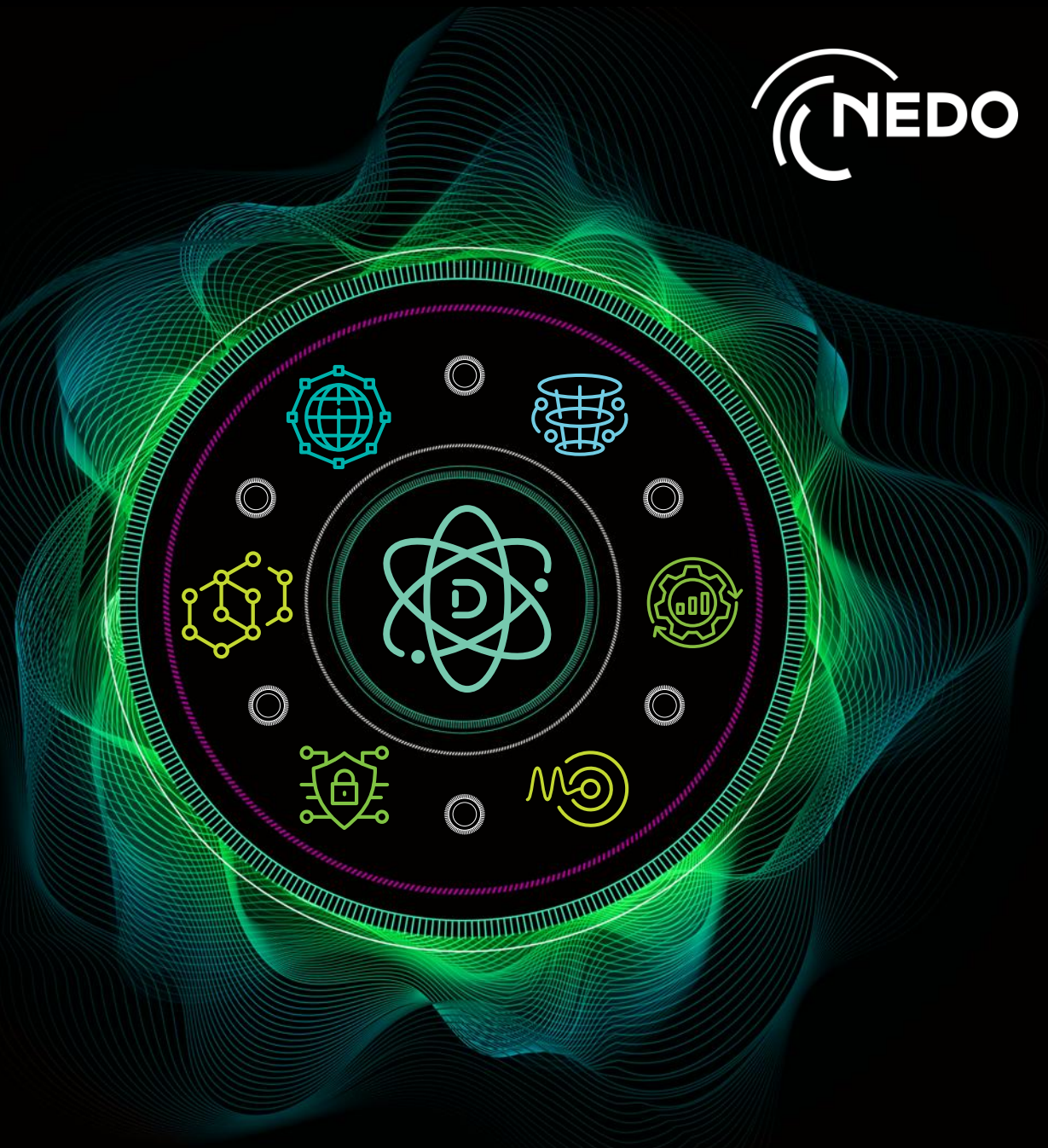
Quantum Computing Use Cases

Molecular simulations of the electronic structure of drug-metabolizing enzymes

Boehringer Ingelheim



New Energy and Industrial Technology Development Organization (NEDO)

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Concept

Industry	Drug Discovery and Healthcare
Process	research and development
Method	Simulation
Category	Gate*

Background

- The development of innovative new drugs for diseases with significant unmet medical needs is a process requiring huge budgets and a time span of ~10 years, in which **molecular simulations are required in the R & D phase to understand the molecular states (electronic states in molecules) of molecules related to disease mechanisms (targets) and compounds that are effective against targets (leads).**
- Identification of energetically stable structures and molecular states through high-precision simulations of materials with complex molecular structures will facilitate accurate understanding of target molecules and compounds and accelerate the drug development process.

Issues and motivation to be solved

- On the other hand, **when a classical computer such as a supercomputer is used, if the accuracy of the simulation is increased (the number of electrons in a molecule = the number of orbitals), the calculation time becomes enormous,** and **the accuracy is lowered so that the calculation can be made in a realistic time.**
  - ✓ In classical calculations, increasing the number of orbits increases the computational complexity exponentially and requires more computational resources to obtain accurate results.
- Therefore, against the potential of molecular simulation, due to the increase in necessary computer resources, **utilization of molecular simulation for understanding molecular states is limited** such as target molecules at the stage of drug discovery.
- **Boehringer Ingelheim worked with Google to** estimate **the machine resources needed for molecular simulations to understand the electronic structure of CYP (cytochrome P450), a drug-metabolizing enzyme involved in the breakdown of drugs into the body.**
  - ✓ **CYP (cytochrome P 450)** is a biologically important enzyme, **a drug-metabolizing enzyme that plays an important role in drug metabolism and detoxification,** and the chemical intermediates involved in the catalytic cycle of CYP **have very complex electronic structures.**

Reference: GeneQuest "What is CYP (drug-metabolizing enzyme) " (https://www.pnas.org/doi/full/10.1073/pnas. 2203533119) and" What is CYP (drug-metabolizing enzyme) " (https://genequest.jp/glossary/cyp#:~:text=CYP%E3%81%A8%E3%81%AF%E3%80%81%E3%82%B7%E3%83%88%E3%82%AF%E3%83%AD%E3%83%A0P450,%E3%81%99%E3%82%8B%E3%81%A8%E8%A8%80%E3%82%8F%E3%82%8C%E3%81%A6%E3%81%84%E3%81%BE%E3%81%99%E3%80%82)

*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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Concept

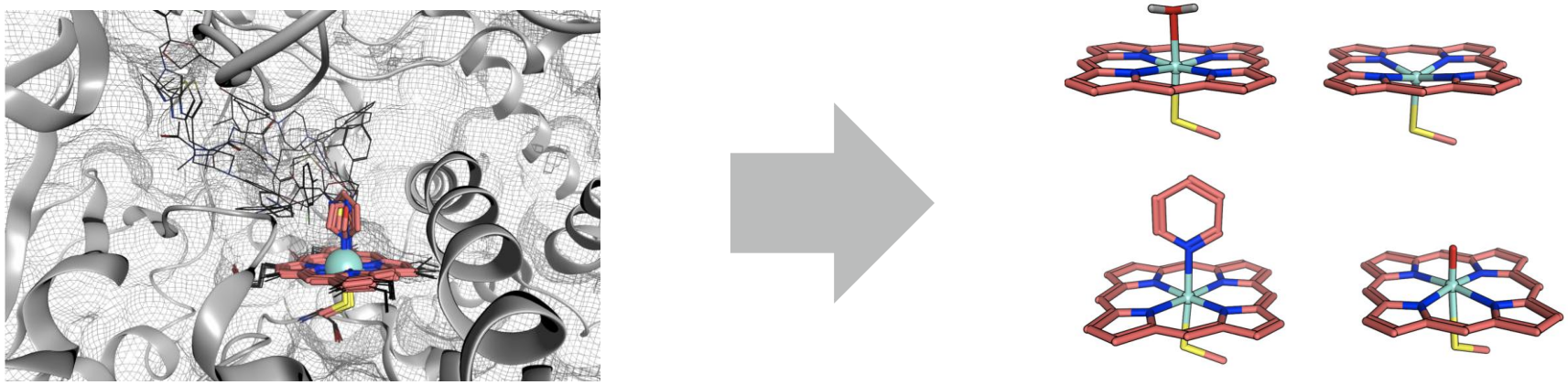
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Problem setting as a quantum computer

- **This demonstration is expected to be used in the lead search phase of drug discovery and medical research and development.** * Toward **understanding the electronic structure of CYP (cytochrome P 450), we estimated the resources required for molecular simulations using a CPU-based classical computer and a quantum computer.**

*Since CYP is a drug-metabolizing enzyme involved in the breakdown of drugs that enter the body, it is assumed that CYP is not a target molecule that causes disease but a lead that exerts an effect on the target.

- For classical computers, simulation by density matrix renormalization group is assumed, and **for quantum computers, simulation using FTQC and quantum phase estimation (QPE) algorithm** is assumed.



Cytochrome P450 enzymes to be calculated
Proteins which are intrinsically complex electronic structures (left), and simple model systems (right) for quantum computer calculations.

Reference: PNAS "Reliably assessing the electronic structure of cytochrome P450 on today's classical computers and tomorrow's quantum computer"(https://www.pnas.org/doi/full/10.1073/pnas. 2203533119)
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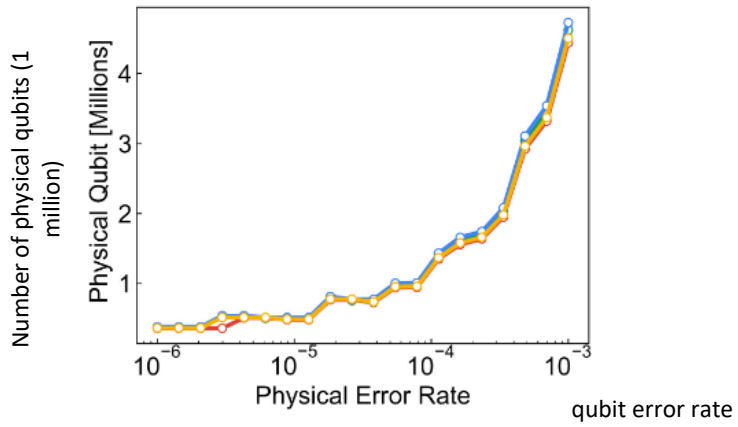
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Expected business benefits

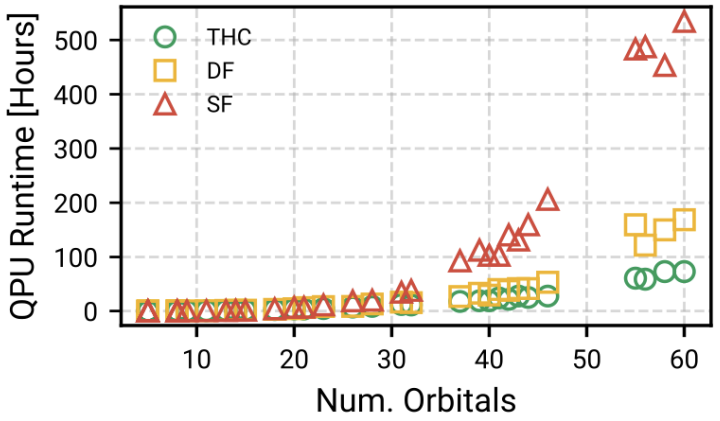
- **Molecular simulation using a classical computer requires several years of computation time for the largest model (58 orbitals) and high accuracy (M=3000).**
  - ✓ M in the right table is an approximate parameter in quantum chemical calculation, and the larger the parameter, the higher the accuracy, but the higher the calculation load.
- The quantum computer **predicts that the largest model of an enzyme (cytochrome P450) can be simulated with THC in less than 100 hours of quantum computing time.**
  - ✓ THC is a tensor factorization scheme that affects resource estimation in quantum computers and is the least computationally expensive.
  - ✓ **FTQC, assuming a realistic error rate (0.1%), would require approximately 5 million physical qubits**



Physical qubit requirements for computation

	G ($M = 1500$)	X ($M = 1500$)	X ($M = 3000$)
CPU time (hrs)	1800	4570	36564
Memory (Gb)	48	87	348
Disk (Gb)	235	572	2288

Estimated resources required for computation on classical computers
(G: 43 orbitals, X: 58 orbitals)



Estimated resources needed for computation on a quantum computer

*Quantum bit error rate is assumed to be 0.1%

*Markers are results at specific value settings

- SF: Single factorization is a basic method of decomposing a tensor into a single factor.
- DF: Double factorization is a method of decomposing a tensor into two factors.IT decomposes tensors more efficiently than single factorization and reduces computational costs.
- THC: The tensor hypershrinkage scheme is method that reduces the computational cost most and is an advanced decomposition method that shrinks tensors in multiple dimensions.

Reference: PNAS "Reliably assessing the electronic structure of cytochrome P450 on today's classical computers and tomorrow's quantum computer"(https://www.pnas.org/doi/full/10.1073/pnas. 2203533119)
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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

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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”.