The Centre for Computational Science
Department of Chemistry

Opportunities for extending quantum computing through subspace, embedding and classical molecular dynamics techniques

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Quantum Autumn School, Stockholm, Sweden

11am CET, 4th November 2025

Introduction

Previously: MSci Chemistry and Physics, Durham University

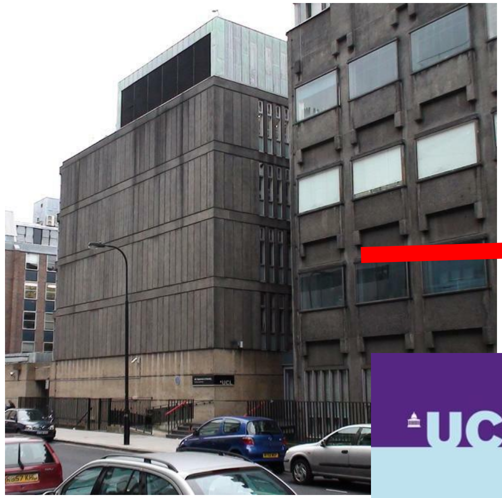
Steered towards physical and computational chemistry. Masters thesis in density functional theory.

Supervisor: David Tozer

Currently: 3rd year PhD student at University College London

Quantum chemistry and quantum computing.

Supervisor: Peter Coveney



Talk overview

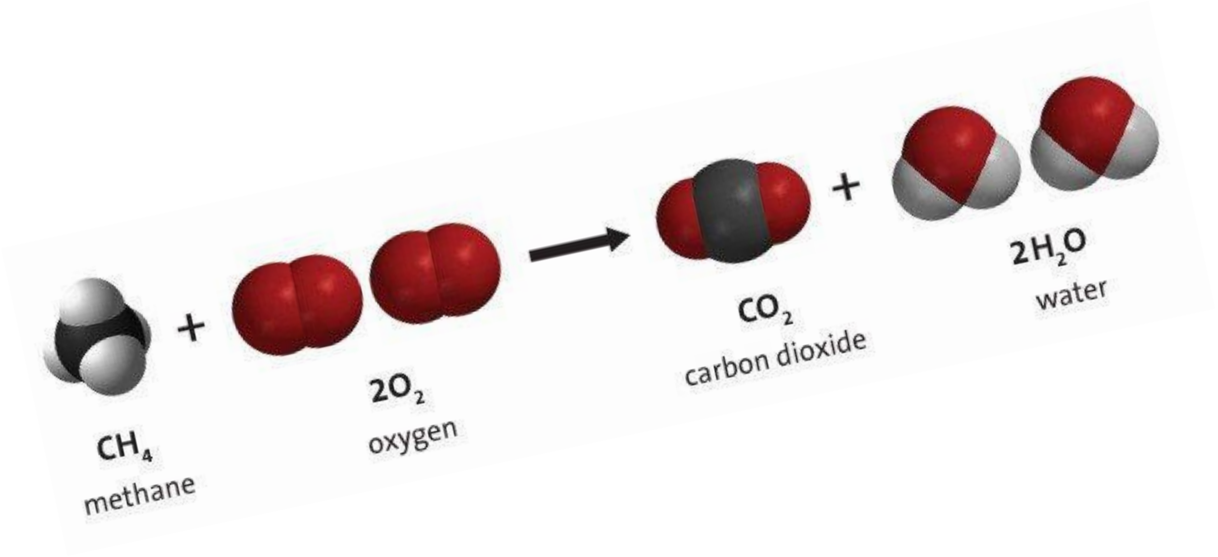
- **What is quantum chemistry?**
- **How might quantum computers help?**
- **How might classical compute complement quantum computing in the chemical domain?**
- **Some proof-of-concept work**
- **Outlook**

Key takeaways by the end:

- Quantum chemistry is often touted as one of the key application areas for quantum computing – why?
- There are many challenges along the way before we can do interesting chemistry using quantum computers.
- We expect that quantum-classical hybrid approaches will be crucial for advancing the field as we move towards the fault-tolerant regime.

What is quantum chemistry?

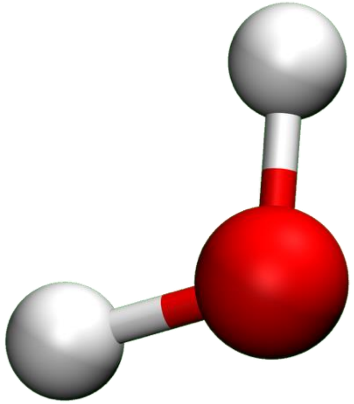
- A broad field, on the interface of theoretical and computational chemistry.
- Fundamentally, chemistry is the interaction of electrons and nuclei.
- How can we map reality onto a set of solvable equations?



?

$$\hat{\mathcal{H}}\Psi = E\Psi$$

What is quantum chemistry?



- Quantum chemistry and quantum computing is ***usually*** concerned with molecular electronic structure theory.
- This concerns the time-independent non-relativistic Schrödinger equation under the Born-Oppenheimer approximation:

$$H_{\mathrm{el}}(\mathbf{R})\Psi_{\mathrm{el}}(\mathbf{r};\mathbf{R}) = E_{\mathrm{el}}(\mathbf{R})\Psi_{\mathrm{el}}(\mathbf{r};\mathbf{R})$$

$$\hat{H}_{\mathrm{el}} = -\frac{1}{2}\sum_{i}^{N}\nabla_i^2 + \sum_{i}^{N} v(\mathbf{r}_i) + \sum_{i<j}^{N}\frac{1}{r_{ij}}$$

electron kinetic energy

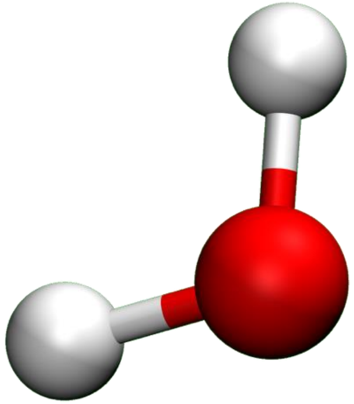
electron-nuclear repulsion

electron-electron repulsion

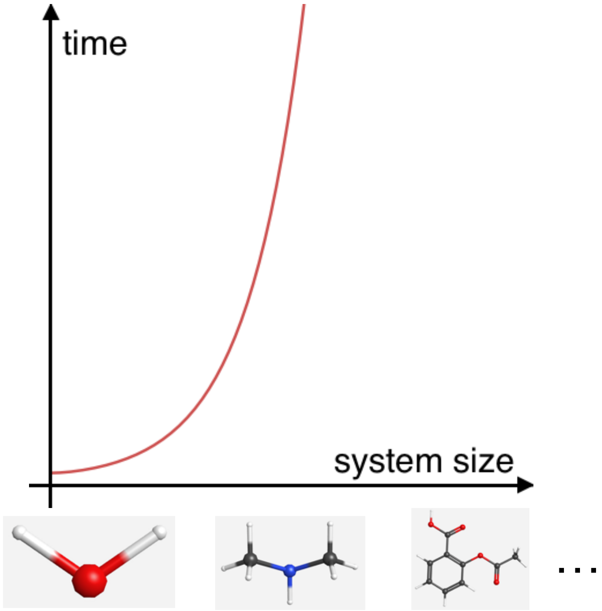
Solutions to this give the electronic energy of the system of interest. Useful for:

- Determining chemical structures
- Predicting reaction pathways
- Transition states and spectroscopy

What is quantum chemistry?



- The equations can look deceptively simple – there is in fact a huge scaling issue.
- Exact solutions of the electronic Schrödinger are only solvable for the smallest systems.

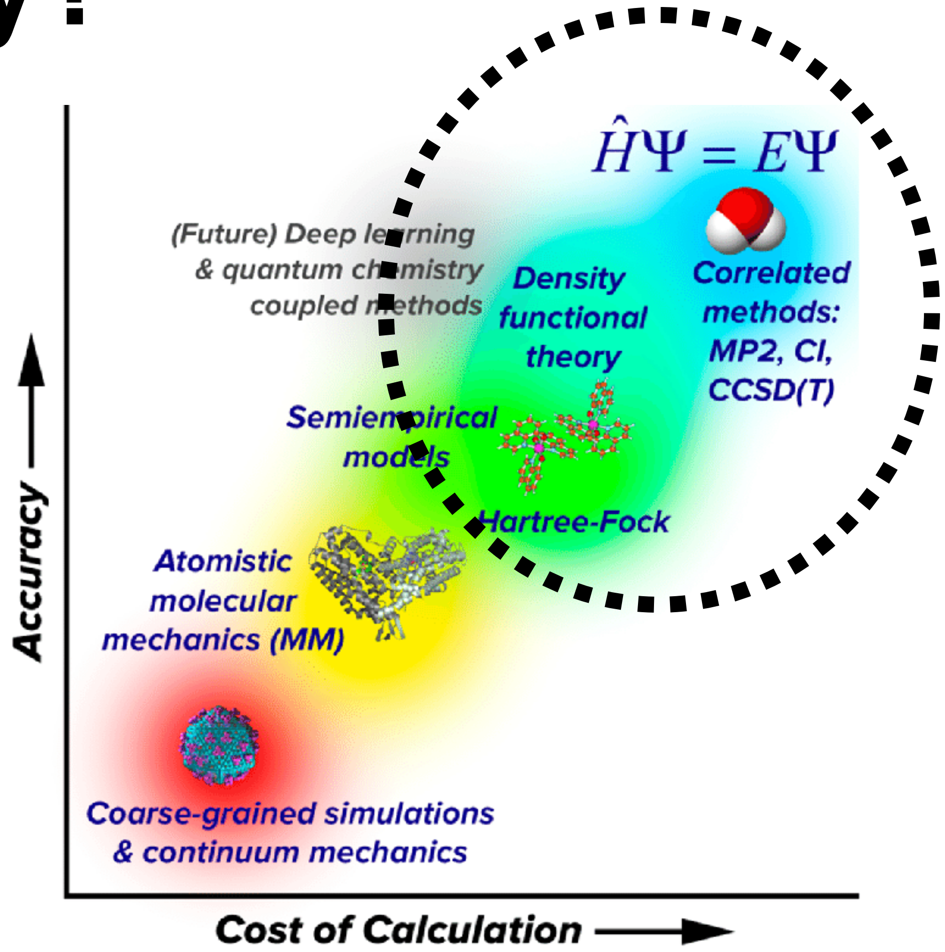


- The exact solution (FCI) in a given basis set scales exponentially with system size! $\mathcal{O}(\exp(M))$
- Approximations are needed for larger molecules to be considered.

What is quantum chemistry?

- There are a variety of methods which aim to scale more favorably whilst still yielding good electronic energies.

- Hartree Fock (HF): a mean-field method, ignores electron correlation. $\mathcal{O}(M^4)$
- Configuration Interaction (CI): accounts for correlation. Can be truncated but still poor scaling. CISD: $\mathcal{O}(M^6)$
- Density Functional Theory (DFT): Expresses wavefunction as functional of electron density. Good accuracy to cost ratio. Scaling varies but around $\mathcal{O}(M^3)$
- **Gold-standard**: Coupled Cluster Singles and Doubles with perturbative Triples (CCSD(T)): $\mathcal{O}(M^7)$



Borges, R. M., Colby, S. M., Das, S., Edison, A. S., Fiehn, O., Kind, T., ... & Renslow, R. S. (2021). Quantum Chemistry Calculations for Metabolomics: Focus Review. *Chemical reviews*, *121*(10), 5633-5670.

How might quantum computing help?

- As we know, there are a range of theoretical speed-ups which quantum algorithms can provide in several domains:
  - Ordered search (Grover's algorithm)
  - Factoring (Shor's algorithm)
  - Eigenvalue-finding (Quantum Phase Estimation)

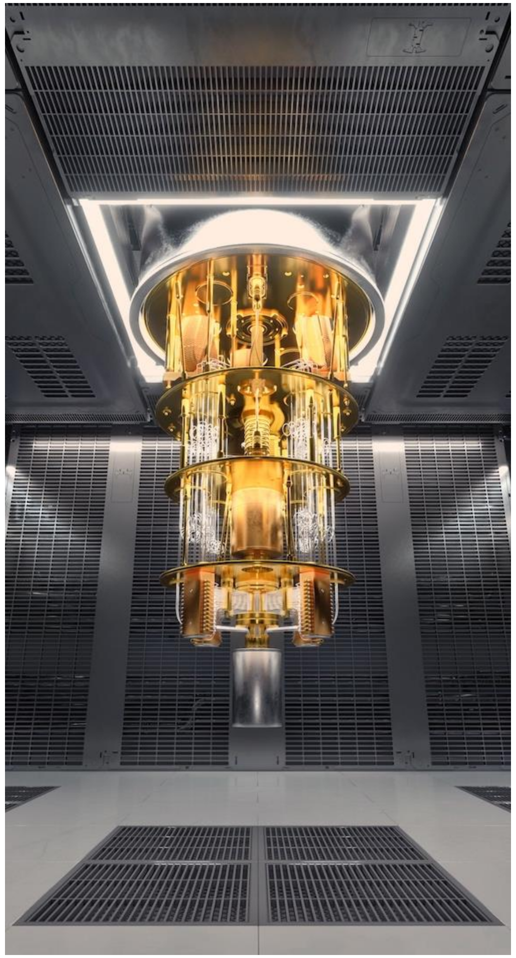
- We also know that a quantum computer can, in principle, represent the molecular wavefunction in a linear number of qubits.

$$\left(\sum_{ij} h_{ij} a_i^* a_j + \sum_{ijkl} h_{ijkl} a_i^* a_j^* a_k a_l\right)\psi = E\psi$$

2^M classical bits

M quantum bits

electronic Hamiltonian in 2nd quantized form



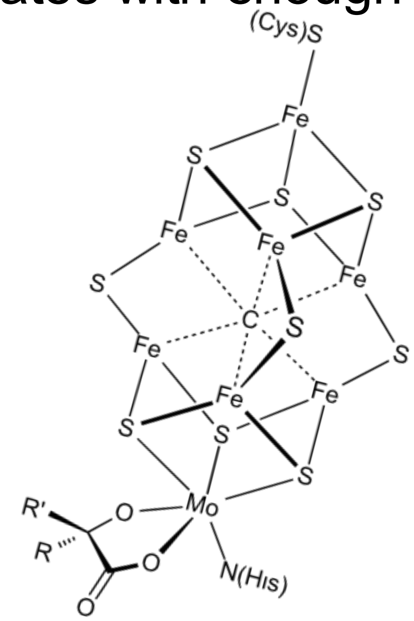
How might quantum computing help?

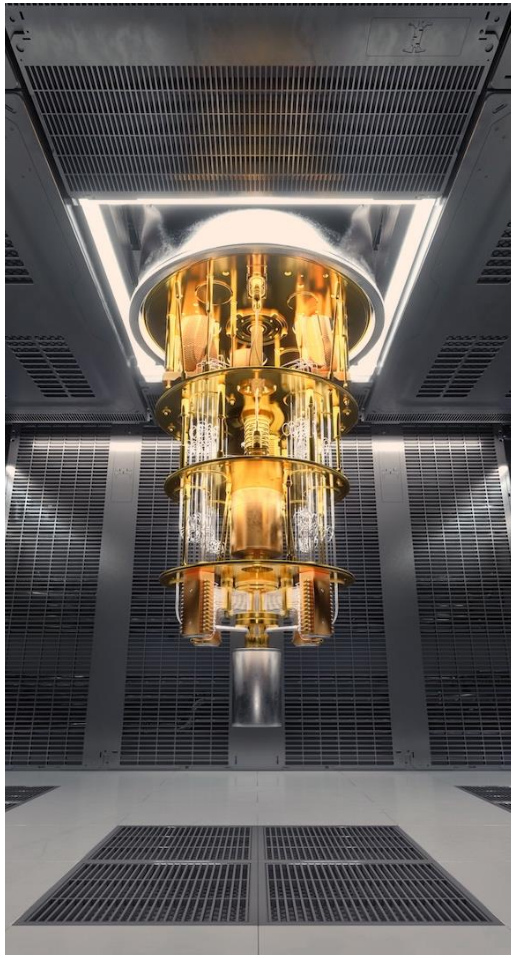
- So for quantum chemistry, use QPE right?
- Ideally yes, QPE would be used to return eigenvalues of the molecular Hamiltonian.
- However, circuits are extremely deep, so general implementations are limited to the fault tolerant regime.
- There is also the underlying issue of preparing initial states with enough ground state overlap…

Year	Innovation	FeMoco-54 [37]			FeMoco-76 [38]		
		Qubits	Toffolis	Reference	Qubits	Toffolis	Reference
2017	First resource estimate by Trotterization [37]	111	5.0×10^{13}	[37]	-	-	-
2019	Qubitization of Single-Factorization [17]	3320	9.5×10^{10}	[7]	3628	1.2×10^{11}	[7]
2020	Qubitization of Double-Factorization (DF) [9]	3600	2.3×10^{10}	[9]	6404	5.3×10^{10}	[7]
2020	Tensor-Hyper-Contraction (THC) [7]	2142	5.3×10^{9}	[7]	2196	3.2×10^{10}	[7]
2024	Symmetry compression of DF [39]	1994	2.6×10^{9}	[39]	-	-	-
2025	Symmetry compression of THC [8]	-	-	-	1512	4.3×10^{9}	[8]
This work	Spectrum amplification & DFTHC	1137	3.41×10^{8}		1459	9.99×10^{8}	
Improvement of this work over [39] and [8][a]		1.8×	7.0×		1.0 ×	4.3 ×	

[a] Our approach is distinct and independent of recent results by Caesura et. al [8].

TABLE I. Improvements in Toffoli and qubit costs on benchmark molecules for performing phase estimation targeting ground-state energies with a standard deviation of at most chemical accuracy $\epsilon_{\text{chem}} = 1.6\text{mHa}$. Total Toffoli counts are based on a phase estimation uncertainty of $\sigma_{\text{PEA}} = 1\text{mHa}$.

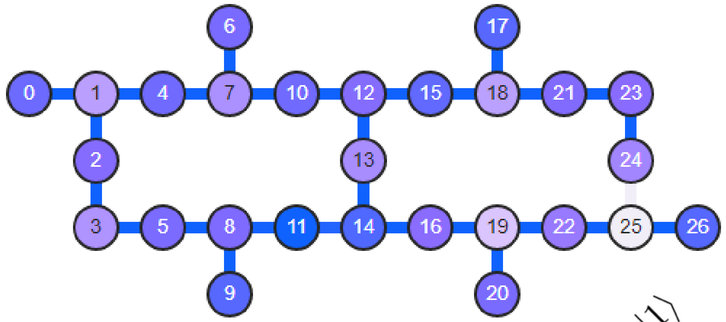




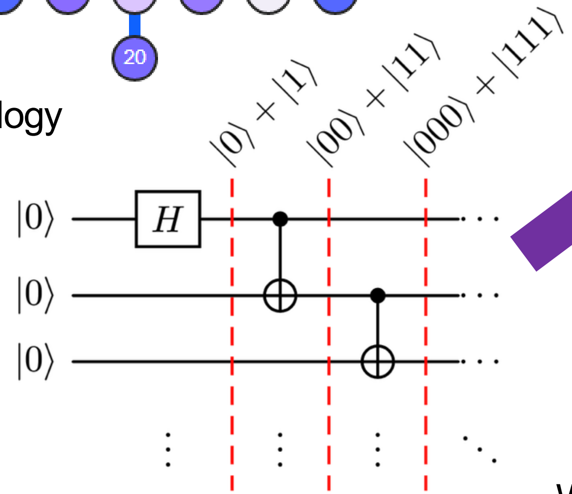
Low, G. H. et al. arXiv:2502.15882

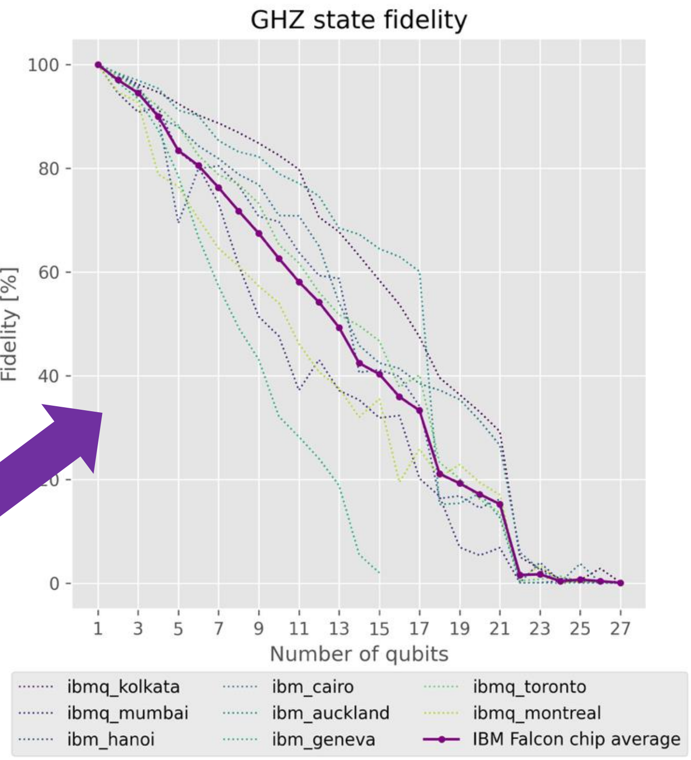
Current quantum computers

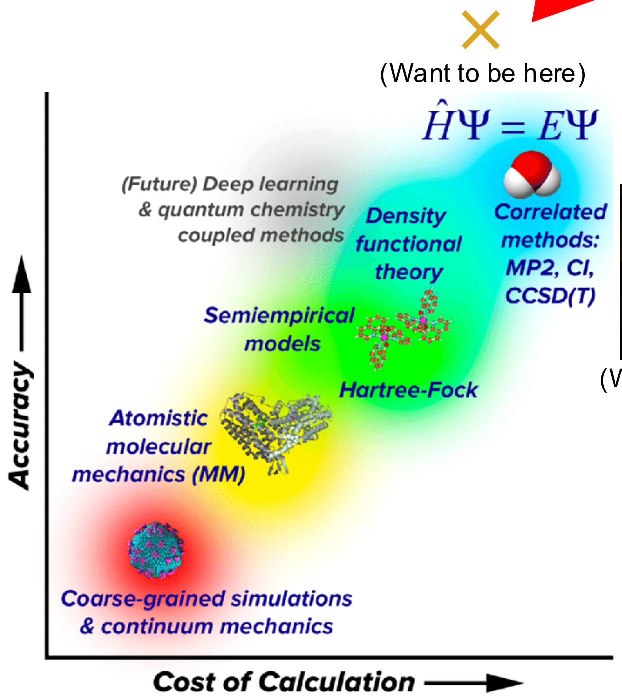
- Current devices are **noisy**, requiring heavy error mitigation
- **Limited coherence** means shallow circuits
- Qubit **topologies** are **restrictive**



IBM *Falcon* chip topology





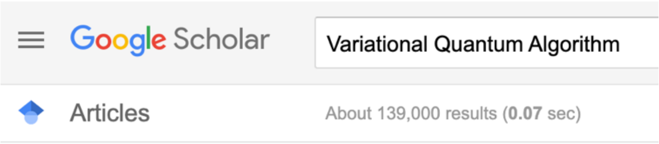


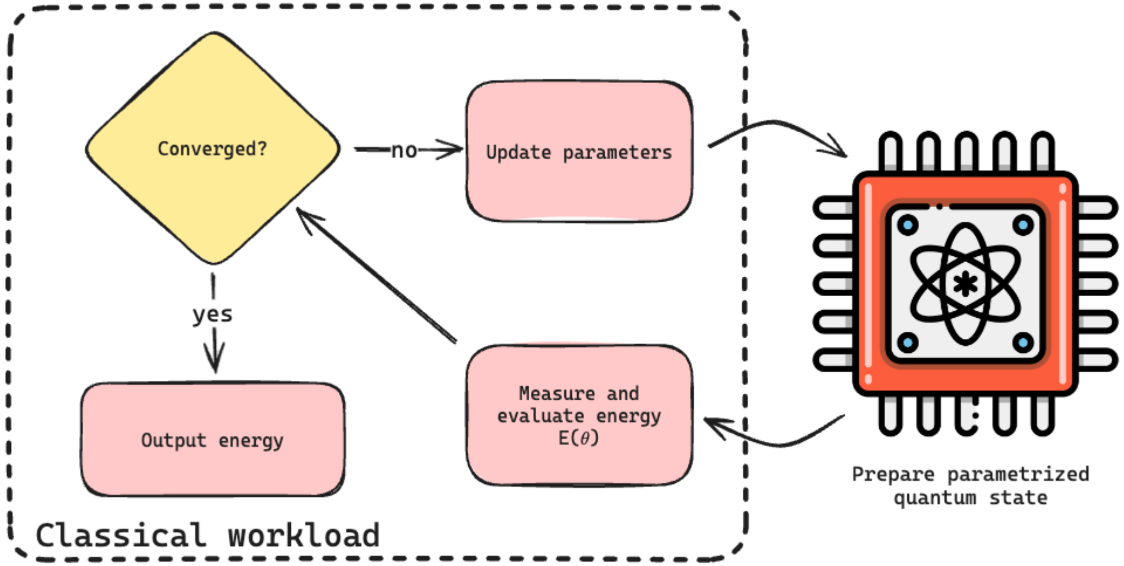
(We are here)

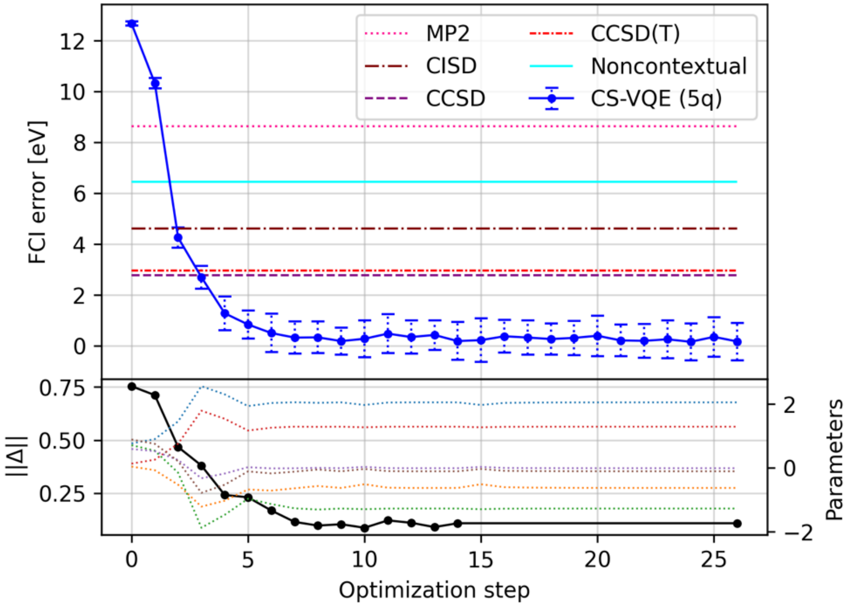
Weaving, T. et al. Phys. Rev. Research 5, 043054 (2023)

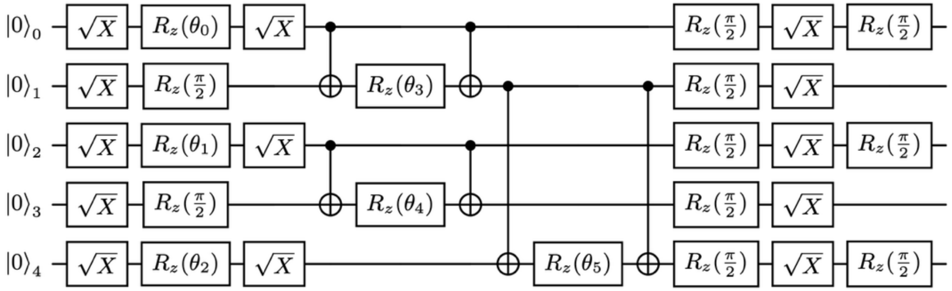
Quantum-Classical Hybrid Algorithms

- Due to these limitations, the field has looked towards **hybrid** algorithms, where a **quantum subroutine** is embedded within a **classical framework.**
- **Variational Quantum Algorithms (VQAs)** are most commonly used.



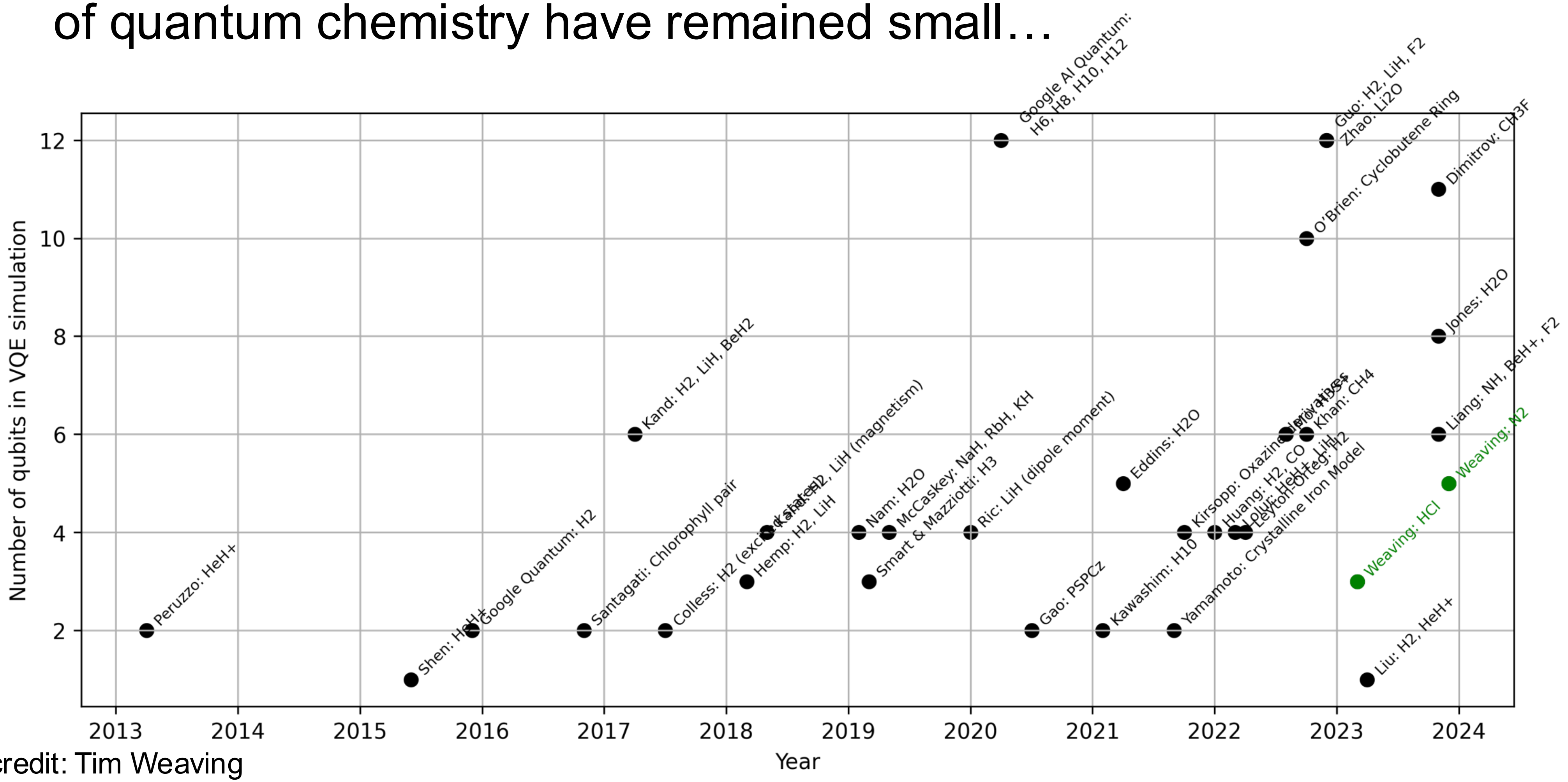






VQAs in Chemistry

- Despite VQAs easing the load on the QPU, demonstrations of quantum chemistry have remained small…

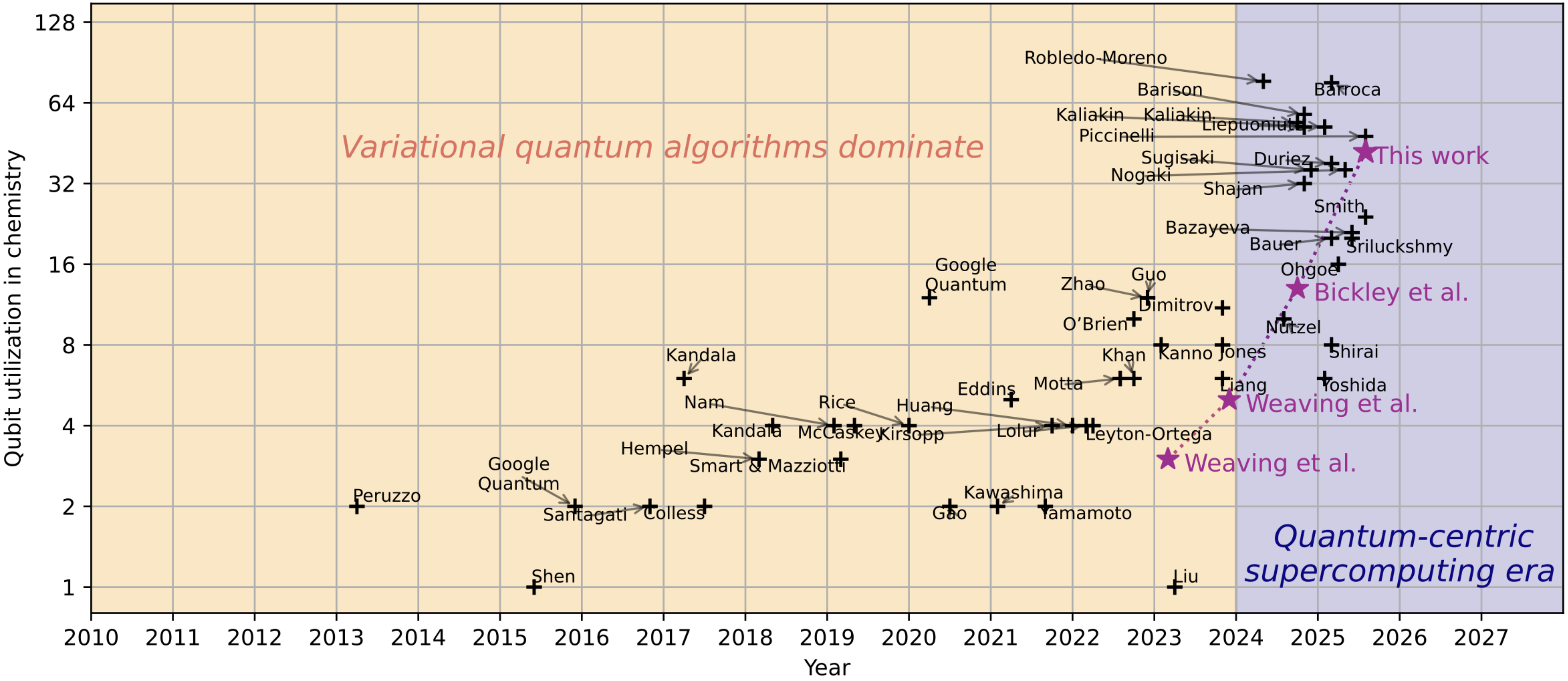


credit: Tim Weaving

- Measurement overhead is prohibitive
- Hardware noise corrupts results and worsens at scale.
- Looming issue of barren plateaus

Quantum Selected Configuration Interaction (QSCI)

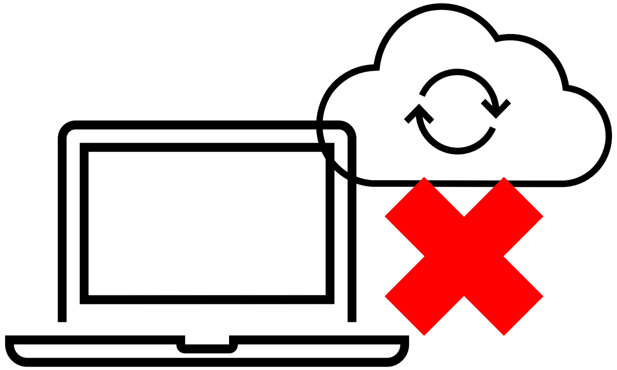
- Recently, many researchers have turned to a different approach.
- QSCI (aka SQD) uses the quantum computer as a sampling device for the electronic configuration space of your system, with the resulting subspace solved classically.
- Hardware noise does not corrupt the energy evaluation – it is only the selection of subspace which dictates the energy.
- The classical energy evaluations lends itself to HPC integration, especially as size of molecules is scales up.
- However, there are still unanswered questions on the efficacy of QSCI vs. comparable fully classical methods.

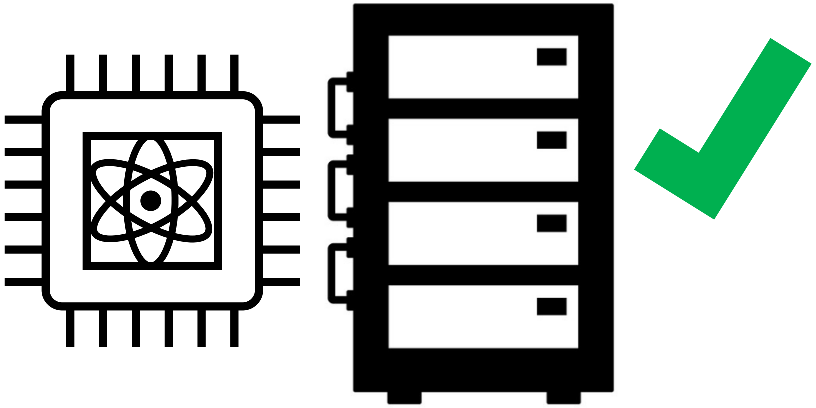


Weaving, T. et al. arXiv:2509.02525v2

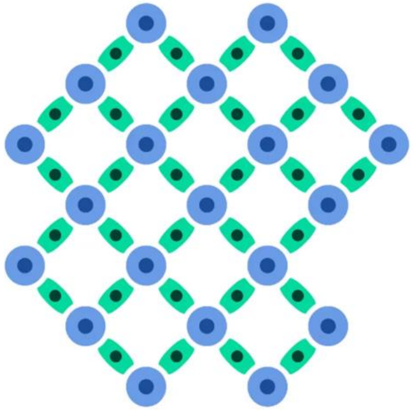
HPC Integration Extends Quantum Capabilities

- Quantum hardware is most commonly provided via cloud services...
- … but this places limitations on classical compute availability.
- There are also latency issues.
- Integrating quantum resources into HPC platforms allows optimal performance.
- Workflows can be designed to challenge both quantum *and* classical resources.





LRZ Integrated System



- QPU+HPC architecture

Median T1 Time	40 μs
Median T2 Time	20 μs
Single qubit gate fidelity	>0.998
Two qubit gate fidelity	>0.990
Readout fidelity	>0.97

- **LRZ SuperMUC-NG:**
  - 6,336 “thin” nodes with 48 cores and 96GB memory
  - 144 “fat” nodes with 48 cores and 768GB memory

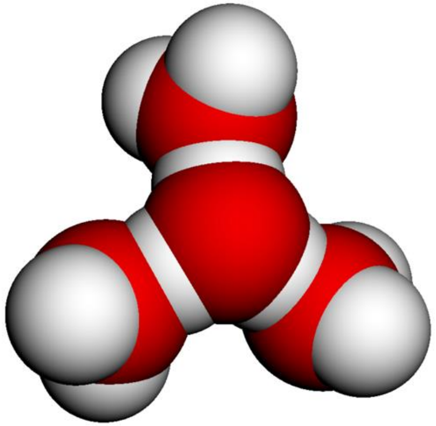
- **IQM QExa20 Chip:**
  - 20 qubit superconducting chip with a square lattice topology
  - Tunable coupler architecture enables fast gates with high fidelities

Leibniz Supercomputing Centre
of the Bavarian Academy of Sciences and Humanities

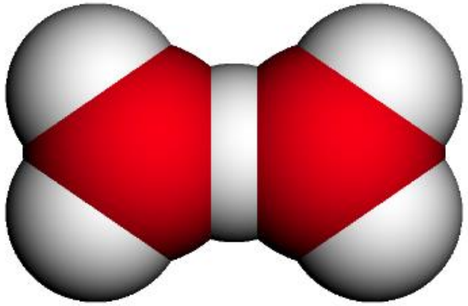
IQM

Application – Hydronium

- Hydronium is the protonated form of water, i.e. H_3O^+.
- It exists in two solvated forms, the Eigen and Zundel cations.
- The extra proton can "hop" between adjacent water molecules in solution, known as the **Grotthuss mechanism**.
- It is important for many biological processes.
- In this study, we consider the planar form of the Zundel cation, where the free proton can move between two water molecules.



Eigen cation

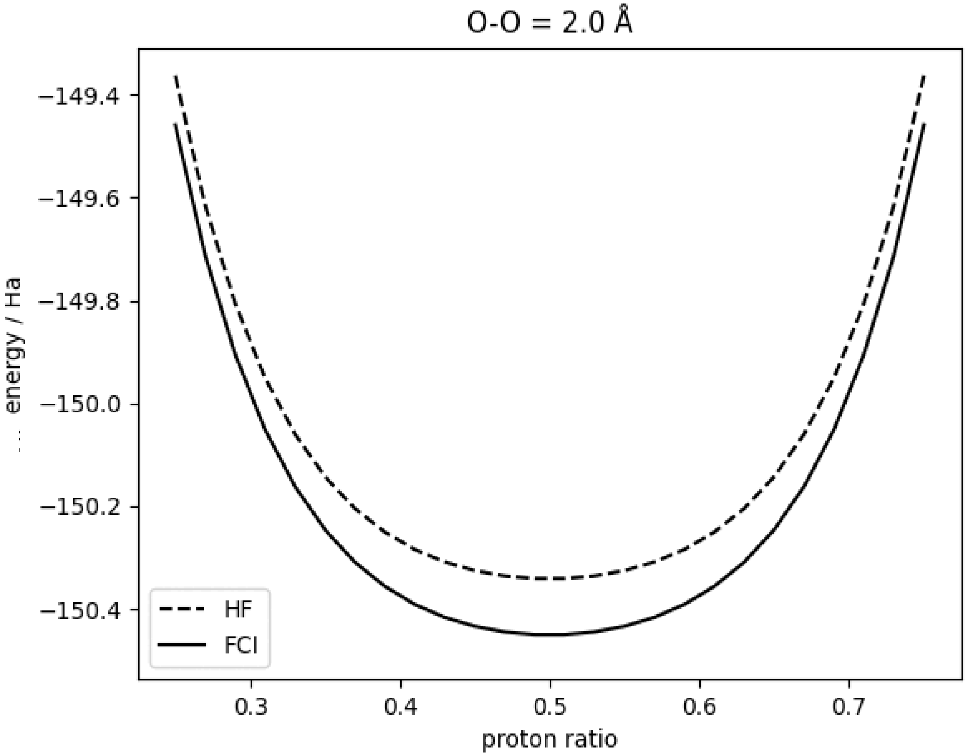


planar Zundel cation

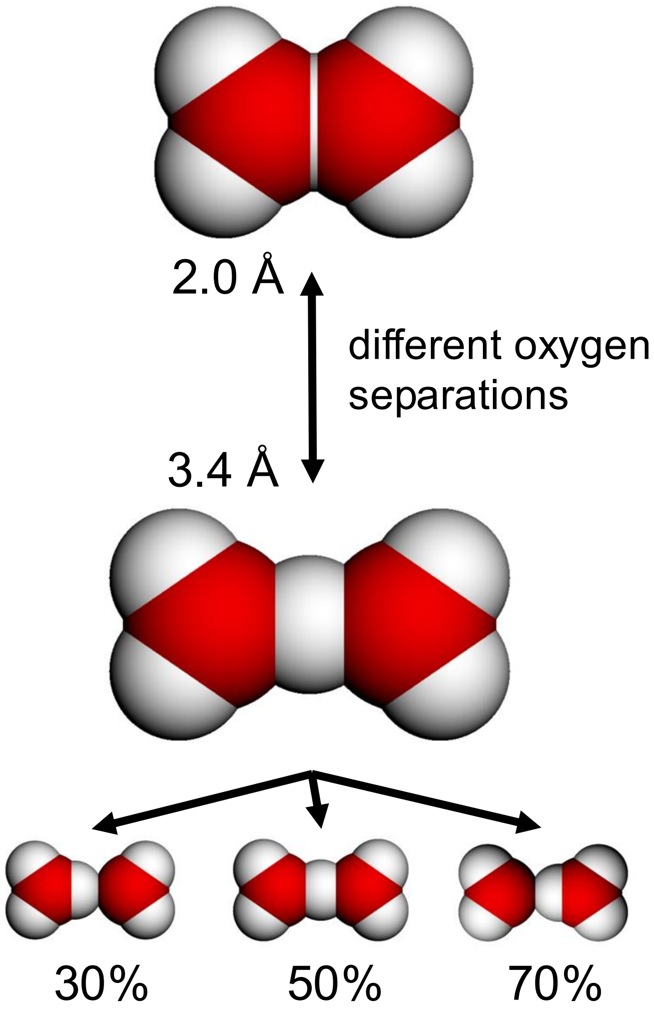
Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

Proton Transfer

- **When compressed**, the proton transfer energy surface has a single minimum.
- **When extended**, two potential wells emerge where the proton is localized on either of the two waters.
- **Ideal proton transfer** mechanics occur when the PE surface between the two waters is mainly flat, allowing proton hopping with minimal energy input.
- With full configuration interaction energy computations, we see that this ideal behavior occurs at **around 2.6 angstrom** oxygen separation.



Dashed line: Hartree-Fock
Solid line: full configuration interaction

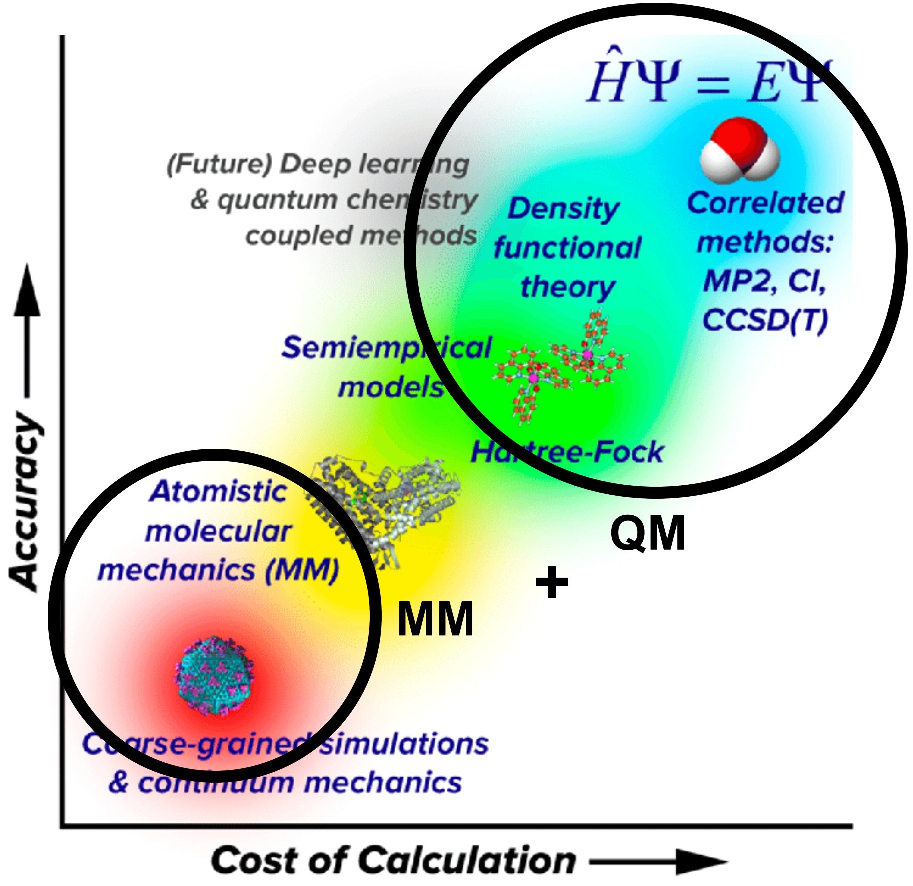


different proton ratios

Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

Multiscale Modelling

- The highest accuracy quantum chemistry methods scale too poorly for large/complex chemical systems.
- Therefore, multiscale modelling in chemistry allows such methods to be embedded within lower accuracy, but less computationally demanding schemes.
- For example, QM/MM is ubiquitous within modern drug discovery pipelines.



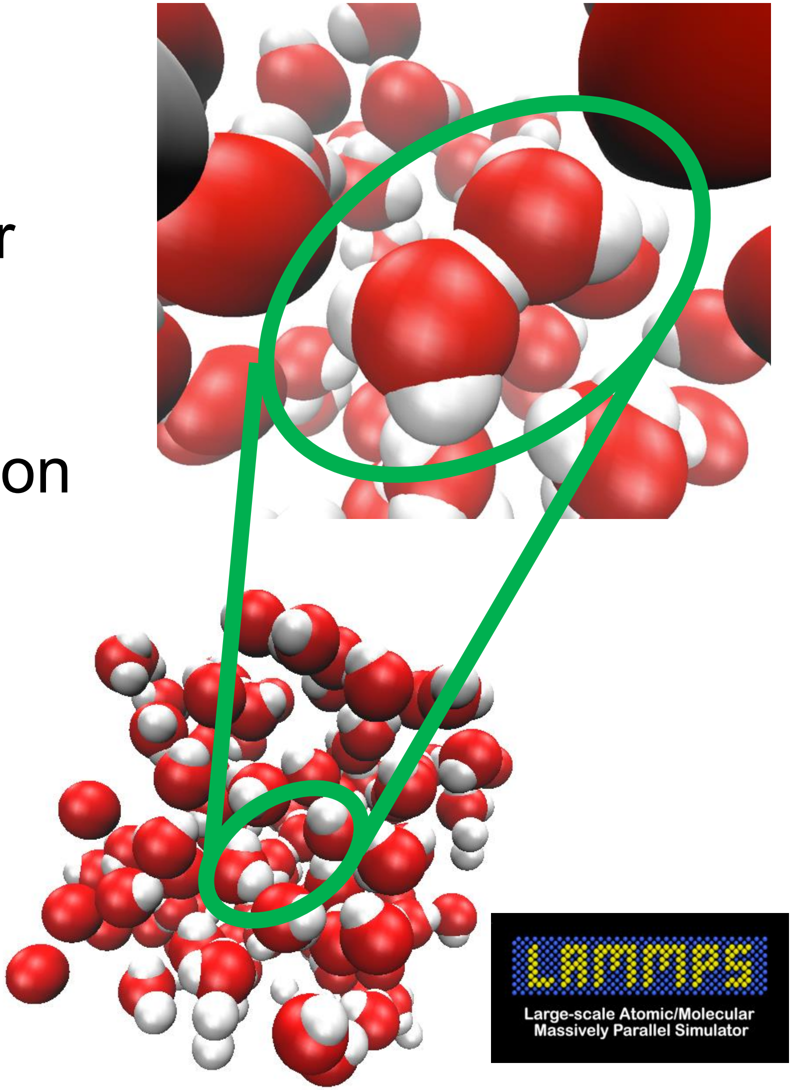
Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

QM/MM

- We use the LAMMPS code to propagate the solvent water molecules around the central Zundel system, which is initially fixed in space.
- The MolSSI Driver Interface (MDI) facilitates communication between LAMMPS and PySCF, which drives the quantum chemistry calculations on the Zundel region.
- QM/MM interactions are treated with electrostatic embedding:

$$\hat{H}_{\mathrm{QM/MM}} = \hat{H}_{\mathrm{QM}} + \hat{V}_{\mathrm{nuc-MM}} + \hat{V}_{\mathrm{el-MM}}$$

$$= \underbrace{-\frac{1}{2}\sum_{i}^{N_{\mathrm{el}}}\nabla_i^2 + \sum_{i}^{N_{\mathrm{el}}} v(\mathbf{r}_i) + \sum_{i<j}^{N_{\mathrm{el}}}\frac{1}{r_{ij}}}_{\text{electronic Hamiltonian}} + \underbrace{\sum_{A}^{N_{\mathrm{MM}}}\sum_{B}^{N_{\mathrm{QM}}}\frac{Q_A Q_B}{|\mathbf{R}_A - \mathbf{R}_B|}}_{\text{MM-QM nuclear repulsion}} - \underbrace{\sum_{A}^{N_{\mathrm{MM}}}\sum_{i}^{N_{\mathrm{el}}}\frac{Q_A}{|\mathbf{R}_A - \mathbf{r}_i|}}_{\text{MM nuclear QM electron attraction}}$$

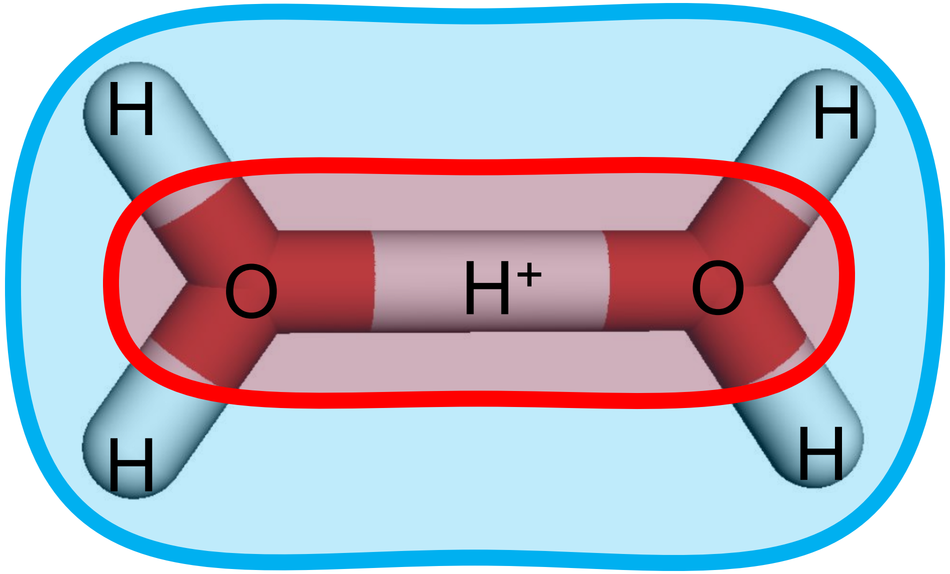


Large-scale Atomic/Molecular Massively Parallel Simulator

Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

Projection Based Embedding

- Projection based embedding splits the orbital description of a molecule into two regions which can be computed at different levels of theory.
- We use a wavefunction-in-DFT embedding, allowing a small region to be converted into a qubit Hamiltonian.
- We generate Hamiltonians for the O-H-O atoms of the Zundel cation, which generates an 18 qubit Hamiltonian. Upon symmetry tapering this reduces to 16 qubits.
- Our custom package *Nbed* drives the PBE method, with PySCF as the quantum chemistry backend.



Active region:
16 qubit
Hamiltonian

Environment region:
Density functional
theory

pyscf + *Nbed:*
https://github.com/UCL-CCS/Nbed

A. Ralli, M. Williams de la Bastida, P. V. Coveney, "Scalable approach to quantum simulation via projection-based embedding", ***Physical Review A*** **109, 022418 (2024)**

Full embedding scheme

1. Quantum core

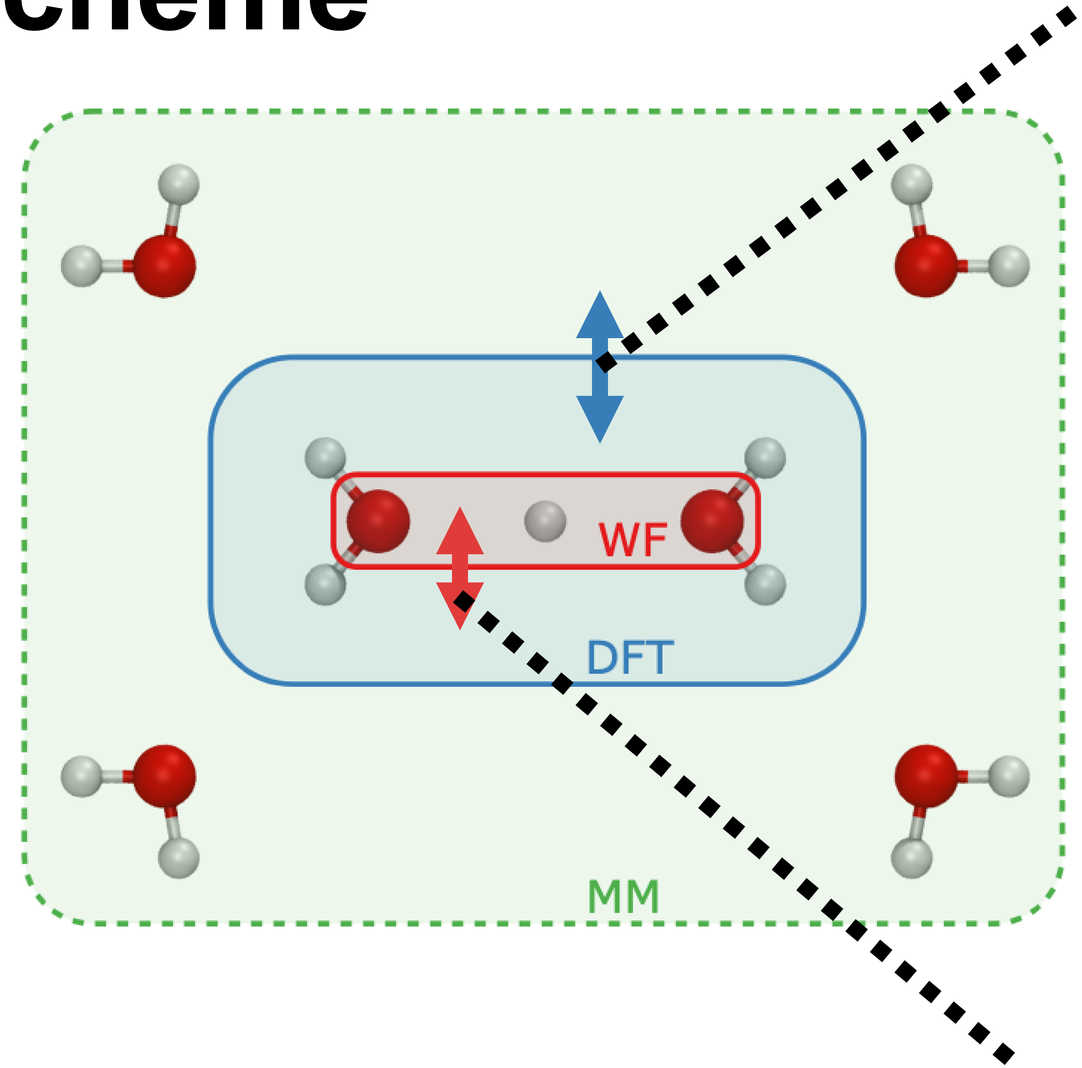
A set of localised molecular orbitals which ideally capture the region of highest electron correlation. Can be represented with correlated-wavefunction methods (CI, CC) or quantum circuits (VQE, QSCI).

2. DFT environment

The remainder of the quantum chemistry calculation, evaluated with DFT. Interactions between ***1*** and ***2*** handled with projection-based embedding (PBE).

3. Classical environment

An explicit solvent or larger biomolecular structure treated with force fields, and propagated with MD. Interactions between ***3*** and **(*1*+*2*)** handled with electrostatic QM/MM.



QM/MM interaction

$$= \underbrace{-\frac{1}{2}\sum_{i}^{N_{\mathrm{el}}}\nabla_i^2 + \sum_{i}^{N_{\mathrm{el}}} v(\mathbf{r}_i) + \sum_{i<j}^{N_{\mathrm{el}}}\frac{1}{|\mathbf{r}_i - \mathbf{r}_j|}}_{\text{electronic Hamiltonian}} \underbrace{+ \sum_{A}^{N_{\mathrm{MM}}}\sum_{B}^{N_{\mathrm{QM}}}\frac{Q_A Q_B}{|\mathbf{R}_A - \mathbf{R}_B|}}_{\text{MM-QM nuclear repulsion}} \underbrace{- \sum_{A}^{N_{\mathrm{MM}}}\sum_{i}^{N_{\mathrm{el}}}\frac{Q_A}{|\mathbf{R}_A - \mathbf{r}_i|}}_{\text{MM-QM (nuclear-electron) attraction}},$$

$$= \underbrace{\left\langle \Psi_{emb}^{act} \middle| H_{emb} \middle| \Psi_{emb}^{act} \right\rangle}_{\text{active region}} + \underbrace{E[\gamma_{env}]}_{\text{environment}} + \underbrace{g(\gamma^{act}, \gamma^{env})}_{\text{non-additive}} - \underbrace{\mathrm{Tr}\Big(\gamma^{act}(V_{emb} + P_{proj}^{env})\Big)}_{\text{correction}}.$$

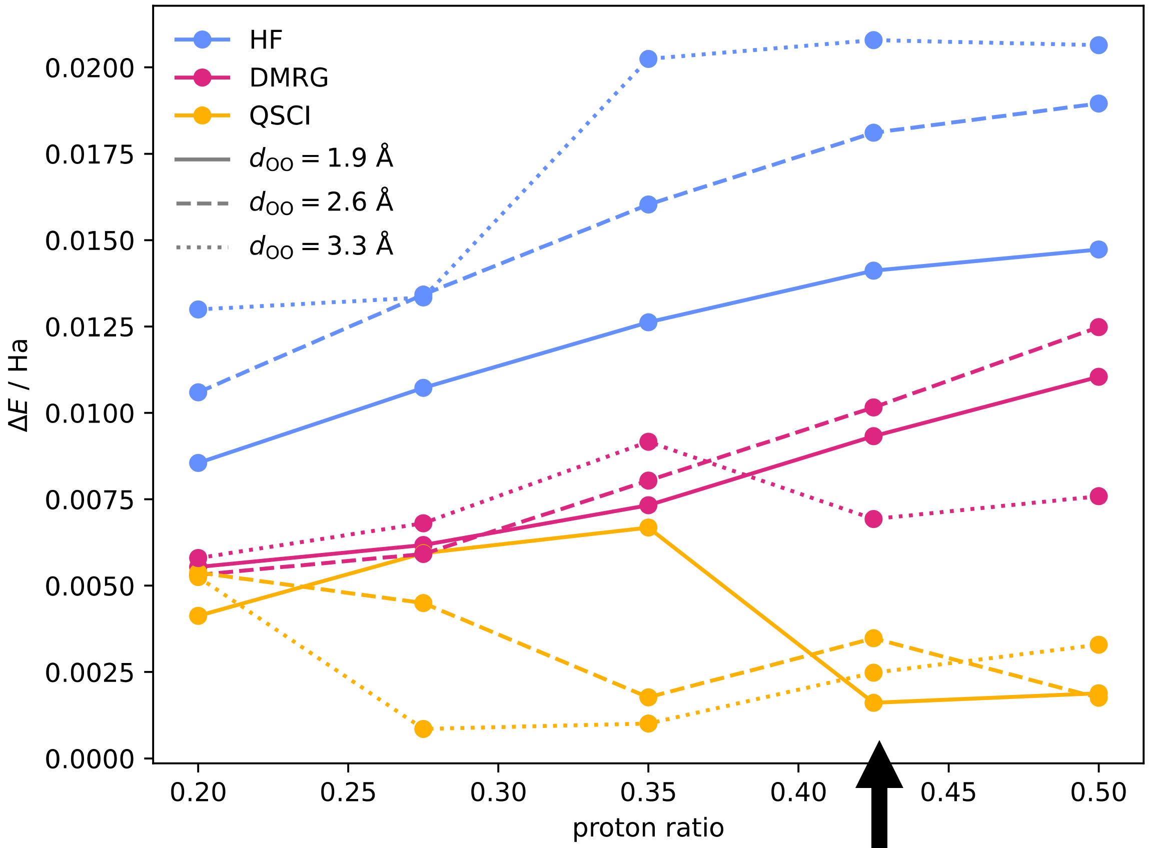
PBE interaction

Bickley, Thomas M., et al. “Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques”, **Digital Discovery, 2025 (will be published very soon)**

Proof-of-concept results

Natively a 30-qubit problem, a reduced 13-qubit quantum core for the O-H-O region is extracted. For a set of core geometries, a quantum circuit is prepared using a low bond dimension DMRG solution on IQM's Q-Exa 20 qubit superconducting device.

With respect to the exact energy, the data from Q-Exa 20 device achieves **"chemical accuracy"** for some points along the proton transfer coordinate, and outperforms the DMRG solution used to initialize the circuit at each step.



Hartree-Fock

DMRG
(Used to initialize the QSCI circuit)

QSCI

chemical accuracy

IQM Q-Exa 20 device

Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

Next steps

Scale-up classical and quantum compute workloads:

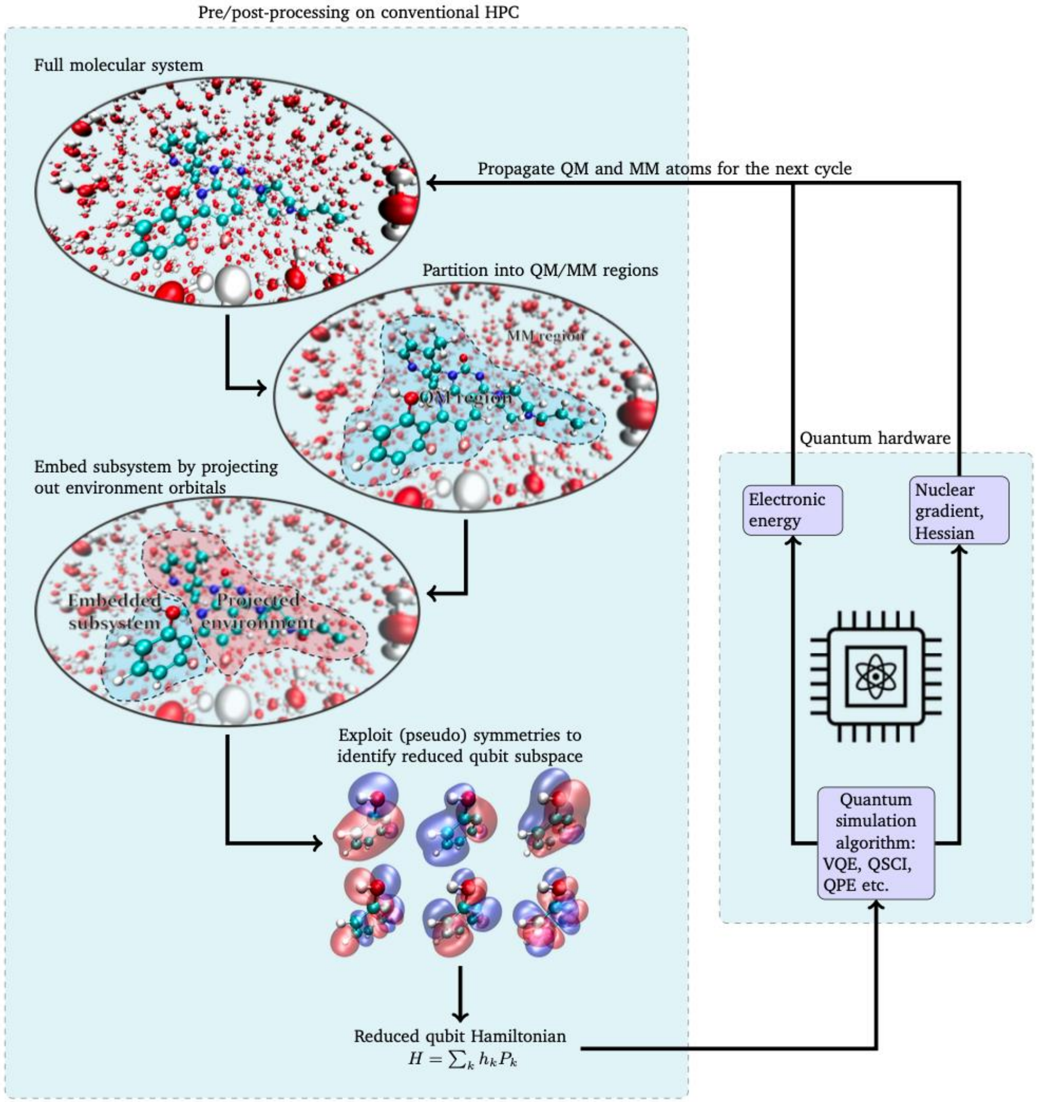
- Expand the size of the MM region and propagation time for larger classical compute demand.
- Could consider up to 20 qubits on the QExa device, and beyond as new hardware becomes available.

Perform full QM/MM propagation of the QM region nuclei:

- Initially we kept the QM atoms clamped in space to facilitate the proton sweep, however we could also allow these atoms to move for a full QM/MM simulation.

Further develop our tensor network assisted quantum SCI method:

- Improve warm-starting and error mitigation to handle larger systems and increase accuracy



Bickley, Thomas M., et al. "Extending Quantum Computing through Subspace, Embedding and Classical Molecular Dynamics Techniques", **Digital Discovery, 2025 (will be published very soon)**

Next steps

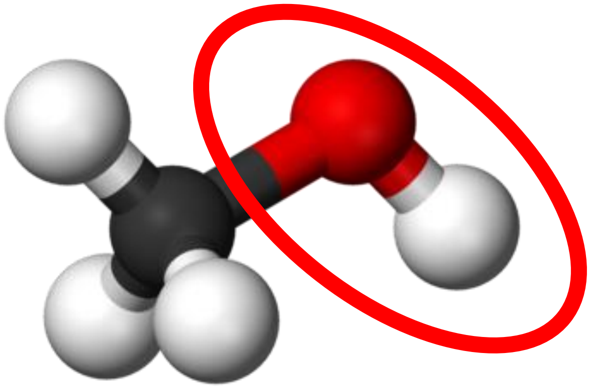
One option is to approximate the exact embedded energy gradient with the global DFT gradient.

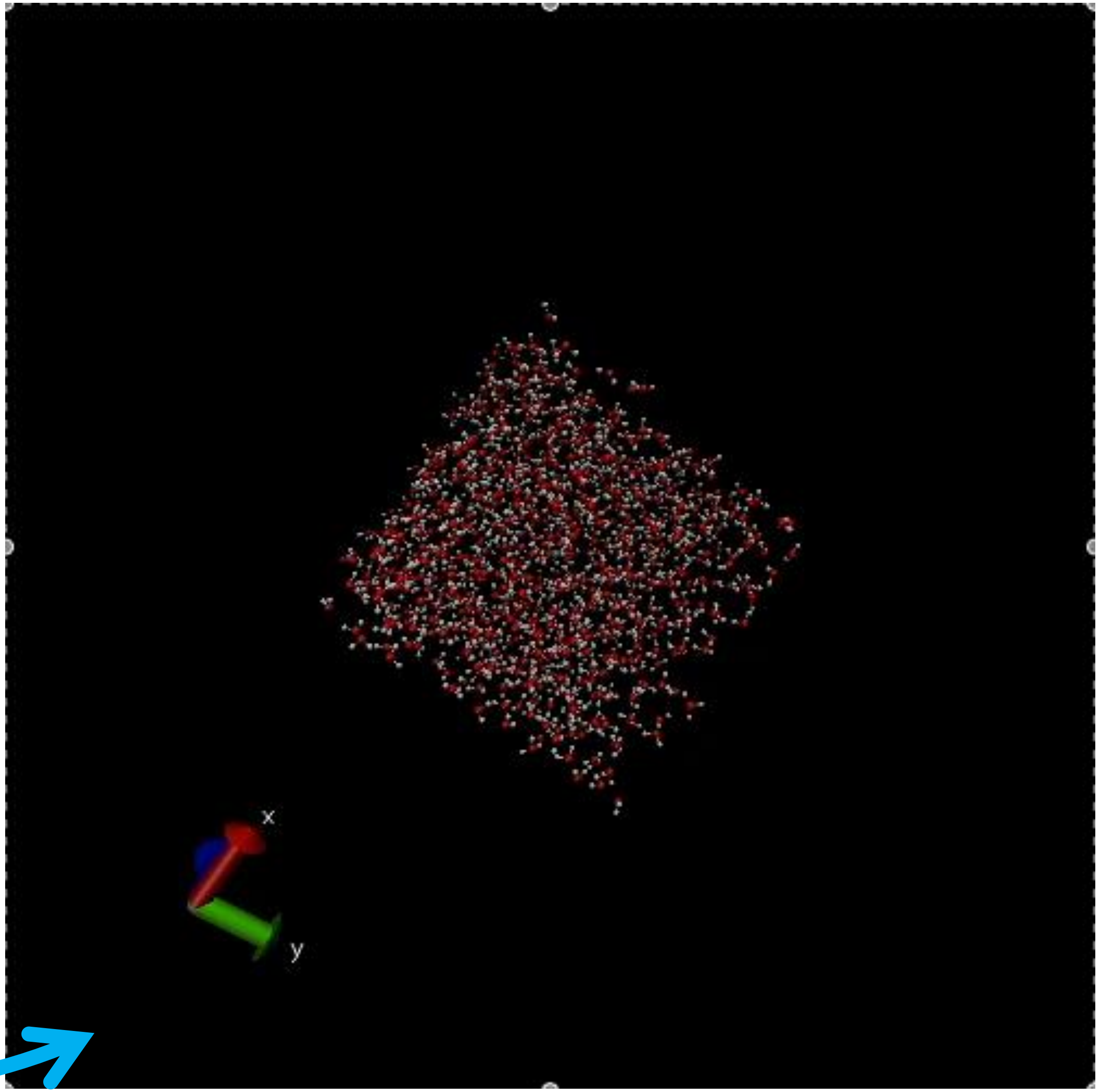
This allows movement of the QM atoms, and a potential path to tighter classical / quantum integration.

Here we see a methanol molecule solvated in water.

With a similar embedding scheme, the OH (alcohol) group is targeted as the core quantum region.

This is a 20 qubit problem, but could be reduced further.





Recent HPC and QC news

Platform Architecture for Tight Coupling of High-Performance Computing with Quantum Processors

SHANE A. CALDWELL, MOEIN KHAZRAEE, ELENA AGOSTINI, TOM LASSITER, COREY SIMPSON, OMRI KAHALON, MRUDULA KANURI, JIN-SUNG KIM, SAM STANWYCK, MUYUAN LI, JAN OLLE, CHRISTOPHER CHAMBERLAND, BEN HOWE, BRUNO SCHMITT, JUSTIN G. LIETZ, and ALEX MCCASKEY, NVIDIA Corporation, USA
JUN YE, Institute of High Performance Computing (IHPC), Agency for Science, Technology and Research (A*STAR), Singapore
ANG LI, Pacific Northwest National Laboratory, USA and University of Washington, USA
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We propose an architecture, called NVQLink, for connecting high-performance computing (HPC) resources to the control system of a quantum processing unit (QPU) to accelerate workloads necessary to the operation of the QPU. We aim to support every physical modality of QPU and every type of QPU system controller (QSC). The HPC resource is optimized for real-time (latency-bounded) processing on tasks with latency tolerances of tens of microseconds. The network connecting the HPC and QSC is implemented on commercially available Ethernet and can be adopted relatively easily by QPU and QSC builde [illegible] latency measurement of 3.96 μs (max) with prospects of further optimization. We describe an ext [illegible] n to the C [illegible] ng model and runtime architecture to support real-time callbacks and data marshaling b [illegible] een the HPC a [illegible] QSC. [illegible] NVQLink extends heterogeneous, kernel-based programming to the QSC, allowing the p [illegible] amm [illegible] o add [illegible] s CPU, [illegible] U, a [illegible] bsystems in the QSC, all in the same C++ program, avoiding the use of a performance-li [illegible] ng H [illegible] TP i [illegible] ve pr [illegible] a [illegible] for QSC builders to integrate with this architecture by making use of multi-level intermedia [illegible] epres [illegible] ation dial [illegible] nd progres [illegible] lowering to encapsulate QSC code.

29 October 2025
arXiv:2510.25213

Real-time decoding of the gross code memory with FPGAs.

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[1]IBM Quantum

Oct 24, 2025

Abstract

We introduce a prototype FPGA decoder implementing the recently discovered Relay-BP algorithm and targeting memory experiments on the $[[144, 12, 12]]$ bivariate bicycle quantum low-density parity check code. The decoder is both fast and accurate, achieving a belief propagation iteration time of 24ns. It matches the logical error performance of a floating-point implementation despite using reduced precision arithmetic. This speed is sufficient for an average per cycle decoding time under 1 μs assuming circuit model error probabilities are less than 3×10^{-3}. This prototype decoder offers useful insights on the path toward decoding solutions for scalable fault-tolerant quantum computers.

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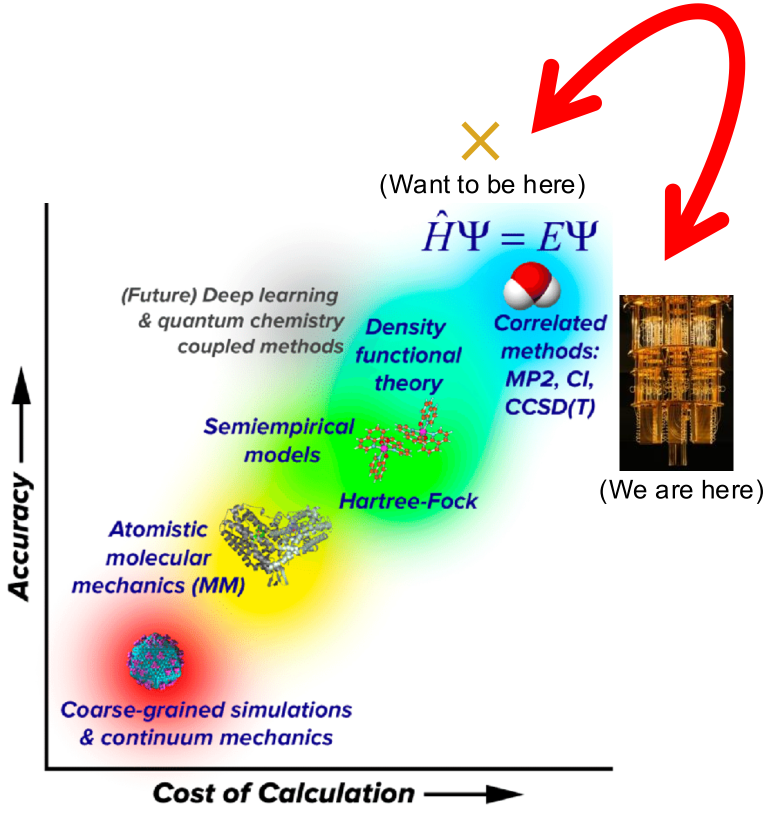
Conclusions

- Quantum chemistry is an important tool for chemists to predict chemical properties.
- Scaling issues necessitate approximation in classical algorithms.
- Quantum computers may offer exciting benefits in the area, but practical implementations are extremely challenging.
- However long it takes, good quantum and classical algorithm overlap will be important.
- Multiscale chemistry methods provide one potential option for using high accuracy quantum chemistry calculations in larger classical frameworks.
- QSCI is an emerging algorithm in chemistry which also benefits from HPC integration.
- More work is required!



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Any questions?

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lrz Leibniz Supercomputing Centre of the Bavarian Academy of Sciences and Humanities