The Historical Background of Quantum Mechanics

From the late 19th to the early 20th century, physicists developed quantum mechanics while studying phenomena that classical mechanics could not explain. In 1897, J.J. Thomson discovered the electron through cathode ray experiments, revealing that atoms are composed of smaller particles [1]. Later, Rutherford discovered in 1911 through the gold foil experiment that the atom consists of a nucleus concentrated in the center and electrons orbiting around it [2]. In 1900, Max Planck, in the process of solving the black-body radiation problem, proposed that energy is emitted in discrete units (quanta). Subsequently, in 1905, Albert Einstein explained the photoelectric effect, demonstrating that light can behave as particles (photons).

In 1913, Niels Bohr proposed the hydrogen atom model, asserting that electrons can move along specific orbits corresponding to energy levels [3]. Following this, in 1924, Louis de Broglie suggested that matter, including electrons, can possess both particle and wave properties [4]. This was confirmed in 1927 by the Davisson-Germer experiment, which verified the wave nature of electrons [5]. In the same year, Heisenberg announced the uncertainty principle, stating that position and momentum cannot be simultaneously measured with exact precision [6], suggesting that a probabilistic interpretation is necessary for quantum mechanics.

In 1926, Schrödinger proposed the famous wave equation, establishing a mathematical framework for quantum mechanics that describes the state of electrons probabilistically [7]. In 1935, the Einstein-Podolsky-Rosen (EPR) paradox argued that quantum mechanics is incomplete, raising the issue of quantum entanglement [8]. Later, through research such as Bell's theorem in 1964, the non-locality of quantum mechanics was proven, laying the foundation for modern quantum information theory.

The History of Quantum Computing Development

In 1982, Richard Feynman pointed out in his paper "Simulating Physics with Computers" that it is difficult to simulate quantum systems with existing classical computers [9], proposing a new computational paradigm utilizing quantum

mechanical principles [10]. This soon became the conceptual basis of today's quantum computers. Subsequently, in the process of investigating problems where quantum computing has a clearer computational advantage over classical computing, David Deutsch and Richard Jozsa proposed the Deutsch-Jozsa Algorithm in 1992, which demonstrated that a quantum computer can determine whether a specific function is uniform much faster than a classical computer [11]. This is one of the first instances that proved quantum computers can perform calculations faster than existing computers [12].

In 1994, MIT professor Peter Shor developed Shor's Algorithm, demonstrating that quantum computers can efficiently factor very large numbers [13]. This algorithm led to the significant result that RSA cryptography could be threatened, and it became a major driving force in subsequent quantum computer research [14]. In the same year, Bell Laboratories researcher Lov Grover proposed Grover's Algorithm, a type of quantum search algorithm, which showed that quantum computers can perform calculations much faster than classical computers in database searches, optimization problems, and more [15].

In 1998, IBM researchers implemented a 2-qubit quantum algorithm for the first time using a nuclear magnetic resonance (NMR) quantum computer, and later succeeded with a 3-qubit experiment as well [16]. To date, various physical implementation methods such as superconducting qubits and ion traps have been studied [17].

Currently, quantum computer research has entered the Noisy Intermediate-Scale Quantum (NISQ) era, and quantum processors containing hundreds to thousands of qubits, but with incomplete error correction, have been developed [18]. As of 2024, research is underway to realize quantum supremacy through technologies such as the VQE algorithm and quantum machine learning, even in the still-lacking hardware environment [19]. Quantum computers have not yet reached a fully practical stage, but with continued research, the development of a complete quantum computer with powerful computational capabilities is expected in the future [20].

Innovative New Drug Development Utilizing Quantum Computing

The new drug development process requires enormous computational costs, which are a major cause of high costs and long development periods [21]. In the stages of discovering new drug candidates and analyzing genomes, millions of compound libraries must be virtually screened. Predicting protein-drug binding structures requires molecular dynamics (MD) and molecular mechanics (MM) simulations, which are computationally burdensome [22]. In addition, the process of drug design and optimization requires evaluating various chemical structures and making predictions using QSAR and machine learning models. The selection of final candidate substances requires complex calculations for ADMET (absorption, distribution, metabolism, excretion, toxicity) analysis and evaluation of drug efficacy and safety [23]. According to a 2020 study, the median cost of launching a new drug on the overseas market was estimated to be $985 million (₩1.4314 trillion) [24].

In addressing this issue, quantum computing and artificial intelligence (AI) are gaining attention as potentially industry-changing technologies and are expected to play an important role in accelerating the speed of new drug development and reducing costs [25]. Quantum computers are a technology that can revolutionize new drug development, accelerate the search for drug candidates, accurately simulate molecular interactions, and lead the development of personalized treatments [26]. Algorithms such as VQE and Quantum Approximate Optimization Algorithm (QAOA) can be used to calculate the physical and chemical properties of molecules more accurately [27]. Optimizing drug design is possible through molecular dynamics simulations that are up to 10^4 times faster than conventional computers.

In fact, companies such as D-Wave Systems and Biogen are conducting new drug development research using quantum annealing [28], and IBM is applying quantum computers to molecular interaction simulations for cancer treatment development in its European laboratory [29]. These technological advancements accelerate the speed of new drug development, improve therapeutic effects, reduce medical costs, and enable more patients to receive economically effective treatments. Ultimately, this contributes to the achievement of UN Sustainable

Development Goal (SDG) #3 (Good Health and Well-being) and is expected to open new possibilities for the treatment of intractable diseases such as cancer and Alzheimer's disease.

Case Study I: Quantum Computing and Innovation in New Drug Development[1)]

Quantum computing excels in solving high-dimensional and multi-variable problems in drug development, such as calculating the stability and binding affinity of substances, and predicting toxicity. In particular, in analyzing ligand-protein binding interactions, quantum technology helps accurately model drug-protein binding mechanisms in real biological environments.

Traditional new drug development is time-consuming and expensive due to the immense complexity of intermolecular interactions. It is particularly difficult to analyze the complex 3D structure and binding pockets of proteins, where the role of water molecules acts as a critical variable. Water molecules penetrate into the protein, changing its shape and stability, and also affect how ligands bind. The process of analyzing this is called protein hydration analysis and requires a large amount of computation.

Recently, the French quantum computing company Pasqal and the American pharmaceutical company Qubit Pharmaceuticals developed a hybrid quantum-classical approach that predicts the water distribution inside proteins using classical algorithms (3D-RISM) and precisely arranges the positions of water molecules using quantum algorithms.[2)] In this process, the principles of superposition and entanglement in quantum computing are used to perform calculations much faster and more accurately than conventional computers. This study is the first case to propose and validate a hybrid quantum-classical algorithm that can analyze 'the distribution of water inside proteins' during the protein-drug binding analysis process.

Proteins are large molecules that perform various functions in the body, and abnormal modifications of proteins can cause diseases (e.g., cancer). New drugs

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1) https://www.weforum.org/stories/2025/01/quantum-computing-drug-development/

2) Pasqal. "Quantum Algorithm Can Help Drug Discovery." *Pasqal*, https://www.pasqal.com/news/quantum-algorithm-can-help-drug-discovery/. Accessed 16 Feb. 2025.

for treating diseases are usually developed as small molecules called 'ligands,' which bind to specific parts of harmful proteins to inhibit their action. However, the protein-drug binding process is not a simple chemical reaction but is strongly influenced by the internal cellular environment (especially water molecules). Water molecules can exist in the 'pockets' inside proteins, and these water molecules greatly affect the structure of the protein and the binding affinity of drugs. Therefore, accurately identifying the location and number of water molecules inside proteins is essential for effective new drug development. Although current protein hydration analysis technology using computer simulations is advancing, analyzing the water distribution in the deep (occluded pockets) inside proteins presents several problems that are difficult for conventional computers to solve.

First, there are limitations to X-ray crystallography techniques. X-ray crystallography is a technique that identifies the three-dimensional structure of a protein by analyzing the diffraction pattern of X-rays irradiated onto a protein crystal. However, it lacks the resolution to accurately determine the location of water molecules in narrow spaces or deep pockets inside the protein. In addition, the location of water molecules can be calculated using classical molecular dynamics (MD) simulations, but this is very computationally expensive and time-consuming.

Quantum computers have excellent parallel processing capabilities that consider many combinations simultaneously, so they can calculate the locations where water molecules are likely to exist inside proteins more quickly and accurately. The research team conducted experiments on Fresnel 1 (a neutral atom-based quantum computer) using Major Urinary Protein-1 (MUP-1) protein as a model. The experimental results showed a high degree of agreement between the location of water molecules calculated by the quantum algorithm and the results of existing classical simulations. However, since the number of qubits in current quantum computers is limited, further research is needed on expansion and error correction, as well as optimization of quantum algorithms so that they can be applied to larger systems.

Case Study II : Research on Protein Structure Prediction Using Quantum Computing[3)]

A recent study published in the *Journal of Chemical Theory and Computation* by researchers from the Cleveland Clinic and IBM presented the possibility of protein structure prediction using quantum computing. Proteins perform functions in a folded state with a specific three-dimensional structure, and this structure plays an important role in how diseases progress and in developing treatments. Therefore, accurately predicting protein structures is essential for establishing disease treatment strategies.

Previously, computer-based prediction techniques have been used, and recently, machine learning (ML)-based models, especially deep learning technologies such as AlphaFold2, have made great progress. However, machine learning models rely on experimentally revealed protein structure data, so they have limitations in predicting gene mutations (mutated proteins) or proteins that are significantly different from existing data. On the other hand, another way to predict protein structures is to calculate all possible protein folding pathways through physical simulations. However, this method is an extremely difficult problem even for classical supercomputers. For example, a complete search of a protein consisting of 100 amino acids would require as much computation as the age of the universe.

To overcome these computational limitations, the research team developed a hybrid framework combining quantum and classical computing. Quantum computing was used to address areas that are difficult for classical computing to solve, such as structural disorder, mutations, and the physical complexity of the folding process, which occur as the size of the protein increases. In this paper, the research team used the 7-amino acid catalytic P-loop structure of the Zika virus NS3 helicase as an experimental target and calculated the minimum energy state (energy conformation) using a quantum algorithm. In other words, the process of predicting the backbone folding of the protein is the most computationally demanding step, and this was performed by a quantum computer.

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3) Doga, Hakan, et al. "A Perspective on Protein Structure Prediction Using Quantum Computers." *Journal of Chemical Theory and Computation*, vol. 20, no. 9, 14 May 2024, pp. 3359-3378. https://pubmed.ncbi.nlm.nih.gov/38703105/. Accessed 16 Feb. 2025.

Subsequently, a classical algorithm was used to add the side chains of the protein based on the results calculated by the quantum computer, and the precise structure was corrected using molecular dynamics.

The results showed that the quantum-classical hybrid approach was more accurate than the classical physics-based model method. In addition, it showed more accurate results in small protein predictions than AlphaFold2. AlphaFold2 has strengths in large proteins, but it has limitations in new structures because it relies on training data.

This study is considered an important example of demonstrating the potential of quantum computing to be used in new drug development and protein research. Dr. Bryan Raubenolt (Cleveland Clinic) and Dr. Hakan Doga (IBM), who led the research, explained that this study would be the first step in applying quantum computing to protein structure prediction. Currently, there is a problem that it is difficult to predict larger proteins due to the limitations of quantum computer hardware, and optimization of quantum algorithms is needed to solve this problem. In particular, error correction and efficient computational method improvements are required, and additional research should be conducted to ensure that quantum computing can be effectively applied in real-world new drug development environments.

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