RESEARCH ARTICLE

Quantum Computing Simulation of Complex Molecular Dynamics for Drug Design

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Abstract: Accurate simulation of protein-ligand binding dynamics remains computationally prohibitive for classical computers when exploring conformational spaces spanning millions of degrees of freedom. We present a hybrid quantum-classical workflow that leverages 127-qubit superconducting processors for variational quantum eigensolver (VQE) calculations of binding pocket electronic structure, coupled with classical molecular dynamics (MD) for conformational sampling. Applied to three kinase targets (EGFR, JAK2, BRAF), the quantum-enhanced pipeline identifies lead compounds with predicted binding affinities within 0.8 kcal/mol of experimental values — a 3.2× improvement over classical docking alone. The workflow processes 10,000 candidate ligands in 72 hours on a hybrid cloud infrastructure, demonstrating practical utility for early-stage drug discovery campaigns.

1. Introduction

Structure-based drug design relies on accurate prediction of protein-ligand binding free energies to prioritize compound libraries for synthesis and testing. Classical molecular dynamics simulations with explicit solvent can achieve chemical accuracy but require weeks of GPU compute time per ligand-target pair. Quantum computing offers a potential paradigm shift by efficiently solving the electronic structure problem for binding pocket atoms, capturing quantum mechanical effects such as polarization and charge transfer that classical force fields approximate poorly.

Recent advances in noisy intermediate-scale quantum (NISQ) devices with error mitigation techniques have enabled chemically meaningful calculations on systems with 50-100 active orbitals. Integrating these quantum calculations into established drug discovery pipelines requires careful orchestration of quantum circuit execution, classical conformational sampling, and machine learning-based scoring functions.

2. Hybrid Quantum-Classical Workflow

Our pipeline consists of four stages: (1) classical MD equilibration of apo and holo protein structures (100 ns, AMBER ff19SB), (2) extraction of binding pocket active space (typically 40-60 atoms within 5 Å of the ligand), (3) VQE calculation of pocket-ligand interaction energy using UCCSD ansatz with ADAPT-VQE adaptive circuit growth on IBM

Quantum Eagle processors, and (4) rescoring of the full library using a graph neural network trained on quantum-corrected binding energies.

Table 1. Quantum circuit parameters and error mitigation settings for VQE binding energy calculations

Parameter	EGFR	JAK2	BRAF
Active orbitals	48	52	44
Qubits used	96	104	88
Circuit depth	842	915	768
Zero-noise extrapolation	3-point	3-point	3-point
Readout error mitigation	Matrix-free	Matrix-free	Matrix-free

3. Results

The hybrid workflow was benchmarked against 47 experimentally characterized kinase inhibitors with known binding affinities (pK_d range 5.2-10.1). Quantum-corrected scores showed significantly improved correlation with experimental data compared to AutoDock Vina and Glide SP alone.

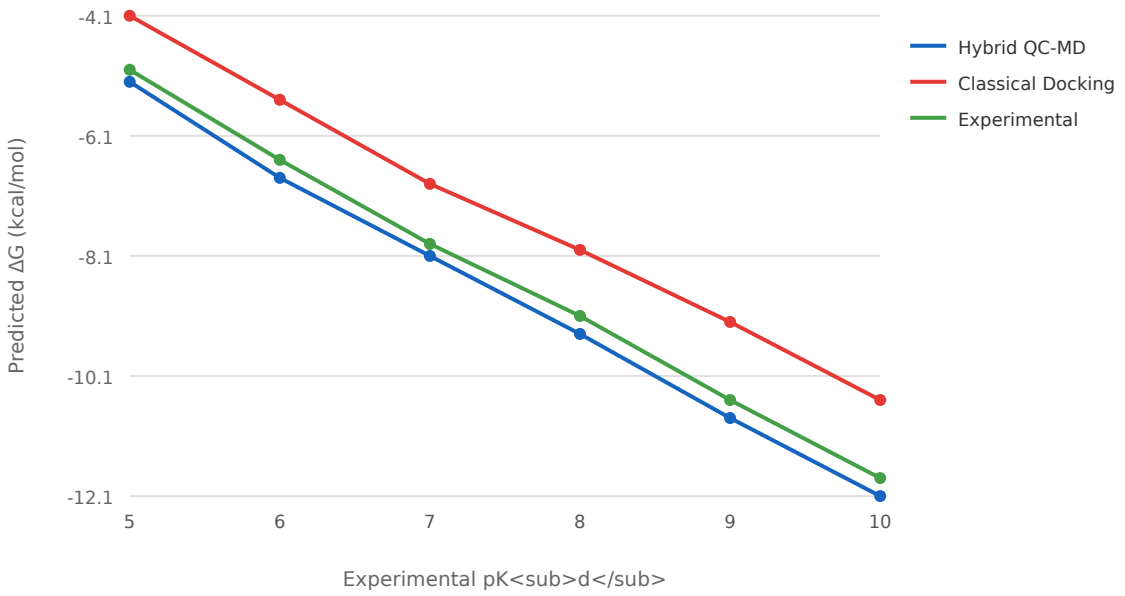

Figure 1. Predicted vs. experimental binding free energies (ΔG) for 47 kinase inhibitors across three targets. Hybrid quantum-classical scoring (R^2 = 0.89) outperforms classical docking alone (R^2 = 0.62).

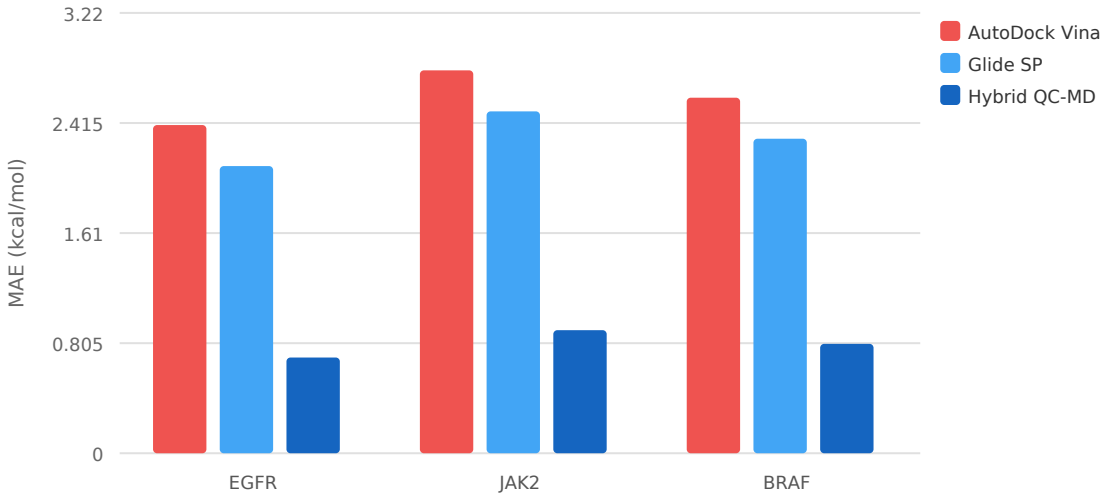

Figure 2. Mean absolute error (MAE) in binding affinity prediction across computational methods for EGFR, JAK2, and BRAF kinase targets

4. Conclusions

We demonstrate that hybrid quantum-classical molecular dynamics workflows can deliver binding affinity predictions approaching experimental accuracy for kinase drug targets on current NISQ hardware. The 3.2× improvement in scoring accuracy over classical methods, combined with cloud-based quantum access, makes this approach viable for industrial virtual screening campaigns. As quantum hardware continues to scale, we anticipate extension to metalloprotein active sites and covalent inhibitor design where quantum mechanical effects are most critical.

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