Quantum-Enhanced Computational Drug Discovery: Leveraging Variational Quantum Algorithms for Accurate

Binding Affinity Prediction and Lead Optimization in Complex Biological Targets

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***Abstract*—Accurate prediction of binding affinities and efficient lead optimization remain central challenges in computational drug discovery, particularly for complex biological targets characterized by rugged energy landscapes, conformational heterogeneity, and high-dimensional interaction spaces. Classical computational methods—such as molecular docking, force-field–based simulations, and deep learning models—have made substantial progress, yet they often struggle to capture quantum-mechanical effects and long-range correlations critical to molecular recognition. This study explores a quantum-enhanced framework that integrates Variational Quantum Algorithms (VQAs), quantum-inspired Hamiltonian modeling, and hybrid quantum–classical optimization workflows to improve the fidelity and scalability of drug discovery pipelines. By encoding molecular interactions into parameterized quantum circuits, the framework leverages quantum superposition and entanglement to explore complex chemical space more efficiently, enabling refined estimation of binding energies and accelerated identification of high-quality leads. Preliminary simulations indicate that VQA-based estimators outperform classical baselines for challenging protein–ligand systems, reducing prediction error while maintaining computational tractability. These findings highlight the emerging potential of quantum technologies to enable more accurate, data-efficient, and mechanistically grounded drug discovery for next-generation therapeutics.**

Computational drug discovery plays a critical role in accelerating therapeutic development by reducing experimental costs, narrowing chemical search space, and enabling early prediction of drug-target interactions [9]. Over the past decade, advancements in classical computational chemistry, molecular dynamics, and machine learning have significantly improved the ability to screen compounds and model binding phenomena. However, many biological systems—particularly those involving flexible proteins, allosteric sites, metal centers, or quantum-mechanical interaction effects—pose fundamental challenges to classical simulation approaches [2].

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