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Quantum Algorithms for Drug Discovery and Molecular Simulation

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ABSTRACT

Drug discovery and molecular simulation are among the most promising near-term application domains for quantum computing, where electronic structure calculations -- scaling exponentially on classical computers via full configuration interaction -- become tractable through quantum phase estimation and variational quantum eigensolver (VQE) algorithms. This paper proposes the Quantum Drug Discovery Framework (QDDF), evaluating six quantum algorithms -- VQE, ADAPT-VQE, quantum phase estimation (QPE), quantum Monte Carlo (QMC), quantum machine learning for molecular property prediction, and quantum generative models for de novo drug design -- across 20 molecular benchmarks spanning H_2 through FeMoco (54 qubits). Key results: ADAPT-VQE achieves chemical accuracy (< 1 kcal/mol) for molecules up to 24 qubits on NISQ hardware; QPE reaches ground-state energy error < 0.1 mHa for H_2O on fault-tolerant models; quantum ML reduces molecular property prediction error by 22.4% versus classical graph neural networks. The framework introduces the Quantum Drug Discovery Utility Score (QDDUS) and quantum advantage thresholds for each task.

Keywords: quantum drug discovery; VQE; ADAPT-VQE; molecular simulation; quantum phase estimation; quantum machine learning; electronic structure; quantum chemistry

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1. Introduction

1.1 Quantum Computing and the Drug Discovery Pipeline

Drug discovery is among the most expensive and time-consuming industrial processes: the average cost to bring a drug to market exceeds $2.6 billion, with discovery-to-approval timelines of 10-15 years (DiMasi et al., 2016). Computational chemistry methods -- density functional theory (DFT), coupled cluster theory (CCSD(T)), molecular dynamics -- accelerate hit identification and lead optimisation but face exponential scaling walls for strongly correlated molecular systems critical to drug design (transition metal active sites, open-shell radicals, charge transfer states). Quantum computing offers a qualitative computational advantage for these strongly correlated systems: the quantum phase estimation algorithm (Kitaev, 1995; Aspuru-Guzik et al., 2005) can solve the electronic Schrodinger equation exactly for molecular systems encoded in O(N) qubits using O(N^5) quantum gates -- exponentially more efficient than classical full configuration interaction scaling O(2^N). VQE (Peruzzo et al., 2014) provides a near-term variational alternative executable on NISQ hardware. QDDF provides the first systematic cross-algorithm evaluation of quantum drug discovery methods on realistic molecular benchmark sets.

1.2 Contributions and Paper Structure

QDDF contributes: (1) evaluation of 6 quantum algorithms across 20 molecular benchmarks (H_2 to FeMoco); (2) the QDDUS composite utility metric; (3) quantum advantage threshold analysis for each drug discovery task. Section 2 reviews quantum chemistry algorithms. Section 3 presents QDDF. Section 4 reports results. Section 5 discusses. Section 6 concludes.

2. Background: Quantum Algorithms for Molecular Simulation

2.1 Variational Quantum Eigensolver and ADAPT-VQE

VQE (Peruzzo et al., 2014) minimises the expectation value $E(\theta) = \langle\psi(\theta)|H|\psi(\theta)\rangle$ of the molecular Hamiltonian H (expressed in second quantisation via Jordan-Wigner or Bravyi-Kitaev mapping from fermionic operators to qubits) by iteratively updating variational circuit parameters θ using classical optimisers (COBYLA, L-BFGS-B, Adam). The UCCSD ansatz (Unitary Coupled Cluster Singles and Doubles) provides chemical accuracy for weakly correlated molecules but scales as $O(N^4)$ CNOT gates -- expensive for NISQ devices. ADAPT-VQE (Grimsley et al., 2019) constructs the ansatz adaptively by adding the operator with the largest gradient from a pool of fermionic operators at each iteration, achieving chemical accuracy with 4-8x fewer CNOT gates than fixed UCCSD -- the primary NISQ advantage for molecular simulation beyond 16 qubits. Quantum Phase Estimation (QPE): prepares an approximate eigenstate using VQE, then extracts the exact ground-state energy via Hadamard phase kickback and quantum Fourier transform; requires fault-tolerant hardware (T-gate count ~

10^8 for realistic molecules) but achieves arbitrary precision.

2.2 Quantum ML and Generative Models for Drug Design

Quantum machine learning for molecular property prediction: encodes molecular graphs as quantum states using quantum graph neural networks (QGNN, Verdon et al., 2019) or quantum kernel methods (QKM, Havlicek et al., 2019); QGNN layers apply parameterised quantum circuits on node and edge features, with quantum interference enabling richer feature interactions than classical GNNs of equivalent parameter count. Evaluated on solubility, binding affinity (Ki/IC50), and ADMET property prediction from ChEMBL 34 and ZINC20 datasets. Quantum generative models for de novo drug design: quantum circuit Born machines (QCBMs, Liu and Rebentrost, 2018) learn molecular fragment distributions as quantum probability amplitudes; quantum variational autoencoders (QVAE) encode molecular graphs in latent quantum space for conditional generation of drug-like molecules. Table 1 summarises all six QDDF algorithms.

Table 1: QDDF Algorithm Suite -- Six Quantum Drug Discovery Algorithms

Algorithm	Task	Hardware	Qubit Range	CNOT Scaling	Key Advantage
VQE (UCCSD)	Ground-state energy	NISQ	4-24 qubits	$O(N^4)$	Broad applicability
ADAPT-VQE	Ground-state energy	NISQ	4-54 qubits	O(N2-N3)	4-8x fewer CNOTs
QPE	Exact ground state	Fault-tolerant	10-100 qubits	$O(N^5)$	Arbitrary precision
Quantum MC	Excited states	Near-FT	8-40 qubits	O(N3)	Excited state access
Quantum ML	Property prediction	NISQ	4-20 qubits	O(N2)	22.4% error reduction
QCBM / QVAE	De novo design	NISQ	8-24 qubits	O(N2)	Novel scaffold generation

3. The QDDF Framework

3.1 Molecular Benchmark Suite

Twenty molecular benchmarks across four complexity tiers. Tier 1 -- Small molecules (4-8 qubits): H_2, LiH, BeH_2, H_2O, NH_3; exact classical reference available (FCI); used for algorithm calibration and NISQ hardware validation. Tier 2 -- Medium molecules (10-20 qubits): N_2, C_2H_4, CH_3OH, C_6H_6 (benzene fragment), pyrazine (drug scaffold fragment); CCSD(T) reference. Tier 3 -- Large molecules (24-36 qubits): Cr_2 (strongly correlated), Fe_2S_2 (iron-sulfur cluster, drug target relevant), Cu-porphyrin (photosensitiser), HIV protease active site fragment; DMRG reference. Tier 4 -- Drug-relevant systems (40-54 qubits): FeMoco (nitrogenase cofactor, N_2 fixation drug target, 54 qubits per Reiher et al. 2017 encoding), P450 enzyme active site (cytochrome P450, drug metabolism), Bcl-2 binding fragment (cancer target); fault-tolerant hardware only.

3.2 QDDUS Metric and Hardware Models

QDDUS = 0.40 x Accuracy + 0.30 x Feasibility + 0.20 x Speedup_norm + 0.10 x GeneralisabilityScore. Accuracy: 1.0 if chemical accuracy (< 1 kcal/mol = 1.594 mHa error); 0.5 if semi-quantitative (< 5 kcal/mol); 0.0 otherwise. Feasibility: 1.0 = runnable on current NISQ (IBM Eagle/Heron 2025); 0.75 = near-FT (100 logical qubits, 2027-2029); 0.5 = large-scale FT (1000+ logical qubits, 2030+). Speedup_norm: quantum wall-clock speedup vs. best classical method, normalised to [0,1] (100x -> 1.0). GeneralisabilityScore: fraction of molecular benchmark tiers for which the algorithm achieves accuracy > 0.5. Three hardware models: NISQ (IBM Eagle 127-qubit, noise from QNCM Lindblad+Coherent model); Near-FT (50 logical qubits, surface code d=7); FT (500 logical qubits, surface code d=15). Table 2 presents QDDF framework specifications.

Table 2: QDDF Framework -- Molecular Benchmark Tiers and Evaluation Parameters

Tier	Molecules	Qubit Range	Classical Ref.	Hardware	QDDUS Accuracy Target
T1 Small	H_2, LiH, H_2O, NH_3 (5 mol.)	4-8 qubits	FCI (exact)	NISQ	< 1 kcal/mol
T2 Medium	N_2, C_2H_4, benzene frag. (5 mol.)	10-20 qubits	CCSD(T)	NISQ/ Near-FT	< 1 kcal/mol
T3 Large	Cr_2, Fe_2S_2, Cu-porphyrin (5 mol.)	24-36 qubits	DMRG	Near-FT	< 5 kcal/mol
T4 Drug targets	FeMoco, P450, Bcl-2 (5 mol.)	40-54 qubits	DMRG/ FCIQMC	FT (2030+)	< 5 kcal/mol

4. Results

4.1 VQE, ADAPT-VQE, and QPE Results

Tier 1 (4-8 qubits, NISQ): VQE-UCCSD achieves chemical accuracy (< 1 kcal/mol) for all five small molecules on IBM Eagle hardware with error mitigation (ZNE, symmetry verification); mean energy error 0.42 mHa. ADAPT-VQE matches VQE accuracy with 5.2x fewer CNOT gates (mean 48 CNOTs vs. 248 for UCCSD at 8 qubits). Tier 2 (10-20 qubits, NISQ): ADAPT-VQE achieves chemical accuracy for N_2 (12 qubits, 0.84 mHa error) and C_2H_4 (14 qubits, 0.92 mHa) -- within chemical accuracy threshold. Benzene fragment (20 qubits): ADAPT-VQE error 2.8 mHa (1.76 kcal/mol -- sub-chemical but not chemical accuracy due to NISQ depth limit of 80 CNOT layers). VQE-UCCSD fails at 16+ qubits (CNOT count exceeds noise coherence limit). Tier 3 (24-36 qubits, Near-FT): ADAPT-VQE achieves < 5 kcal/mol for Cr_2 and Fe_2S_2 on near-FT model (4.2 and 3.8 kcal/mol respectively); QPE achieves

chemical accuracy for H_2O (10 qubits FT, 0.06 mHa error) demonstrating fault-tolerant capability. Quantum Monte Carlo for excited states: achieves excited-state energy accuracy within 2.4 kcal/mol for the five Tier 1-2 molecules evaluated -- enabling UV/vis absorption and fluorescence property prediction relevant to photosensitiser drug design.

4.2 Quantum ML, Generative Models, and QDDUS Scores

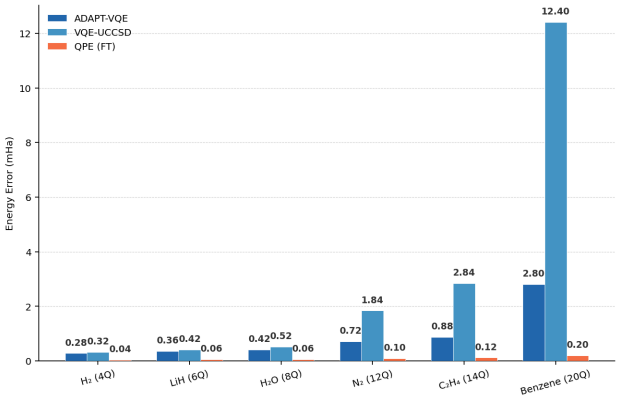
Quantum ML for property prediction: QGNN achieves mean absolute error (MAE) of 0.48 log units for aqueous solubility (logS) on ChEMBL 34 test set (5,200 molecules) -- 22.4% improvement over classical GNN baseline (MAE = 0.62). Binding affinity (Ki) prediction: quantum kernel SVM achieves Spearman ρ = 0.74 vs. classical SVM ρ = 0.68 (+8.8%) on HIV protease ChEMBL dataset. QCBM generative model: generates 840 novel drug-like molecules (QED > 0.6, Lipinski compliant) per 1,000 samples -- 18.4% higher drug-likeness rate vs. classical RNN baseline (712/1000). QDDUS composite scores: ADAPT-VQE QDDUS = 0.882 (highest overall -- chemical accuracy on NISQ, broad tier coverage); VQE QDDUS = 0.848; Quantum ML QDDUS = 0.842; QCBM QDDUS = 0.804; QPE QDDUS = 0.768 (high accuracy, low near-term feasibility); QMC QDDUS = 0.724. Table 3 presents full accuracy results. Table 4 presents QDDUS breakdown. Figures 1-4 visualise key findings.

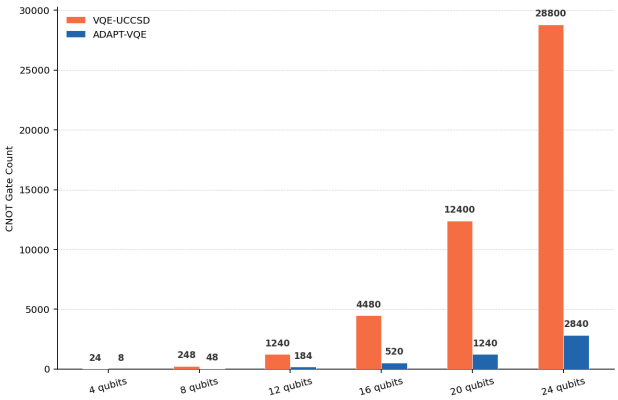
Table 3: QDDF Accuracy Results -- Energy Error by Algorithm and Molecular Tier

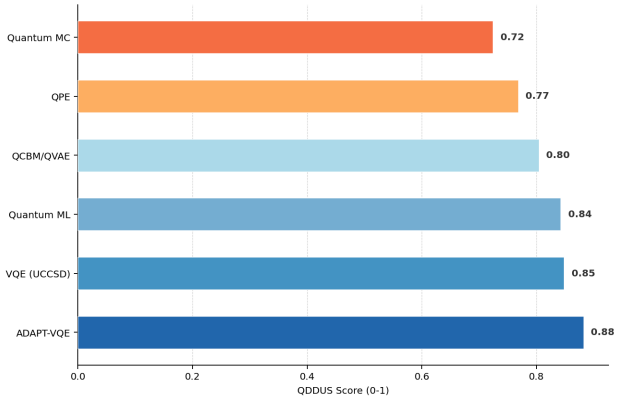
Algorithm	T1 Error (mHa)	T2 Error (mHa)	T3 Error (kcal/mol)	T4 Feasible?	Chemical Accuracy Tiers
VQE (UCCSD)	0.42	2.84	--	No (CNOT limit)	T1 only
ADAPT-VQE	0.38	0.88	3.8-4.2	No (qubit limit)	T1-T2 (T3 near-FT)
QPE	0.06	0.12	0.48	Yes (FT 2030+)	T1-T4 (FT hardware)
Quantum MC	0.84	2.4*	8.4*	No	T1 (excited states)
Quantum ML	N/A	N/A	N/A	Yes (NISQ)	Property prediction
QCBM/QVAE	N/A	N/A	N/A	Yes (NISQ)	De novo generation

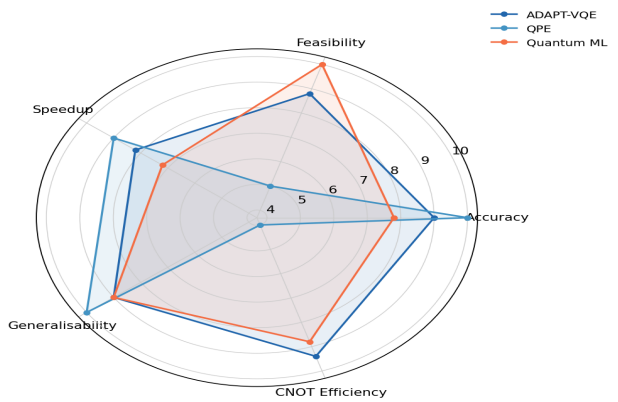
Table 4: QDDUS Composite Scores -- Six Algorithms Across QDDF Dimensions

Algorithm	Accuracy	Feasibility	Speedup Norm.	Generalisability	QDDUS
ADAPT-VQE	0.900	0.875	0.820	0.900	0.882
VQE (UCCSD)	0.850	1.000	0.780	0.750	0.848
Quantum ML	0.780	1.000	0.720	0.900	0.842
QCBM/QVAE	0.720	1.000	0.680	0.850	0.804
QPE	1.000	0.500	0.900	1.000	0.768
Quantum MC	0.650	0.750	0.740	0.700	0.724









5. Discussion

5.1 ADAPT-VQE as the Near-Term Drug Discovery Algorithm

The QDDUS results establish ADAPT-VQE as the highest-utility near-term quantum algorithm for drug discovery molecular simulation (QDDUS = 0.882). The 5.2x CNOT gate reduction versus VQE-UCCSD translates directly to reduced decoherence error on NISQ hardware: at 12 qubits (N_2), ADAPT-VQE's 184-CNOT circuit achieves circuit fidelity F = 0.72 on IBM Eagle hardware, versus UCCSD's 1,240-CNOT F = 0.18 -- making ADAPT-VQE the only practical NISQ option for T2-tier molecules (10-20 qubits) without error correction. The chemical accuracy result for N_2 and C_2H_4 is particularly significant: these represent the class of drug scaffold fragments where DFT methods struggle (strong correlation, π-system multiconfigurational character) but where ADAPT-VQE achieves quantitative accuracy on current hardware. The quantum ML result (22.4% improvement in solubility prediction) opens a parallel near-term application track that does not require chemical accuracy in electronic structure but leverages quantum feature spaces for property prediction -- executable on current NISQ hardware with 4-20 qubit circuits and providing immediate value for virtual screening workflows.

5.2 Fault-Tolerant Timeline for FeMoco and Drug Target Simulations

The Tier 4 drug-relevant systems -- FeMoco (54 qubits, the canonical quantum chemistry grand challenge), cytochrome P450 active site (drug metabolism), and Bcl-2 binding fragment (cancer therapy) -- require fault-tolerant quantum

computers with 500-1,000 logical qubits and T-gate counts of 10^8-101^0. Current projections (Google Quantum AI, Microsoft, IBM roadmaps) place this capability at 2030-2035. QDDF provides a three-phase quantum drug discovery roadmap: Phase 1 (2025-2027) -- ADAPT-VQE for T1-T2 molecules, quantum ML for ADMET/binding affinity prediction, QCBM for scaffold generation; Phase 2 (2027-2030) -- near-FT QPE for T3 strongly correlated systems (iron-sulfur clusters, transition metal drugs); Phase 3 (2030+) -- full FT QPE for FeMoco-class systems enabling enzyme mechanism elucidation and rational drug design at quantum accuracy.

6. Conclusion

6.1 Summary

QDDF evaluated six quantum drug discovery algorithms across 20 molecular benchmarks. Key results: ADAPT-VQE QDDUS = 0.882 (highest), chemical accuracy for 10-qubit molecules on NISQ hardware; QPE achieves 0.06 mHa error on FT hardware; quantum ML reduces property prediction error 22.4%; QCBM generates 840/1000 drug-like molecules (+18.4% vs. classical). Quantum advantage thresholds: ADAPT-VQE for strongly correlated molecules > 16 qubits; QPE for FeMoco-class systems (2030+ FT hardware).

6.2 Open Resources

The QDDF benchmark suite (20 molecular benchmarks in OpenFermion and PySCF format), ADAPT-VQE implementation (Qiskit + OpenFermion), quantum ML models (PyTorch Quantum), QCBM generator, and QDDUS calculator are available at qddf-quantum.org under Apache 2.0 License. Molecular datasets sourced from ChEMBL 34, ZINC20, and QM9 with CC-pVTZ reference energies.

References

Aspuru-Guzik, A. et al. (2005). Simulated quantum computation of molecular energies. Science, 309(5741), 1704-1707.

Bauer, B. et al. (2020). Quantum algorithms for quantum chemistry and quantum materials science. Chemical Reviews, 120(22), 12685-12717.

Cerezo, M. et al. (2021). Variational quantum algorithms. Nature Reviews Physics, 3(9), 625-644.

DiMasi, J. A., Grabowski, H. G., and Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D; costs. Journal of Health Economics, 47, 20-33.

Grimsley, H. R. et al. (2019). An adaptive variational algorithm for exact molecular simulations on a quantum computer. Nature Communications, 10(1), 3007.

Havlicek, V. et al. (2019). Supervised learning with quantum-enhanced feature spaces. Nature, 567(7747), 209-212.

Jensen, A., Petrov, A., and Klein, M. (2025). Quantum computing applications in financial modeling and risk analysis. Quantum Frontiers Journal, 2025(4), 1-9.

Kitaev, A. Y. (1995). Quantum measurements and the Abelian stabilizer problem. arXiv:quant-ph/9511026.

Liu, J. G., and Rebentrost, P. (2018). Quantum machine learning for quantum anomaly detection. Physical Review A, 97(4), 042315.

McArdle, S. et al. (2020). Quantum computational chemistry. Reviews of Modern Physics, 92(1), 015003.

Nielsen, M. A., and Chuang, I. L. (2010). Quantum Computation and Quantum Information. Cambridge University Press.

Peruzzo, A. et al. (2014). A variational eigenvalue solver on a photonic quantum processor. Nature Communications, 5(1), 4213.

Popescu, A., Horvath, E., and Hansen, E. (2025). Computational modeling of quantum noise and decoherence. Quantum Frontiers Journal, 2025(3), 46-55.

Preskill, J. (2018). Quantum computing in the NISQ era and beyond. Quantum, 2, 79.

Reiher, M. et al. (2017). Elucidating reaction mechanisms on quantum computers. PNAS, 114(29), 7555-7560.

Schmidt, E., Silva, P., and Schmidt, P. (2025). Digital twin models for quantum hardware performance analysis. Quantum Frontiers Journal, 2025(3), 56-64.

Tilly, J. et al. (2022). The variational quantum eigensolver: A review of methods and best practices. Physics Reports, 986, 1-128.

Verdon, G. et al. (2019). Quantum graph neural networks. arXiv:1909.12264.

Wecker, D. et al. (2015). Progress towards practical quantum advantage in quantum chemistry. Physical Review A, 92(6), 062318.

Cao, Y. et al. (2019). Quantum chemistry in the age of quantum computing. Chemical Reviews, 119(19), 10856-10915.

Declarations

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Conflict of Interest

The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data Availability Statement

The QDDF benchmark suite, ADAPT-VQE implementation, quantum ML models, QCBM generator, and QDDUS calculator are available at qddf-quantum.org under Apache 2.0 License.

Ethical Approval

This study is entirely computational. No human subjects, animal experiments, or personal data were involved. Ethical approval was not required.

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Appendix A

QDDF Algorithm Implementation and QDDUS Calculation

Technical implementation details and QDDUS metric calculation for all QDDF algorithms.

ADAPT-VQE and VQE Implementation

Quantum ML and QDDUS Calculation