

Real Science on Hybrid Quantum-Classical Computers

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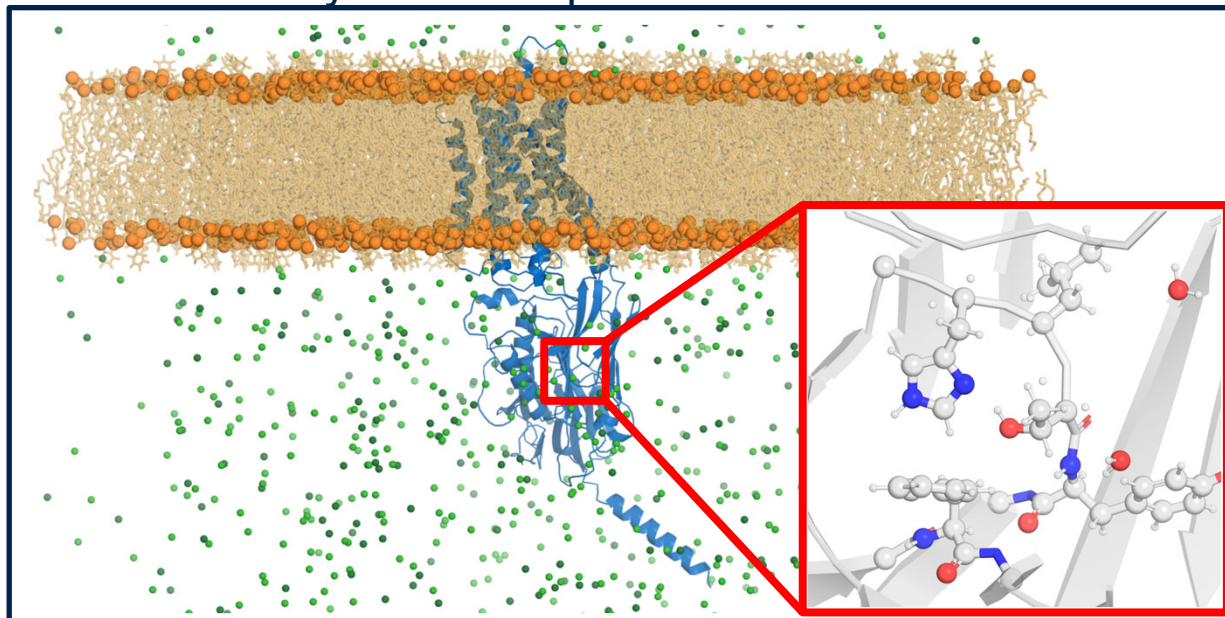
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Studying the Chemistry of Life with Quantum Computers

Biomolecular systems couple local chemical reactions to million-atom environments



- **Goal: Understanding and predicting biomolecular processes** (for, e.g., life sciences and drug development¹)
- **Multi-scale methods** link local electronic structure to complex environments³
- **Quantum computing** as a solver for correlated chemical processes²

The target molecule of this work: ADGRG1 from the family of adhesion G protein coupled receptors⁴ (aGPCRs).

¹ Salo-Ahen et al. (2020): Molecular dynamics simulations in drug discovery and pharmaceutical development.

² Warshel & Levitt (1976): Theoretical studies of enzymic reactions: Dielectric, electrostatic and steric stabilization of the carbonium ion in the reaction of lysozyme.

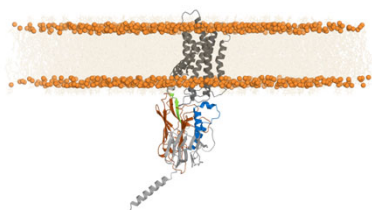
³ Aspuru-Guzik et al. (2005): Simulated quantum computation of molecular energies.

⁴ Vizurraga et al. (2020): Mechanisms of adhesion G protein-coupled receptor activation.

A QPU-Integrated HPC Workflow for Biochemistry

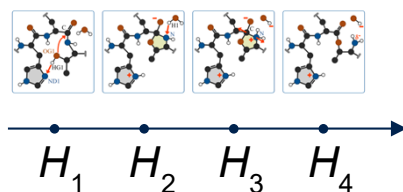
This work's simulation pipeline uses Quantum Selected Configuration Interaction

**Structural Biology
and Molecular
Dynamics**



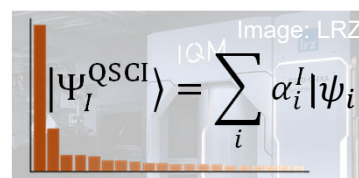
I. 3D model of the
biomolecule's initial
state

**QM/MM
Reaction Path
and Embedding**



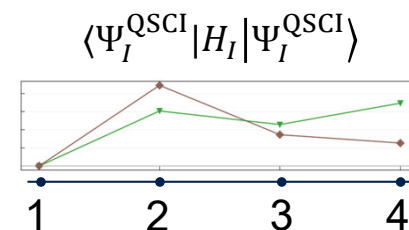
II. Embedded
Hamiltonians along
the reaction sequence

**QPU-Sampling
and HPC Post-
processing**



III. Approximate ground
state energies for the
four Hamiltonians

**WF-in-DFT-in-
MD Reaction
Energy Profile**



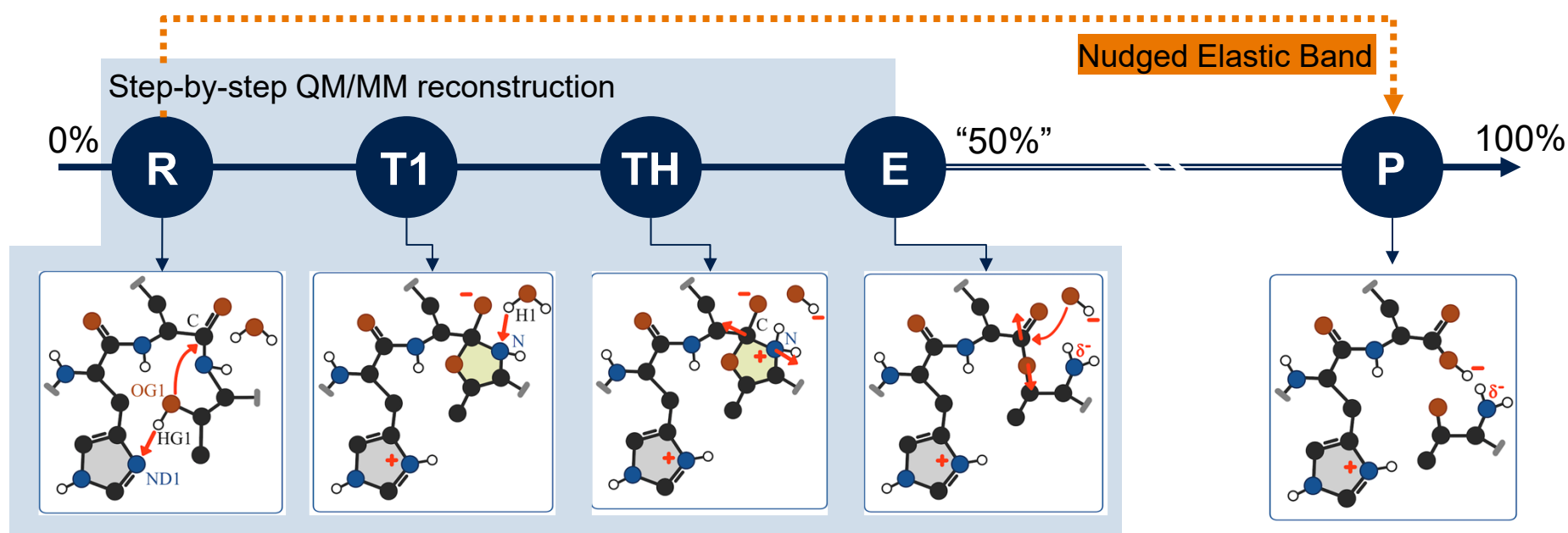
**Quantum-corrected
reaction energy
profile**

QM/MM: quantum mechanics / molecular mechanics | QPU: quantum processing unit | HPC: high-performance computing | QSCI: quantum selected configuration interaction | WF: wavefunction | DFT: density functional theory | MD: molecular dynamics

We Trace the Full Autoproteolytic Reaction

Work in Progress

Autoproteolysis consists of an N-O acyl shift and a subsequent hydrolysis

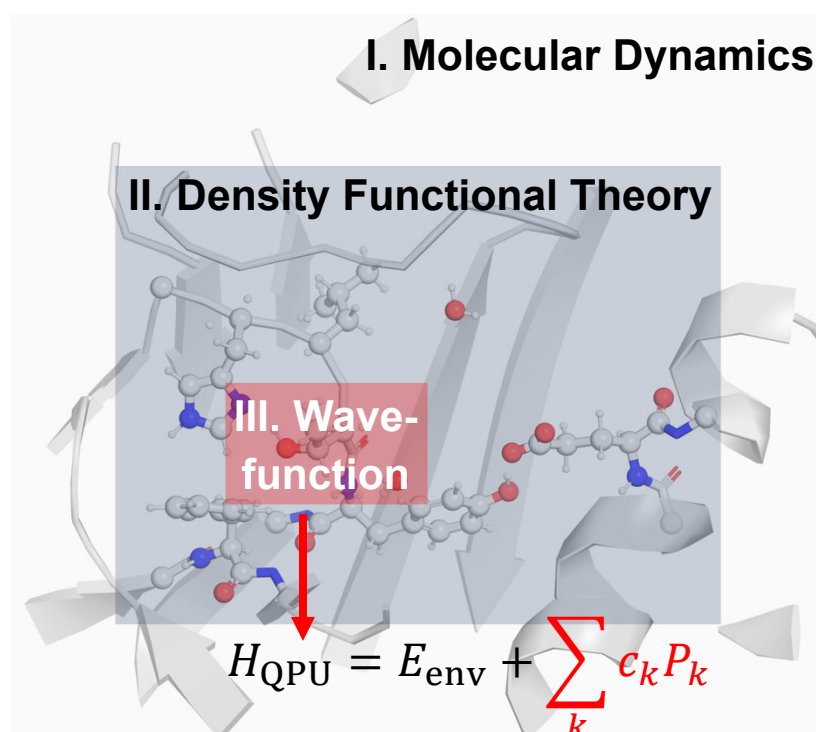


Reaction pathway and QM/MM methodology following Seufert et al. (2025): Mechanistic insights into adhesion GPCR autoproteolysis by a multiscale computational approach.

QM/MM: quantum mechanics / molecular mechanics | MM: molecular mechanics | DFT: density functional theory | MD: molecular dynamics

Embedding Reduces the Simulation to QPU Scale

The wavefunction-in-DFT-in-MD framework



Three levels of theory

- I. **Classical Physics:** molecular dynamics¹
- II. **Mean-field Quantum Physics:** density functional theory²
- III. **Wavefunction:** e.g., quantum-selected configuration interaction³

Multiscale embedding

- I. **Quantum Mechanics/Molecular Mechanics⁴ (QM/MM):** electrostatic embedding
- II. **Projection-based embedding⁵**

¹ Berendsen et al. (1995): GROMACS: A message-passing parallel molecular dynamics implementation.

² Kohn & Sham (1965): Self-Consistent equations including exchange and correlation effects.

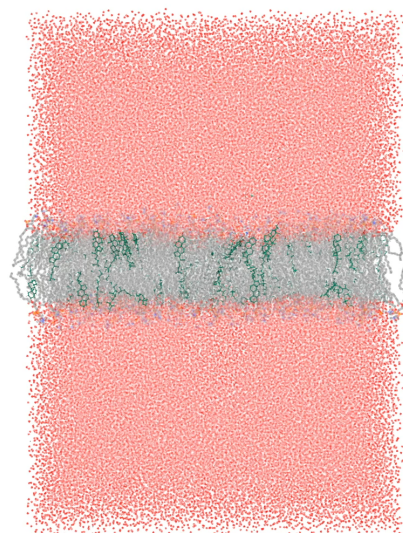
³ Kanno et al. (2023): Quantum-Selected Configuration Interaction: classical diagonalization of Hamiltonians in subspaces selected by quantum computers

⁴ Warshel & Levitt (1976): Theoretical studies of enzymic reactions: Dielectric, electrostatic and steric stabilization of the carbonium ion in the reaction of lysozyme.

⁵ Ralli et al. (2024): Scalable approach to quantum simulation via projection-based embedding.

The QPU Constraints the Active Quantum Space Size

Zooming into the QPU-simulated region



We simulate the full 1,000,000 atom system with HPC software and the chemically active region with DFT and quantum computing methods.

The QPU Samples Relevant Electronic Configurations

Approximate time evolution populates the relevant wavefunction components

Initial Guess

$|000 \dots 01 \dots 111\rangle$

Reaction Path Hamiltonian

$$H_{\text{QPU}} = E_{\text{env}} + \sum_k c_k P_k$$

QPU



Sampled Bitstrings

000...01...111

001...10...111

011...00...011

⋮

Sample P_k
according
to $|c_k|$

Approximate time evolution

$$U_{\text{qDRIFT}} \approx \exp[-iH_{\text{QPU}}t]$$

Repeat for
different P_k
and t

QSCI – Kanno et al. (2023): Quantum-Selected Configuration Interaction: classical diagonalization of Hamiltonians in subspaces selected by quantum computers.

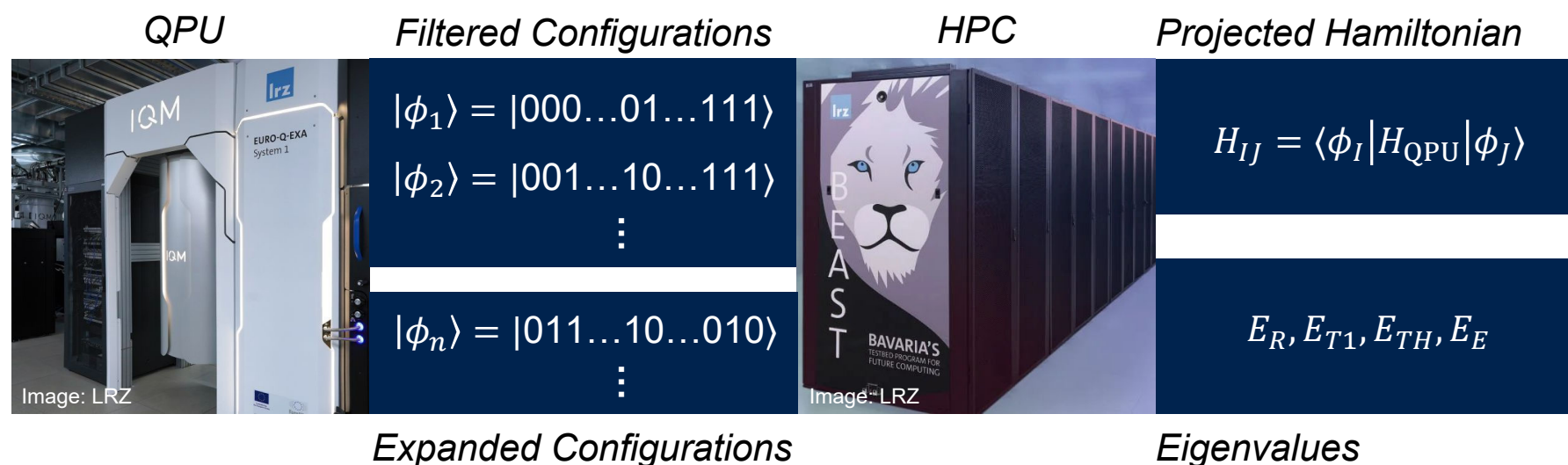
Time-evolution QSCI – Mikkelsen & Nakagawa (2025): Quantum-selected configuration interaction with time-evolved state.

qDRIFT – Campbell (2019): Random compiler for fast Hamiltonian simulation.

QPU: quantum processing unit | QSCI: quantum selected configuration interaction | env: environment | qDRIFT: quantum stochastic drift protocol 8

The Sampled Configurations Inform the Diagonalization

Classical postprocessing on HPC systems produces the final QSCI energies



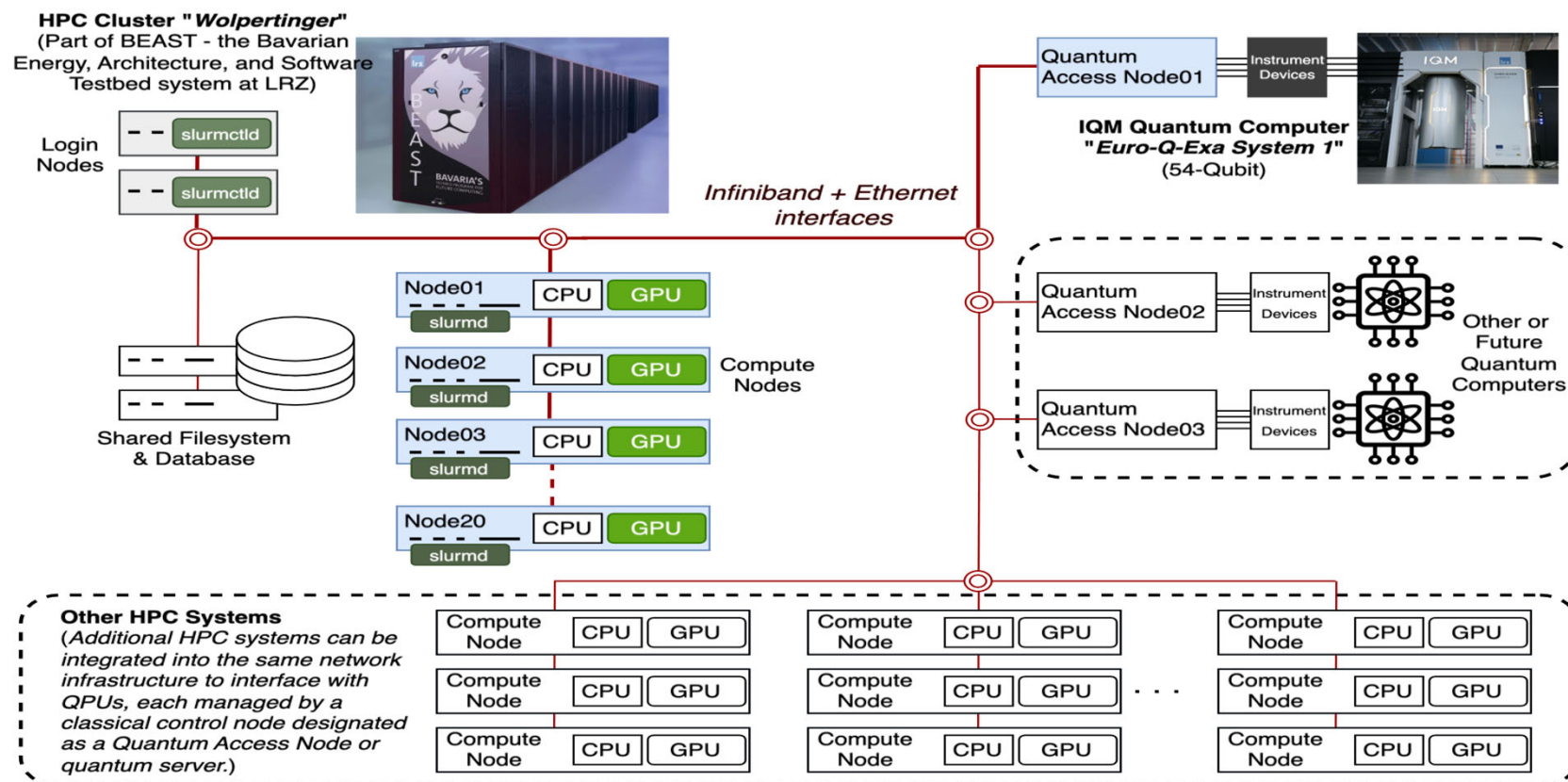
QSCI – Kanno et al. (2023): Quantum-Selected Configuration Interaction: classical diagonalization of Hamiltonians in subspaces selected by quantum computers.

Configuration expansion – Weaving et al. (2026): Selected configuration interaction using Time-Evolved Population Statistics.

GPU-acceleration – QMatter (2026): A new era of biomolecular simulation.

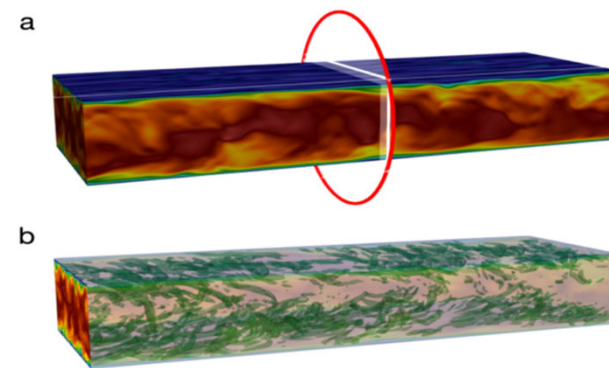
HPC: high-performance computing | QSCI: quantum selected configuration interaction | QPU: quantum processing unit

Quantum – HPC: integrated infrastructure



Part 3: Quantum-Informed Machine Learning for Predicting Spatiotemporal Chaos

- Modelling **high-dimensional dynamical systems** remains one of the most persistent challenges in computational science
- **Quantum machine learning (QML)** has emerged as a possible candidate due to its ability to **represent and manipulate high-dimensional probability distributions in Hilbert space**
- QML for such problems has been unrealized, largely due to the **limitations of current hardware**



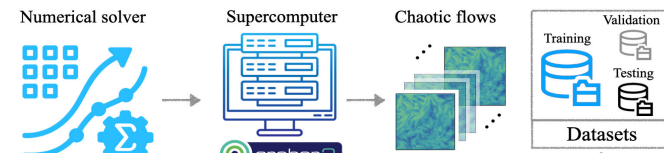
Generation of synthetic turbulent inflow from turbulent channel flow data.

A New Quantum Paradigm for Machine Learning

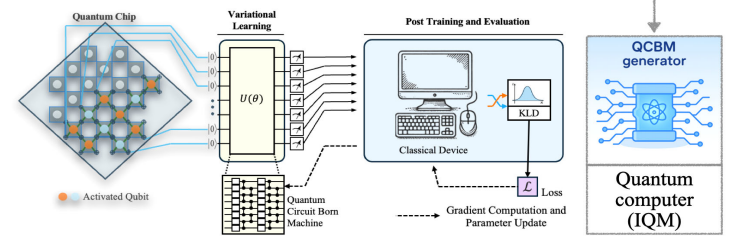
- Here, we introduce a **quantum-informed machine learning (QIML)** framework for predicting spatiotemporal chaos.
- First, a **quantum generator is trained** in a one-time, offline process to learn the invariant measure from trajectory data, termed a “**Q-Prior**”.
- This prior is then embedded as a **differentiable constraint within the loss function of a classical Koopman-based model**, which learns the step-by-step evolution.

The Structure of the Quantum-Informed Machine Learning

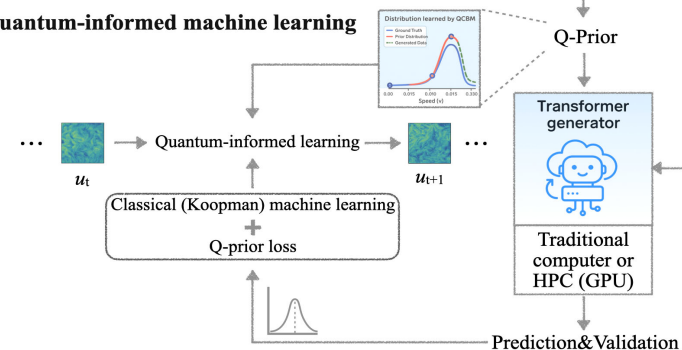
a. Data generation



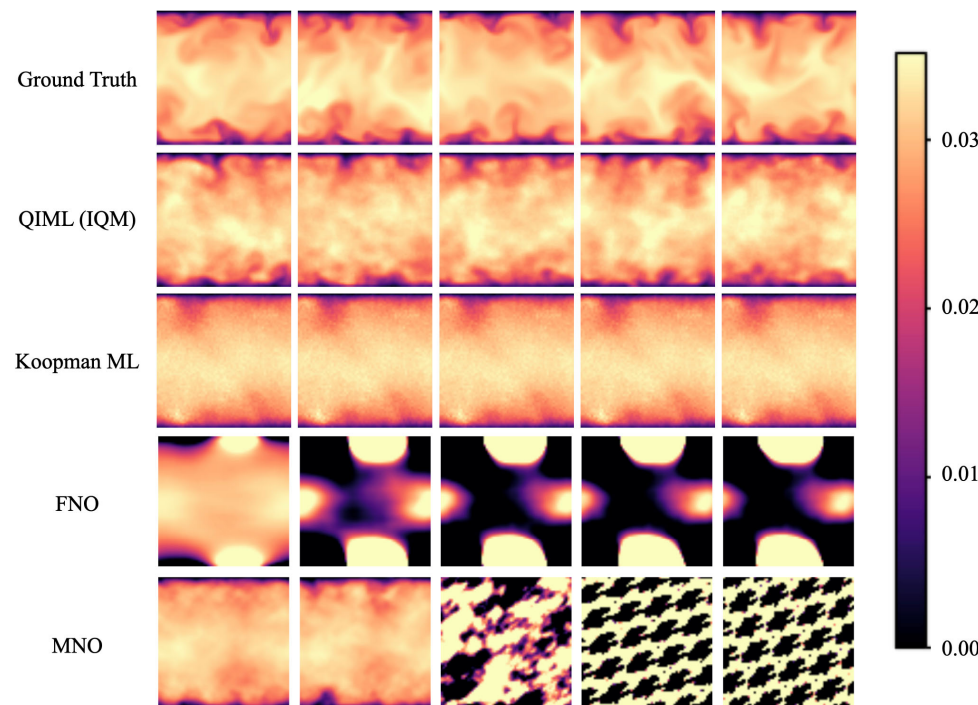
b. Q-Prior learning



c. Quantum-informed machine learning



Results on Turbulent Channel Flow Inflow



The comparison highlights the **superior performance of the QIML**, which is the **only method to maintain structural fidelity with the ground truth**, whereas the classical baselines either collapse to an overly smooth, time-averaged field or diverge into non-physical artifacts.

Quantum Advantages in QIML

Model	Total Parameters
Q-Prior (in the QIML)	≈ 300
QIML (this work)	4,535,172
Koopman	4,534,872
FNO	35,971,333
MNO	45,823,681

Dynamical System	Raw data (full set)	Q-Prior (full set)	Compression (ratio)
Kuramoto–Sivashinsky	300 MB	0.25 MB	$\approx 1.2 \times 10^3 : 1$
2D Kolmogorov flow	400 MB	0.40 MB	$\approx 10^3 : 1$
Turbulent channel flow	500 MB	2.3 MB	$\approx 2.2 \times 10^2 : 1$

Quantum parameter efficiency and storage compression achieved by the QIML (Q-Prior)

Summary:

- ✓ Addressing the Challenge
- ✓ Performance Gain
- ✓ Quantum Memory Advantage
- ✓ Use of NISQ Device