Design of Drug Compounds using Quantum Machine Learning

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Quantum computing and drug discovery

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Will Quantum Computing Transform Biopharma R&D?

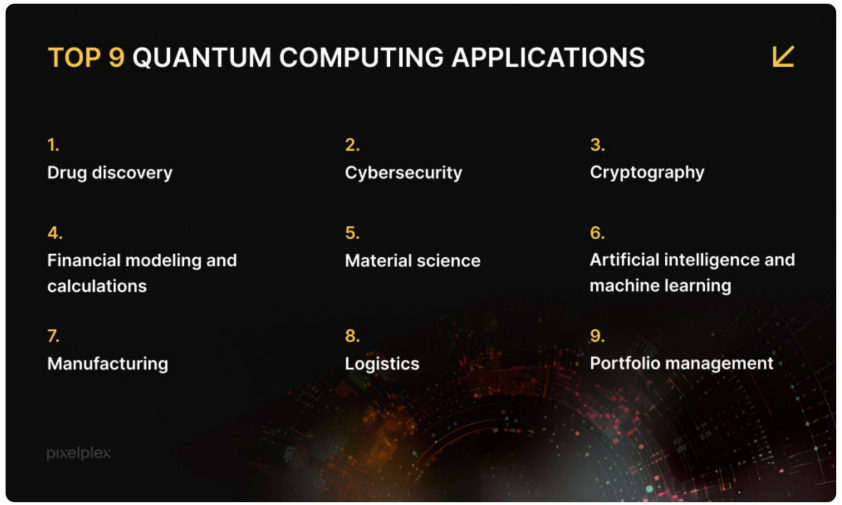
DECEMBER 10, 2019

By Matt Langione, Jean-François Bobier, Chris Meier, Sebastian Hasenfuss, and Ulrik Schulze

Of the many industries in which quantum computing is expected to have a far-reaching impact, biopharma is among the most promising. Quantum computing has the potential to significantly accelerate, enhance the quality of, and reduce the costs of data-rich R&D processes. The earliest uses are likely to involve the early stages of R&D (drug discovery and design), but the impact will extend into the later stages of R&D, thanks to higher clinical success rates from better early design.

Quantum computing is still very much an emerging technology, and the pathway to practical application remains under

9 most promising quantum computing applications



While only small quantum processors are currently available and large-scale quantum computers are still in the early stages of development, researchers and companies are nevertheless exploring a range of promising quantum computing applications. Some of these applications include:

1. Drug discovery

For an R&D department, new drugs take an average of $2 billion and more than ten years to reach the market after discovery. Quantum computing has the potential to dramatically speed up the process of developing new drugs by improving target identification, drug design, and toxicity testing. These processes would be less reliant on trial and error and could result in faster time to market.

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Feynman's idea of quantum computing

- Feynman was famously quoted as saying "The real use of computer simulation of physics would be with quantum mechanics. Nature isn't classical. If you want to make a simulation of Nature, you'd better make it quantum mechanical".
- He was, in essence, envisioning a computer with quantum mechanically behaving components to simulate quantum phenomena.
- Drugs are molecules and their behavior is intrinsically quantum mechanical.

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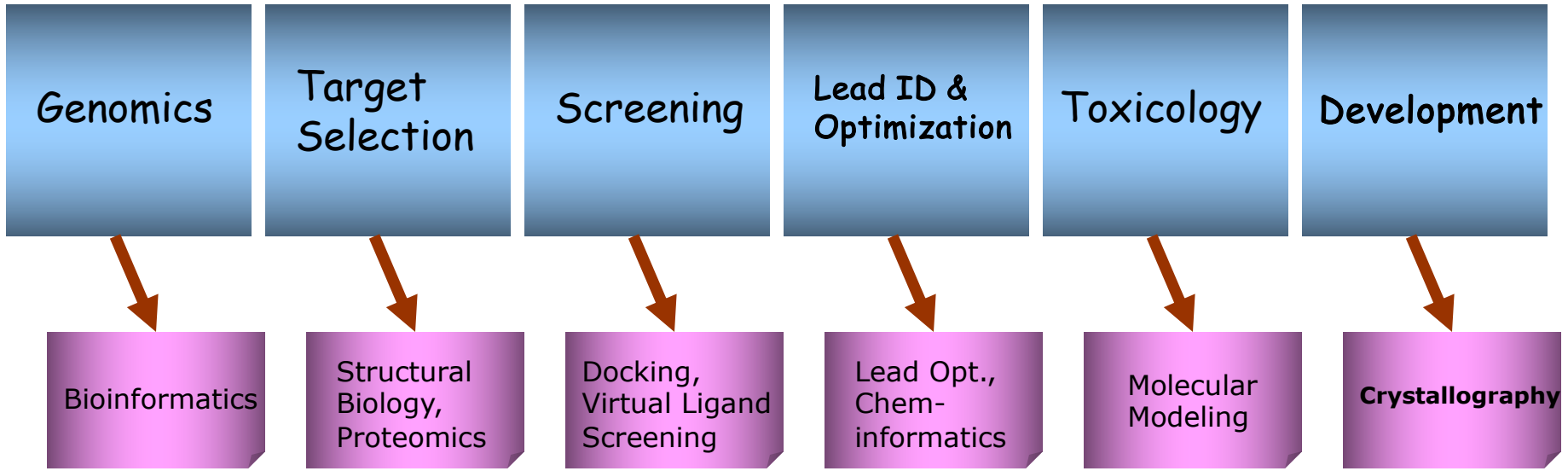
Drug discovery pipeline



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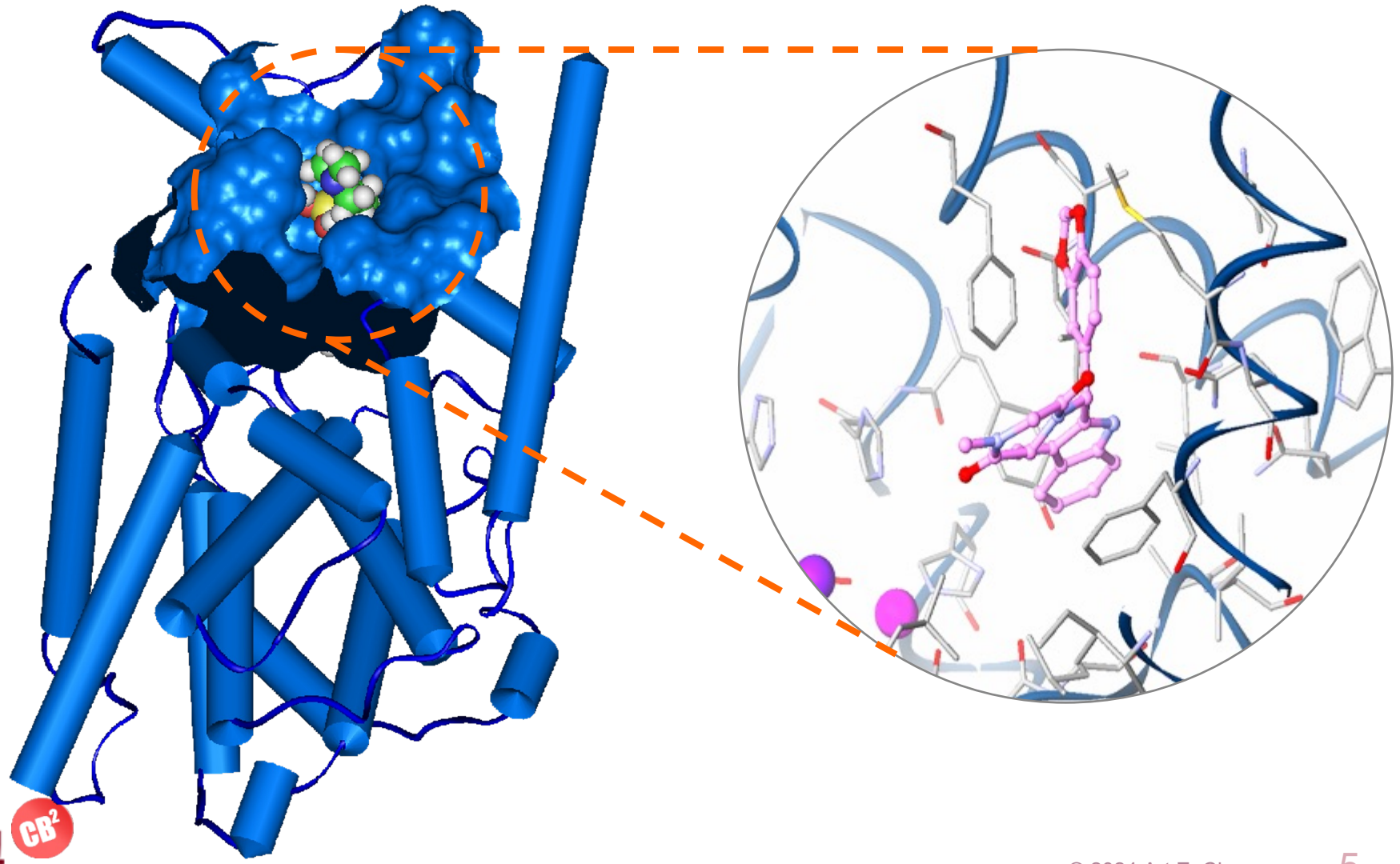
Protein-ligand (drug) binding



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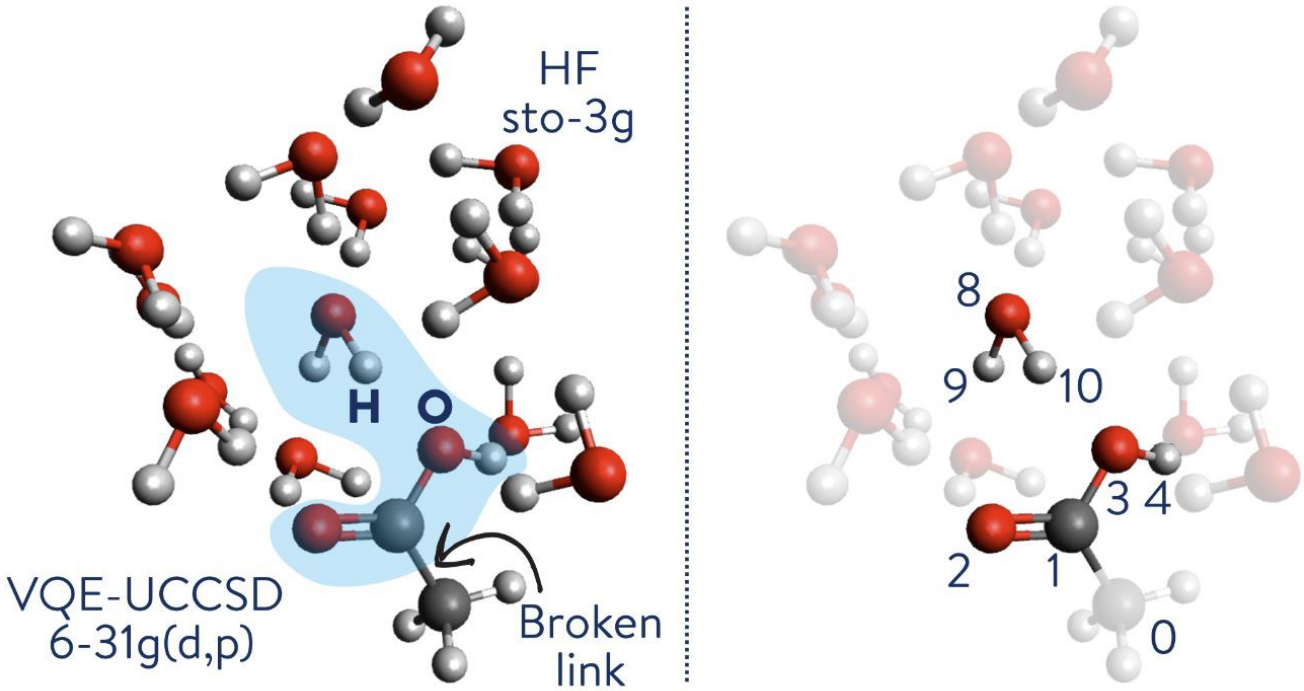
Decomposition of binding problem: ONIOM/VQE

$$E_{\mathrm{ONIOM}} = E^{\mathrm{Low}}_{\mathrm{All}} + \sum_{i=1}^{N} (E^{\mathrm{High}}_{\mathrm{Fragment}_i} - E^{\mathrm{Low}}_{\mathrm{Fragment}_i})$$



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Protein-ligand binding and QC

- To achieve better accuracy than the current digital-computer-based methods such as density functional theory, one would need thousands of physical Qubits for at least a few logical Qubits to represent orbitals.
- Until we get our hands on such hardware, QC does not help drug discovery in this path.

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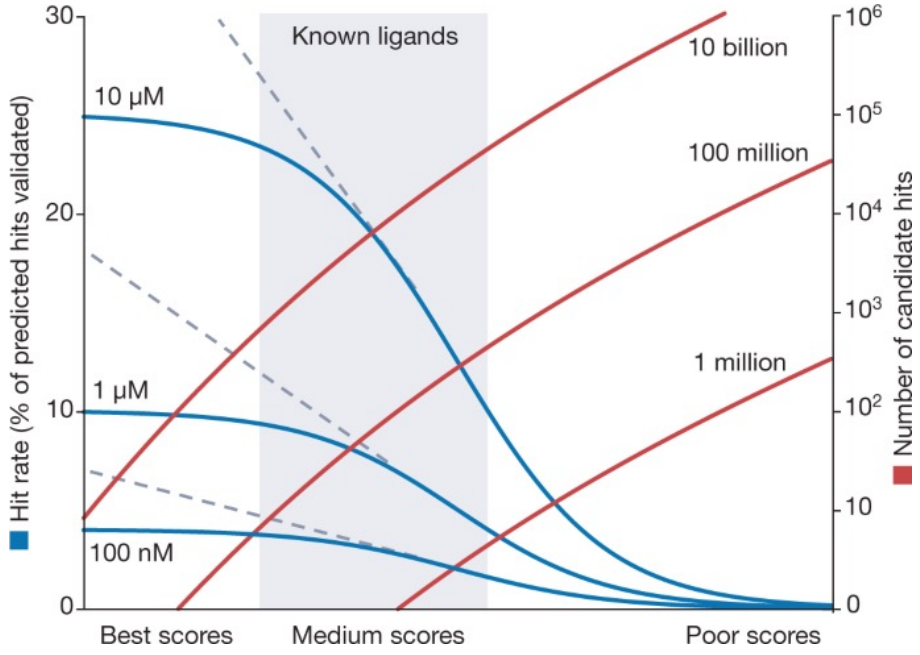
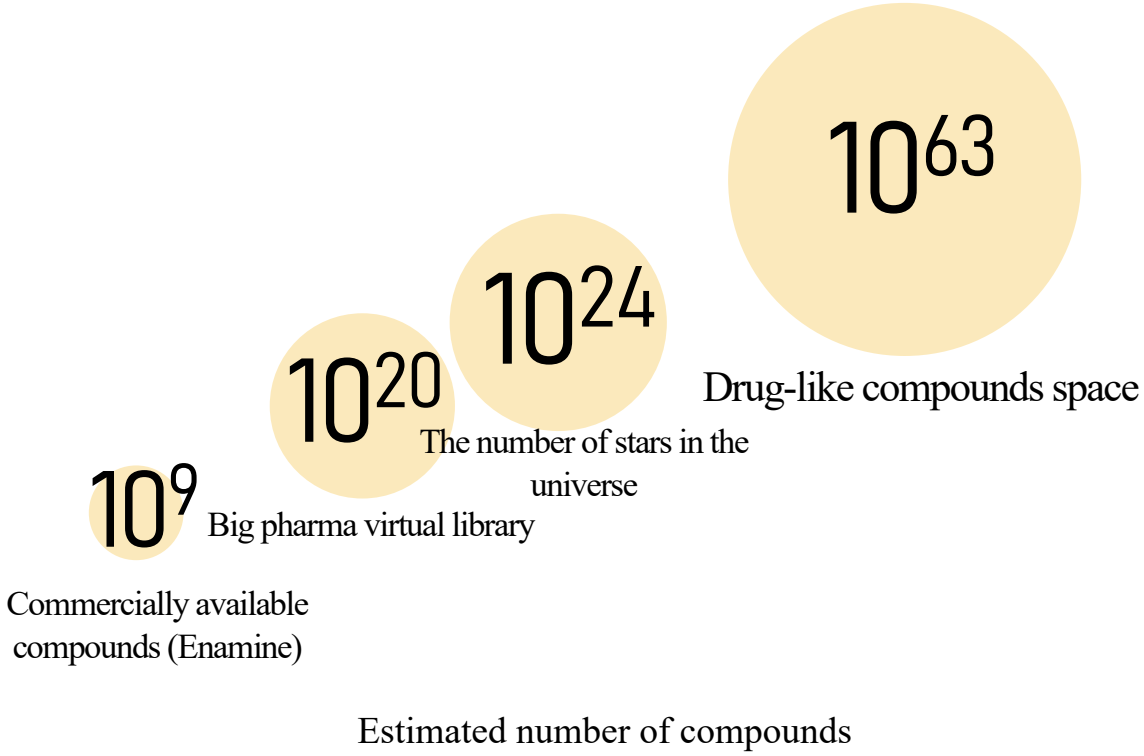
Drug screening: importance of the size of libraries



Better performance with larger libraries to screen

Sadybekov and Katritch, Nature, 616, 673-685 (2023)



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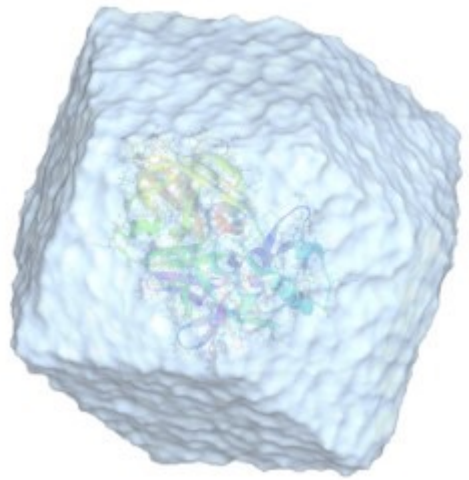
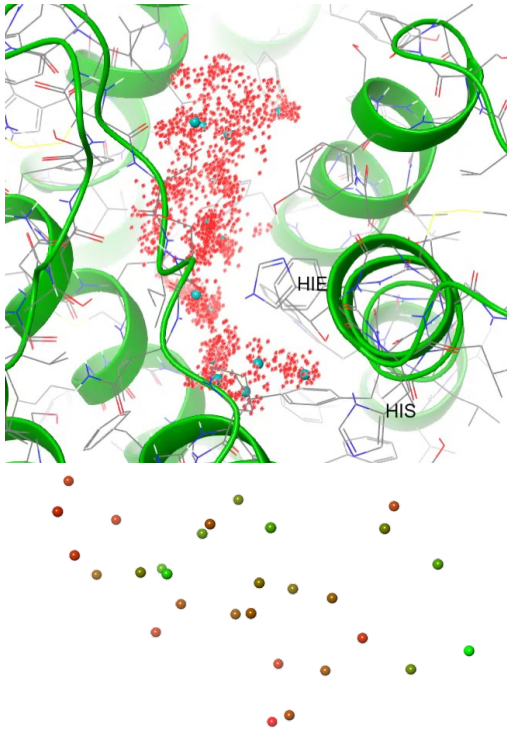
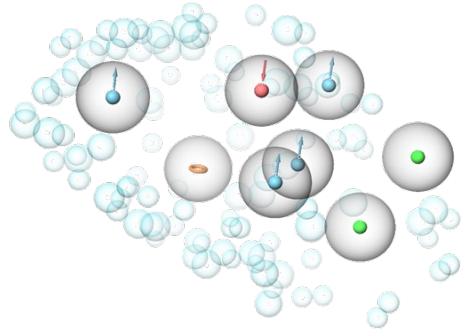
Water Pharmacophore: Target Information



1 Molecular Dynamics Simulation



2 Clustering Water Molecules



3 Generation of the Water Pharmacophore Features

4 Ligand library screening

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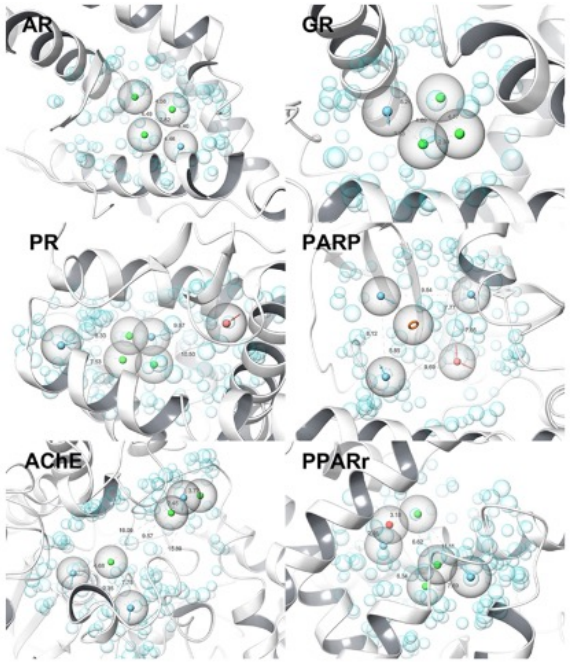
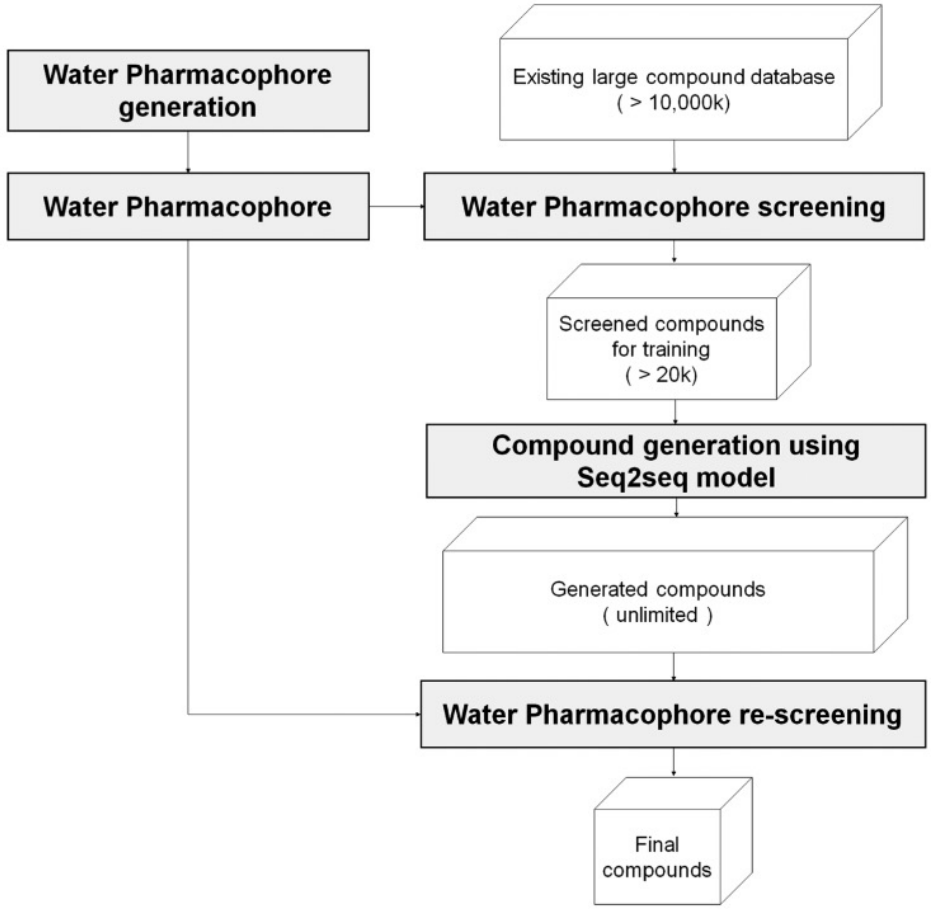
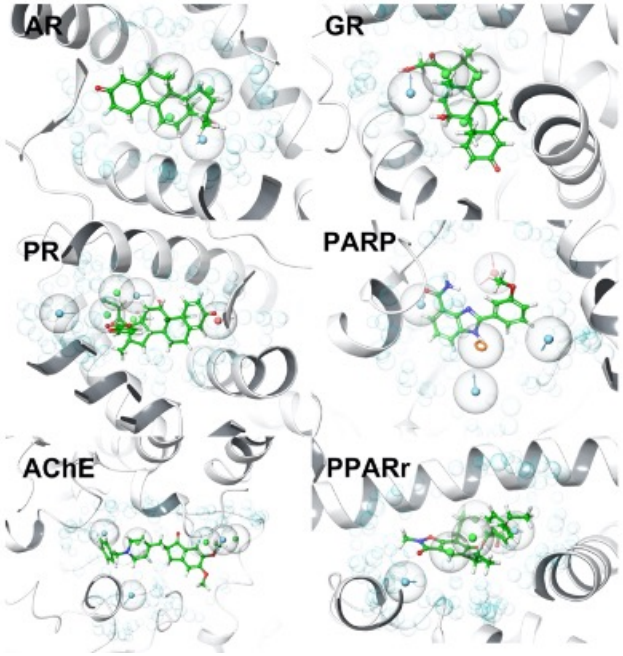
Water Pharmacophore Deep Learning



Target WP



WPDL Workflow



WPDL-generated compounds

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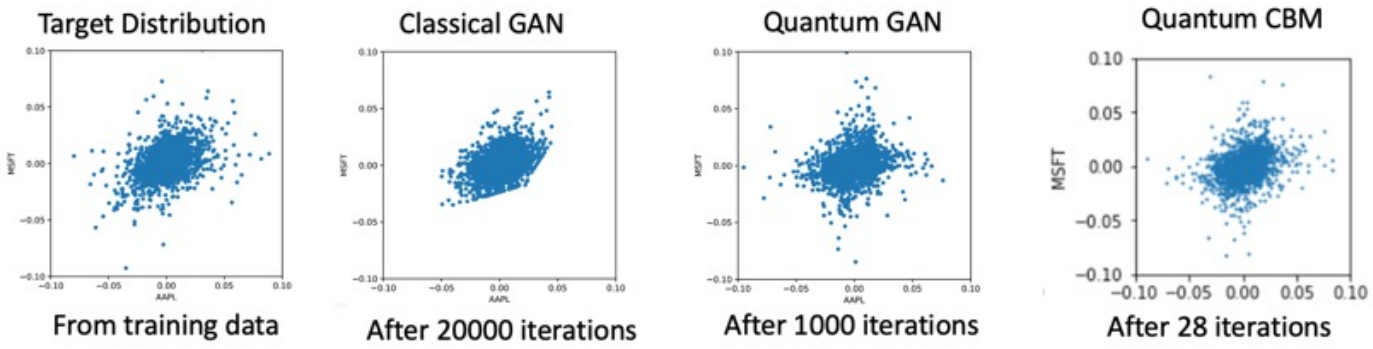
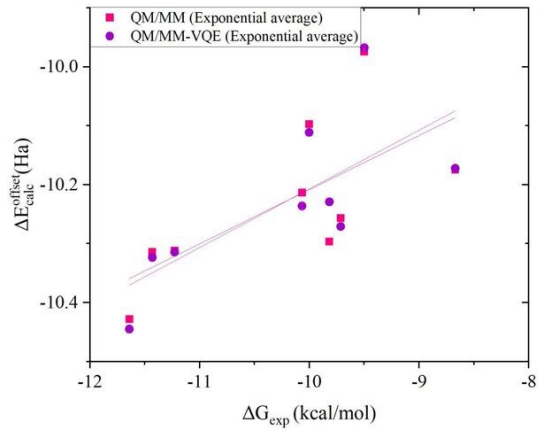
Realization of quantum advantage in drug discovery



Quantum Machine Learning

Virtual Ligand Library Generation



Variational Quantum Eigensolver

Protein-Ligand Interaction Energy

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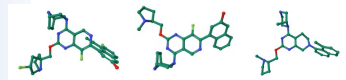
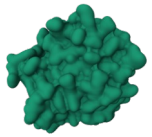
WPDL with QML

Training set generation



Experimentally known binders



Target protein

Virtual screening

Ligand library

Virtual screening hits

New compound generation

Generative QML on Quantum Hardware

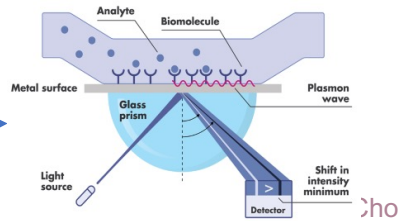
Target-Specific Chemical Library

Virtual Hit Selection

Virtual Hits

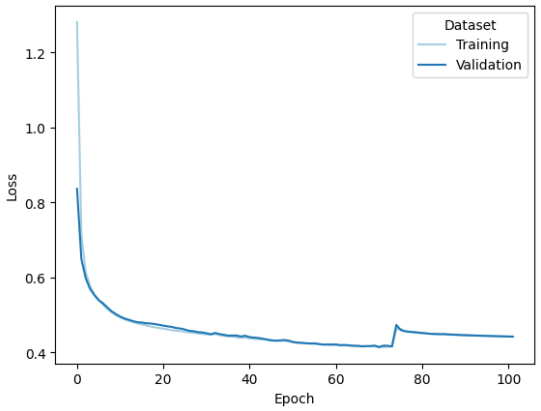
Experimental Verification

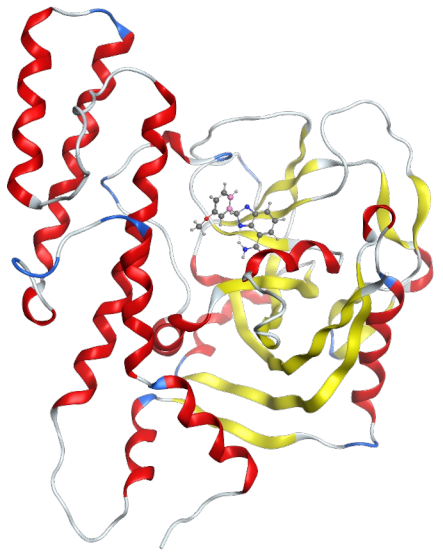
Synthesis



SPR assay

Pilot Test of WPDL/QML using Quantum Simulator

Test details		
Period	2023.12~2024.03	
Data used	Data size	• Sequence length: 135 • One-hot-encoding vector 36 dimension • 29700 molecules
Simulator	Pennylane	
No. of Qubits	4	
Training plot		



Target: PARP (PDB ID: 1EFY)

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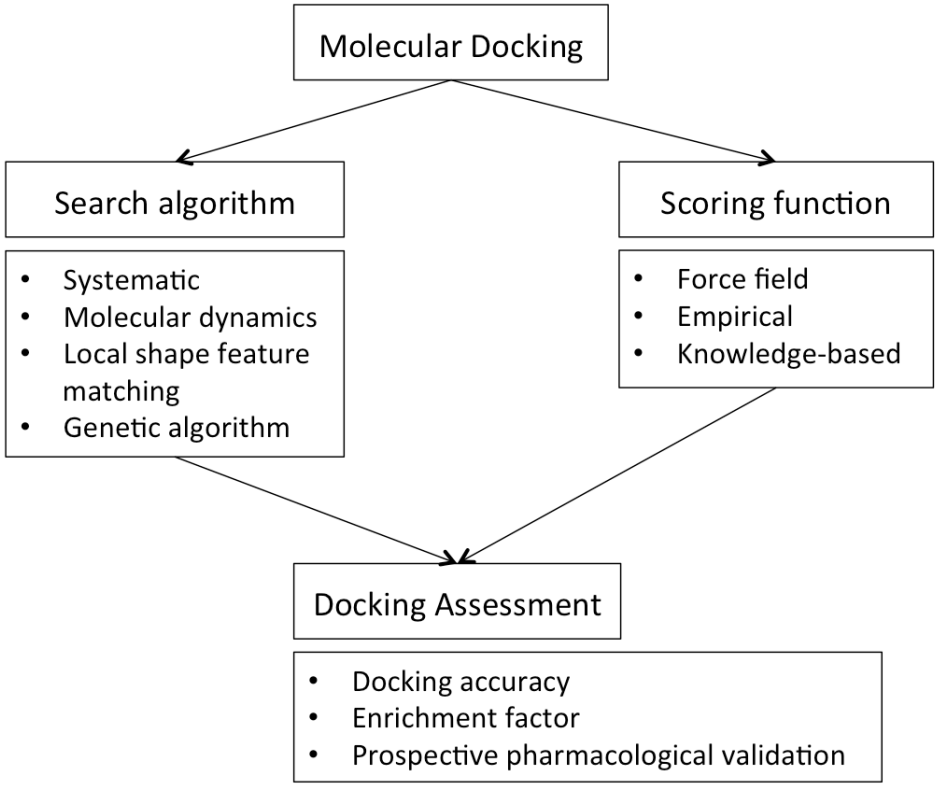
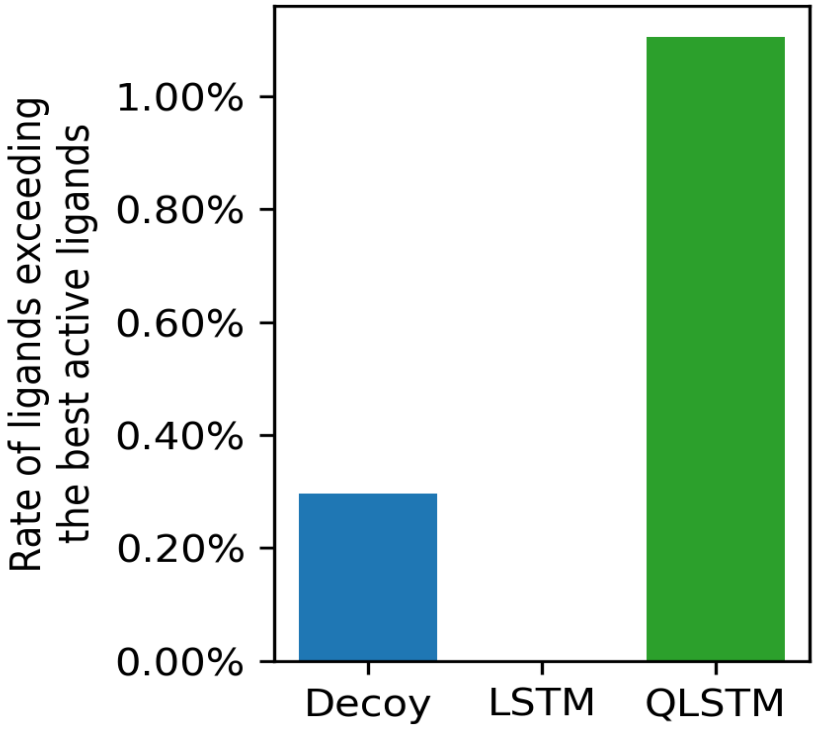
Classical ML vs. Quantum ML (binding affinities)





QLSTM generates more compounds with higher affinities

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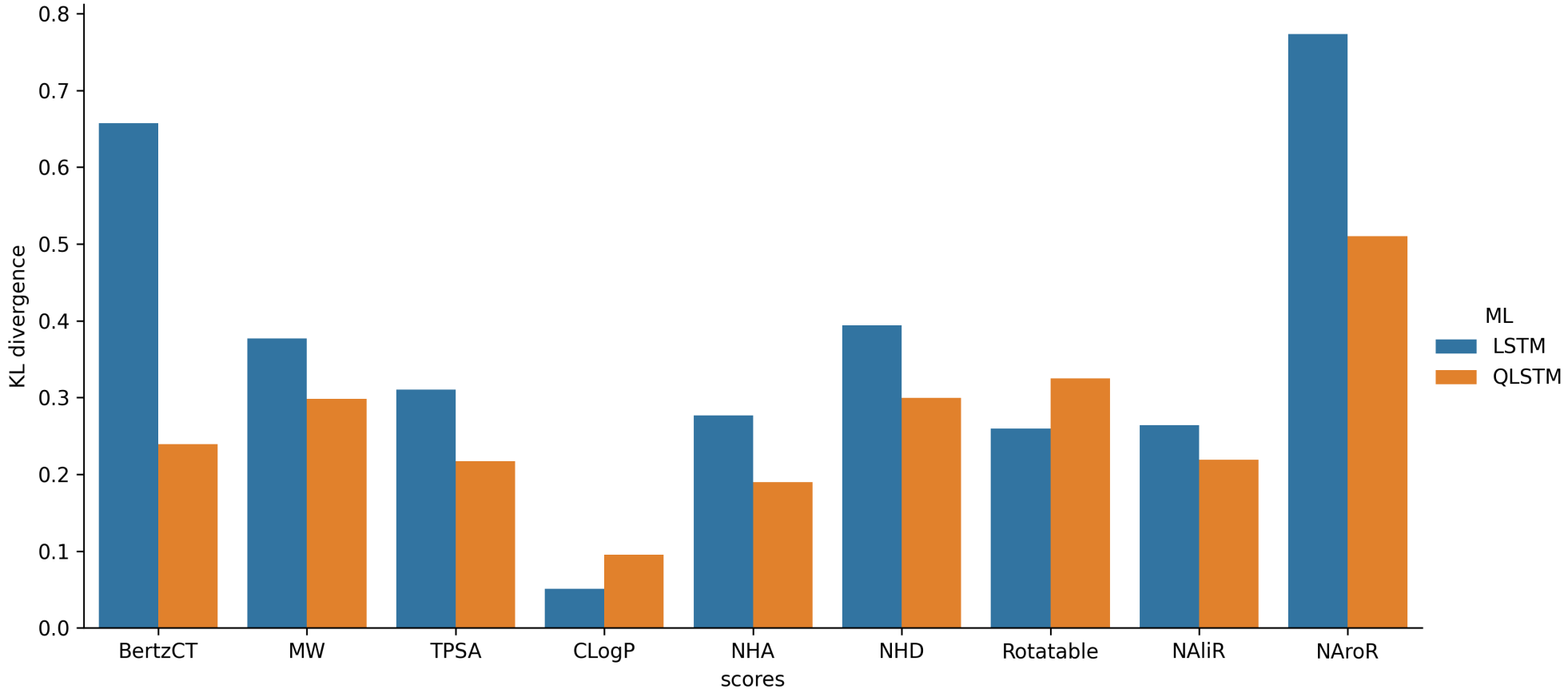
Classical ML vs. Quantum ML (divergence)



QML generates compounds that are more like the training set.

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Summary

- Quantum-based protein-ligand binding affinity calculation shows promise for the future. Yet, the current state of quantum hardware is incapable of realizing quantum advantage.

- However, QML, even at the level of current quantum hardware, does seem to give improvement in ligand generation.

- Further research is needed to realize quantum advantage in drug discovery.

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Appendix

Quantum enhanced drug discovery pipeline