

Quantum Walk-Based Exploration of Drug-Like Chemical Space

Authors: Mohamed Iheb Hergli, Adel Trabelsi, Afef Abdelkrim, Emna Harigua-Souiai

Motivation

Drug lead optimization requires navigating a chemical space estimated at 10^{60} molecules. Classical approaches like evolutionary algorithms, bayesian optimization, and reinforcement learning build their exploration distributions from past fitness evaluations. By construction, they cannot amplify probability toward unobserved, high-fitness molecular regions. This is a structural limitation, not a scaling one.

Approach

Starting from a known active molecule, we construct a local molecular subspace as a structured graph, nodes are synthetically accessible compounds generated by applying a set of standard medicinal chemistry transformations, and edges connect molecules reachable by a single transformation step. Subspace size is chosen to keep the resulting circuit within a bounded qubit and depth budget. A Quantum Walk Optimization Algorithm (QWOA) is then deployed on this graph: a fitness oracle encodes molecular quality as a phase into the quantum register, and alternating walk and phase-separation unitaries drive coherent amplitude concentration toward high-fitness regions through constructive interference. Circuit depth follows from the graph's structural properties and the number of walk/phase-separation layers needed for convergence, and is reported alongside the oracle's own circuit cost. Measurement provides an exploration distribution that is statistically biased toward promising molecules, without gradient information and without exhaustive enumeration.

Expected results

The local subspace remains small enough to be classically precomputable and circuit-compilable, placing the method firmly within the NISQ-feasible regime. We ground this claim in bounded register size and circuit depth, rather than qubit count alone. The parameter schedule is derived analytically from the graph structure, eliminating the outer variational optimization loop and its associated trainability issues. The result is a non-variational, hardware-ready sampler that produces structured exploration distributions over synthetically accessible chemical space.

Significance

To our knowledge, this is the first application of QWOA to chemical space exploration framed as a graph-structured combinatorial search over synthetically accessible molecules. The work establishes a concrete, hardware-feasible methodology for quantum-probabilistic lead optimization and identifies the structural conditions under which a quantum exploration advantage can be expected.

Keywords: quantum walks · chemical space exploration · drug discovery · lead optimization · combinatorial optimization