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ICSC Centro Nazionale di Ricerca in HPC, Big Data and Quantum Computing

MoSeGAD : MOlecular StructurE Generation And Docking with Quantum Computing

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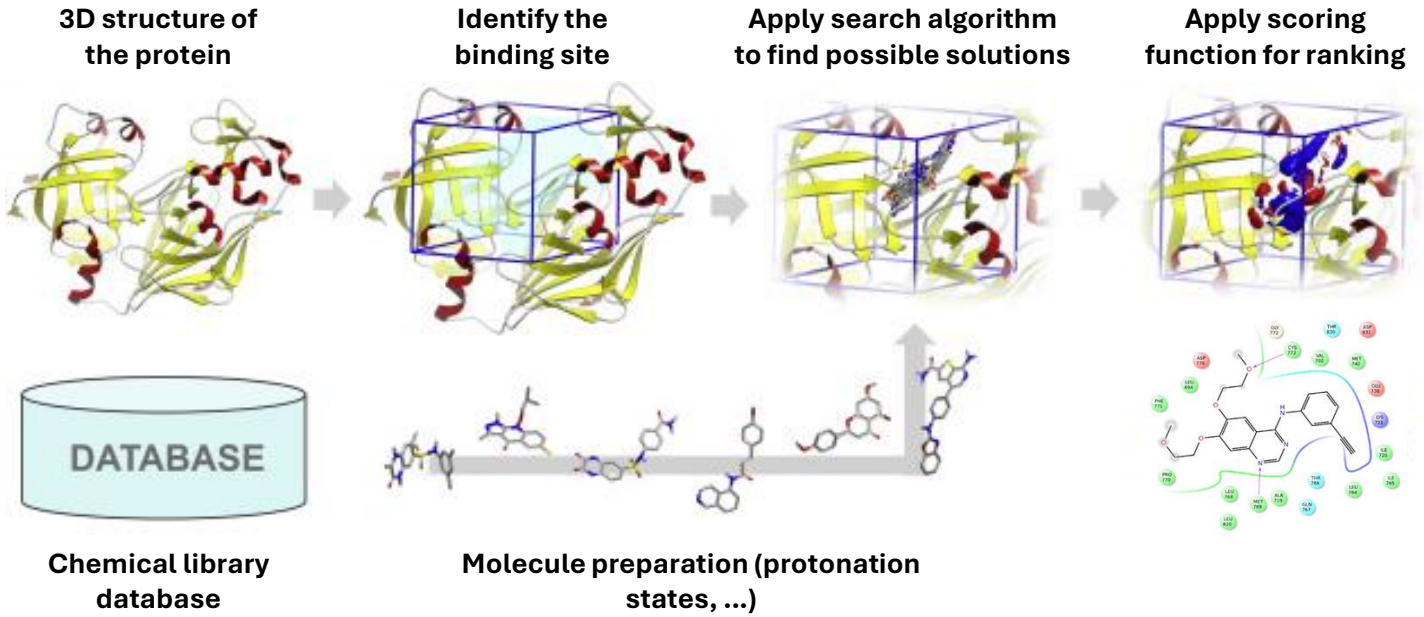
ICSC Innovation and Community Day

Why Quantum for Drug discovery ?

Drug discovery requires finding molecules that bind effectively to protein targets. This binding prediction—molecular docking—is a computational bottleneck. Classical methods explore this vast search space through iterative refinement. Quantum computing suggests a fundamentally different approach.



The molecular docking challenge

- Billions of molecules to screen
- Combinatorial explosion
- Classical approach: iterative search → doesn't scale

Quantum computing ?

Validated Quantum Docking PoC (EuroCC)

Previously in 2021 in partnership with CINECA and Politecnico di Milano, we successfully validated the quantum-native reformulation of molecular docking, yielding a reproducible and polynomially scalable methodology that generates valid binding poses and is now ready for extension.

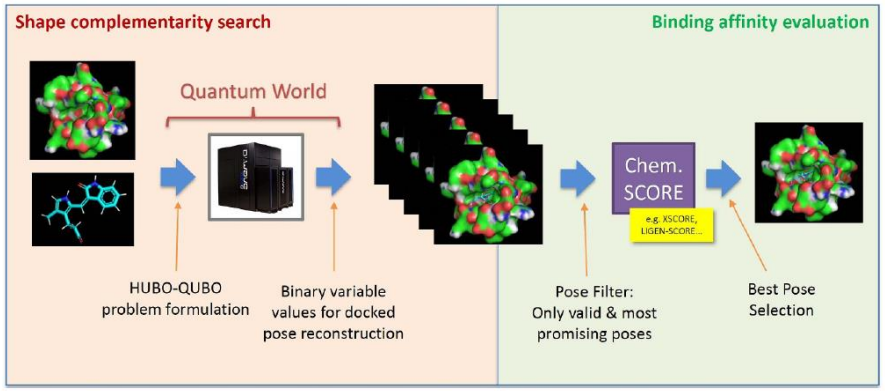


Figure 1. Complete workflow. The proposed approach tackles the Shape Complementarity search using quantum annealing, producing a set of valid configurations. Subsequently, the pose filter in the Binding Affinity evaluation identifies the most promising poses based on their chemical scores.

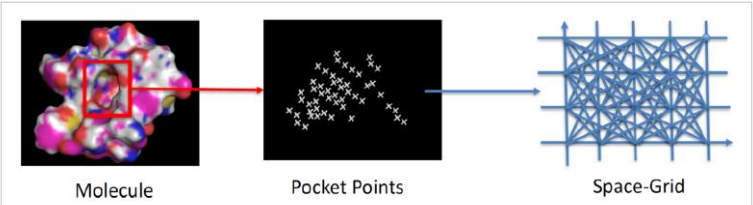


Figure 3. From the molecular pocket, we select the pocket points that are used to construct the 3D space grid inside the pocket.

Initial PoC

- Docking encoded as a geometric matching QUBO problem (subgraph isomorphism).
- PoC validated on 6 experimental complexes.

Open Points

- Accuracy: need to incorporate physicochemical energy terms.
- Scaling: need validation on larger ligands and more diverse set.

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MoSeGAD: From Geometry to Physics-Informed Docking

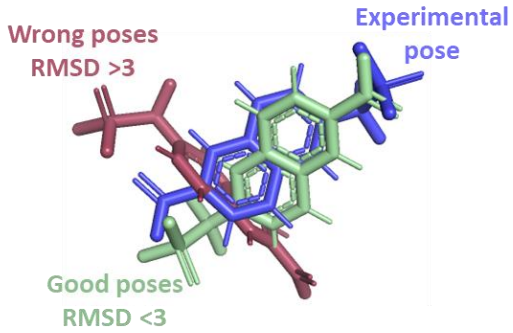
Moving beyond the geometric success, MoSeGAD integrated physicochemical properties and an optimized quantum formulation for improved hardware mapping. This enabled the scaling up of the process and significantly improving the quality of results.

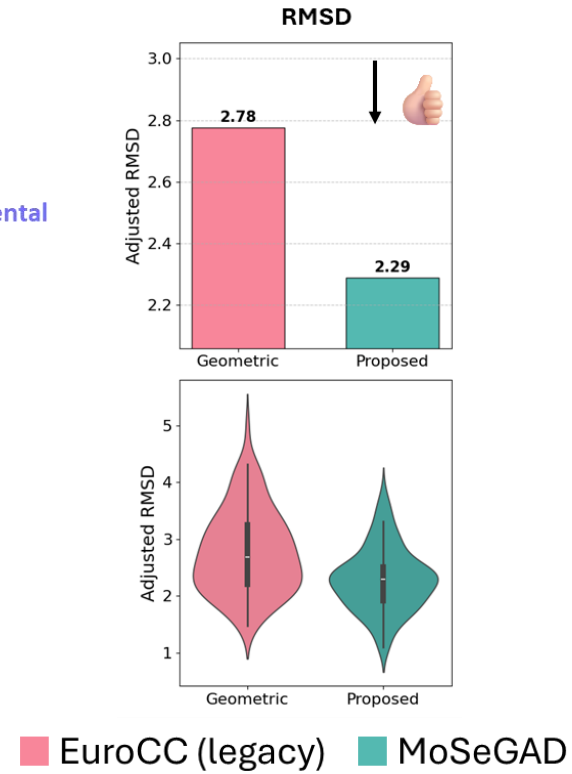
- **Added physics:** Five interactions (electrostatics, van der Waals, hydrogen bonds, hydrophobic effects, π-stacking).
- **Scaled up:** From 6 complexes to 103 complexes.
- **Optimized hardware:** Better encoding. Less qubit overhead.

	EuroCC (legacy)	MoSeGAD (2024-25)
Approach	Geometric	Geometry + Physics
Ligand complexity	6 atoms, no rotation	Up to 8 atoms, rotatable bonds
Dataset	8 protein-ligand complexes	103 protein-ligand complexes
Encoding	Pure QUBO	Optimized encoding

MoSeGAD: From Geometry to Physics-Informed Docking - Results

Physics-informed docking outperforms pure geometry across 103 real protein-ligand complexes. Adding chemical interactions improves binding pose prediction and reduces prediction variance.





- **Physics matters:** Adding interactions consistently improves pose accuracy.
- **More reliable:** Variance shrinks. Predictions are more predictable across diverse molecules.
- **Real validation:** Validated on 103 complexes from real-world dataset.
- **Ready to deploy:** The methodology scales.

Conclusions

MoSeGAD : MOlecular StructurE Generation And Docking with Quantum Computing (6/2024 – 9/2025)

- The methodology works: Validated across 103 real complexes. Results are reproducible and consistent.
- Ready for the next phase: We have the approach. When quantum hardware improves, integration is possible.
- Competitive position: Early investment in methodology means we're prepared when the technology matures.
- Scientific dissemination:
  - 🎤 QUANTUM COMPUTING MEETING Talk (2025)
  - 📄 3+ Research Papers in Prep
  - 📑 1 Patent Application Under Assessment

Grazie per l'attenzione

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