Fullqubit alchemist:
Quantum algorithm for alchemical free energy calculation

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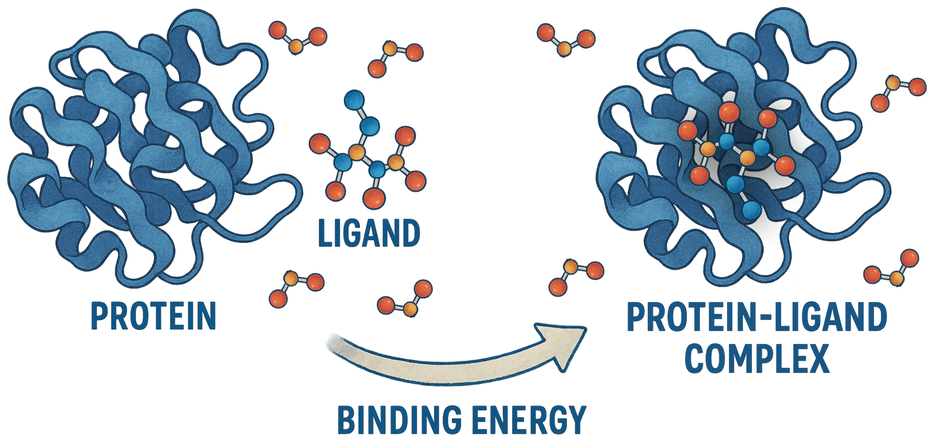
TL;DR: We introduce quantum algorithms for molecular dynamics with a logarithmic dependency on precision and alchemical free energy difference calculation without entropy estimation.

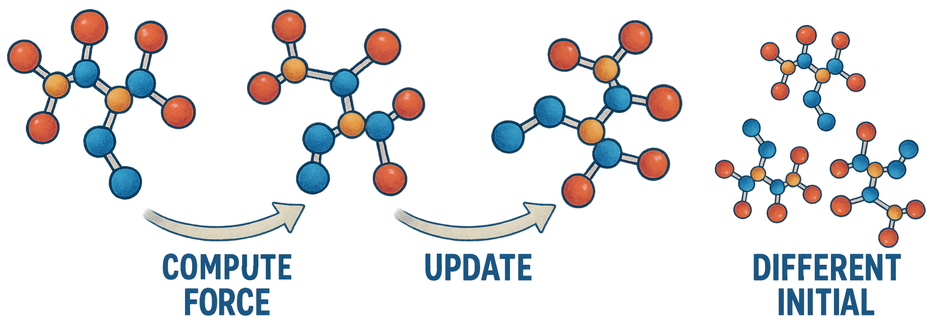
Drug Design

Modern drug design rely on binding free energy to rank candidates.



Molecular Dynamics

Molecular dynamics simulate the motion of molecules over time.

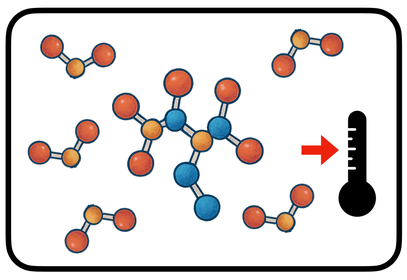


Evolution under the NVT Liouvillian

Evolution under the NVT Liouvillian generates thermal states.

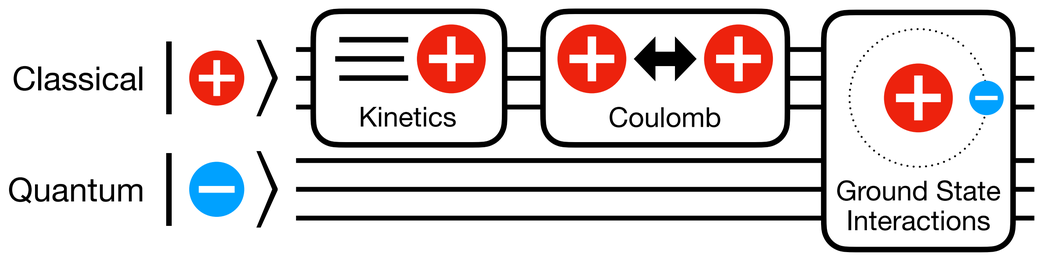
$$\rho_t = e^{-iLt}\rho_0$$

$$L = -i\left(\frac{\partial H}{\partial \boldsymbol{p}}\frac{\partial}{\partial \boldsymbol{x}} - \frac{\partial H}{\partial \boldsymbol{x}}\frac{\partial}{\partial \boldsymbol{p}}\right)$$



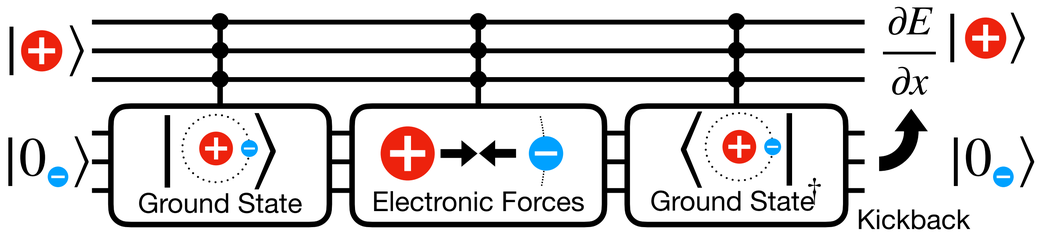
Modeling Mixed Quantum-Classical Systems

Classical and quantum systems can be modeled separately via the Born-Oppenheimer approximation.



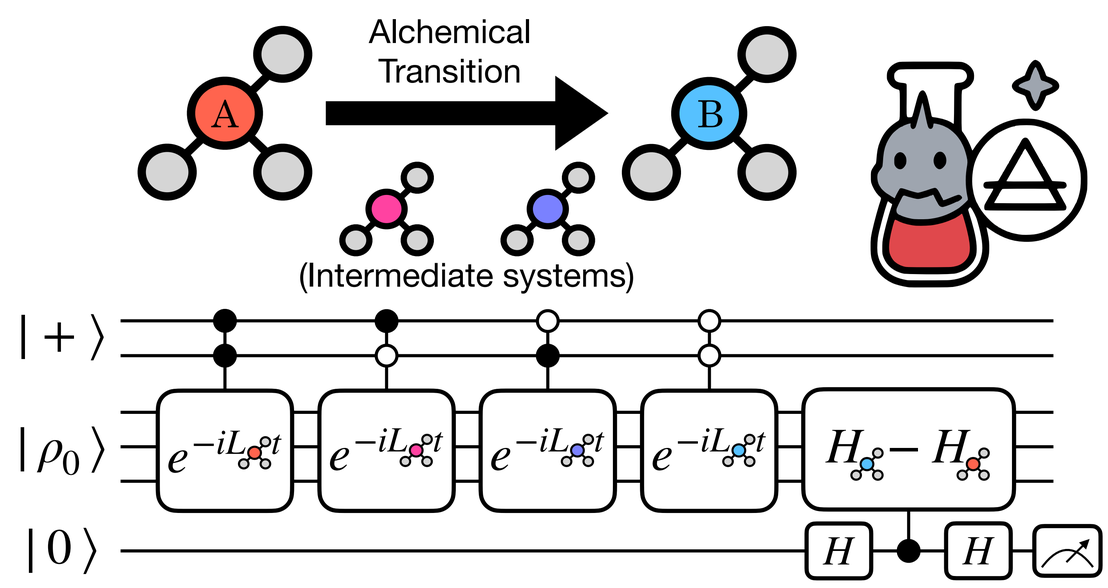
Electronic Register Kickback

Electronic forces are "kicked-back" into the nuclear register after computation via Hellmann-Feynman theorem.



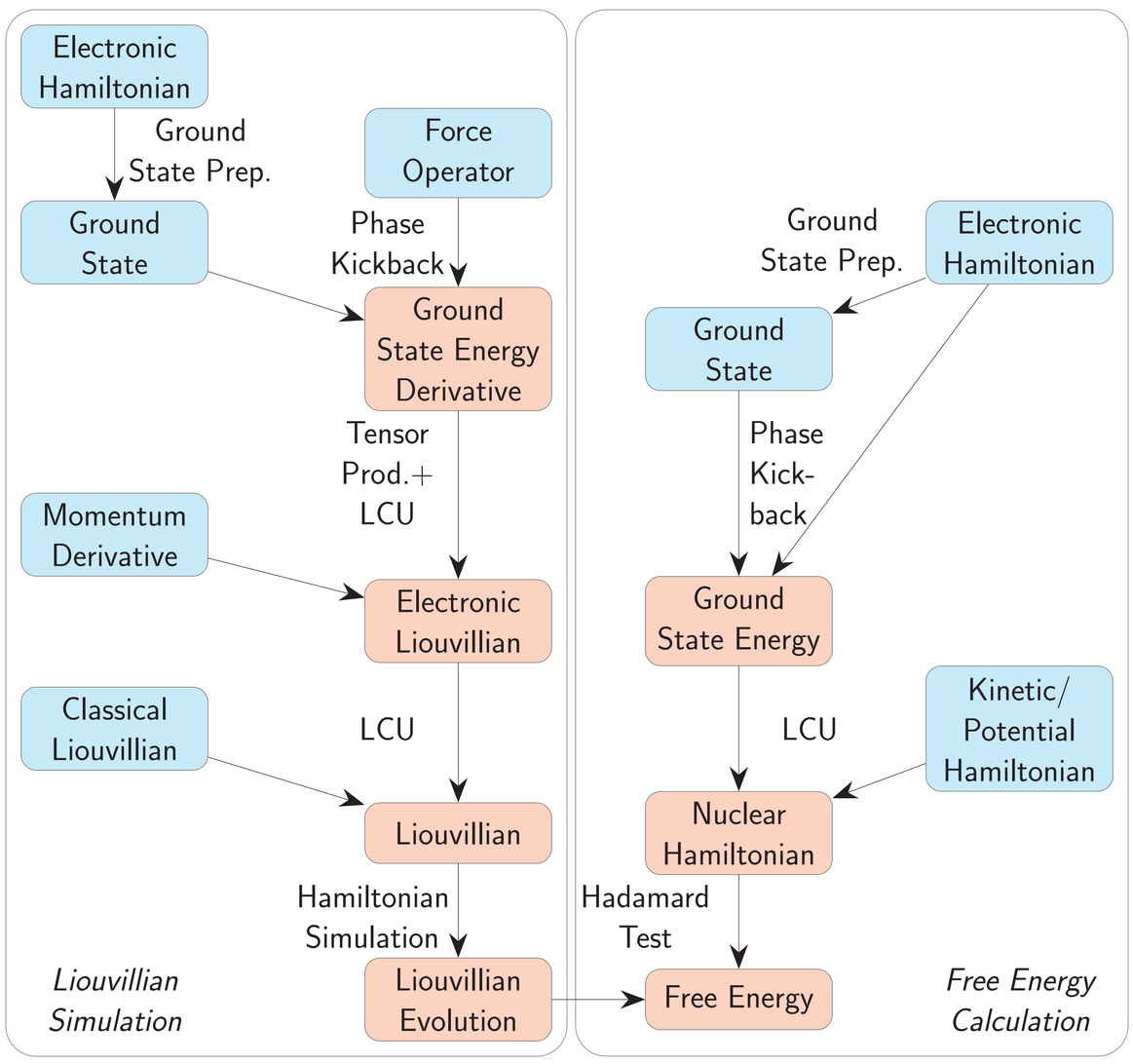
Alchemical Free Energy Calculation

Alchemical methods calculate free energy differences by integrating across different thermal states without explicit entropy estimation.



Algorithm Design

We recursively construct block encodings to obtain the final result.



Performance Comparison

	MD simulation	Free energy calculation
QPE + Euler Int. [1]	$\tilde{\mathcal{O}}(\varepsilon^{-1})$	—
Liouville + Trott. [2]	$\tilde{\mathcal{O}}(\varepsilon^{-o(1)})$	$\tilde{\mathcal{O}}(\eta^{1+o(1)}\varepsilon^{-1.5} + \varepsilon^{-2})$
Our work	$\mathcal{O}(\log^3 \varepsilon^{-1})$	$\tilde{\mathcal{O}}(\varepsilon^{-1})$

References

[1] T. E. O'Brien et al., *Phys. Rev. Res.* **2022**, *4*, 043210.

[2] S. Simon et al., *PRX Quantum* **2024**, *5*, 010343.

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