IEEE Access
Multidisciplinary ⋮ Rapid Review ⋮ Open Access Journal

Received 31 January 2024, accepted 20 February 2024, date of publication 11 March 2024, date of current version 13 May 2024.

Digital Object Identifier 10.1109/ACCESS.2024.3376408

SURVEY

Recent Advances in Quantum Computing for Drug Discovery and Development

GAUTAM KUMAR[1], SAHIL YADAV[1], ANIRUDDHA MUKHERJEE[1], VIKAS HASSIJA[1], AND MOHSEN GUIZANI[2], (Fellow, IEEE)

[1]School of Computer Engineering, Kalinga Institute of Industrial Technology, Bhubaneshwar 751024, India
[2]Machine Learning Department, Mohamed Bin Zayed University of Artificial Intelligence (MBZUAI), Abu Dhabi, United Arab Emirates

Corresponding author: Vikas Hassija (vikas.hassijafcs@kiit.ac.in)

This work was supported by the Mohamed Bin Zayed University of Artificial Intelligence (MBZUAI) under Project 8481000021.

ABSTRACT Preserving human health is of utmost importance, and unrestricted availability of medications is essential for overall wellness. Pharmaceuticals, which consist of a wide range of therapeutic substances utilized to diagnose, treat, and improve various diseases and conditions, play a crucial part in healthcare. However, the drug research and development process is widely recognized for its lengthy duration, demanding nature, and substantial expenses. To enhance the effectiveness of this complex process, interdisciplinary groups have converged, giving rise to the field known as ''Bioinformatics''. The emergence and future advancements of Quantum Computing (QC) technologies have the potential to significantly enhance and accelerate the complex process of drug discovery and development. This paper explores various disciplines, such as Computer-Aided Drug Design (CADD), quantum simulations, quantum chemistry, and clinical trials, that stand to gain significant advantages from the rapidly advancing field of quantum technology. This study explores a range of fundamental quantum principles, intending to facilitate a thorough understanding of this revolutionary technology.

INDEX TERMS Ab initio methods, ansatz, computer-aided drug designing, molecular docking, quantum computing, quantum simulations, virtual screening.

I. INTRODUCTION

The current challenge that confronts us pertains to drug development and discovery. This issue is underscored by the time-intensive and exorbitant nature of formulating effective pharmaceuticals, with costs potentially soaring to a staggering one billion dollars [1]. The urgency to tackle this problem is rooted in historical instances such as the prolonged 35-year endeavor to develop a Malaria cure [2], which resulted in numerous fatalities due to such prolonged absence of a remedy. As a result, there is a pressing need to accelerate the process of drug development while working within constrained timeframes and budgets.

The process of developing drugs is complex and involves several stages, including identifying potential targets, screening for initial compounds, optimizing lead candidates, conducting pre-clinical tests, and undertaking clinical trials [3]. The efforts to leverage artificial intelligence (AI) in overcoming the challenges associated with drug discovery and development face significant obstacles. These challenges comprise issues related to the quality of data, a lack of high-quality information particularly for uncommon diseases, difficulties in modelling the complex nature of biological systems, and the opacity of AI, which can result in safety concerns and potentially inaccurate predictions [4]. Ethical dilemmas may arise due to AI's limitations in modeling biological systems' intricate and dynamic nature, potentially leading to inaccurate outcomes. QC offers a potential solution, leveraging its superiority over classical computers. Quantum computers can tackle problems that even today's supercomputers struggle with. Google's 'Sycamore' system, containing 53 programmable superconducting qubits, achieved quantum supremacy in 2019 [5], [6].

The evolution of QC holds promise for drug discovery and development. Quantum generative models offer advantages by comprehensively covering distributions due to their

The associate editor coordinating the review of this manuscript and approving it for publication was Yifan Zhou.

intrinsic probabilistic nature [7]. Quantum computers excel at molecular simulations, predicting drug behavior and properties, thus enhancing in-depth drug understanding as they reinforce drug design with more precise predictions [8]. Furthermore, QC accelerates machine learning algorithms by rapidly processing extensive data volumes, managing complex computations, and generating more precise predictions [9]. Quantum computers' speed accelerates solving complex problems compared to traditional methods and AI [10].

The primary motivation behind this research lies in expediting drug development, reducing costs, and redefining the foundational approach in creating new drugs, diverging from conventional methods. QC's unique advantages extend to chemistry simulations [11], opening avenues to explore its potential in medicine. This research delves into quantum computers' capabilities in medicine, analyzing drug behavior under diverse conditions using tailored algorithms.

The organization of this paper is as follows. A summary of previous works, their contribution, and their advantages and disadvantages have been covered under Section II with their core technology being discussed in their work. A basic overview of core and fundamental quantum computing concepts is discussed in Section III. Section IV comprises various steps of simulations in the process and discusses quantum integration at each sub-process. Quantum chemistry is discussed in Section V, which helps cover drug interaction with their target and basic molecular structure. Section VI discusses the complete pipeline of the quantum-enhanced drug development process. Moreover, in Section VII, we discuss the potential use of quantum computers for final stage trial and testing for human use. Despite having numerous advantages, quantum computers still possess various technological and ethical challenges, which are explored in Section VIII. Section IX provides an overview of future prospects and further new applications in the field. Lastly, Section X concludes and summarizes the work of this paper.

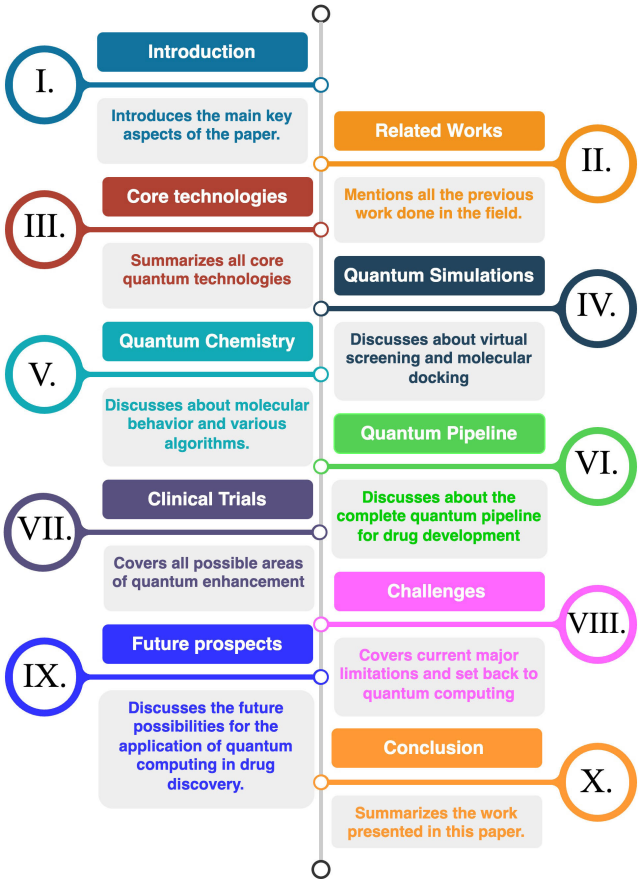


FIGURE 1. Sections of the paper.

II. RELATED WORKS

The field of QC has witnessed remarkable advancements in recent years. Historically, computers were not extensively employed in drug discovery. However, a noticeable paradigm shift has occurred with new terminologies, including CADD, Computer-Aided Molecular Modeling (CAMM), and the overarching concept known as Computer-Aided Drug Discovery and Design (CADDD). Quantum computers are poised to serve as the next frontier for computer-aided design.

Numerous researchers have undertaken extensive investigations in this domain. QC, as a subject, has been under deliberation since the 1980s [15], and a substantial body of research already exists [16]. This section aims to provide compact summaries of key prior works and research papers, offering a comprehensive overview of the extensive groundwork conducted in the field of QC for drug development and discovery.

Wang et al. [3] provide a brief overview of the various steps involved in the process of drug development and design. Their work explores steps such as quantum simulation, molecular docking and Quantitative structure-activity relationships (QSAR). Their paper discusses how quantum computers can combine the knowledge of bio-informatics, cheminformatics, and medicinal chemistry precisely and concisely.

Cao et al. [17] highlights a distinctive focus, the exploration of quantum simulations for molecular system detection, which sets this approach apart from existing traditional methods for drug development. They also support the idea that a hybrid quantum-classical approach should be employed for quantum simulation and quantum machines to develop a fault-tolerant system capable of overcoming the limitations of current quantum computers, which are still in the development phase.

QC significantly enhances the development of genetic algorithms through its evolutionary iterations, as discussed by Duela et al. [12]. This paper delves into the synergistic relationship between quantum theory and genetic programming, highlighting how they mutually benefit each other's advancement. On one hand, quantum computers offer increased computational capabilities; on the other, genetic programming contributes an element of true randomness. This combination opens up new frontiers in both fields, allowing for more complex and efficient problem-solving strategies.

Lau et al. [13] discuss the concept of HypaCADD, a hybrid classical-quantum workflow method for determining ligand

TABLE 1. Related works.

Author	Summary	Advantages	Disadvantages	Quantum Technologies
Wang et al. [3]	This paper discusses the integration of bio-informatics with QC, focusing on the potential for improved data analysis and processing.	- Discussion of QSAR prediction model and usage in drug discovery - Improved accuracy and speed of bio-informatics computations	The entanglement of many qubits at once is currently a significant challenge, limiting practical applications.	- Molecular Docking - Quantum Simulation - QML
Duela et al. [12]	Provided an overview of quantum-assisted genetic algorithms and their applications in various fields.	- Complimenting of QC and genetic algorithms for optimized solutions - Potential to solve complex problems more efficiently	- All currently used encryption mechanisms would be rendered obsolete - High computational cost for implementation	- Quantum Genetic Algorithm - Quantum Gates - Quantum Annealing
Lau et al. [13]	Provides a brief overview of HypaCADD and its applications in QC.	- Provides an overview of all basic topics and applications concisely	It does not discuss the limitations of current quantum technologies.	- QML - Qubit-Rotation Gates - Quantum Fourier Transform
Mustafa et al. [14]	Discuss various algorithms used, such as Variation Quantum Eigensolver (VQE), in QC for bio-informatics.	Discusses - Protein folding - Various quantum algorithms and their applications in bio-informatics	It does not provide a brief discussion of quantum theory and its principles.	- VQE - Quantum Annealing - Quantum Fourier Transform
Our work [2024]	This paper provides an in-depth analysis of the state of QC in bioinformatics.	- Comprehensive overview of QC - Analysis of current research and future trends	It does not provide in-depth knowledge about the physical implementation of quantum computers.	- VQE - QML - Quantum Simulation

binding to proteins, and also considers genetic mutations. They discussed how HypaCADD helps combine classical docking and molecular dynamics with Quantum Machine Learning (QML) to get a report on the impact of mutation. This paper outlines a neural network constructed using qubit-rotation gates. It maps a classical machine learning module onto QC. This is explained by taking a case study of the novel coronavirus (SARS-CoV-2) protease and its mutants. This paper also states how QML performs on par with classical computing, if not better. It summarises a successful strategy for leveraging QC for CADD by HypaCADD.

Mustafa et al. [14] discuss using QC to understand the concept of protein folding. Understanding the concept of protein folding is relatively hard because of the difficulty of understanding and finding a stable shape with increased size. A moderate protein consists of around 100 amino acids, and there is a certain point where a classical computer cannot devise a solution for the protein's structure or properties. This paper also discusses how two different algorithms, Variational Quantum Eigensolver (VQE) and Quantum Approximate Optimization Algorithm (QAOA), are used using Qiskit Nature.

In conclusion, the research mentioned above have significantly contributed to drug discovery development using quantum computers. They have all provided various aspects towards improvement at various steps in the process. They also mentioned various techniques and algorithms to ease the process and reduce the cost of production.

III. BRIEF ANALYSIS OF CORE CONCEPTS OF QC TECHNOLOGY

Currently, we have supercomputers that can perform any assigned task very quickly, but the scenario has changed in today's world, where data is vast and time is limited. For effective analysis, we need even more powerful computers to reduce the time required [18], and one of its potential answers to this requirement is quantum computers. Although quantum computers are still in their early stages, they are highly expected to solve these problems as they can leverage principles like superposition and entanglement, presenting exponential speedup and transformative potential [19]. The field of QC and all of its technology, in itself, is new to the world, so it becomes crucial to understand its fundamentals. For that very reason, we delve into this section, grasping

the core concepts to the fullest for a better understanding of this technology. The first and foremost difference between classical and quantum computers is bits and qubits. Classical computers use bits (binary digits) as 1s and 0s. In contrast, quantum computers use quantum bits or qubits. These qubits represent 0, 1, or any superposition of these states [20]. Here, qubits leverage quantum superposition and entanglement, allowing quantum computers to process vast amounts of data simultaneously, leading to exponential speedups compared to classical computers.

A. SUPERPOSITION

The principle of superposition is foundational; it allows qubits to exist in multiple states simultaneously, increasing computational power exponentially compared to classical bits and ultimately enabling parallel computation. This principle underpins algorithms such as Grover's algorithm for unstructured search problems and Shor's algorithm for integer factorization, both of which leverage the inherent parallelism of quantum states to achieve a computational speedup unattainable by classical counterparts. For an illustrative analogy, one might consider Schrödinger's cat thought experiment [21], wherein the feline subject is presumed to exist in a coherent superposition of orthogonal states - namely, "alive" $|0\rangle$ and "dead" $|1\rangle$ - until an observation induces the collapse of the wavefunction. Mathematically, the state of a qubit in superposition can be expressed as a linear superposition of its basis states, represented by complex probability amplitudes. The probability of observing the qubit in a given state post-measurement is determined by the modulus squared of these amplitudes, as formulated by:

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

where $|\psi\rangle$ denotes the quantum state of the qubit, and α and β are complex numbers such that $|\alpha|^2 + |\beta|^2 = 1$. Upon measurement, the qubit's wavefunction collapses to one of the basis states $|0\rangle$ or $|1\rangle$, with respective probabilities $|\alpha|^2$ and $|\beta|^2$, as depicted by:

$$P(|0\rangle) = |\alpha|^2, \quad P(|1\rangle) = |\beta|^2. \tag{2}$$

This non-classical correlation between the states, a characteristic of quantum entanglement, is central to the computational advancements brought about by quantum processing.

B. QUANTUM ENTANGLEMENT

To signify the peculiar role in quantum particle correlation, Erwin Schrödinger coined the idea of quantum entanglement [22]. Quantum entanglement and teleportation plays a significant and vital role as the backbone of various quantum technologies, such as quantum communications, quantum networks, and quantum computations [23]. Quantum entanglement is a phenomenon where two quantum particles become deeply interconnected so that the state of any particle cannot be described independently without considering the state of the other particles. $|\psi\rangle = \frac{1}{\sqrt{2}}(|\uparrow\rangle_A \otimes |\downarrow\rangle_B - |\downarrow\rangle_A \otimes |\uparrow\rangle_B)$. The entangled state $|\Psi\rangle$ signifies the joint quantum state of two particles, where $|0\rangle_A$ and $|1\rangle_A$ represent possible states for particle A, and $|0\rangle_B$ and $|1\rangle_B$ represent states for particle B. The tensor product $\otimes$ combines these states, and the coefficient $\frac{1}{\sqrt{2}}$ ensures proper normalization, adhering to quantum probability principles.

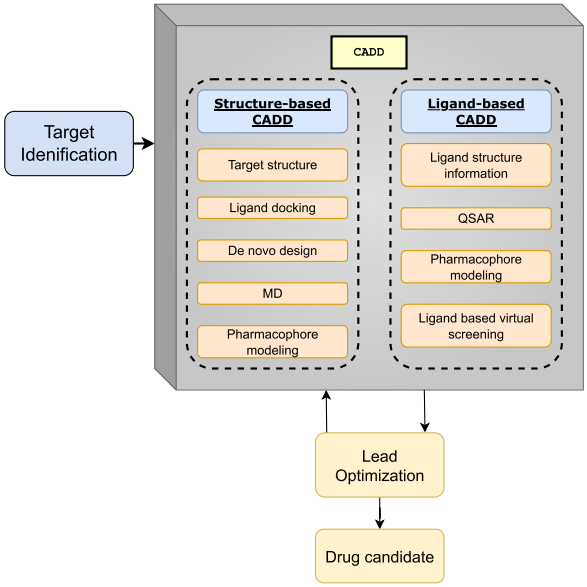


FIGURE 2. Types of computer aided drug designing.

C. QUANTUM GATES

The primary driver behind the development of quantum computers is their superior computational capabilities, realized through the manipulation of quantum bits, or qubits [24]. Quantum gates manipulate data to carry out complex computation tasks. They are analogous to classical logic gates, which are responsible for manipulating logic bits. This means that quantum gates are building blocks in QC circuits; they manipulate qubits, the fundamental units of quantum information [25]. Quantum gates are represented as unitary matrices, which are reversible, meaning that if a quantum gate is applied to the qubits and its inverse is applied, it will return to its original state [26]. Quantum gates also normalize the possibilities to 1. When a quantum gate is applied, all amplitude components may change, but the overall summation of all possibilities of all potential outcomes remains constant. Some of the most famous examples of quantum gates are Pauli Gate, CNOT Gate, Swap Gate [27], Hadamard Gate [28], and Toffoli Gate [29].

D. QUANTUM INTERFERENCE

Quantum interference, an intrinsic phenomenon in quantum mechanics, arises when the probability amplitudes of two quantum states converge. This process is analogous to classical wave interference and is described by the principle of superposition. Constructive interference occurs when the

phases of the amplitudes align, enhancing the probability ($\Psi_{constructive} = \Psi_1 + \Psi_2$), while destructive interference occurs when the phases are opposed, diminishing the probability ($\Psi_{destructive} = \Psi_1 - \Psi_2$). In QC, qubits leverage this principle; aligned states ($|0\rangle$ or $|1\rangle$) result in constructive interference, amplifying computational pathways, whereas opposing states lead to destructive interference, effectively pruning the computational landscape. Exploiting these interference patterns enables quantum algorithms to outperform their classical counterparts in specific problem sets. Despite its potential, mastering quantum interference for robust quantum information processing remains a formidable challenge in advancing quantum technologies.

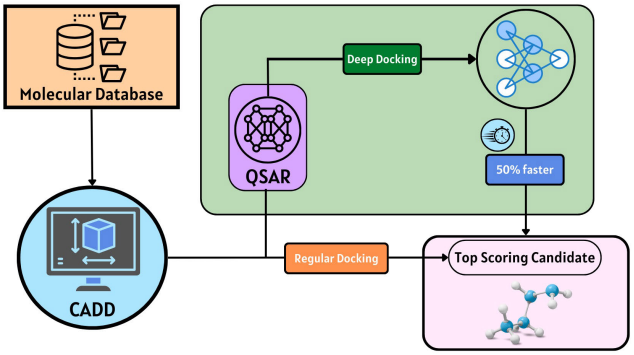


FIGURE 3. Computational steps in molecular docking.

IV. QUANTUM SIMULATIONS IN DRUG DISCOVERY

Traditionally, drug discovery starts with identifying a disease-linked molecule (target). Then, researchers screen vast libraries or use computer models to find compounds (hits) that interact with the target. These hits are further refined (hit-to-lead) to improve their potency, minimize side effects, and ensure they are absorbed and eliminated correctly. This multi-stage process, though successful, can be slow and expensive.

Despite the success of traditional drug discovery, it still struggles to simulate complex molecules, leading to inaccurate predictions of how drugs interact with targets. This can cause wasted time, unforeseen side effects, and limitations in exploring new drug possibilities.

Quantum simulation is a technique that possesses the ability to solve complex issues faced by traditional methods. It is a computational technique that uses various high-level, complex quantum algorithms to simulate and model complex molecule and material designs [30]. It uses QC to model molecular interactions accurately. By simulating various quantum phenomena such as superposition and entanglement, researchers can potentially predict drug behavior, accelerating the drug discovery process and enabling the design of more effective pharmaceuticals with fewer experimental iterations. The advantages of quantum simulation primarily benefit large-scale molecules, though they are not restricted to them; small-scale molecules can also gain from it. Below are some of the benefits:

- **Accurate Modeling:** Quantum simulation accounts for the quantum behavior of molecules, enabling more accurate predictions of their interaction with each other and with biological systems [31].
- **Understanding Complex Reactions:** Quantum simulation can provide insights into chemical reactions and processes vital for drug development, such as enzyme interactions and protein folding [32].
- **Optimising Drug Candidates:** Quantum simulations can predict the properties of potential drug candidates, helping researchers identify molecules that are likely to have the desired therapeutic effects [33].
- **Reducing Experimental Efforts:** Quantum simulation can guide experimental efforts by providing insights into which compounds are worth synthesizing and testing in the lab [34].
- **Personalized Medicine:** Quantum simulations can help tailor drug treatments to individual patients by predicting how specific molecules will interact with a person's unique biological makeup [35].

In summary, quantum simulation promises to transform drug discovery by providing a more accurate and efficient way to model and understand complex molecular interactions [36]. As QC technology matures, it could also significantly accelerate the development of new drugs and treatments. The following subsections explain the various steps involved in drug discovery simulation, which has the potential to be enhanced by QC.

A. MOLECULAR DOCKING AND QC

In molecular biology, for drug design, it is vital to predict the interaction between ligands (typical small molecules) and receptors (usually proteins) for the formation of a stable complex. Molecular docking is a tool widely used for the prediction of these complexes [37]. Ligands typically bind within the binding site of receptors, and docking tools provide the best optimal orientation and conformation from them. These tools offer insights into the ligand's binding affinity and biological activity.

Molecular docking in drug discovery synergistically employs sophisticated computational methodologies, encompassing CADD, QSAR, and advanced deep docking techniques [38]. This integrative computational approach enables a refined analysis of the intricate interactions between small molecules and protein targets. Through the application of these techniques, molecular databases are systematically screened with heightened efficiency, culminating in the identification of top-scoring candidates poised for optimized drug development. The streamlined process, depicted in Fig. 3, underscores the technical prowess of molecular docking, showcasing its ability to expedite the selection of promising drug candidates through a meticulously guided computational exploration of molecular interactions.

First, molecules are selected from a huge pool of databases, and after that, they are employed against CADD. Here, CADD

aims to expedite the identification of molecules with desired pharmacological properties while minimizing the time and cost associated with experimental testing [39]. It encompasses a range of computational techniques, including molecular modeling, virtual screening, molecular dynamics simulations, and more [40]. CADD is divided into structure-based and ligand-based subtypes. In drug discovery, ligand-based methods scrutinize small molecule-protein interactions using quantum algorithms, optimizing drug design. Structure prediction employs quantum models to simulate biomolecular structures, aiding target identification, which is explained in Fig. 2. QC promises a transformative era in intricate molecular analyses.

Molecular docking follows various steps, which are listed below :

1) **Preparation of Ligand and Receptor Structures:** Experimental techniques like X-ray crystallography and NMR spectroscopy provide accurate 3D structures of molecules such as ligands and receptors. In cases where experimental data is unavailable, computational methods can be used to predict the structures of these molecules [41].
2) **Grid Generation and Scoring Function:** Using manual and automated methods, the receptor's binding site is defined where ligands are expected to interact. A grid is generated or created around the binding site to sample different positions and orientations of the ligand. A successful function is established to evaluate the relationship between a ligand and a receptor. The separation energy, which measures the nature of ligand-receptor interaction, is estimated using the established function [42]. A stronger binding similarity is desired, with lower energy values [43].
3) **Search and Docking:** To investigate various conformations, the ligand is positioned into the binding site and repeatedly rotated and translated. The scoring function is utilized throughout this search procedure to evaluate the energy of the ligand in various positions and orientations within the binding site. The placement and orientation of the ligand in the binding site are optimized using a variety of search algorithms, including genetic algorithms and Monte Carlo techniques [44].
4) **Scoring and Ranking:** The computed binding energies of the created ligand conformations are used to rank them. Conformations with the lowest binding energy are considered to have the highest binding affinity and are chosen as potential binding sites [45].
5) **Analysis and Interpretation:** To better understand how the ligand and receptor interact, additional analysis is done on the top-ranked ligand conformations [46]. Types of interactions, such as hydrogen bonding, van der Waals forces, and electrostatic interactions, are identified. The binding postures and interactions between ligands and receptors are visualized using software and visualization tools [47].
6) **Validation and Further Experiments:** Experiments using X-ray crystallography or binding tests can be used to verify the predicted binding postures. If the docking predictions are correct, additional research can be directed towards improving ligands' binding affinity and selectivity, such as structure-based medication design [48].

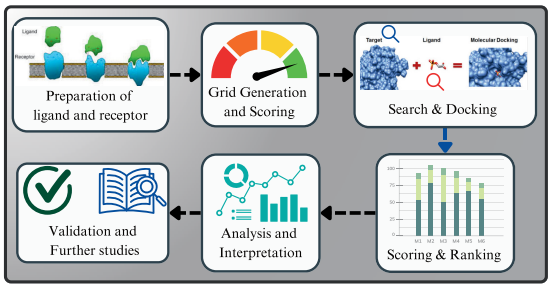


FIGURE 4. Process of molecular docking.

Despite having various advantages molecular docking faces several critical challenges, and the integration of quantum computers holds promise in addressing these issues [49]. One prominent challenge is the treatment of protein flexibility. Classical molecular docking often assumes rigid structures for small molecule ligands and target proteins, even though proteins can undergo conformational changes and exhibit flexibility, influencing binding interactions [50]. Quantum computers offer the potential to model protein flexibility more accurately by considering multiple protein conformations and their energetic contributions, providing a more realistic representation of binding events [51]

Another significant challenge in classical molecular docking is the simplified treatment of solvation effects. The solvent environment plays a crucial role in molecular interactions. However, traditional docking simulations often employ simplified solvation models that may not fully capture the complexities of solvent influences on binding. As examined by Gioia et al. [52], classical docking methods suffer from limitations related to the static or semi-flexible treatment of ligands and targets, neglecting solvation and entropic effects. This deficiency strongly limits the predictive power of traditional docking approaches. Quantum computers can conduct more sophisticated and precise simulations of solvation effects, enhancing our understanding of the stability and energetics of ligand-protein complexes [53].

Molecular docking demands substantial computational resources, particularly for larger and more intricate biomolecular systems [54]. Quantum computers, with their inherent parallelism [55], [56], [57] and efficiency in quantum chemistry calculations, have the potential to accelerate these computations significantly, reducing the time required for molecular docking studies.

Quantum mechanical accuracy is also crucial. While quantum mechanics-based methods offer a more precise

TABLE 2. Advantages of Quantum Simulations.

Benefits of Quantum Simulation	Description
1. Highly accurate predictions	Enhances comprehension of molecular interactions.
2. Insights into chemical reactions	Vital in drug development, including enzyme interactions and protein folding
3. Property forecasting for drugs	Identifies molecules with desired therapeutic effects
4. Streamlined Experimental Efforts	Guided selection of compounds for synthesis and testing.
5. Personalized Medicine	Tailors drug treatments to individual patients based on biological profiles.

description of molecular interactions than classical force fields [54], their computational demands have limited their application to relatively small systems on classical computers [58]. Quantum computers can expand the applicability of quantum mechanical calculations to larger and more biologically relevant systems, thereby enhancing the precision of binding affinity predictions [58].

Furthermore, quantum computers can revolutionize the exploration [59] of chemical space by efficiently sampling a broader range of chemical compounds for potential drug candidates, potentially unveiling novel therapeutic molecules that might be overlooked using classical approaches.

In summary, the integration of QC into molecular docking offers promising solutions to these challenges, advancing the field of drug discovery and development.

B. QML FOR VIRTUAL SCREENING

Virtual screening in drug discovery is the filtering of massive libraries for potential drug candidates using computers. It analyzes the structures of countless molecules to identify those with the potential to interact with a specific disease-linked target. This helps researchers narrow the search and prioritize promising leads for further testing, saving the drug discovery process time and resources.

Traditional virtual screening in drug discovery has various limitations. Simplified models can lead to inaccurate predictions, wasting time on ineffective candidates. These methods can also be computationally expensive and generate many false positives requiring validation. Additionally, exploring the vast chemical space and considering complex biological interactions remain challenges. Quantum simulations offer promise to overcome these limitations, potentially leading to a more efficient and accurate drug discovery process.

To develop potential drug compounds, we need to identify and understand the interaction of a target biomolecule, which can be achieved through virtual screening using QML [60]. QML is an interdisciplinary field that integrates and unites QC and machine learning to address complex problems [61].

Here are the following quantum-enhanced computer technologies that can potentially help to increase the effectiveness of the virtual screening process:

1. **Quantum Simulations:** Simulations of quantum systems have always been significantly faster on quantum computers when compared with classical computers. In drug discovery, accurate modeling of molecular interactions is required, allowing researchers to study various complex biochemical processes. This can be achieved by quantum systems, which are hard to stimulate classically [62].
2. **Quantum Feature Encoding:** The more compact the representation of molecules is, the more efficient and faster the analysis of potential drug candidates. QML can encode various molecular structures and properties in the quantum state [63].
3. **Quantum Neural Networks:** Neural networks can understand and learn the patterns of quantum data that might not be easily perceivable using classical methods. To process quantum data and to perform quantum computations, quantum neural networks or quantum circuits are used [64].
4. **Quantum Kernels:** Quantum kernels are equivalents to classical kernels, which are used in Support Vector Machines (SVMs) in classical machine learning [60]. We can use quantum kernels to capture quantum correlations to increase the accuracy of machine-learning models for drug discovery tasks.
5. **Quantum Molecular Data:** For determination of molecular structures and properties of the complex, we use various processes and data technologies such as Nuclear Magnetic Resonance (NMR), X-ray and crystallography, and QML can be used to improve and increase its efficiency.
6. **Quantum Search Algorithms:** Various quantum algorithms can be applied in this context. For instance, Grover's algorithm can search through an extensive database of potential compounds [65]. These algorithms quickly speed up the process.

QML techniques are expected to save a huge cost and increase time efficiency. A real-life example of this approach was recently seen in research conducted by McKinsey & Company in 2019, which examined and calculated the potential cost and time efficiencies achievable through integrating QC and machine learning techniques in drug research and development. These analyses explored diverse scenarios to estimate the savings that could be realized by adopting these advanced technologies in the pharmaceutical industry [66].

C. QUANTUM ALGORITHMS FOR MOLECULAR DYNAMICS SIMULATIONS

Molecular dynamics simulations (MD) mimic how molecules move and interact. This helps us see how drugs bind to targets in the body. However, traditional MD struggles with complex systems and accuracy. Quantum algorithms, using the power of quantum mechanics, offer a potential solution. They could speed up calculations and improve the accuracy of MD simulations, leading to better drug discovery. While still early days, this combo holds promise for more effective drugs, faster development, and lower costs.

Quantum algorithms for molecular dynamics simulations leverage various QC techniques to stimulate the behaviors and interactions of molecules at the quantum level. Quantum algorithms can provide more accurate and efficient simulations by exploiting the inherent quantum properties of the systems being modeled [67].

- **Wavefunction Simulations:** Quantum systems and molecules are both described by wavefunctions that capture the probability amplitudes of different quantum states [68]. To enable more accurate calculation of molecular properties and behaviors, quantum computers directly simulate the time evolution of these wavefunctions.
- **Quantum Phase Estimation:** To gain insights into molecular dynamics and chemical reactions, we must determine energy levels. This algorithm is used to estimate the eigenvalues of the quantum system, which are equivalent to the energy levels of the molecule [69].
- **Quantum Walks and Quantum Monte Carlo Methods:** This algorithm helps provide insights into the dynamics, conformational changes, and thermodynamics properties by stimulating the behaviors of molecules and their components [73].
- **Excited State Calculations:** Quantum computers can accurately compute the excited state properties of molecules, which are crucial for understanding processes like electronic transitions and energy transfer [74].

V. QUANTUM CHEMISTRY FOR DRUG DESIGN

For the development and discovery of pharmaceuticals, it is imperative to gain an understanding of the electronic configuration, characteristics, and quantum-level interactions of molecules. This objective can be realized through the support of quantum chemistry [75]. The main factors in drug development are efficiency and the reduction of side effects. Quantum chemistry enables the comprehension of the essential, foundational behavior of molecules, enables the prediction of their properties, and assists in creating novel drug candidates that fulfill the above criteria [76].

1) **Electronic Structure Calculation:** Quantum chemistry techniques and methods, like Hartree-Fock, Density Functional Theory (DFT), and correlated different wavefunction methods, are used to calculate the electronic structure of molecules accurately [77]. This information includes the distribution of electrons and their energy levels, which are critical for understanding molecular properties and reactivity.
2) **Binding Energy and Affinity Prediction:** Quantum chemistry calculations can predict the binding energy and affinity between a drug molecule and its target protein or biomolecule [78]. This information is essential for assessing the strength and quality of drug-target interaction and designing molecules with optimal binding affinities.
3) **Transition State Analysis:** Quantum chemistry enables us to study reaction mechanisms and transition states, which are crucial for understanding enzymatic reactions, metabolic processes, and chemical transformations in drug metabolism [79].
4) **Quantum Mechanics/Molecular Mechanics (QM/MM) Simulations:** In drug design and discovery, QM/MM simulation combines the accuracy of quantum chemistry with the efficiency of classical molecular dynamics simulations [80]. They study reactions occurring in complex environments, such as enzymatic active sites.
5) **Solvent Effects:** It is very indicative to understand how molecules behave in different solvents, as it is essential for predicting drug solubility, stability, and bioavailability [81]. Quantum chemistry can account for the effects of solvents on molecular interactions.
6) **Electrostatic Interactions and Charge Distribution:** For researchers, it is vital to understand how electrostatic interactions contribute to binding and reactivity, and quantum chemistry helps to reveal this distribution of charges [82].
7) **Prediction of Spectroscopic Properties:** Quantum chemistry methods can predict spectroscopic properties, including UV and visible absorption spectra, NMR chemical shifts, and vibrational frequencies [83]. These predictions aid in characterizing molecules and understanding their behaviors.
8) **Design of Ligands and Inhibitors:** Quantum chemistry also guides the design of ligands and enzyme inhibitors by optimizing their structures for maximum binding affinity and selectivity [84].
9) **High-Throughput Screening:** Quantum chemistry calculations can be used in high-throughput virtual screening to quickly assess large libraries of potential drug candidates and prioritize molecules for experimental testing [85].

A. QUANTUM ALGORITHMS FOR VQE IN QUANTUM CHEMISTRY

Quantum chemistry involves studying molecular and material behavior at a quantum level, which is challenging and complex. To solve the challenge of understanding complex quantum mechanics, we can use quantum algorithms such as VQE, as they tend to approach the problem more efficiently [86]. The following points describe the VQE concisely:

- **Objective:** The VQE algorithm is used to approximate the lowest energy state (ground state) of a given molecule [87]. The Hamiltonian ($\hat{\mathcal{H}}$) represents the total energy of the molecule's quantum states.

TABLE 3. Real-life application of QCs.

Study	Molecule(s)	Quantum Devices	Variational Ansatz	Optimizer	Results
Xie et al. [70]	Small molecule	IBM Quantum	UCCSD	COBYLA	Qubit-Frugal Low-Variational Quantum Eigensolver (L-VQE)
Tkachenko et al. [71]	Drug candidate	Rigetti Aspen-9	RYRZ	L-BFGS-B	Permutation Variational Quantum Eigensolver (PermVQE): Connectivity-Optimized Quantum Chemistry
Rattew et al. [72]	Protein-ligand	Google Sycamore	UCCSD	SLSQP	Evolutionary Variational Quantum Eigensolver(EVQE) Advancements

- **Ansatz:** VQE uses a parameterized quantum circuit (ansatz) to prepare a trial quantum state [88]. This state is prepared using quantum gates, each controlled by specific parameters that can be adjusted.
- **Quantum Measurements:** Measurement of ansatz state is done on a quantum computer to estimate its energy concerning molecule's Hamiltonian [89].
- **Classical Optimisation:** The estimated energy is used as a cost function in a classical optimization process. The goal is to adjust the parameters of the ansatz so that energy is minimized, thus finding an approximation to the ground state energy [90].
- **Iterative Process:** The optimization is an iterative process. After each iteration, the ansatz is updated based on the classical optimization results. The process continues until the energy converges to a minimum.
- **Hybrid Nature:** VQE is a hybrid algorithm because it combines quantum and classical computing [91]. Quantum computers perform the quantum measurements and gate operations, while classical computers handle the optimization and control of the quantum hardware.
- **Application:** VQE finds applications in quantum chemistry, optimizing molecular structures and electronic configurations. It also addresses complex problems in optimization, material science, and drug discovery, showcasing its versatility across diverse scientific domains.

One of the current and major examples of quantum algorithms was seen and implemented by FRESNEL1 by PASQAL [92]. A noteworthy example of this quantum algorithm designed to expedite the drug discovery process motivates more ventures in this field.

B. QUANTUM COMPUTATIONAL METHODS FOR MOLECULAR STRUCTURE PREDICTION

Quantum computational methods for molecular structure prediction are advanced techniques employed in research for the accurate modeling and prediction of molecules' three-dimensional structures [93]. These methods harness the principles of quantum mechanics, a fundamental theory describing the behavior of matter and energy at the quantum level. In molecular structure prediction, quantum methods offer several advantages over classical approaches, enabling researchers to gain deeper insights into molecular properties, interactions, and behavior. The following technologies are currently being explored for molecular structure prediction:

1) DENSITY FUNCTIONAL THEORY

Density Functional Theory (DFT) is a powerful computational method used in quantum chemistry and condensed matter physics to study the electronic structure and properties of molecules, solids, and materials [94]. It is particularly beneficial for systems with many electrons, which makes solving the Schrödinger equation extremely challenging or even impossible due to its high computational cost. DFT provides a more practical approach by focusing on the electronic density rather than the wavefunction of the system [95].

2) AB INITIO METHODS

Beyond DFT, Ab Initio methods, such as Hartee-Fock and post-Hartee-Fock methods, offer higher levels of accuracy by accounting for electron correlation effects [96]. These methods are particularly useful for understanding complex molecular systems and reaction mechanisms. Ab initio quantum chemistry approaches aim to address the electronic Schrödinger equation, taking into account the positions of nuclei and the electron count, in order to generate valuable insights like electron distributions, energy levels, and additional characteristics of the system.

Incorporating quantum computational methods into molecular structure prediction research requires a solid foundation in quantum mechanics, access to quantum chemistry software, and understanding the specific algorithms and methods relevant to the research goals [97]. As the field advances, researchers can leverage these methods to achieve more accurate and detailed insights into the behavior of molecules, opening up new avenues for discovery and innovation.

Quantum computing has the potential to augment both Density Functional Theory (DFT) and ab initio techniques, mirroring their prospective advantages in predicting molecular structures. These methods are effective for modeling the electronic structures of molecules, though they require significant computational resources, particularly for intricate and large-scale systems. Quantum computers excel in executing certain quantum simulations with greater efficiency than traditional computers, offering substantial speed advantages. This capability is especially advantageous for examining

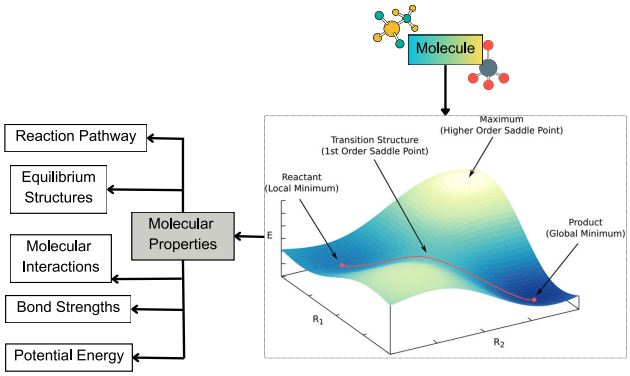


FIGURE 5. Potential energy surfaces.

complex chemical reactions or large molecules. By providing swift resolutions to electronic structure challenges that classical ab initio methods struggle with, quantum computers could enhance computational feasibility. Moreover, quantum computers may achieve superior precision by more accurately simulating quantum phenomena and electron correlations. This improved accuracy holds promise for more dependable forecasts of molecular characteristics and dynamics, such as reaction pathways, bond dissociation energies, and spectroscopic features.

C. POTENTIAL ENERGY SURFACES AND REACTION PATHWAYS

Potential energy surfaces (PES) are essential for understanding molecular behavior, chemical reactions, reaction pathways, and equilibrium structures [98]. PES maps the relationship between a molecule's potential energy and its atomic coordinates, aiding in studying molecular properties and reaction pathways [99]. We can observe all of the major chemical properties mapped by PES in Fig. 5. Recent advances in QC have significantly improved PES calculations, providing a powerful tool for drug discovery.

QC's computational capabilities have the potential to enhance the accuracy of PES calculations, thereby improving the precision of drug development [100]. Additionally, it helps identify transition states on PES, which is crucial for determining reaction rates and mechanisms. This quantum-driven precision accelerates drug optimization, synthetic route design, and complex chemical process comprehension, with applications spanning materials science, catalysis, and environmental chemistry. QC stands as a transformative force in modern drug discovery. For research purposes, studying potential energy surfaces and reaction pathways requires the application of quantum chemistry methods, computational algorithms, and visualization tools [101]. Researchers delve into the intricate details of molecular energetics and dynamics to uncover the underlying mechanisms driving chemical transformations. These insights have far-reaching implications for drug discovery, materials science, catalysis, and environmental chemistry.

VI. COMPLETE PIPELINE FOR DRUG DEVELOPMENT USING QUANTUM COMPUTING

The drug development pipeline, as illustrated in Fig. 6, serves as a comprehensive roadmap for understanding the intricacies of the entire process. Initiated by the key phase of target identification and characterization, this process uses quantum algorithms and simulations to resolve the complexities of biomolecular systems [102]. This foundational step provides a molecular-level comprehension of disease mechanisms, setting the stage for subsequent stages in the pipeline.

Advancing from target identification, the workflow transitions to hit search, where the integration of quantum-enhanced algorithms expedites the virtual screening of chemical libraries [103]. This accelerated process efficiently identifies potential drug candidates, establishing a solid foundation for the subsequent stages.

Building on the identified hits, the next critical phase is lead search and optimization. Here, quantum simulations and algorithms are central in predicting molecular properties and guiding an iterative optimization process [104]. This iterative refinement aims to enhance binding affinity and reduce toxicity, laying the groundwork for the ensuing stages.

The pipeline further branches into Computer-Aided Drug Design (CADD), where the contrast between structure-based and ligand-based approaches becomes apparent [105]. In structure-based methodologies, quantum algorithms come to the forefront, predicting three-dimensional structures and interactions of molecules with target proteins. Quantum technologies, exemplified by the VQE, contribute significantly to refining the accuracy of these predictions [106].

Simultaneously, ligand-based approaches within CADD leverage quantum algorithms to analyze existing drugs and predict the binding affinities of lead compounds [107]. Integrating quantum machine learning into these approaches refines the comprehension of structure-activity relationships, providing valuable insights for decision-making in drug development.

Fig. 6 serves as a visual guide, highlighting key quantum technologies pivotal for advancing drug discovery. NISQ (Noisy Intermediate-Scale Quantum) computing, Fault-Tolerant QC (FTQC), VQE in Quantum Mechanics/Molecular Mechanics (VQE in QM/MM), Quantum Phase Estimation in Quantum Mechanics/Molecular Mechanics (PEA in QM/MM), and hybrid classical schemes for both protein folding and machine learning are emphasized [108]. Together, these technological advancements mark a significant breakthrough in drug discovery, initiating an unprecedented period of opportunities through the exploitation of quantum computing (QC). Incorporating quantum machine learning strategies amplifies this groundbreaking capacity, providing a deeper understanding of intricate connections in extensive datasets, supporting improved decision-making processes [109]. In essence, this holistic workflow, enriched by key quantum technologies, underlines a paradigm shift in drug discovery, showcasing the immense potential of QC to

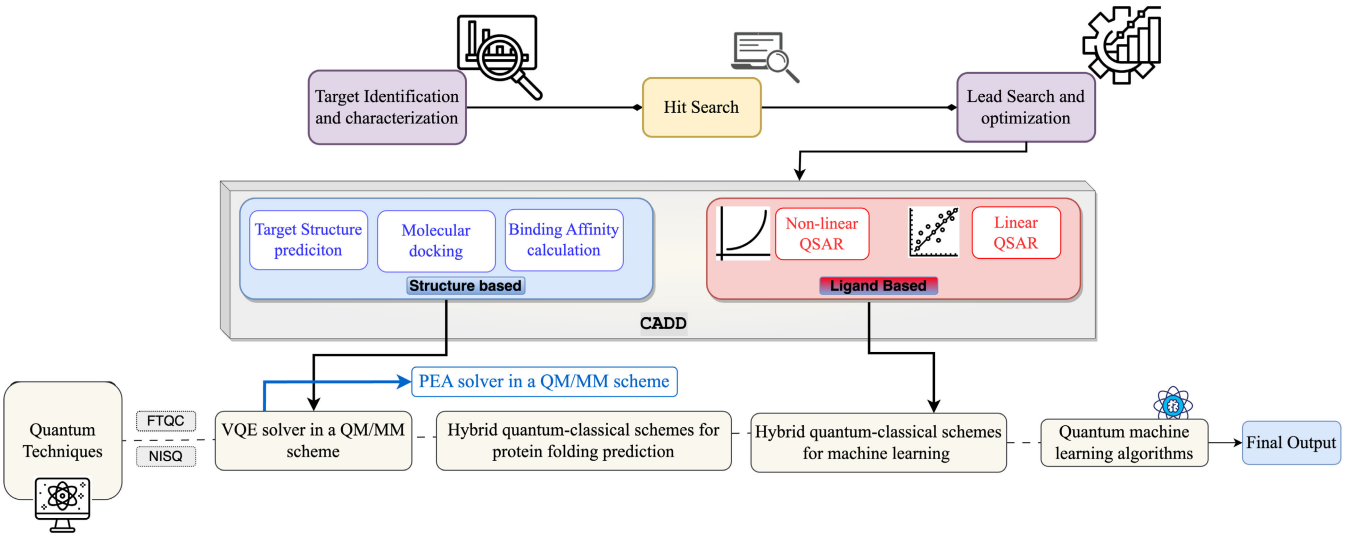


FIGURE 6. Pipeline for drug development using quantum techniques.

revolutionize the field and expedite the development of novel therapeutic agents.

A. REAL LIFE IMPLICATIONS OF QUANTUM COMPUTERS FOR DRUG DISCOVERY PIPELINE

The discourse surrounding the "quantum revolution" in drug discovery evokes visions of futuristic laboratories dominated by quantum computers. However, the present reality unfolds in a more nuanced yet equally promising manner. Although comprehensive drug discovery endeavors solely propelled by the powers of QC remain unrealized, the burgeoning field is affecting tangible advancements. QC contributes to specific pivotal stages within the conventional drug development pipeline [110].

Strategic collaborations between industry leaders and innovative QC entities drive this progress. A notable instance is the collaboration between Boehringer Ingelheim [111] and Rigetti Computing [112], yielding a remarkable 20-fold enhancement in the solubility of an existing drug molecule—an impediment frequently encountered in formulation and delivery.

QC's impact extends beyond materials and delivery aspects. Merck's [113] partnership with Zapata Computing [114] focuses on the intricate dynamics of protein-ligand interactions—the cornerstone of drug action. Quantum simulations achieved a noteworthy 2x acceleration in simulating these interactions, potentially expediting drug discovery pipelines substantially. Additionally, Vertex Pharmaceuticals [115] and QuantumScape [116] are pioneering the utilization of quantum simulations to design novel antibiotics targeting specific bacterial vulnerabilities. Although in its nascent stages, this collaboration holds promise for discovering antibiotics crucial in addressing the escalating threat of antimicrobial resistance.

Moreover, Quantum technologies, including quantum computers and simulators, are recognized for their potential transformative impacts across various sectors, with a particular emphasis on applications in the life sciences. These technologies are already making significant progress in drug development, the simulation of chemical processes, and genetic and genomic sequencing [117].

While these instances do not yet represent fully quantum-driven drug discovery pipelines, they underscore the transformative potential of this nascent technology. From optimizing existing drugs to identifying novel delivery materials, deciphering protein-ligand interactions, and designing antibiotics, QC's impact on specific yet pivotal drug development stages is undeniable. As QC continues its evolution, its role in revolutionizing drug discovery is poised to expand, ultimately culminating in the development of more effective and innovative medications. This is not merely a futuristic aspiration; it is an ongoing quantum leap, unfolding step by impactful step [17].

VII. QUANTUM INTEGRATED CLINICAL TRIAL

Clinical trials play a pivotal role in evaluating the safety and efficacy of new medical interventions like drugs. However, traditional clinical trial methodologies often face challenges related to the complexity of data analysis, patient recruitment, trial optimization, and time-to-market for new treatments [118]. QC and quantum technologies offer a unique perspective to address challenges in areas like drug discovery, leveraging quantum phenomena such as superposition and entanglement for accelerated computation and optimization. These advancements can significantly impact the efficiency and effectiveness of clinical trials in the pharmaceutical industry [119].

Clinical trials have become more efficient over time. Nevertheless, they still face various challenges. Designing an effective clinical drug requires optimization at various and multiple parameters such as sample size, treatment protocols,

TABLE 4. Comparative Analysis between Classical and QC in Drug Discovery.

Stage of Drug Development	Classical Computing	QC
Target Identification and Characterization	Analyze known biological data for targets based on existing knowledge.	Simulates complex molecular structures for insights into protein interactions.
Hit and Lead Optimization	Molecular dynamics, classical optimization algorithms.	Quantum algorithms (e.g., VQE) for complex optimization problems.
Molecular Docking	Simulations with limited accuracy due to computational cost.	Quantum algorithms enhance accuracy by efficiently exploring multiple configurations simultaneously.
Quantitative Structure-Activity Relationship (QSAR)	Well-established classical QSAR models.	Quantum-enhanced QSAR methods for more accurate predictions.
Machine Learning in Drug Discovery	Classical machine learning widely used.	QML for potential speedup, particularly with large datasets.
Quantum Chemistry Simulations	Classically computationally intensive. Struggles with large molecular systems.	Quantum algorithms excel in simulating molecular structures and electronic configurations.
Computational Cost and Scalability	Bottlenecks with high-dimensional parameter spaces and large datasets.	Potential exponential speedup in certain calculations, but constrained by current hardware and error issues.

and patient selection to ensure statistically meaningful results [120]. The second major challenge is the analysis of large, intricate clinical trial datasets, which can be time-consuming and susceptible to errors. The third major problem is biomarker identification, which means identifying relevant biomarkers that predict a patient's response to a drug, which is crucial for personalized medicine and targeted therapies. There are also many more problems like drug target interaction modeling, clinical trial simulation, drug toxicity prediction, drug formulation and delivery optimization challenge, regulatory compliance and validation, patient recruitment and stratification, predictive modeling for patient outcomes, and much more.

With the help of quantum computers, we can easily streamline the process because it can accelerate complex optimization tasks, enabling researchers to consider a larger number of variables simultaneously and find optimal trial designs that lead to faster and more reliable outcomes [121]. Quantum computers also possess the ability to handle massive datasets and perform complex calculations that could speed up data analysis, helping researchers uncover subtle patterns and correlations that might be missed using classical methods. Additionally, QML algorithms could enhance biomarker identification by analyzing intricate molecular interactions and patient data, leading to the discovery of more accurate and predictive biomarkers [122]. Quantum simulations can provide a more detailed understanding of molecular interactions, enabling researchers to design drugs with higher binding affinity and specificity. Quantum-enhanced simulations can also offer more precise predictions of drug interactions, assisting in the refinement of trial designs and reducing the need for numerous physical trials.

Quantum computers can also model the quantum behavior of molecules within various delivery systems, leading to optimized drug formulations that improve efficacy and minimize side effects. Quantum-enhanced methods would need to be validated to meet regulatory standards. QC could provide more accurate and efficient validation processes [123]. QML algorithms can potentially revolutionize data analysis in healthcare by enabling the analysis of diverse patient data sources to identify potential participants and stratify them more effectively based on complex patterns [124]. Quantum-enhanced predictive models could incorporate intricate molecular interactions and patient data, leading to more accurate outcome predictions [108].

VIII. CHALLENGES IN QC FOR DRUG DISCOVERY

Despite holding great promise for development in drug discovery, there are still several challenges in QC capabilities for this purpose [125]. The most critical and significant challenge is scalability and error mitigation.

A. SCALABILITY AND ERROR MITIGATION

Quantum computers demand a substantial number of qubits to model complex molecular systems. The requirement to have a system that needs a large number of coherent qubits poses a significant challenge regarding the scalability of the system [126]. Current quantum devices typically have limited qubit counts. Thus, substantial advancements are necessary to meet the demands of drug discovery applications. Furthermore, scaling quantum gate operations is crucial, as intricate algorithms for molecular simulations involve numerous gate operations, potentially increasing error rates [127].

Error mitigation is another critical concern in quantum drug discovery. Quantum computers are susceptible to errors due to decoherence and gate imperfections, impacting simulation accuracy [128]. Developing error-correction techniques and error-robust quantum algorithms is vital for dependable quantum simulations. Lowering error rates in quantum hardware is also a pressing issue, as existing devices often exhibit error rates far above what is acceptable for precise drug discovery simulations.

Quantum computers are highly sensitive to environmental factors, including temperature fluctuations and external interference, which can introduce noise and errors [129]. Thus, creating controlled environments for QC is essential to mitigate these influences. Adapting classical drug discovery algorithms to the quantum paradigm poses a formidable challenge, demanding the development of quantum algorithms tailored for real-world drug problems.

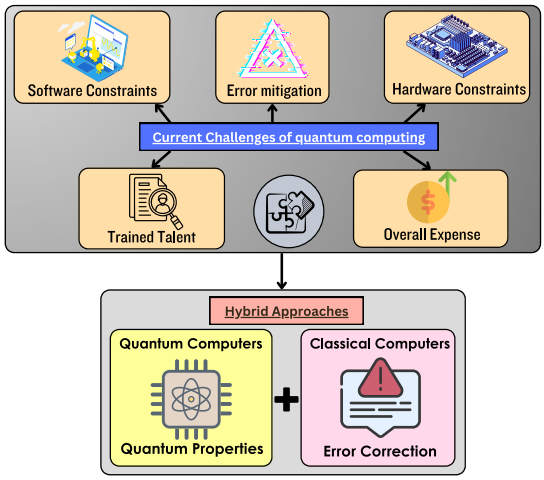


FIGURE 7. Hybrid approaches.

B. HARDWARE AND SOFTWARE CONSTRAINTS

Hardware and software constraints are pivotal factors influencing the integration of QC into drug discovery. On the hardware front, the limitations regarding qubit count and connectivity present formidable challenges [130]. Drug discovery often involves the intricate modeling of complex molecular systems, necessitating many qubits and intricate qubit connections [13]. Unfortunately, contemporary quantum devices generally feature a restricted number of qubits and connectivity, constraining their capacity to simulate large molecules accurately. Furthermore, it is crucial to acknowledge that the error rates inherent in quantum hardware, arising from challenges such as decoherence, gate imperfections, and readout errors, play a substantial role in the context of drug discovery [131]. In drug discovery processes, where precision and accuracy are paramount, addressing and mitigating these error sources becomes a critical focus [132].

The reliability of quantum gates and the coherence times of qubits represent further hardware constraints. Quantum gates must exhibit high fidelity and stability, yet current hardware often struggles to meet these strict requirements [133]. Coherence times determine the duration of a qubit as it can maintain its quantum state without errors, impacting the feasibility of conducting complex drug discovery simulations. Quantum volume, a comprehensive metric encompassing qubit count, gate fidelity, and connectivity, offers insight into a quantum computer's overall computational capability [134]. Shortcomings in quantum volume can restrict the networks and complexity of drug discovery simulations achievable through QC.

Developing quantum algorithms customized for drug discovery represents a significant endeavor on the software front. Adapting classical algorithms to the quantum realm requires strong foundational knowledge in quantum physics and a comprehensive understanding of the unique challenges intrinsic to drug discovery. Creating efficient quantum algorithms that harness the strengths of QC while mitigating its limitations remains a focal point of ongoing research [135].

Establishing a robust quantum software ecosystem is another software constraint [136]. This ecosystem should encompass quantum compilers, programming languages, and libraries specifically designed for drug discovery tasks. The absence of mature and user-friendly quantum software tools can slow down the widespread adoption of QC in the field.

C. CRYPTOGRAPHY AND SECURITY

The advent of quantum computers, driven by algorithms like Grover's and Shor's, introduces a formidable challenge to the security landscape of drug discovery and development systems, with particular ramifications for safeguarding patient data, privacy, and sensitive drug-related information [137]. The inherent potential of quantum computers to efficiently compromise conventional encryption methods, analogous to their threat to public key cryptographic systems, raises substantial concerns regarding the vulnerability of critical data within the pharmaceutical domain. Notably, patient confidentiality and the integrity of drug data face potential compromise.

While Quantum Key Distribution (QKD) has emerged as a suggested quantum-safe alternative, it is not immune to security issues. Implementation flaws and the looming prospect of advancements in quantum hacking methods pose risks that could undermine patient confidentiality and the integrity of drug-related data [138]. The transition towards quantum-resistant cryptography in the pharmaceutical sector is a complex and resource-intensive endeavor, compounded by the limited availability of thoroughly evaluated quantum-resistant algorithms. Current efforts are directed towards developing and standardizing robust quantum-resistant standards, necessitating continuous vigilance to address unforeseen developments in quantum security [139].

Moreover, the vast repository of drug and patient response data in the pharmaceutical industry raises significant concerns about data leakage, presenting substantial privacy issues [140]. This information's sheer volume and sensitivity elevate the

TABLE 5. Scope of quantum computers in clinical trials.

Challenge	Current Approach	Potential Quantum Solution
Drug target interaction modeling	Approximate models	Improved understanding of drug design
Clinical trial simulation	Extensive physical trials	Reduction in physical trials through quantum insights
Drug toxicity prediction	Inaccurate predictions	Enhanced predictive modeling for better drug toxicity prediction
Drug formulation and delivery optimization	Trial and error	Optimised drug formulations
Regulatory compliance and validation	Time-consuming	More accurate and efficient validation processes
Patient recruitment and stratification	Ineffective patient selection	Effective participant identification and stratification
Predictive modeling for patient outcomes	Limited accuracy	More accurate drug-human body interaction outcome prediction

risk of inadvertent disclosures, underscoring the need for stringent measures to protect patient privacy and uphold the integrity of drug-related data. These challenges prompt a critical examination of the security infrastructure in drug discovery and development, urging a comprehensive reassessment of existing practices to mitigate vulnerabilities effectively.

However, amidst these challenges, it is crucial to recognize that quantum technologies also unveils opportunities for innovative cryptographic techniques [141]. While grappling with security concerns, the field offers prospects for novel approaches that can enhance the resilience of drug discovery systems. This emphasizes the need for ongoing research and adaptation to the changing landscape of drug discovery and development security issues. Future cryptographic developments must meet the special needs of the pharmaceutical industry to protect sensitive data and promote medical research.

D. HYBRID APPROACHES: COMBINING CLASSICAL AND QC

Integrating QC with classical computing in a seamless, effective manner—called hybrid quantum-classical integration—is a complex challenge [142]. Given the constraints of qubit count and gate operations on quantum hardware, optimizing resource utilization is paramount. Nevertheless, as quantum hardware advances, the hybrid approach remains scalable, adapting to incorporate more quantum processing as quantum devices become more capable [143]. Developing hybrid approaches becomes more pivotal because it capitalizes on several advantages. It maximizes the strengths of classical and QC, allowing each to excel in tasks where they are most proficient. Classical computers provide robust error correction and can handle well-understood computations, while quantum computers tackle complex, quantum-specific aspects of drug discovery. Moreover, this approach optimizes the utilization of quantum resources, which are often constrained, by incorporating quantum processing selectively within a larger classical workflow [144].

In summary, hardware and software constraints represent substantial hurdles in harnessing QC's potential to accelerate drug discovery [145]. Addressing these constraints is essential to unlock the transformative power of QC fully in this critical research field.

IX. FUTURE PROSPECTS AND IMPLICATIONS

As we stand on the edge of a rapidly changing future, new technologies are reshaping how we live and work. This transformation brings both exciting possibilities and significant challenges. Navigating this evolving landscape demands a clear understanding of the forces shaping our societies and economies.

A. REVOLUTIONIZING DRUG DEVELOPMENT THROUGH QC

QC stands at the forefront of revolutionizing drug development pipelines, presenting unprecedented opportunities for innovation and efficiency [146]. This paradigm shift in computational processes holds immense potential to accelerate drug discovery by simulating intricate molecular interactions and complex chemical reactions with unparalleled speed and precision. The speed and power of QC offer the potential to expedite drug discovery processes significantly. Rapid and precise molecular modeling enables a deeper understanding of disease mechanisms and drug interactions at the quantum level. Moreover, it streamlines drug re-purposing efforts by efficiently analyzing existing databases, potentially saving valuable time and resources [147].

B. HOLISTIC INTEGRATION APPROACH:

The integration of QC into pharmaceutical companies is expected to follow a holistic approach, encompassing strategic partnerships, collaborations, and workforce development [148]. In order to seamlessly infuse QC capabilities into drug development pipelines, companies are likely to

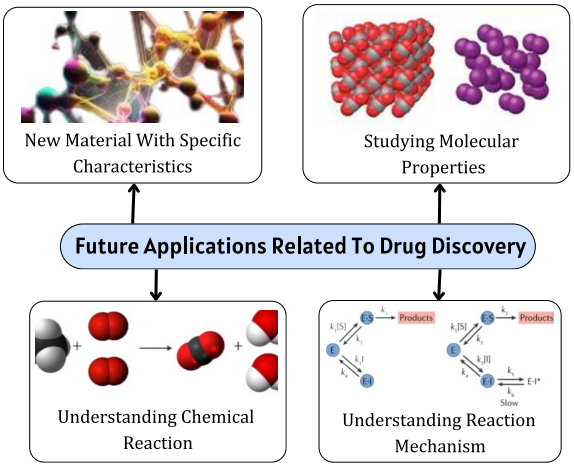


FIGURE 8. Future applications of QC.

engage in strategic partnerships and collaborations with QC firms or research institutions. Simultaneously, investments in QC infrastructure or utilizing cloud-based quantum resources may be explored to enhance competitiveness. An integral part of this integration strategy involves acquiring QC experts and data scientists. These skilled professionals will play a crucial role in bridging the gap between quantum technologies and pharmaceutical research, ensuring the effective utilization of these powerful tools. This holistic approach aims to position pharmaceutical companies at the forefront of QC advancements in the context of drug development.

C. ETHICAL CONSIDERATIONS IN QC FOR DRUG DISCOVERY:

As QC reshapes the pharmaceutical landscape, ethical considerations and responsible use become paramount. Data security and privacy concerns are heightened, necessitating a renewed focus to safeguard sensitive patient information and intellectual property [149]. When QC converges with artificial intelligence (AI) for drug discovery, additional ethical concerns arise, including those related to AI bias, transparency, and accountability [150]. Ensuring unbiased and safe outcomes is essential for maintaining the integrity of the drug development process. Ethical considerations also extend to accessibility and equity, demanding that the benefits of quantum-powered drug development reach underserved communities and diverse patient populations. Striking a balance between transformative potential and ethical responsibility is key to realizing the full benefits of QC.

D. REGULATORY COMPLIANCE:

Finally, regulatory compliance remains essential [151]. Pharmaceutical companies must navigate and adhere to evolving regulations governing the ethical use of QC in drug development. Adherence to these regulations ensures ethical standards are maintained throughout the transformative journey of QC in drug discovery.

X. CONCLUSION

This survey investigated the disruptive potential of QC in the field of drug development, as well as its applications and future prospects. QC has improved pharmaceutical CADD, chemical simulations, and clinical trial simulations. The technology's capacity to accurately and rapidly replicate intricate chemical reactions has brought about a transformative impact on drug research. The system performs complex calculations and analyses large datasets to enhance the efficiency of clinical trials.

To effectively characterize complex chemical processes, it is essential to have scalability, error mitigation, and a sufficient number of qubits. Interdisciplinary collaboration is necessary for the application of quantum computers in pharmaceutical research, as it enables a comprehensive understanding of both quantum physics and pharmaceutical processes.

Future research goals include the development of quantum algorithms for drug discovery, quantum hardware for complex simulations, and hybrid classical-quantum models for resource optimization. Ethics, particularly concerning data security and patient privacy, are also significant.

QC has the potential to enhance simulations and data processing, leading to accelerated drug discovery and improved treatment effectiveness. To harness this potential, it is imperative to conduct research focused on technology and its applications. The industry cannot overlook the significant potential of QC, despite the obstacles it presents.

REFERENCES

[1] N. Berdigaliyev and M. Aljofan, "An overview of drug discovery and development," *Future Medicinal Chem.*, vol. 12, no. 10, pp. 939–947, May 2020, doi: 10.4155/fmc-2019-0307.

[2] Smithsonian Magazine. (Jun. 2022). *Why Did It Take 35 Years to Get a Malaria Vaccine?* [Online]. Available: https://www.smithsonianmag.com/science-nature/why-did-it-take-35-years-to-get-a-malaria-vaccine-180980151/

[3] P.-H. Wang, J.-H. Chen, Y.-Y. Yang, C. Lee, and Y. J. Tseng, "Recent advances in quantum computing for drug discovery and development," *IEEE Nanotechnol. Mag.*, vol. 17, no. 2, pp. 26–30, Apr. 2023.

[4] A. Blanco-González, A. Cabezón, A. Seco-González, D. Conde-Torres, P. Antelo-Riveiro, Á. Piñeiro, and R. Garcia-Fandino, "The role of AI in drug discovery: Challenges, opportunities, and strategies," *Pharmaceuticals*, vol. 16, no. 6, p. 891, Jun. 2023.

[5] F. Arute, K. Arya, R. Babbush, D. Bacon, and J. C. Bardin, "Quantum supremacy using a programmable superconducting processor," *Nature*, vol. 574, no. 7779, pp. 505–510, Oct. 7779.

[6] M. Zinner, F. Dahlhausen, P. Boehme, J. Ehlers, L. Bieske, and L. Fehring, "Quantum computing's potential for drug discovery: Early stage industry dynamics," *Drug Discovery Today*, vol. 26, no. 7, pp. 1680–1688, Jul. 2021. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1359644621002750

[7] R. Biswas, A. Basu, A. Nandy, A. Deb, K. Haque, and D. Chanda, "Drug discovery and drug identification using AI," in *Proc. Indo–Taiwan 2nd Int. Conf. Comput., Anal. Netw. (Indo-Taiwan ICAN)*, Feb. 2020, pp. 49–51.

[8] M. D. Parenti and G. Rastelli, "Advances and applications of binding affinity prediction methods in drug discovery," *Biotechnol. Adv.*, vol. 30, no. 1, pp. 244–250, Jan. 2012.

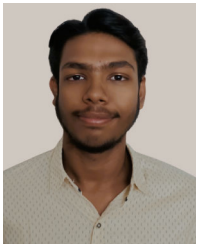
[9] J. Li, R. O. Topaloglu, and S. Ghosh, "Quantum generative models for small molecule drug discovery," *IEEE Trans. Quantum Eng.*, vol. 2, pp. 1–8, 2021.

[10] V. Chauhan, S. Negi, D. Jain, P. Singh, A. K. Sagar, and A. K. Sharma, "Quantum computers: A review on how quantum computing can boom AI," in *Proc. 2nd Int. Conf. Advance Comput. Innov. Technol. Eng. (ICACITE)*, Apr. 2022, pp. 559–563.

[11] S. McArdle, S. Endo, A. Aspuru-Guzik, S. C. Benjamin, and X. Yuan, "Quantum computational chemistry," *Rev. Mod. Phys.*, vol. 92, Mar. 2020, Art. no. 015003, doi: 10.1103/RevModPhys.92.015003.
[12] S. Duela, A. Umamageswari, R. Prabavathi, P. Umapathy, and K. Raja, "Quantum assisted genetic algorithm for sequencing compatible amino acids in drug design," in *Proc. 3rd Int. Conf. Adv. Electr., Comput., Commun. Sustain. Technol. (ICAECT)*, Jan. 2023, pp. 1–7.
[13] B. Lau, P. S. Emani, J. Chapman, L. Yao, T. Lam, P. Merrill, J. Warrell, M. B. Gerstein, and H. Y. K. Lam, "Insights from incorporating quantum computing into drug design workflows," *Bioinformatics*, vol. 39, no. 1, Jan. 2023, Art. no. btac789.
[14] H. Mustafa, S. N. Morapakula, P. Jain, and S. Ganguly, "Variational quantum algorithms for chemical simulation and drug discovery," in *Proc. Int. Conf. Trends Quantum Comput. Emerg. Bus. Technol. (TQCEBT)*, Oct. 2022, pp. 1–8.
[15] *Quantum Computing: Progress and Prospects*, Nat. Academies Sci., Eng., Med., Washington, DC, USA, 2019.
[16] O. Dupouët, Y. Pitarch, M. Ferru, and B. Bernela, "Community dynamics and knowledge production: Forty years of research in quantum computing," *J. Knowl. Manage.*, vol. 28 no. 3, pp. 651-672, 2024, doi: 10.1108/JKM-01-2023-0083.
[17] Y. Cao, J. Romero, and A. Aspuru-Guzik, "Potential of quantum computing for drug discovery," *IBM J. Res. Develop.*, vol. 62, no. 6, pp. 6:1–6:20, Nov. 2018.
[18] J. Singh and M. Singh, "Evolution in quantum computing," in *Proc. Int. Conf. Syst. Model. Advancement Res. Trends (SMART)*, Nov. 2016, pp. 267–270.
[19] S. K. Sood and Pooja, "Quantum computing review: A decade of research," *IEEE Trans. Eng. Manag.*, vol. 71, pp. 6662–6676, 2024, doi: 10.1109/TEM.2023.3284689.
[20] E. h. Shaik and N. Rangaswamy, "Implementation of quantum gates based logic circuits using IBM qiskit," in *Proc. 5th Int. Conf. Comput., Commun. Secur. (ICCCS)*, Oct. 2020, pp. 1–6.
[21] G. T. Sridhar, P. Ashwini, and N. Tabassum, "A review on quantum communication and computing," in *Proc. 2nd Int. Conf. Appl. Artif. Intell. Comput. (ICAAIC)*, May 2023, pp. 1592–1596.
[22] J. Bub, "Quantum entanglement and information," in *The Stanford Encyclopedia of Philosophy*, E. N. Zalta and U. Nodelman, Eds. Stanford, CA, USA: Metaphysics Research Lab., Stanford University, Summer 2023.
[23] A. Zeilinger, "Quantum entanglement and information," in *Proc. Quantum Electron. Laser Sci. Conf. (QELS). Tech. Dig.*, vol. 10, May 2000, p. 163.
[24] S. Gamble, "Quantum computing: What it is, why we want it, and how we're trying to get it," in *Frontiers of Engineering: Reports on Leading-Edge Engineering From the 2018 Symposium*. Washington, DC, USA: National Academies Press, 2018.
[25] T. S. Humble, H. Thapliyal, E. Muñoz-Coreas, F. A. Mohiyaddin, and R. S. Bennink, "Quantum computing circuits and devices," *IEEE Des. Test. IEEE Des. Test. Comput.*, vol. 36, no. 3, pp. 69–94, Jun. 2019.
[26] M. Möttönen[1] and J. J. Vartiainen, "Decompositions of general quantum gates," in *Trends in Quantum Computing Research*. Nova Publishers, 2006, p. 149.
[27] M. Swathi and B. Rudra, "Implementation of reversible logic gates with quantum gates," in *Proc. IEEE 11th Annu. Comput. Commun. Workshop Conf. (CCWC)*, Jan. 2021, pp. 1557–1563.
[28] P. K. Roy, "Quantum logic gates," Tech. Rep., Aug. 2020.
[29] L. Banchi, N. Pancotti, and S. Bose, "Quantum gate learning in qubit networks: Toffoli gate without time-dependent control," *NPJ Quantum Inf.*, vol. 2, no. 1, pp. 1–6, Jul. 2016.
[30] H. Ma, M. Govoni, and G. Galli, "Quantum simulations of materials on near-term quantum computers," *NPJ Comput. Mater.*, vol. 6, no. 1, pp. 1–8, Jul. 2020.
[31] Y. Shi, S. T. Lam, and T. L. Beck, "Deep neural network based quantum simulations and quasichemical theory for accurate modeling of molten salt thermodynamics," *Chem. Sci.*, vol. 13, no. 28, pp. 8265–8273, 2022.
[32] M. Reiher, N. Wiebe, K. M. Svore, D. Wecker, and M. Troyer, "Elucidating reaction mechanisms on quantum computers," *Proc. Nat. Acad. Sci.*, vol. 114, no. 29, pp. 7555–7560, Jul. 2017.
[33] D. Prada-Gracia, S. Huerta-Yépez, and L. M. Moreno-Vargas, "Application of computational methods for anticancer drug discovery, design, and optimization," *Boletín Médico del Hospital Infantil de México*, vol. 73, no. 6, pp. 411–423, Nov. 2016.
[34] X. Lin, X. Li, and X. Lin, "A review on applications of computational methods in drug screening and design," *Molecules*, vol. 25, no. 6, p. 1375, Mar. 2020.
[35] D. Solenov, J. Brieler, and J. F. Scherrer, "The potential of quantum computing and machine learning to advance clinical research and change the practice of medicine," *Missouri Med.*, vol. 115, no. 5, pp. 463–467, 2018.
[36] W. L. Jorgensen, "Efficient drug lead discovery and optimization," *Accounts Chem. Res.*, vol. 42, no. 6, pp. 724–733, Jun. 2009, doi: 10.1021/ar800236t.
[37] G. M. Morris and M. Lim-Wilby, "Molecular docking," in *Molecular Modeling of Proteins*. Cham, Switzerland: Springer, 2008, pp. 365–382.
[38] F. Gentile, J. C. Yaacoub, J. Gleave, M. Fernandez, A.-T. Ton, F. Ban, A. Stern, and A. Cherkasov, "Artificial intelligence–enabled virtual screening of ultra-large chemical libraries with deep docking," *Nature Protocols*, vol. 17, no. 3, pp. 672–697, Mar. 2022.
[39] A. Veselovsky and A. Ivanov, "Strategy of computer-aided drug design," *Current Drug Target-Infectious Disorders*, vol. 3, no. 1, pp. 33–40, Mar. 2003.
[40] W. Yu and A. D. MacKerell, "Computer-aided drug design methods," in *Antibiotics: Methods and Protocols*, vol. 1520, P. Sass, Ed. New York, NY, USA: Humana Press, 2017, doi: 10.1007/978-1-4939-6634-9_5.
[41] G. M. Sastry, M. Adzhigirey, T. Day, R. Annabhimoju, and W. Sherman, "Protein and ligand preparation: Parameters, protocols, and influence on virtual screening enrichments," *J. Comput.-Aided Mol. Design*, vol. 27, no. 3, pp. 221–234, Mar. 2013.
[42] K. K. Chaudhary and N. Mishra, "A review on molecular docking: Novel tool for drug discovery," *JSM Chem.*, vol. 3, no. 4, p. 1029, 2016.
[43] A. Axenopoulos, P. Daras, G. Papadopoulos, and E. Houstis, "A shape descriptor for fast complementarity matching in molecular docking," *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 8, no. 6, pp. 1441–1457, Nov. 2011.
[44] I. Halperin, B. Ma, H. Wolfson, and R. Nussinov, "Principles of docking: An overview of search algorithms and a guide to scoring functions," *Proteins: Struct., Function, Bioinf.*, vol. 47, no. 4, pp. 409–443, Jun. 2002.
[45] D. B. Kitchen, H. Decornez, J. R. Furr, and J. Bajorath, "Docking and scoring in virtual screening for drug discovery: Methods and applications," *Nature Rev. Drug Discovery*, vol. 3, no. 11, pp. 935–949, Nov. 2004.
[46] Y. Fang, "Ligand–receptor interaction platforms and their applications for drug discovery," *Expert Opinion Drug Discovery*, vol. 7, no. 10, pp. 969–988, Oct. 2012.
[47] J. Vaidyanathan, T. K. Vaidyanathan, P. Yadav, and C. E. Linaras, "Collagen–ligand interaction in dentinal adhesion: Computer visualization and analysis," *Biomaterials*, vol. 22, no. 21, pp. 2911–2920, Nov. 2001.
[48] V. Rusinov, V. Baev, I. N. Minkov, and M. Tabler, "MicroInspector: A web tool for detection of miRNA binding sites in an RNA sequence," *Nucleic Acids Res.*, vol. 33, no. 2, pp. W696–W700, Jul. 2005.
[49] D. E. Bernal, A. Ajagekar, S. M. Harwood, S. T. Stober, D. Trenev, and F. You, "Perspectives of quantum computing for chemical engineering," *AIChE J.*, vol. 68, no. 6, Jun. 2022, Art. no. e17651.
[50] S.-Y. Huang and X. Zou, "Advances and challenges in protein-ligand docking," *Int. J. Mol. Sci.*, vol. 11, no. 8, pp. 3016–3034, Aug. 2010.
[51] A. Pyrkov, A. Aliper, D. Bezrukov, Y.-C. Lin, D. Polykovskiy, P. Kamya, F. Ren, and A. Zhavoronkov, "Quantum computing for near-term applications in generative chemistry and drug discovery," *Drug Discovery Today*, vol. 28, no. 8, Aug. 2023, Art. no. 103675. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1359644623001915
[52] D. Gioia, M. Bertazzo, M. Recanatini, M. Masetti, and A. Cavalli, "Dynamic docking: A paradigm shift in computational drug discovery," *Molecules*, vol. 22, no. 11, p. 2029, Nov. 2017.
[53] I. Kassal, J. D. Whitfield, A. Perdomo-Ortiz, M.-H. Yung, and A. Aspuru-Guzik, "Simulating chemistry using quantum computers," *Annu. Rev. Phys. Chem.*, vol. 62, no. 1, pp. 185–207, May 2011.
[54] P. H. M. Torres, A. C. R. Sodero, P. Jofily, and F. P. Silva-Jr., "Key topics in molecular docking for drug design," *Int. J. Mol. Sci.*, vol. 20, no. 18, p. 4574, Sep. 2019.
[55] V. Kulkarni. (Dec. 2021). *Quantum Parallelism—Where Quantum Computers Get Their Mojo From | Towards Data Science*. Medium. [Online]. Available: https://towardsdatascience.com/quantum-parallelism-where-quantum-computers-get-their-mojo-from-66c93bd09855
[56] M. Nabil. (Feb. 2023). *Quantum Parallelism*. Medium. [Online]. Available: https://medium.com/
[57] SciU. (Jan. 2024). *The Power of Quantum Computing: Parallelism*. Accessed: Jan. 26, 2024. [Online]. Available: https://blogs.iu.edu/sciu/2019/07/13/quantum-computing-parallelism

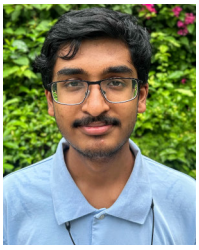
[58] O. A. Arodola and M. E. Soliman, "Quantum mechanics implementation in drug-design workflows: Does it really help?" *Drug Design, Develop. Therapy*, vol. 11, pp. 2551–2564, Aug. 2017.
[59] S. Yu et al., "A universal programmable Gaussian boson sampler for drug discovery," *Nature Comput. Sci.*, vol. 3, no. 10, pp. 839–848, Oct. 2023.
[60] S. Mensa, E. Sahin, F. Tacchino, P. K. Barkoutsos, and I. Tavernelli, "Quantum machine learning framework for virtual screening in drug discovery: A prospective quantum advantage," *Mach. Learn., Sci. Technol.*, vol. 4, no. 1, Mar. 2023, Art. no. 015023.
[61] C. Gorgulla, A. Jayaraj, K. Fackeldey, and H. Arthanari, "Emerging frontiers in virtual drug discovery: From quantum mechanical methods to deep learning approaches," *Current Opinion Chem. Biol.*, vol. 69, Aug. 2022, Art. no. 102156.
[62] I. M. Georgescu, S. Ashhab, and F. Nori, "Quantum simulation," *Rev. Mod. Phys.*, vol. 86, no. 1, p. 153, 2014.
[63] H. Yano, Y. Suzuki, K. M. Itoh, R. Raymond, and N. Yamamoto, "Efficient discrete feature encoding for variational quantum classifier," *IEEE Trans. Quantum Eng.*, vol. 2, pp. 1–14, 2021.
[64] S. K. Jeswal and S. Chakraverty, "Recent developments and applications in quantum neural network: A review," *Arch. Comput. Methods Eng.*, vol. 26, no. 4, pp. 793–807, Sep. 2019.
[65] J. A. Jones, M. Mosca, and R. H. Hansen, "Implementation of a quantum search algorithm on a quantum computer," *Nature*, vol. 393, no. 6683, pp. 344–346, May 1998.
[66] M. Evers, A. Heid, and I. Ostojic. (Jun. 2021). *Pharma's Digital Rx: Quantum Computing in Drug Research and Development*. McKinsey & Company. [Online]. Available: https://www.mckinsey.com/industries/life-sciences/our-insights/pharmas-digital-rx-quantum-computing-in-drug-research-and-development
[67] Y. Fan, "Quantum simulation of simple many-body dynamics," 2009, *arXiv:0901.4163*.
[68] X.-S. Ma, B. Dakic, W. Naylor, A. Zeilinger, and P. Walther, "Quantum simulation of the wavefunction to probe frustrated Heisenberg spin systems," *Nature Phys.*, vol. 7, no. 5, pp. 399–405, May 2011.
[69] U. Dorner, R. Demkowicz-Dobrzanski, B. J. Smith, J. S. Lundeen, W. Wasilewski, K. Banaszek, and I. A. Walmsley, "Optimal quantum phase estimation," *Phys. Rev. Lett.*, vol. 102, no. 4, Jan. 2009, Art. no. 040403.
[70] Q. Xie, W. Zhang, X. Xu, S. Liu, and Y. Zhao, "Qubit unitary coupled cluster with generalized single and paired double excitations ansatz for variational quantum eigensolver," *Int. J. Quantum Chem.*, vol. 122, no. 24, Dec. 2022, Art. no. e27001.
[71] N. V. Tkachenko, J. Sud, Y. Zhang, S. Tretiak, P. M. Anisimov, A. T. Arrasmith, P. J. Coles, L. Cincio, and P. A. Dub, "Correlation-informed permutation of qubits for reducing ansatz depth in the variational quantum eigensolver," *PRX Quantum*, vol. 2, no. 2, Jun. 2021, Art. no. 020337.
[72] A. G. Rattew, S. Hu, M. Pistoia, R. Chen, and S. Wood, "A domain-agnostic, noise-resistant, hardware-efficient evolutionary variational quantum eigensolver," 2019, *arXiv:1910.09694*.
[73] D. M. Ceperley, "An overview of quantum Monte Carlo methods," *Rev. Mineralogy Geochemistry*, vol. 71, no. 1, pp. 129–135, 2010, doi: 10.2138/rmg.2010.71.6.
[74] Q.-X. Xie, S. Liu, and Y. Zhao, "Orthogonal state reduction variational eigensolver for the excited-state calculations on quantum computers," *J. Chem. Theory Comput.*, vol. 18, no. 6, pp. 3737–3746, Jun. 2022.
[75] T. Zhou, D. Huang, and A. Caflisch, "Quantum mechanical methods for drug design," *Current Topics Medicinal Chem.*, vol. 10, no. 1, pp. 33–45, Jan. 2010.
[76] M. Manathunga, A. W. Götz, and K. M. Merz, "Computer-aided drug design, quantum-mechanical methods for biological problems," *Current Opinion Structural Biol.*, vol. 75, Aug. 2022, Art. no. 102417.
[77] D. R. Bowler and T. Miyazaki, "$\mathcal{O}(N)$ methods in electronic structure calculations," *Rep. Prog. Phys.*, vol. 75, no. 3, Feb. 2012, Art. no. 036503, doi: 10.1088/0034-4885/75/3/036503.
[78] R. Guareschi, I. Lukac, I. H. Gilbert, and F. Zuccotto, "SophosQM: Accurate binding affinity prediction in compound optimization," *ACS Omega*, vol. 8, no. 17, pp. 15083–15098, May 2023.
[79] V. L. Schramm, "Transition states, analogues, and drug development," *ACS Chem. Biol.*, vol. 8, no. 1, pp. 71–81, Jan. 2013.
[80] M. W. van der Kamp and A. J. Mulholland, "Combined quantum mechanics/molecular mechanics (QM/MM) methods in computational enzymology," *Biochemistry*, vol. 52, no. 16, pp. 2708–2728, Apr. 2013.
[81] C. Reichardt, "Solvents and solvent effects: An introduction," *Organic Process Res. Develop.*, vol. 11, no. 1, pp. 105–113, Jan. 2007.
[82] C. T. Sebens, "Electron charge density: A clue from quantum chemistry for quantum foundations," *Found. Phys.*, vol. 51, no. 4, p. 75, Aug. 2021.
[83] V. Barone, S. Alessandrini, M. Biczysko, J. R. Cheeseman, D. C. Clary, A. B. McCoy, R. J. DiRisio, F. Neese, M. Melosso, and C. Puzzarini, "Computational molecular spectroscopy," *Nature Rev. Methods Primers*, vol. 1, no. 1, p. 38, 2021.
[84] L. M. Mihalovits, G. G. Ferenczy, and G. M. Keserű, "The role of quantum chemistry in covalent inhibitor design," *Int. J. Quantum Chem.*, vol. 122, no. 8, Apr. 2022, Art. no. e26768.
[85] A. Irfan, M. Hussien, M. Y. Mehboob, A. Ahmad, and M. R. S. A. Janjua, "Learning from fullerenes and predicting for Y6: Machine learning and high-throughput screening of small molecule donors for organic solar cells," *Energy Technol.*, vol. 10, no. 6, Jun. 2022, Art. no. 2101096.
[86] A. Montanaro, "Quantum algorithms: An overview," *NPJ Quantum Inf.*, vol. 2, no. 1, pp. 1–8, Jan. 2016.
[87] A. Kandala, A. Mezzacapo, K. Temme, M. Takita, M. Brink, J. M. Chow, and J. M. Gambetta, "Hardware-efficient variational quantum eigensolver for small molecules and quantum magnets," *Nature*, vol. 549, no. 7671, pp. 242–246, Sep. 2017.
[88] J.-G. Liu, Y.-H. Zhang, Y. Wan, and L. Wang, "Variational quantum eigensolver with fewer qubits," *Phys. Rev. Res.*, vol. 1, no. 2, Sep. 2019, Art. no. 023025.
[89] S. McArdle, T. Jones, S. Endo, Y. Li, S. C. Benjamin, and X. Yuan, "Variational ansatz-based quantum simulation of imaginary time evolution," *NPJ Quantum Inf.*, vol. 5, no. 1, p. 75, Sep. 2019.
[90] J. Romero, R. Babbush, J. R. McClean, C. Hempel, P. J. Love, and A. Aspuru-Guzik, "Strategies for quantum computing molecular energies using the unitary coupled cluster ansatz," *Quantum Sci. Technol.*, vol. 4, no. 1, Oct. 2018, Art. no. 014008.
[91] G. Nannicini, "Performance of hybrid quantum-classical variational heuristics for combinatorial optimization," *Phys. Rev. E, Stat. Phys. Plasmas Fluids Relat. Interdiscip. Top.*, vol. 99, no. 1, Jan. 2019, Art. no. 013304.
[92] Mirage News. (Jan. 2024). *GENCI/CEA, FZJ, PASQAL Achieve Major Hybrid Computing Milestone*. Accessed: Jan. 20, 2021. [Online]. Available: https://www.miragenews.com/gencicea-fzj-pasqal-achieve-major-hybrid-1120388
[93] J. J. W. McDouall, *Computational Quantum Chemistry: Molecular Structure and Properties in Silico*. Royal Society of Chemistry, Jun. 2013. [Online]. Available: https://doi.org/10.1039/9781849737289
[94] M. Orio, D. A. Pantazis, and F. Neese, "Density functional theory," *Photosynthesis Res.*, vol. 102, pp. 443–453, Feb. 2009.
[95] E. Engel and R. M. Dreizler, *Density Functional Theory*. Berlin, Germany: Springer, 2011. [Online]. Available: https://link.springer.com/book/10.1007/978-3-642-14090-7
[96] I. N. Levine, D. H. Busch, and H. Shull, *Quantum Chemistry*, vol. 6. Upper Saddle River, NJ, USA: Prentice-Hall, 2009.
[97] L. Ahmed, B. Rasulev, M. Turabekova, D. Leszczynska, and J. Leszczynski, "Receptor- and ligand-based study of fullerene analogues: Comprehensive computational approach including quantum-chemical, QSAR and molecular docking simulations," *Organic Biomolecular Chem.*, vol. 11, no. 35, pp. 5798–5808, 2013.
[98] A. Teplukhin and D. Babikov, "Visualization of potential energy function using an isoenergy approach and 3D prototyping," *J. Chem. Educ.*, vol. 92, no. 2, pp. 305–309, Feb. 2015.
[99] G. C. Schatz, "The analytical representation of electronic potential-energy surfaces," *Rev. Mod. Phys.*, vol. 61, no. 3, pp. 669–688, Jul. 1989.
[100] A. Baiardi, M. Christandl, and M. Reiher, "Quantum computing for molecular biology," *ChemBioChem*, vol. 24, no. 13, 2023, Art. no. e202300120.
[101] A. Baiardi, S. A. Grimmel, M. Steiner, P. L. Türtscher, J. P. Unsleber, T. Weymuth, and M. Reiher, "Expansive quantum mechanical exploration of chemical reaction paths," *Accounts Chem. Res.*, vol. 55, no. 1, pp. 35–43, Dec. 2021, doi: 10.1021/acs.accounts.1c00472.
[102] R. E. Amaro and A. J. Mulholland, "Multiscale methods in drug design bridge chemical and biological complexity in the search for cures," *Nature Rev. Chem.*, vol. 2, no. 4, p. 0148, Apr. 2018.
[103] B. Bonde, P. Patil, and B. Choubey, "The future of drug development with quantum computing," *Methods Mol. Biol.*, vol. 2716, pp. 153–179, 2024, doi: 10.1007/978-1-0716-3449-3_7.
[104] G. W. Richings and S. Habershon, "Predicting molecular photochemistry using machine-learning-enhanced quantum dynamics simulations," *Accounts Chem. Res.*, vol. 55, no. 2, pp. 209–220, Jan. 2022.
[105] N. Schaduangrat, S. Lampa, S. Simeon, M. P. Gleeson, O. Spjuth, and C. Nantasenamat, "Towards reproducible computational drug discovery," *J. Cheminformatics*, vol. 12, no. 1, pp. 1–30, Dec. 2020.

[106] Y. Liu, J. Liu, J. R. Raney, and P. Wang, "Quantum computing for solid mechanics and structural engineering—A demonstration with Variational Quantum Eigensolver," *Extreme Mech. Lett.*, vol. 67, Mar. 2024, Art. no. 102117.
[107] S. K. Niazi and Z. Mariam, "Computer-aided drug design and drug discovery: A prospective analysis," *Pharmaceuticals*, vol. 17, no. 1, p. 22, Dec. 2023.
[108] P. Hassanzadeh, "Towards the quantum-enabled technologies for development of drugs or delivery systems," *J. Controlled Release*, vol. 324, pp. 260–279, Aug. 2020.
[109] M. Sajjan, J. Li, R. Selvarajan, S. H. Sureshbabu, S. S. Kale, R. Gupta, V. Singh, and S. Kais, "Quantum machine learning for chemistry and physics," *Chem. Soc. Rev.*, vol. 51, no. 15, pp. 6475–6573, 2022.
[110] C. Outeiral, M. Strahm, J. Shi, G. M. Morris, S. C. Benjamin, and C. M. Deane, "The prospects of quantum computing in computational molecular biology," *WIREs Comput. Mol. Sci.*, vol. 11, no. 1, p. e1481, Jan. 2021.
[111] (Jan. 2024). *Boehringer Ingelheim—Life Forward*. Accessed: Jan. 30, 2024. [Online]. Available: https://www.boehringer-ingelheim.com
[112] (Jan. 2024). *Quantum Computing*. Accessed: Jan. 30, 2024. [Online]. Available: https://www.rigetti.com
[113] (Jan. 2024). *Merck | Home*. Accessed: Jan. 31, 2024. [Online]. Available: https://www.merck.com
[114] (Jan. 2024). *Home*. Accessed: Jan. 30, 2024. [Online]. Available: https://zapata.ai
[115] (Jan. 2024). *Vertex Pharmaceuticals | Home*. Accessed: Jan. 30, 2024. [Online]. Available: https://www.vrtx.com
[116] (Oct. 2023). *Building the Best Solid State Battery | QuantumScape*. Accessed: Jan. 30, 2024. [Online]. Available: https://www.quantumscape.com
[117] S. Gunashekar, I. Flanagan, C. d'Angelo, I. D. Motsi-Omoijiade, M. Virdee, C. Feijao, and S. Porter, "Using quantum computers and simulators in the life sciences: Current trends and future prospects," RAND Corp., Santa Monica, CA, USA, 2022. [Online]. Available: https://www.rand.org/pubs/research_reports/RRA1899-1.html
[118] P. Kouvelis, J. Milner, and Z. Tian, "Clinical trials for new drug development: Optimal investment and application," *Manuf. Service Oper. Manage.*, vol. 19, no. 3, pp. 437–452, Jul. 2017.
[119] F. Bova, A. Goldfarb, and R. G. Melko, "Commercial applications of quantum computing," *EPJ Quantum Technol.*, vol. 8, no. 1, p. 2, Dec. 2021.
[120] A. D. Roses, "Pharmacogenetics and drug development: The path to safer and more effective drugs," *Nature Rev. Genet.*, vol. 5, no. 9, pp. 645–656, Sep. 2004.
[121] M. Langione, J.-F. Bobier, C. Meier, S. Hasenfuss, and U. Schulze, *Will Quantum Computing Transform Biopharma R&D*. Boston Consulting Group, 2019. [Online]. Available: https://www.bcg.com/publications/2019/quantum-computing-transform-biopharma-research-development
[122] K. Dwivedi and A. Nigam, "Quantum deep learning for phoniatrics biomarker based disease detection deep learning model for disease detection by phoniatrics biomarkers using quantum computation," in *Proc. 2nd Int. Conf. Data, Eng. Appl. (IDEA)*, Feb. 2020, pp. 1–8.
[123] A. S. Bhatia, M. K. Saggi, and S. Kais, "Quantum machine learning predicting ADME-Tox properties in drug discovery," *J. Chem. Inf. Model.*, vol. 63, no. 21, pp. 6476–6486, Nov. 2023.
[124] Y. Zhang and Q. Ni, "Recent advances in quantum machine learning," *Quantum Eng.*, vol. 2, no. 1, p. e34, Mar. 2020.
[125] A. K. Fedorov and M. S. Gelfand, "Towards practical applications in quantum computational biology," *Nature Comput. Sci.*, vol. 1, no. 2, pp. 114–119, Feb. 2021.
[126] P. Lolur, M. Skogh, W. Dobrautz, C. Warren, J. Biznárová, A. Osman, G. Tancredi, G. Wendin, J. Bylander, and M. Rahm, "Reference-state error mitigation: A strategy for high accuracy quantum computation of chemistry," *J. Chem. Theory Comput.*, vol. 19, no. 3, pp. 783–789, Feb. 2023.
[127] S. Carretta, D. Zueco, A. Chiesa, Á. Gómez-León, and F. Luis, "A perspective on scaling up quantum computation with molecular spins," *Appl. Phys. Lett.*, vol. 118, no. 24, Jun. 2021, Art. no. 240501, doi: 10.1063/5.0053378.
[128] S. Endo, Z. Cai, S. C. Benjamin, and X. Yuan, "Hybrid quantum-classical algorithms and quantum error mitigation," *J. Phys. Soc. Jpn.*, vol. 90, no. 3, Mar. 2021, Art. no. 032001.
[129] L.-M. Duan and G.-C. Guo, "Suppressing environmental noise in quantum computation through pulse control," *Phys. Lett. A*, vol. 261, nos. 3–4, pp. 139–144, Oct. 1999.
[130] G. Li, A. Wu, Y. Shi, A. Javadi-Abhari, Y. Ding, and Y. Xie, "On the co-design of quantum software and hardware," in *Proc. 8th Annu. ACM Int. Conf. Nanosc. Comput. Commun.*, 2021, pp. 1–7.
[131] J. M. Baker and F. T. Chong, "Emerging technologies for quantum computing," *IEEE Micro*, vol. 41, no. 5, pp. 41–47, Sep. 2021.
[132] J. Singh and K. S. Bhangu, "Contemporary quantum computing use cases: Taxonomy, review and challenges," *Arch. Comput. Methods Eng.*, vol. 30, no. 1, pp. 615–638, Jan. 2023.
[133] N. P. de Leon, K. M. Itoh, D. Kim, K. K. Mehta, T. E. Northup, H. Paik, B. S. Palmer, N. Samarth, S. Sangtawesin, and D. W. Steuerman, "Materials challenges and opportunities for quantum computing hardware," *Science*, vol. 372, no. 6539, Apr. 2021, Art. no. eabb2823.
[134] P. Jurcevic et al., "Demonstration of quantum volume 64 on a superconducting quantum computing system," *Quantum Sci. Technol.*, vol. 6, no. 2, Apr. 2021, Art. no. 025020.
[135] E. Knill, R. Laflamme, and G. J. Milburn, "A scheme for efficient quantum computation with linear optics," *Nature*, vol. 409, no. 6816, pp. 46–52, Jan. 2001.
[136] V. Stirbu, M. Haghparast, M. Waseem, N. Dayama, and T. Mikkonen, "Full-stack quantum software in practice: Ecosystem, stakeholders and challenges," 2023, *arXiv:2307.16345*.
[137] C. Ugwuishiwu, U. Orji, C. Ugwu, and C. Asogwa, "An overview of quantum cryptography and Shor's algorithm," *Int. J. Adv. Trends Comput. Sci. Eng.*, vol. 9, no. 5, pp. 8397–8405, 2020.
[138] E. Diamanti, H.-K. Lo, B. Qi, and Z. Yuan, "Practical challenges in quantum key distribution," *NPJ Quantum Inf.*, vol. 2, no. 1, pp. 1–12, Nov. 2016.
[139] D. Garisto. (2022). *What Is the Future of Quantum-Proof Encryption?* IEEE Spectrum. [Online]. Available: https://spectrum.ieee.org/post-quantum-cryptography-nist
[140] U. Tariq, I. Ahmed, A. K. Bashir, and K. Shaukat, "A critical cybersecurity analysis and future research directions for the Internet of Things: A comprehensive review," *Sensors*, vol. 23, no. 8, p. 4117, Apr. 2023. [Online]. Available: https://www.mdpi.com/1424-8220/23/8/4117
[141] G. Trifirò and S. Crisafulli, "A new era of pharmacovigilance: Future challenges and opportunities," *Frontiers Drug Saf. Regulation*, vol. 2, Feb. 2022, Art. no. 866898. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fdsfr.2022.866898
[142] S. Fadli, B. S. Rawal, and A. Mentges, "Hybrid quantum machine learning using quantum integrated cloud architecture (QICA)," in *Proc. Int. Conf. Comput., Netw. Commun. (ICNC)*, Feb. 2023, pp. 419–425.
[143] L. Wang, F. Tang, and H. Wu, "Hybrid genetic algorithm based on quantum computing for numerical optimization and parameter estimation," *Appl. Math. Comput.*, vol. 171, no. 2, pp. 1141–1156, Dec. 2005.
[144] M. Perelshtein, A. Sagingalieva, K. Pinto, V. Shete, A. Pakhomchik, A. Melnikov, F. Neukart, G. Gesek, A. Melnikov, and V. Vinokur, "Practical application-specific advantage through hybrid quantum computing," 2022, *arXiv:2205.04858*.
[145] S. P. Leelananda and S. Lindert, "Computational methods in drug discovery," *Beilstein J. Organic Chem.*, vol. 12, no. 1, pp. 2694–2718, 2016.
[146] N. Jyothi Ahuja and S. Dutt, "Implications of quantum science on Industry 4.0: Challenges and opportunities," in *Quantum and Blockchain for Modern Computing Systems: Vision and Advancements: Quantum and Blockchain Technologies: Current Trends and Challenges*, 2022, pp. 183–204.
[147] J. Kietzmann, D. S. Demetis, T. Eriksson, and A. Dabirian, "Hello quantum! How quantum computing will change the world," *IT Prof.*, vol. 23, pp. 106–111, 2021, doi: 10.1109/MITP.2021.3086917.
[148] R. de Wolf, "The potential impact of quantum computers on society," *Ethics Inf. Technol.*, vol. 19, no. 4, pp. 271–276, Dec. 2017.
[149] P. B. Upama, M. J. H. Faruk, M. Nazim, M. Masum, H. Shahriar, G. Uddin, S. Barzanjeh, S. I. Ahamed, and A. Rahman, "Evolution of quantum computing: A systematic survey on the use of quantum computing tools," in *Proc. IEEE 46th Annu. Comput., Softw., Appl. Conf. (COMPSAC)*, Jun. 2022, pp. 520–529.
[150] J. Davids, N. Lidströmer, and H. Ashrafian, "Artificial intelligence in medicine using quantum computing in the future of healthcare," in *Artificial Intelligence in Medicine*. Cham, Switzerland: Springer, 2022, pp. 423–446, doi: 10.1007/978-3-030-64573-1_338.
[151] S. Sinha and D. Vohora, "Chapter 2—Drug discovery and development: An overview," in *Pharmaceutical Medicine and Translational Clinical Research*, D. Vohora and G. Singh, Eds. Boston, MA, USA: Academic, 2018, pp. 19–32. [Online]. Available: https://www.sciencedirect.com/science/article/pii/B978012802103300002X



GAUTAM KUMAR is currently pursuing the B.Tech. degree with Kalinga Institute of Industrial Technology (KIIT), Bhubaneshwar. He is also doing his research internship with the Birla Institute of Technology and Science (BITS), Pilani, under Dr. Vikas Hassija. His research interests include machine learning, computer vision, and deep learning.

SAHIL YADAV is currently pursuing the B.Tech. degree with Kalinga Institute of Industrial Technology (KIIT), Bhubaneshwar. He is also doing his research internship with the Birla Institute of Technology and Science (BITS), Pilani, under Dr. Vikas Hassija. His research interests include machine learning, reinforcement learning, and deep learning.



ANIRUDDHA MUKHERJEE is currently pursuing the B.Tech. degree with Kalinga Institute of Industrial Technology (KIIT), Bhubaneshwar. He was with the Birla Institute of Technology and Science (BITS), Pilani, during the summer of 2023. On campus, he was pursuing his research internship under Dr. Vinay Chamola. He has two published patents to his name. His research interests include machine learning, natural language processing, computer vision, and deep learning for privacy and security.

VIKAS HASSIJA received the M.E. degree from Birla Institute of Technology and Science (BITS), Pilani, India, in 2014. He is currently an Associate Professor with the School of Computer Engineering, Kalinga Institute of Industrial Technology, Bhubaneshwar. He was a Postdoctoral Research Fellow with the National University of Singapore (NUS). His current research interests include blockchain, non fungible tokens, the IoT, privacy and security, and distributed networks.

MOHSEN GUIZANI (Fellow, IEEE) is currently a Professor of Machine Learning with the Mohamed Bin Zayed University of Artificial Intelligence (MBZUAI), Abu Dhabi, UAE. Previously, he worked in different institutions in the USA. His research interests include applied machine learning and artificial intelligence, smart city, the Internet of Things (IoT), intelligent autonomous systems, and cybersecurity. He was listed as a Clarivate Analytics Highly Cited Researcher in computer science in 2019, 2020, 2021, and 2022.