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Quantum-centric high performance computing for quantum chemistry

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High performance computing (HPC) is renowned for its capacity to tackle complex problems. Meanwhile, quantum computing (QC) provides a potential way to accurately and efficiently solve quantum chemistry problems. The emerging field of quantum-centric high performance computing (QCHPC), which merges these two powerful technologies, is anticipated to enhance computational capabilities for solving challenging problems in quantum chemistry. The implementation of QCHPC for quantum chemistry requires interdisciplinary research and collaboration across multiple fields, including quantum chemistry, quantum physics, computer science and so on. This perspective provides an introduction to the quantum algorithms that are suitable for deployment in QCHPC, focusing on conceptual insights rather than technical details. Parallel strategies to implement these algorithms on quantum-centric supercomputers are discussed. We also summarize high performance quantum emulating simulators, which are considered a viable tool to explore QCHPC. We conclude with challenges and outlooks in this field.

1 Introduction

An exact solution of the Schrödinger equation is a longstanding problem in the community of quantum chemistry.[1] Due to an exponential growth of computational costs with the increase of the system size, the exact computational method that refers to the full configuration interaction (CI) for solving electronic structure problems[2,3] is limited to small complete active space (CAS) with less than 20 electrons and 20 orbitals.[4] In order to overcome this exponential wall problem, a variety of approximate methods with polynomial computational complexity have been proposed. For example, in the case of ground state problems near the equilibrium geometry, the coupled-cluster singles, doubles, and perturbative triples [CCSD(T)] method is regarded as the "gold standard" in quantum chemistry for accurately treating weakly interacting electrons.[5–8] An accurate description of strongly correlated problems, *e.g.* transition-metal catalysis, and electronically excited states is a much more challenging task. A popular scheme is to employ multiconfiguration self-consistent field to treat the static correlation[9,10] and the perturbation theory to account for the dynamics correlation.[11–13] Many advanced computational methods, including the density matrix renormalization group (DMRG),[14,15] selected CI,[16–19] full CI quantum Monte Carlo,[20,21] and many-body expanded full CI,[22,23] provide alternative or even better schemes to (near-) exactly describe the electron correlation.

On the other hand, given a computational method, the scale of quantum chemistry problems that are tractable on a classical computer depends heavily on the computing power of central processing units (CPUs). For many years, high performance computing (HPC) with CPUs at its core has been the most powerful computing tool in the field of quantum chemistry. Vogiatzis *et al.* performed the largest single CI iteration calculation of CAS(24e,24o) for the chromium tetramer with a CI expansion of one trillion Slater determinants on 8192 CPU cores of the NERSC Cori machine.[4] Here, CAS(*Ne*,*Mo*) defines a CAS problem with *N* electrons and *M* orbitals. Brabec *et al.* ran large-scale DMRG calculations on a supercomputer platform, with the largest calculation of CAS(113e,76o) for the nitrogenase FeMo cofactor cluster.[24] This parallel calculation scales up to approximately 2000 CPU cores when setting the bond dimension equal to 6000. In the past few years, the emergence of AI-centric supercomputers, where CPUs and graphics processing units (GPUs) work together in giant systems, has achieved tremendous success in handling heavy quantum chemistry tasks. Xiang *et al.* extended the DMRG calculation of CAS(114e,76o) for the P-cluster to an unprecedentedly large bond dimension of 14 000 on 48 A100 GPUs.[25] Datta *et al.* accelerated the CCSD(T) calculation for the C60 molecule with GPUs at the level of the cc-pVDZ/aug-cc-pVTZ-RI basis sets. The whole calculation was finished in 7 minutes on Frontier using 12 288 AMD GPUs.[26] In the field of density functional theory (DFT), HPC has significantly

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extended the simulation scale,[27–34] from simulating 1000 atoms with 1200 CPUs at a parallel efficiency of ~20% in the early stage[27] to simulating SARS-CoV-2 spike proteins with up to 83 million atoms on a high performance platform with 70 400 CPUs plus 4400 GPUs.[34] Overall, HPC is a leading tool to push the electronic structure theory to the limit on modern supercomputers.

With the development of quantum information techniques, quantum computers are emerging as another promising computing platform for solving the Schrödinger equation.[35–44] This research field has gained significant attention in recent years, especially after the demonstration of quantum advantage in experiments for certain problems, *e.g.* Gaussian Boson sampling, on several quantum computing (QC) platforms.[45–47] QC, utilizing quantum mechanical principles including quantum superposition and quantum entanglement, is anticipated to be a more efficient approach to solve quantum many-body problems than classical computing. However, in the current stage, QC suffers from the influence of noise so quantum simulations of quantum chemistry are limited to simple toy models. Many efforts have been devoted to exploring potential applications of noisy intermediate-scale quantum (NISQ) devices in chemistry and materials science.[41,48–50] Meanwhile, recent significant advances herald the advent of early error-corrected quantum computation and shed light on accurately solving quantum chemistry problems with fault-tolerant quantum computers.[51–53] For example, Google Quantum AI team demonstrated that their distance-5 surface code logical qubit outperformed an ensemble of distance-3 logical qubits on average, implying that one could suppress the influence of noise by scaling a surface code logical qubit.[51] In addition, Bluvstein *et al.* realised a programmable quantum processor with a new type of logical encoding quantum circuit, which contains approximately 48 Rydberg atomic logic qubits.[53]

Since 1949, the performance of classical computers has been doubling every 2 years, while Moore's law is invalidating nowadays as integrated circuits are approaching their theoretical performance limits. Quantum computers are expected to significantly enhance computing power while they may exhibit computational advantage only for certain problems. It is thus a natural choice to integrate quantum computers into supercomputers to overcome the limitations of classical computing power. Quantum computers work in a completely different way from classical computers. Therefore, the combination of quantum computers with supercomputers is a challenging task, and it is also attracting growing interest because of its potential to provide powerful computing power for solving complex problems. This new computing platform is referred to quantum-centric supercomputers and the computing mode executed on this platform is named quantum-centric HPC (QCHPC). Here, quantum processing units (QPUs) work together with CPUs/GPUs, with the former one used to run computationally intensive tasks of (near-)exactly solving the Schrödinger equation. Although there are some pilot experiments of integrating small QPUs into the supercomputers, the field is generally still in its infancy. As such, we present a perspective with an emphasis on conceptual rather than technical details of QCHPC for quantum chemistry. A brief introduction to hybrid quantum-classical computing suitable for quantum-centric supercomputer is presented. Parallel strategies for implementing these algorithms are discussed. As a useful tool to explore QCHPC in the NISQ era, state-of-the-art quantum emulating simulators are reviewed.

2 Hybrid quantum-classical computing

QCHPC utilizes QPUs together with CPUs/GPUs to perform large-scale quantum chemistry simulations in a hybrid quantum-classical computing mode. Here, quantum and classical computers can work as a whole to execute a hybrid quantum-classical algorithm or one can combine quantum and classical algorithms to solve a complex quantum chemistry problem. In the following, we will introduce hybrid quantum-classical computing from these two perspectives.

Algorithm-driven hybrid computing

The variational quantum algorithm is a typical hybrid quantum-classical algorithm.[37] It employs a classical optimizer to train parameterized quantum circuits

$$|\Psi(\theta)\rangle = R_l(\theta_l)\cdots R_1(\theta_1)|\Psi_0\rangle \quad (1)$$

where $|\Psi_0\rangle$ is an initial state and $R_k(\theta_k)$ is parameterized one- or two-qubit gates. The cost function is defined as

$$\mathcal{C}(\theta) = \langle\Psi(\theta)|\hat{O}|\Psi(\theta)\rangle, \quad (2)$$

which is often minimized or maximized with respect to parameters to perform a certain task. Variational quantum eigensolver (VQE) is the leading variational quantum algorithm for solving quantum chemistry problems,[39,41,54–58] including ground state and excited state problems. In the VQE algorithm, the physical observable operator $\hat{O}$ in eqn (2) is the many-body Hamiltonian and thus the expectation value of the Hamiltonian, namely the total energy, is the cost function. A parameterized circuit is used to prepare the target quantum state and the total energy (and gradient) is estimated from repeated measurements over the quantum state. Both state preparation and measurement are executed on a quantum computer. The measured results are fed back to the classical computer, which optimizes the circuit parameters to minimize the cost function. It is clear that the VQE algorithm is inherently executed in a hybrid quantum-classical computing mode, where the quantum and classical tasks are executed iteratively and this procedure repeats until converged. The VQE algorithm is considered a near-term quantum algorithm for implementing quantum chemistry simulations on quantum devices with limited coherence time and gate fidelity. The scalability of the VQE for large-scale simulations is hindered by the complexity of quantum circuits required to accurately represent quantum states. In this perspective, we do not introduce the technique details of the VQE algorithm. Comprehensive reviews about the VQE and VQE-base algorithms can be found in ref. 59–61.

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Problem-driven hybrid computing

Quantum computers excel at providing exact solutions of certain problems at a large scale that classical computers find difficult to solve, such as predicting electronic structure properties of the active site that contains multiple coupled transition metal atoms in an enzyme, excited-state properties and dynamics in the light-harvesting complex.[62] While, in these complex systems, strongly correlated particle–particle interactions are usually localized, and meanwhile approximate solutions on a classical computer are usually sufficient to meet the need of applications to describe weakly correlated interactions.[63] Therefore, it is appropriate to decompose a quantum chemistry simulation of a complex system into different tasks according to the required computational accuracy and execute them separately on quantum and classical computers according to their computational costs. This hybrid quantum-classical computing mode provides an appealing scheme to leverage the benefits of both quantum and classical computers.

The characteristics of the problems in quantum chemistry are diverse, so the decomposition strategies need to be tailored to specific issues. Here, we introduce three typical problem decomposition strategies for simulating complex systems, as shown in Fig. 1.

• Case 1: An active site and the environment

For a complex system, *e.g.* an enzyme, one only needs to treat the central region, referred to the active site that contains transition metals, with the exact computational method. In such a case, it is promising to embed quantum algorithms into classical algorithms to describe the whole system with moderate computational costs. The quantum algorithm is responsible for an accurate description of the active site, and approximate algorithms are carried out on the classical computers to handle the environment. Inspired by the traditional quantum mechanics/molecular mechanics (QM/MM) method,[64–66] in which the Hamiltonian is written as

$$H = H_{\mathrm{QM}} + H_{\mathrm{MM}} + H_{\mathrm{QM\text{–}MM}} \tag{3}$$

with $H_{\mathrm{QM\text{–}MM}}$ being the interactions between the active site and the environment, it is straightforward to extend it for quantum simulations as

$$H = H_{\mathrm{QC}} + H_{\mathrm{CC}} + H_{\mathrm{QC\text{–}CC}} \tag{4}$$

with "CC" indicating classical computational approaches, *e.g.* molecular force field methods.[67,68] Furthermore, one can employ Hartree–Fock, density functional theory or even low-scaling wave function approaches, *e.g.* linear scaling second-order Møller–Plesset perturbation theory (MP2)[69] and CCSD(T) approaches,[70] as the mediate-level schemes to describe the neighbouring environment, and classical mechanical approaches as the low-level scheme to describe the outermost environment.

• Case 2: Weakly coupled multiple active sites

Consider a complex system consisting of multiple active sites, *e.g.* chlorophyll pigments in the light-harvesting complex of plants, these sites are weakly coupled while the many-body interactions in each site are strongly correlated. One can approximate the Hamiltonian as

$$H = \sum_I H_I^{\mathrm{QC}} + \sum_{I<J} H_{IJ}^{\mathrm{CC}} + \cdots \tag{5}$$

where H_I is the Hamiltonian of the I-th site and H_{IJ} is the interaction between I-th and J-th sites. In principle, one should include all high-order interactions while these interactions are often truncated at a finite order in practice. For each site, the exact quantum algorithm is used to describe the electron correlation and meanwhile, approximate computational methods are employed to treat the interactions between different sites. This scheme is analogous to the traditional fragmentation theory that partitions a system into fragments.[71–77]

Alternatively, the interactions between one active site and the others can be included in an effective Hamiltonian,

$$H = \sum_I H_{\mathrm{eff},I}^{\mathrm{QC}} \tag{6}$$

Here, the effective Hamiltonian is diagonalized on a quantum computer but the construction of the effective Hamiltonian is conducted on a classical computer. In the context of QC, this strategy is able to significantly reduce the requirement of quantum resources and thus implements large-scale quantum simulations of quantum chemistry with small-sized quantum devices.[78]

• Case 3: Fully entangled sites

When the electrons in a complex system are fully entangled, it is a challenging task to accurately describe the electron correlation. A popular scheme is to decompose the electron

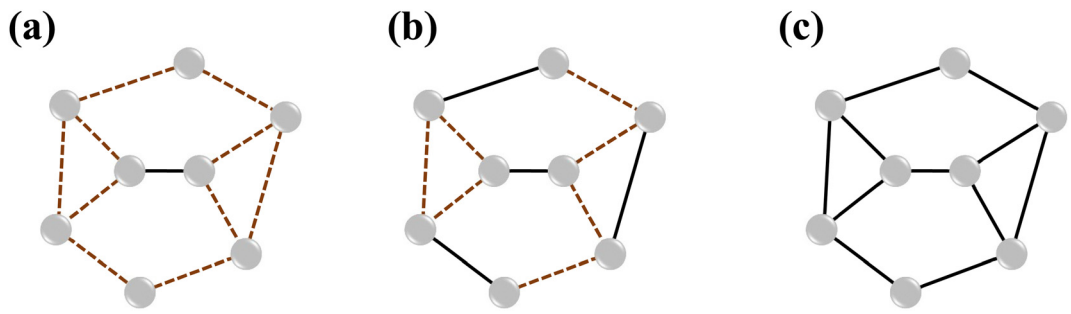

Fig. 1 (a) An active site and the surrounding environment; (b) multiple active sites coupled by weak interactions; (c) fully entangled sites. Solid and dashed lines indicate strong and weak interactions between two sites, respectively.

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correlation into static and dynamic ones and treat them with different numerical methods. In this scheme, the single-particle orbital space is often divided into a small active space and a large inactive space. The Hamiltonian is written as

$$H = H_0^{QC} + V^{CC} \quad (7)$$

where H_0^{QC} is the zeroth-order Hamiltonian defined in the active space and V^{CC} is the perturbed Hamiltonian to account for dynamic correlation. H_0^{QC} should be exactly diagonalized on a quantum computer. Note that integrated QPUs consisting of many logical qubits may be necessary to execute this task since multiple sites are strongly coupled. The perturbation theory can be used to take into consideration the electron correlation beyond the active space. Analogous to the multireference perturbation theory, high-order reduced density matrices extracted from QC calculations are necessary to evaluate the perturbation correction.[79]

It is clear that this problem-driven hybrid computing is far from being a block-box method, as it always requires defining the boundary of quantum computing and classical computing through careful consideration of the balance between accuracy and efficiency. In the context of QC, multiscale quantum computing (MQC) provides a unified framework for constructing a problem-driven hybrid computing algorithm.[80]

3 Multiscale quantum computing

Analogous to classical multiscale modeling, MQC integrates multiple numerical models at different scales of resolution to give a reasonable description of different interactions as shown in Fig. 2. MQC is designed not only for fault-tolerant quantum computers but also for near-term noisy quantum computers with self-adapted quantum resources. Except for a simple partition of a complex system into the QM and MM region, MQC further introduces the Divide-and-Conquer strategy to treat the QM region, namely decomposing the QM problem into small subproblems. In the solution of each subproblem, the correlation energy is partitioned into static and dynamic ones, with only the former one evaluated on a quantum computer.

One of the key appealing aspects of MQC is its capacity to accurately describe the electron correlation of complex systems using a small number of qubits and shallow quantum circuits. As such, error mitigation techniques can be applied to these small-scale quantum circuit simulations to efficiently suppress the effects of noise.[82] Another advantage of MQC originates from the introduction of the Divide-and-Conquer strategy, which allows independent executions of QC task for solving each subproblem so that one can easily implement massively parallel quantum simulations with a batch of small-scale quantum devices. Finally, MQC can improve its computational accuracy through apriori or posterior corrections, which can be efficiently carried out on classical computers. In this section, we briefly review the Divide-and-Conquer and active space schemes for large-scale quantum simulations within the framework of MQC and leave the discussions of parallel quantum simulations to the next section.

Divide-and-Conquer

Divide-and-Conquer is a widely used strategy to break down a problem into smaller, simpler subproblems until these subproblems can be easily solved. Ma *et al.* combined a simple many-body expansion (MBE) fragmentation scheme and the VQE to study the relative energies of water hexamers.[80] The total energy is approximated at the second order MBE (MBE2) fragmentation method as

$$E \approx E_{QM}^{MBE2} = \sum_I E_I + \sum_{I<J} E_{IJ}^{(2)}, \quad (8)$$

where $E_{IJ}^{(2)} = E_{IJ} - E_I - E_J$. E_I and E_{IJ} are the energies of I-th

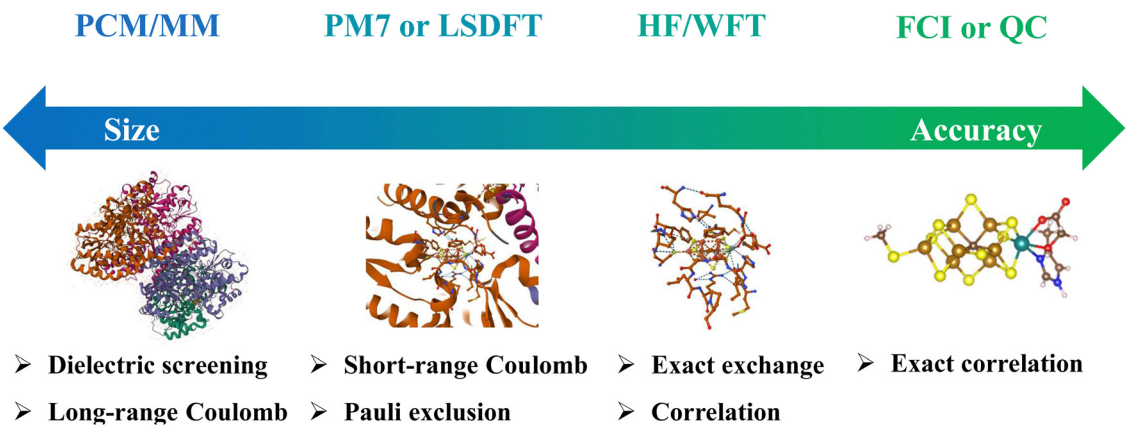

Fig. 2 A brief introduction of different interactions and numerical models used to account for them in a complex system. (1) The long-range interactions between the outermost region and the active region can be described by the classical mechanics methods, *e.g.* polarizable continuum models (PCM) for the dielectric screening effect and molecular mechanics (MM) force field models for long-range Coulomb interactions. (2) The short-range Coulomb and Pauli exclusion can be treated with semiempirical methods,[81] such as AM1, PM7 and OMx, or linear-scaling density functional theory (LSDFT) methods.[28] (3) The exact exchange can be handled by the Hartree–Fock (HF) method. It is difficult to describe the electron correlation in an accurate manner. (4) The wave function theory (WFT) is considered a systematic way to approach the exact solution. Theoretical chemists have been trying to achieve a subtle balance between accuracy and efficiency in the WFT approaches for half a century. Quantum computing provides another potential solution of the Schrödinger equation.

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monomer and *IJ*-th dimer that is composed of *I*-th and *J*-th monomers. Except for the MBE approach, fragment molecular-orbital method,[71] molecular fragmentation with conjugated caps method,[72,73] and the (generalized) many-body expansion[74–76] are also popular energy-based fragmentation approaches for problem decomposition.

The density matrix embedding theory (DMET)[83–87] is an alternative Divide-and-Conquer scheme to reduce the computational complexity. The core concept of DMET is to construct a set of localized orbitals to define fragments and then construct an effective Hamiltonian in an active space that is composed of the fragment orbitals and corresponding bath orbitals, with the latter one used to account for the interactions between the fragment and the environment.[86] As a pilot of implementation the DMET on a trapped-ion quantum computer, Kawashima *et al.* realized quantum simulations of a ring of 10 hydrogen atoms based on the VQE.[78] Here, the ground-state potential energy surface of H_{10} is estimated by running ten 2-qubit VQE simulations. Lv and coworkers carried out quantum emulating simulations of a C_{18} molecule at the level of the cc-pVDZ basis (up to 144 qubits) using the DMET-VQE method.[88] Furthermore, they have generalized this method to simulate periodic materials.[89] Shang *et al.* have realized a massively parallelized VQE circuit simulation of Atazanavier (a small drug molecule for COVID-19 containing 103 atoms) by integrating a matrix product state (MPS) simulator with DMET.[90] It is worth mentioning that Divide-and-Conquer is a powerful scheme to carry out large-scale quantum chemistry simulations while it is not suitable for decomposing strongly correlated electrons.

Active space

The active space method is a common strategy to carry out large-scale high-accuracy quantum chemistry simulations, in which the Hamiltonian in the active space is diagonalized with near-exactly computational methods, such as DMRG[14,15] and selected CI.[16–19] A simple way to describe the correlation energy beyond the active space is the ONIOM method.[91,92] The ONIOM method is an easy-to-implement scheme, in which the total energy can be formulated as

$$E = E^{\mathcal{A}}_{\text{high}} + E_{\text{low}} - E^{\mathcal{A}}_{\text{low}}, \tag{9}$$

to compensate the energy error originating from the active space approximation. Here, 'low' and 'high' indicate low-level and high-level computational methods, and $\mathcal{A}$ indicates the active site. Ma *et al.* employed VQE as the high-level method and MP2 as the low-level method to study the relative energies of molecules.[80] Izsák *et al.* studied dissociation curves of dimethyl acetylene using the CCSD method as the low-level method.[93]

The perturbation theory is a more reliable scheme to evaluate the dynamic correlation. Ryabinkin *et al.* proposed to correct the iterative qubit coupled cluster VQE algorithm based on the qubit version of the second-order Epstein–Nesbet perturbation theory (ENPT) equation.[94] Tammaro and coworkers proposed N-electron valence perturbation theory formulated in the VQE framework to study the relative stability of the hydroxide anion and hydroxyl radical.[95] Liu *et al.* formulated perturbative variational quantum algorithms by combining the VQE and either multireference perturbation theory or an effective Hamiltonian theory.[79] In order to evaluate the perturbation correction energy, one needs to extract high-order reduced density matrices from quantum computing.

Alternatively, one can incorporate the dynamic correlation into an effective Hamiltonian

$$H_{\text{eff}} = \mathrm{e}^{-\sigma} H \mathrm{e}^{\sigma}, \tag{10}$$

which can be diagonalized on a quantum computer. Here, the operator σ usually consists of excitations beyond the active space. One typical example is the coupled cluster-based downfolding methods that partition the cluster operator into internal (including excitations within CAS) and external (namely σ, including excitations outside of CAS) parts.[96–100] Based on downfolding methods, Kowalski *et al.* proposed a pioneering dimensionality-reducing technique, known as the quantum flow (QFlow) approach,[100] which enables the optimization of 684 parameters with only 8 qubits. Similarly, Huang *et al.* proposed a quantum unitary downfolding formalism, known as the quantum driven similarity renormalization group (QDSRG) method, for evaluating the H2 dissociation curve with the cc-pV5Z basis (220 qubits) on a IBM quantum hardware.[101] Additionally, one can combine the explicitly correlated method, such as R12 or F12 method, with the VQE algorithm to approach the complete basis set limit.[102–105] For example, Motta *et al.* employed a canonical transcorrelated F12 Hamiltonian (CT-F12) method to incorporate the dynamic correlation effect from the large basis set.[103] Overall, the combination of the perturbation theory or the effective Hamiltonian with the VQE is an appealing scheme to reduce the complexity of quantum circuits so that one can scale the VQE calculations to complex systems.

4 Quantum-centric high performance computing

IBM stated "*The quantum-centric supercomputer will incorporate quantum processors, classical processors, quantum communication networks, and classical networks, all working together to completely transform how we compute*". The development of quantum processors and communication networks is an ongoing endeavor and is more accurately characterized as a medium to long-term goal. In this work, we focus on implementing QCHPC for quantum chemistry based on the potential architectures of quantum-centric supercomputers.

QC is a computing paradigm that works based on quantum bits and quantum gates, with high computational power and inherent parallelism. Due to the existence of quantum superposition, quantum computers can process a large amount of information at the same time. For example, when n qubits are input, it is possible to obtain $2n$ results. From this perspective, QC is inherently parallel. However, in order to extract information about the quantum state prepared on a quantum computer,

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measurements are needed to understand what happened in the system. After measurement, the quantum state is destroyed so that this parallel mode is useless unless advanced algorithms for reading information exist. In the current stage, the physical observables are estimated by measuring the expectation values of each term in the observable operators. One needs to repeat this process until the statistical error is less than a specified precision threshold. In the case of large-scale quantum circuits, the quantum algorithms can be implemented by processing quantum information on a large number of distinct quantum computers.[106–108] In order to perform multiqubit gates across quantum computers, qubit teleportation and gate teleportation[106] are required, as shown in Fig. 3(a). The quantum circuit is distributed as a series of gate layers, where each layer contains a collection of gates to be applied on the qubits in the system, and the gate times of each gate for each QPU in the system produce a temporal gate execution schedule.

The statistical estimation procedure provides a naive parallel computing mode for QC in the sense that one can prepare a quantum state and measure physical observables on multiple QPUs.[109,110] This enables good parallel scalability using the adapted dynamical distribution algorithm to achieve load balance (see Fig. 3(b)). In the VQE calculation, the electronic molecular Hamiltonian H can be written as a sum of the Pauli strings: $H = \sum_i a_i P_i$, where each Pauli string $P_i \in \{I,\sigma_x,\sigma_y,\sigma_z\}^{\otimes N}$ is a tensor product of N Pauli operators. One can estimate each $\langle\psi|P_i|\psi\rangle$ independently and then sum over all those results with the corresponding coefficients (a_i) to get $\langle\psi|H|\psi\rangle$. Recently, Claudino *et al.* utilized parallel execution of quantum circuits to study the singlet-fission processes using 20 qubits of the Quantinuum H1-1 system in a distributed manner.[111] This pioneering work demonstrated the possibility of parallel hardware simulations on quantum devices. Massive parallelization over measurements is an efficient technique to speed up the VQE calculations. However, it is difficult to extend the VQE methods to accurate simulations of large systems by simply distributing the measurement jobs on multiple QPUs due to the complexity of the quantum circuits.

On top of the VQE parallelization, one can implement task parallelism for concurrent execution of different tasks on QPUs and CPUs/GPUs. When the granularity of task parallelism on classical computers is large and communication is minimal or non-existent, one can implement multiple-level parallelization across a supercomputer platform. This classical parallel strategy has been well established so we will only consider how to distribute tasks onto QPUs and CPUs/GPUs. Task parallelism is naturally suitable for multi-core parallelism, where each core can handle one or more tasks, and multiple cores are mapped to the same or different processors to take advantage of the computing power of multiple cores. According to the different QC tasks, one can categorize QCHPC into two types:

- Sequential parallelism

In sequential parallelism, each task has a clear execution order and there is the dependency between these tasks.

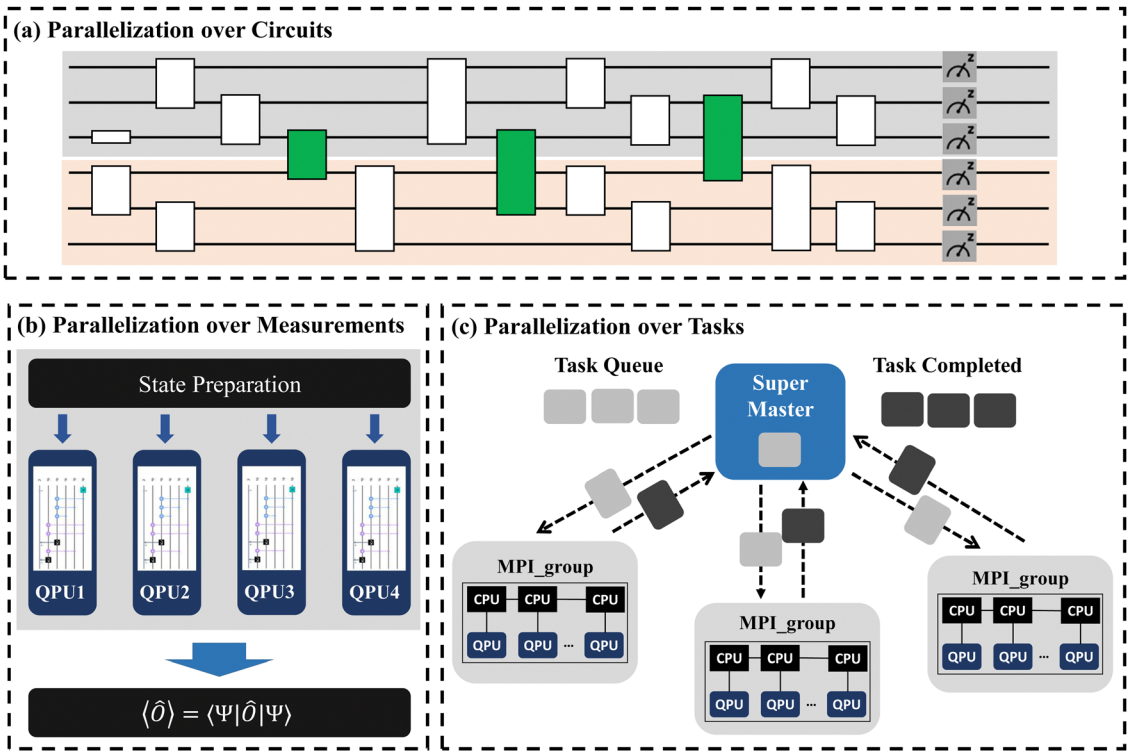

Fig. 3 (a) The distributed logical qubits within the network of quantum computers. The block circuits are executed on different QPUs. (b) The parallelism over quantum measurements based on the statistical estimation of the expectation value of the electronic structure Hamiltonian, which can be expressed as the summation of a polynomial number of mutually uncorrelated Pauli strings. Expectation values of each Pauli string can thus be calculated independently. (c) The dynamical load balancing scheme for implementing the chemical tasks.

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For example, when state preparation and measurement executed on a quantum computer are employed to generate the input for classical calculations, the QC and CC tasks are executed in sequence. As such, one can independently parallelize the QC tasks on multiple QPUs and the CC tasks on the supercomputers.

• Massively parallelism

In massively parallelism, a large batch of tasks are assumed to be executed independently. Here, one can consider QPUs as the same computing unit as CPUs/GPUs. The tasks are statically or dynamically distributed onto QPUs and CPUs/GPUs with special attention needed as QPUs only accept certain computing tasks with high computational complexity. In contrast, one can consider several QPUs plus CPUs/GPUs as a computing unit to execute one task. For example, when Divide-and-Conquer is employed in the MQC, the total energy for each subsystem can be evaluated independently and the data transfer among these calculations is negligible. As such, the calculation for each subsystem can be assigned to a core that is composed of QPUs and CPUs/GPUs. The MQC simulation of a whole complex system can be implemented in a massively parallel manner, without the load balancing problem, as shown in Fig. 3(c).

Although MQC provides an appealing application of QCHPC, it also faces many challenges for solving complex problems, such as task distribution and synchronization and data transmission, due to the completely different characteristics of the QC and CC tasks.

5 Quantum emulating simulator

With the rapid development of quantum techniques, demonstrating quantum computing on multiple quantum platforms has been successfully executed and thus quantum computing is seeking practical applications in chemistry and materials science. However, the quantum resources required to support extensive exploration of these potential applications are still far beyond the capacity of available quantum devices in the near future. It is necessary to develop high performance simulators for quantum algorithm and hardware verification on classical computers. Currently, a large number of classical simulators, including QuEST,[113] Yao.jl,[124] JUQCS,[112,125,126] cuQuantum,[115] Intel Quantum Simulator,[114] ProjectQ,[117] Qulacs,[119] Pennylane,[118] Qiskit[127] and so on, have been proposed for universal quantum circuit emulating simulations. The functionalities supported by these simulators are summarized in Table 1. Due to an exponential growth of physical resources with increasing system sizes, existing simulators commonly suffer from the memory bottleneck so the large-scale emulation of quantum computational chemistry for material and drug design remains challenging. Analogous to classical quantum chemistry simulations, HPC is a powerful tool to perform large-scale simulations of quantum chemistry. In this section, we introduce some typical simulators optimized for HPC to simulate universal quantum circuits.

Jülich universal quantum computer simulator (JUQCS) is a gate-based quantum emulating simulator released as early as 2007.[125] Eleven years later, a massively parallel version compiled to make use of OpenMP and MPI was run on the Sunway TaihuLight and on the K computer to emulate simple quantum circuits and Shors factorization algorithm using up to 48 qubits.[126] Recently, a GPU-accelerated version of JUQCS (JUQCS-G) was implemented to study quantum annealing and the quantum approximate optimization algorithms. JUQCS-G was used to solve exact cover problems with up to 40 qubits on a GPU cluster with 3744 NVIDIA A100 Tensor Core GPUs.[112]

Table 1 Typical simulator for universal quantum circuit emulating simulations. MPI: message passing interface; HPC: high performance computing; N_q: number of qubits. "✓" and "✗" indicate that this function is or is not implemented

Simulator	OpenMP	MPI	GPU	HPC	N_q	Language	Ref.
Q^2Chemistry	✓	✓	✓	✓	1000	Python/Julia	90
JUQCS	✓	✓	✓	✓	48	Fortran	112
QuEST	✓	✓	✓	✓	38	C++	113
IQS	✓	✓	✓	✓	42	C++	114
cuQuantum	✓	✓	✓	✓	40	Python/C++	115
TenCirChem	✓	✗	✓	✗	32	Python	116
ProjectQ	✓	✓	✗	✓	45	Python/C++	117
Pennylane	✓	✗	✓	✗	>20	Python/C++	118
Qulacs	✓	✗	✓	✗	25	Python/C++	119
Qiskit	✓	✓	✓	✓	35	Python	120
Qibo	✓	✓	✓	✗	34	Python	121
Pyquil	✓	✗	✗	✗	36	Python	122
qsim	✓	✓	✓	✓	36	Python/C++	123
Yao.jl	✓	✗	✓	✗	16	Julia	124

QuEST is a hybrid multithreaded and distributed, GPU accelerated simulator of universal quantum circuits. QuEST was used to simulate random circuits of up to 38 qubits, distributed over up to 2048 compute nodes, each with up to 24 cores, on the ARCUS and ARCHER supercomputers.[113] Intel quantum simulator (IQS), formerly known as qHiPSTER, is a HPC simulator that can leverage the available hardware resources provided by supercomputers.[114] By dividing processes into separate groups to simulate a pool of quantum circuits in parallel, IQS was used to carry out 42-qubit simulations on the SuperMUC-NG supercomputer. The cuQuantum SDK provides efficient scalable software building blocks optimized for NVIDIA GPU-based platforms to accelerate and scale up quantum circuit simulators with both state vector and tensor network strategies.[115]

A high-performance and massively parallelized VQE simulator based on matrix product states (MPS), named MPS-VQE, was proposed recently for modeling protein–ligand complex systems.[90,128] In combination with DMET, the MPS-VQE simulator was employed to study the torsional barrier of ethane and the quantification of the protein–ligand interactions on the HPC platform. Without DMET, the largest system modelled by the MPS-VQE simulator is a hydrogen chain containing 500 atoms using the STO-3G basis (1000 qubits). A three-level parallelization scheme was introduced to scale up to about 10 million cores. A peak performance of 216.9 PFLOP/s is achieved on a new Sunway supercomputer, which demonstrates that the MPS-VQE simulator has become the state-of-the-art quantum emulating simulator. This simulator was recently integrated into Q^2chemistry, a cutting-edge software package

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designed for quantum chemistry applications.[129] This software can efficiently simulate medium- to large-sized quantum circuits, handling both molecular and periodic systems with a focus on scalability and performance. Meanwhile, Q^2chemistry combines high-performance computing techniques and advanced quantum algorithms, making it a valuable tool for researchers and practitioners in the field of quantum chemistry.

Another large-scale simulator implemented based on tensor network is TenCirChem,[116] an efficient open-source Python library for solving quantum chemistry problems using variational quantum algorithms. By virtual of advanced tensor network contraction simulation engine in TensorCircuit, TenCirChem exhibits extremely high performance in simulating quantum circuits. For example, it can calculate the potential energy surface of a water molecule at the level of UCCSD/6-31G(d) using a single GPU node, in which the quantum circuit contains 34 qubits and 565 variational parameters.

6 Challenges and outlook

Supercomputers are the most powerful computing tool to carry out large-scale quantum chemistry simulations nowadays, and quantum computers are expected to be a promising computing platform for exactly solving quantum chemistry problems in the future. It is appealing to combine these two tools to solve complex quantum chemistry problems in an accurate and efficient manner. While, the development of quantum-centric high performance computing requires combinin both classical and quantum computing architectures, which brings us lots of challenges:

• When integrating quantum computers into classical computers, it is necessary to consider the efficiency of data transfer, task distribution and synchronization. Quantum computers may deal with a large batch of data much slower than classical computers. Meanwhile, in contrast to classical computer, quantum computers may only exhibit computational advantage for certain problems. Therefore, it may be a challenging task to make quantum computers and supercomputers work together.

• In quantum chemistry, quantum computers are expected to find use in simulating transition metal catalysts,[130,131] photochemistry,[132] high-resolution rovibrational spectroscopy,[133] quantum dynamics[134] and so on. However, quantum algorithms that may exhibit quantum advantage, including higher computational efficiency, less computational time and energy consumption, in solving these problems are still under exploration. Meanwhile, combining quantum computers and classical computers to simulate these problems is a completely new and challenging field.

• There exist a large number of hybrid quantum-classical algorithms. While, in order to take full advantage of the computing power of quantum computers and supercomputers, it is necessary to carry out massively parallel computing on both quantum and classical computers. Therefore, the parallel strategy is different from the classical one. One needs to design efficient parallel strategies for quantum chemistry simulations based on the new hardware architecture.

For years, researchers believed that they might only be able to use noisy quantum devices in the short term, and many were looking for potential applications that could be useful within limited capacity. While progress was unpredictable, this may not matter now. In the past few years, breakthroughs in theory and experiments have led researchers to believe that the error correction problem can be solved.[51–53] A combination of hardware and software strategies is expected to suppress, mitigate, and eliminate quantum errors. This is not a straightforward approach, but it is feasible and may take less time than expected to realize fault-tolerant quantum computers. As such, it is time to explore quantum-centric HPC for solving challenging problems in quantum chemistry.

Conflicts of interest

The authors declare that they have no conflict of interest.

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References

1 P. A. M. Dirac and R. H. Fowler, Quantum mechanics of many-electron systems, *Proc. R. Soc. A*, 1929, **123**, 714–733.
2 J. Olsen, P. Jørgensen and J. Simons, Passing the one-billion limit in full configurationinteraction (FCI) calculations, *Chem. Phys. Lett.*, 1990, **169**, 463–472.
3 A. O. Mitrushenkov, Passing the several billions limit in FCI calculations on a minicomputer, *Chem. Phys. Lett.*, 1994, **217**, 559–565.
4 K. D. Vogiatzis, D. Ma, J. Olsen, L. Gagliardi and W. A. de Jong, Pushing configuration-interaction to the limit: Towards massively parallel MCSCF calculations, *J. Chem. Phys.*, 2017, **147**, 184111.
5 J. F. Stanton, Why CCSD(T) works: a different perspective, *Chem. Phys. Lett.*, 1997, **281**, 130–134.
6 P. Jurečka, J. Šponer, J. Černý and P. Hobza, Benchmark database of accurate (MP2 and CCSD(T) complete basis set limit) interaction energies of small model complexes, DNA base pairs, and amino acid pairs, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1985–1993.
7 K. E. Riley, M. Pitoňák, P. Jurečka and P. Hobza, Stabilization and Structure Calculations for Noncovalent Interactions in Extended Molecular Systems Based on Wave Function and Density Functional Theories, *Chem. Rev.*, 2010, **110**, 5023–5063.

 This journal is © the Owner Societies 2024

Published on 14 2024. Downloaded on 22-11-2025 00:14:04.

8 P. R. Nagy and M. Kállay, Approaching the Basis Set Limit of CCSD(T) Energies for Large Molecules with Local Natural Orbital Coupled-Cluster Methods, *J. Chem. Theory Comput.*, 2019, **15**, 5275–5298.
9 V. Veryazov, P. Malmqvist and B. O. Roos, How to select active space for multiconfigurational quantum chemistry?, *Int. J. Quantum Chem.*, 2011, **111**, 3329–3338.
10 P. G. Szalay, T. Müller, G. Gidofalvi, H. Lischka and R. Shepard, Multiconfiguration Self-Consistent Field and Multireference Configuration Interaction Methods and Applications, *Chem. Rev.*, 2012, **112**, 108–181.
11 B. O. Roos, K. Andersson, M. P. Fülscher, P.-A. Malmqvist, L. Serrano-Andrés, K. Pierloot, *et al.*, *Advances in Chemical Physics*, John Wiley & Sons, Ltd, 1996, pp. 219–331.
12 P. Pulay, A perspective on the CASPT2 method, *Int. J. Quantum Chem.*, 2011, **111**, 3273–3279.
13 H. Lischka, D. Nachtigallová, A. J. A. Aquino, P. G. Szalay, F. Plasser and F. B. C. Machado, *et al.*, Multireference Approaches for Excited States of Molecules, *Chem. Rev.*, 2018, **118**, 7293–7361.
14 S. R. White, Density Matrix Formulation for Quantum Renormalization Groups, *Phys. Rev. Lett.*, 1992, **69**, 2863.
15 G. K.-L. Chan and S. Sharma, The Density Matrix Renormalization Group in Quantum Chemistry, *Annu. Rev. Phys. Chem.*, 2011, **62**, 465.
16 A. A. Holmes, N. M. Tubman and C. J. Umrigar, Heat-Bath Configuration Interaction: An Efficient Selected Configuration Interaction Algorithm Inspired by Heat-Bath Sampling, *J. Chem. Theory Comput.*, 2016, **12**, 3674.
17 W. Liu and M. R. Hoffmann, iCI: Iterative CI toward full CI, *J. Chem. Theory Comput.*, 2016, **12**, 1169.
18 D. S. Levine, D. Hait, N. M. Tubman, S. Lehtola, K. B. Whaley and M. Head-Gordon, CASSCF with Extremely Large Active Spaces Using the Adaptive Sampling Configuration Interaction Method, *J. Chem. Theory Comput.*, 2020, **16**, 2340–2354.
19 N. M. Tubman, C. D. Freeman, D. S. Levine, D. Hait, M. Head-Gordon and K. B. Whaley, Modern Approaches to Exact Diagonalization and Selected Configuration Interaction with the Adaptive Sampling CI Method, *J. Chem. Theory Comput.*, 2020, **16**, 2139.
20 G. H. Booth, A. J. W. Thom and A. Alavi, Fermion Monte Carlo Without Fixed Nodes: A Game of Life, Death, and Annihilation in Slater Determinant Space, *J. Chem. Phys.*, 2009, **131**, 054106.
21 D. Cleland, G. H. Booth and A. Alavi, Communications: Survival of the Fittest: Accelerating Convergence in Full Configuration-Interaction Quantum Monte Carlo, *J. Chem. Phys.*, 2010, **132**, 041103.
22 J. J. Eriksen, F. Lipparini and J. Gauss, Virtual Orbital Many-Body Expansions: A Possible Route towards the Full Configuration Interaction Limit, *J. Phys. Chem. Lett.*, 2017, **8**, 4633.
23 J. J. Eriksen and J. Gauss, Generalized Many-Body Expanded Full Configuration Interaction Theory, *J. Phys. Chem. Lett.*, 2019, **10**, 7910.
24 J. Brabec, J. Brandejs, K. Kowalski, S. Xantheas, O. Legeza and L. Veis, Massively parallel quantum chemical density matrix renormalization group method, *J. Comput. Chem.*, 2021, **42**, 534–544.
25 C. Xiang, W. Jia, W.-H. Fang and Z. Li, Distributed Multi-GPU Ab Initio Density Matrix Renormalization Group Algorithm with Applications to the P-Cluster of Nitrogenase, *J. Chem. Theory Comput.*, 2024, **20**, 775–786.
26 D. Datta and M. S. Gordon, Accelerating Coupled-Cluster Calculations with GPUs: An Implementation of the Density-Fitted CCSD(T) Approach for Heterogeneous Computing Architectures Using OpenMP Directives, *J. Chem. Theory Comput.*, 2023, **19**, 7640–7657.
27 J. Hutter and A. Curioni, Dual-level parallelism for ab initio molecular dynamics: Reaching teraflop performance with the CPMD code, *Parallel Comput.*, 2005, **31**, 1–17.
28 D. R. Bowler and T. Miyazaki, Calculations for millions of atoms with density functional theory: linear scaling shows its potential, *J. Phys.: Condens. Matter*, 2010, **22**, 074207.
29 K. A. Wilkinson, N. D. M. Hine and C.-K. Skylaris, Hybrid MPI-OpenMP Parallelism in the ONETEP Linear-Scaling Electronic Structure Code: Application to the Delamination of Cellulose Nanofibrils, *J. Chem. Theory Comput.*, 2014, **10**, 4782–4794.
30 S. Das, P. Motamarri, V. Gavini, B. Turcksin, Y. W. Li and B. Leback, Fast, Scalable and Accurate Finite-Element Based Ab Initio Calculations Using Mixed Precision Computing: 46 PFLOPS Simulation of a Metallic Dislocation System. Proceedings of the International Conference for High Performance Computing, Networking, Storage and Analysis. New York, NY, USA, 2019.
31 H. Shang, L. Xu, B. Wu, X. Qin, Y. Zhang and J. Yang, The dynamic parallel distribution algorithm for hybrid density-functional calculations in HONPAS package, *Comput. Phys. Commun.*, 2020, **254**, 107204.
32 W. Hu, X. Qin, Q. Jiang, J. Chen, H. An, W. Jia, F. Li, X. Liu, D. Chen, F. Liu, Y. Zhao and J. Yang, High performance computing of DGDFT for tens of thousands of atoms using millions of cores on Sunway TaihuLight, *Sci. Bull.*, 2021, **66**, 111–119.
33 W. Hu, H. An, Z. Guo, Q. Jiang, X. Qin, J. Chen, W. Jia, C. Yang, Z. Luo, J. Li, W. Wu, G. Tan, D. Jia, Q. Lu, F. Liu, M. Tian, F. Li, Y. Huang, L. Wang, S. Liu and J. Yang, 2.5 Million-Atom Ab Initio Electronic-Structure Simulation of Complex Metallic Heterostructures with DGDFT. SC22: International Conference for High Performance Computing, Networking, Storage and Analysis, 2022, pp. 1–13.
34 R. Schade, T. Kenter, H. Elgabarty, M. Lass, T. D. Kühne and C. Plessl, Breaking the exascale barrier for the electronic structure problem in ab-initio molecular dynamics, *Int. J. High Perform. Comput. Appl.*, 2023, **37**, 530–538.
35 A. Aspuru-Guzik, A. D. Dutoi, P. J. Love and M. Head-Gordon, Simulated Quantum Computation of Molecular Energies, *Science*, 2005, **309**, 1704.
36 J. Du, N. Xu, X. Peng, P. Wang, S. Wu and D. Lu, NMR Implementation of a Molecular Hydrogen Quantum

Published on 14 2024. Downloaded on 22-11-2025 00:14:04.

Simulation with Adiabatic State Preparation, *Phys. Rev. Lett.*, 2010, **104**, 030502.
37 A. Peruzzo, J. McClean, P. Shadbolt, M.-H. Yung, X.-Q. Zhou and P. J. Love, *et al.*, A variational eigenvalue solver on a photonic quantum processor, *Nat. Commun.*, 2014, **5**, 4213.
38 P. J. J. O'Malley, R. Babbush, I. D. Kivlichan, J. Romero, J. R. McClean and R. Barends, *et al.*, Scalable Quantum Simulation of Molecular Energies, *Phys. Rev. X*, 2016, **6**, 031007.
39 A. Kandala, A. Mezzacapo, K. Temme, M. Takita, M. Brink and J. M. Chow, *et al.*, Hardware-efficient variational quantum eigensolver for small molecules and quantum magnets, *Nature*, 2017, **549**, 242.
40 C. Hempel, C. Maier, J. Romero, J. McClean, T. Monz and H. Shen, *et al.*, Quantum Chemistry Calculations on a Trapped-Ion Quantum Simulator, *Phys. Rev. X*, 2018, **8**, 031022.
41 F. Arute, K. Arya, R. Babbush, D. Bacon, J. C. Bardin and R. Barends, *et al.*, Hartree-Fock on a superconducting qubit quantum computer, *Science*, 2020, **369**, 1084–1089.
42 J. Preskill, Quantum Computing in the NISQ era and beyond, *Quantum*, 2018, **2**, 79.
43 Y. Cao, J. Romero, J. P. Olson, M. Degroote, P. D. Johnson and M. Kieferová, *et al.*, Quantum Chemistry in the Age of Quantum Computing, *Chem. Rev.*, 2019, **119**, 10856–10915.
44 S. McArdle, S. Endo, A. Aspuru-Guzik, S. C. Benjamin and X. Yuan, Quantum computational chemistry, *Rev. Mod. Phys.*, 2020, **92**, 015003.
45 F. Arute, K. Arya, R. Babbush, D. Bacon, J. C. Bardin and R. Barends, *et al.*, Quantum supremacy using a programmable superconducting processor, *Nature*, 2019, **574**, 505–510.
46 H.-S. Zhong, H. Wang, Y.-H. Deng, M.-C. Chen, L.-C. Peng and Y.-H. Luo, *et al.*, Quantum computational advantage using photons, *Science*, 2020, **370**, 1460–1463.
47 Y. Wu, W.-S. Bao, S. Cao, F. Chen, M.-C. Chen and X. Chen, *et al.*, Strong Quantum Computational Advantage Using a Superconducting Quantum Processor, *Phys. Rev. Lett.*, 2021, **127**, 180501.
48 W. J. Huggins, B. A. O'Gorman, N. C. Rubin, D. R. Reichman, R. Babbush and J. Lee, Unbiasing fermionic quantum Monte Carlo with a quantum computer, *Nature*, 2022, **603**, 416–420.
49 C. H. Valahu, V. C. Olaya-Agudelo, R. J. MacDonell, T. Navickas, A. D. Rao, M. J. Millican, J. B. Pérez-Sánchez, J. Yuen-Zhou, M. J. Biercuk, C. Hempel, T. R. Tan and I. Kassal, Direct observation of geometric-phase interference in dynamics around a conical intersection, *Nat. Chem.*, 2023, **15**, 1503–1508.
50 Y. Kim, A. Eddins, S. Anand, K. X. Wei, E. van den Berg, S. Rosenblatt, H. Nayfeh, Y. Wu, M. Zaletel, K. Temme and A. Kandala, Evidence for the utility of quantum computing before fault tolerance, *Nature*, 2023, **618**, 500–505.
51 G. Q. AI, Suppressing quantum errors by scaling a surface code logical qubit, *Nature*, 2023, **614**, 676–681.
52 Z. Ni, S. Li, X. Deng, Y. Cai, L. Zhang, W. Wang, Z.-B. Yang, H. Yu, F. Yan, S. Liu, C.-L. Zou, L. Sun, S.-B. Zheng, Y. Xu and D. Yu, Beating the break-even point with a discrete-variable-encoded logical qubit, *Nature*, 2023, **616**, 56–60.
53 D. Bluvstein, S. J. Evered, A. A. Geim, S. H. Li, H. Zhou, T. Manovitz, S. Ebadi, M. Cain, M. Kalinowski, D. Hangleiter, J. P. B. Ataides, N. Maskara, I. Cong, X. Gao, P. S. Rodriguez, T. Karolyshyn, G. Semeghini, M. J. Gullans, M. Greiner, V. Vuletić and M. D. Lukin, Logical quantum processor based on reconfigurable atom arrays, *Nature*, 2023, **626**, 58.
54 P. J. Ollitrault, A. Kandala, C.-F. Chen, P. K. Barkoutsos, A. Mezzacapo and M. Pistoia, *et al.*, Quantum equation of motion for computing molecular excitation energies on a noisy quantum processor, *Phys. Rev. Res.*, 2020, **2**, 043140.
55 H. R. Grimsley, S. E. Economou, E. Barnes and N. J. Mayhall, An adaptive variational algorithm for exact molecular simulations on a quantum computer, *Nat. Commun.*, 2019, **10**, 3007.
56 J. Liu, L. Wan, Z. Li and J. Yang, Simulating Periodic Systems on a Quantum Computer Using Molecular Orbitals, *J. Chem. Theory Comput.*, 2020, **16**, 6904–6914.
57 A. Anand, P. Schleich, S. Alperin-Lea, P. W. K. Jensen, S. Sim, M. Díaz-Tinoco, J. S. Kottmann, M. Degroote, A. F. Izmaylov and A. Aspuru-Guzik, A quantum computing view on unitary coupled cluster theory, *Chem. Soc. Rev.*, 2022, **51**, 1659–1684.
58 X. Zeng, Y. Fan, J. Liu, Z. Li and J. Yang, Quantum Neural Network Inspired Hardware Adaptable Ansatz for Efficient Quantum Simulation of Chemical Systems, *J. Chem. Theory Comput.*, 2023, **19**, 8587–8597.
59 M. Cerezo, R. B. Andrew Arrasmith, S. C. Benjamin, S. Endo, K. Fujii and J. R. McClean, *et al.*, Variational quantum algorithms, *Nat. Rev. Phys.*, 2021, **3**, 625–644.
60 J. Tilly, H. Chen, S. Cao, D. Picozzi, K. Setia, Y. Li, E. Grant, L. Wossnig, I. Rungger, G. H. Booth and J. Tennyson, The Variational Quantum Eigensolver: A review of methods and best practices, *Phys. Rep.*, 2022, **986**, 1–128, the variational quantum eigensolver: a review of methods and best practices.
61 J. Liu, Y. Fan, Z. Li and J. Yang, Quantum algorithms for electronic structures: basis sets and boundary conditions, *Chem. Soc. Rev.*, 2022, **51**, 3263–3279.
62 B. Bauer, S. Bravyi, M. Motta and G. Kin-Lic Chan, Quantum Algorithms for Quantum Chemistry and Quantum Materials Science, *Chem. Rev.*, 2020, **120**, 12685–12717.
63 S. Lee, J. Lee, H. Zhai, Y. Tong, A. M. Dalzell, A. Kumar, P. Helms, J. Gray, Z.-H. Cui, W. Liu, M. Kastoryano, R. Babbush, J. Preskill, D. R. Reichman, E. T. Campbell, E. F. Valeev, L. Lin and G. Kin-Lic Chan, Is there evidence for exponential quantum advantage in quantum chemistry?, *Nat. Commun.*, 2023, 1952.
64 M. Levitt, Birth and Future of Multiscale Modeling for Macromolecular Systems (Nobel Lecture), *Angew. Chem., Int. Ed.*, 2014, **53**, 10006–10018.
65 A. Warshel, Multiscale Modeling of Biological Functions: From Enzymes to Molecular Machines (Nobel Lecture), *Angew. Chem., Int. Ed.*, 2014, **53**, 10020–10031.

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Published on 14 2024. Downloaded on 22-11-2025 00:14:04.

66 M. Karplus, Development of Multiscale Models for Complex Chemical Systems: From H + H_2 to Biomolecules (Nobel Lecture), *Angew. Chem., Int. Ed.*, 2014, **53**, 9992–10005.
67 J. Wang, R. M. Wolf, J. W. Caldwell, P. A. Kollman and D. A. Case, Development and testing of a general Amber force field, *J. Comput. Chem.*, 2004, **25**, 1157–1174.
68 M. Masia, *Ab initio* based polarizable force field parametrization, *J. Chem. Phys.*, 2008, **128**, 184107.
69 Y. Guo, W. Li, D. Yuan and S. Li, The relative energies of polypeptide conformers predicted by linear scaling second-order Møller-Plesset perturbation theory, *Sci. China: Chem.*, 2014, **57**, 1393–1398.
70 Y. Guo, C. Riplinger, U. Becker, D. G. Liakos, Y. Minenkov, L. Cavallo and F. Neese, Communication: An improved linear scaling perturbative triples correction for the domain based local pair-natural orbital based singles and doubles coupled cluster method [DLPNO-CCSD(T)], *J. Chem. Phys.*, 2018, **148**, 011101.
71 D. G. Fedorov, T. Nagata and K. Kitaura, Exploring chemistry with the fragment molecular orbital method, *Phys. Chem. Chem. Phys.*, 2012, **14**, 7562–7577.
72 D. W. Zhang and J. Z. H. Zhang, Molecular fractionation with conjugate caps for full quantum mechanical calculation of protein–molecule interaction energy, *J. Chem. Phys.*, 2003, **119**, 3599–3605.
73 X. Wang, J. Liu, J. Z. H. Zhang and X. He, Electrostatically embedded generalized molecular fractionation with conjugate caps method for full quantum mechanical calculation of protein energy, *J. Phys. Chem. A*, 2013, **117**, 7149–7161.
74 E. E. Dahlke and D. G. Truhlar, Electrostatically Embedded Many-Body Expansion for Large Systems, with Applications to Water Clusters, *J. Chem. Theory Comput.*, 2007, **3**, 46–53.
75 R. M. Richard and J. M. Herbert, A generalized many-body expansion and a unified view of fragment-based methods in electronic structure theory, *J. Chem. Phys.*, 2012, **137**, 064113.
76 J. Liu and J. M. Herbert, Pair-Pair Approximation to the Generalized Many-Body Expansion: An Alternative to the Four-Body Expansion for ab Initio Prediction of Protein Energetics via Molecular Fragmentation, *J. Chem. Theory Comput.*, 2016, **12**, 572–584.
77 A. V. Akimov and O. V. Prezhdo, Large-Scale Computations in Chemistry: A Bird's Eye View of a Vibrant Field, *Chem. Rev.*, 2015, **115**, 5797–5890.
78 Y. Kawashima, E. Lloyd, M. P. Coons, Y. Nam, S. Matsuura and A. J. Garza, *et al.*, Optimizing electronic structure simulations on a trapped-ion quantum computer using problem decomposition, *Commun. Phys.*, 2021, **4**, 245.
79 J. Liu, Z. Li and J. Yang, Perturbative variational quantum algorithms for material simulations, *Electron. Struct.*, 2024, **6**, 015007.
80 H. Ma, J. Liu, H. Shang, Y. Fan, Z. Li and J. Yang, Multiscale quantum algorithms for quantum chemistry, *Chem. Sci.*, 2023, **14**, 3190–3205.
81 W. Thiel, Semiempirical quantum-chemical methods, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.*, 2014, **4**, 145–157.
82 A. Kandala, K. Temme, A. D. Córcoles, A. Mezzacapo, J. M. Chow and J. M. Gambetta, Error mitigation extends the computational reach of a noisy quantum processor, *Nature*, 2019, **567**, 491–495.
83 G. Knizia and G. K.-L. Chan, Density matrix embedding: A simple alternative to dynamical mean-field theory, *Phys. Rev. Lett.*, 2012, **109**, 186404.
84 G. Knizia and G. K.-L. Chan, Density matrix embedding: A strong-coupling quantum embedding theory, *J. Chem. Theory Comput.*, 2013, **9**, 1428–1432.
85 Q. Sun and G. K.-L. Chan, Quantum Embedding Theories, *Acc. Chem. Res.*, 2016, **49**, 2705–2712.
86 S. Wouters, C. A. Jiménez-Hoyos, Q. Sun and G. K.-L. Chan, A practical guide to density matrix embedding theory in quantum chemistry, *J. Chem. Theory Comput.*, 2016, **12**, 2706–2719.
87 Z.-H. Cui, T. Zhu and G. K.-L. Chan, Efficient implementation of ab initio quantum embedding in periodic systems: Density matrix embedding theory, *J. Chem. Theory Comput.*, 2019, **16**, 119–129.
88 W. Li, Z. Huang, C. Cao, Y. Huang, Z. Shuai and X. Sun, *et al.*, Toward practical quantum embedding simulation of realistic chemical systems on near-term quantum computers, *Chem. Sci.*, 2022, **13**, 8953–8962.
89 C. Cao, J. Sun, X. Yuan, H.-S. Hu, H. Q. Pham and D. Lv, Ab initio Quantum Simulation of Strongly Correlated Materials with Quantum Embedding, *npj Comput. Mater.*, 2022, **9**, 78.
90 H. Shang, Y. Fan, L. Shen, C. Guo, J. Liu and X. Duan, *et al.*, Towards practical and massively parallel quantum computing emulation for quantum chemistry, *npj Quantum Inf.*, 2023, **9**, 33.
91 S. Dapprich, I. Komáromi, K. S. Byun, K. Morokuma and M. J. Frisch, A new ONIOM implementation in Gaussian98. Part I. The calculation of energies, gradients, vibrational frequencies and electric field derivatives, *J. Mol. Struct.: THEOCHEM*, 1999, **461–462**, 1–21.
92 T. Kerdcharoen and K. Morokuma, ONIOM-XS: An extension of the ONIOM method for molecular simulation in condensed phase, *Chem. Phys. Lett.*, 2002, **355**, 257–262.
93 R. Izsák, C. Riplinger, N. S. Blunt, B. de Souza, N. Holzmann, O. Crawford, J. Camps, F. Neese and P. Schopf, Quantum computing in pharma: A multilayer embedding approach for near future applications, *J. Comput. Chem.*, 2023, **44**, 406–421.
94 I. G. Ryabinkin, A. F. Izmaylov and S. N. Genin, A posteriori corrections to the iterative qubit coupled cluster method to minimize the use of quantum resources in large-scale calculations, *Quantum Sci. Technol.*, 2021, **6**, 024012.
95 A. Tammaro, D. E. Galli, J. E. Rice and M. Motta, N-Electron Valence Perturbation Theory with Reference Wave Functions from Quantum Computing: Application to the Relative Stability of Hydroxide Anion and Hydroxyl Radical, *J. Phys. Chem. A*, 2023, **127**, 817–827.

Published on 14 2024. Downloaded on 22-11-2025 00:14:04.

96 N. P. Bauman, E. J. Bylaska, S. Krishnamoorthy, G. H. Low, N. Wiebe and C. E. Granade, *et al.*, Downfolding of many-body Hamiltonians using active-space models: Extension of the sub-system embedding sub-algebras approach to unitary coupled cluster formalisms, *J. Chem. Phys.*, 2019, **151**, 014107.

97 M. Metcalf, N. P. Bauman, K. Kowalski and W. A. De Jong, Resource-efficient chemistry on quantum computers with the variational quantum eigensolver and the double unitary coupled-cluster approach, *J. Chem. Theory Comput.*, 2020, **16**, 6165–6175.

98 J. Chládek, L. Veis, J. Pittner and K. Karol, *et al.*, Variational quantum eigensolver for approximate diagonalization of downfolded hamiltonians using generalized unitary coupled cluster ansatz, *Quantum Sci. Technol.*, 2021, **6**, 034008.

99 K. Kowalski, Dimensionality reduction of the many-body problem using coupledcluster subsystem flow equations: Classical and quantum computing perspective, *Phys. Rev. A*, 2021, **104**, 032804.

100 K. Kowalski and N. P. Bauman, Quantum flow algorithms for simulating many-body systems on quantum computers, *Phys. Rev. Lett.*, 2023, **131**, 200601.

101 R. Huang, C. Li and F. A. Evangelista, Leveraging small-scale quantum computers with unitarily downfolded hamiltonians, *PRX Quantum*, 2023, **4**, 020313.

102 S. McArdle and D. P. Tew, Improving the accuracy of quantum computational chemistry using the transcorrelated method, *arXiv*, 2020, preprint, arXiv:2006.11181, DOI: **10.48550/arXiv.2006.11181**.

103 M. Motta, T. P. Gujarati, J. E. Rice, A. Kumar, C. Masteran and J. A. Latone, *et al.*, Quantum simulation of electronic structure with a transcorrelated Hamiltonian: improved accuracy with a smaller footprint on the quantum computer, *Phys. Chem. Chem. Phys.*, 2020, **22**, 24270–24281.

104 I. O. Sokolov, W. Dobrautz, H. Luo, A. Alavi and I. Tavernelli, *Phys. Rev. Res.*, 2023, **5**, 023174.

105 A. Kumar, A. Asthana, C. Masteran, E. F. Valeev, Y. Zhang and L. Cincio, *et al.*, Quantum Simulation of Molecular Electronic States with a Transcorrelated Hamiltonian: Higher Accuracy with Fewer Qubits, *J. Chem. Theory Comput.*, 2022, **18**, 5312–5324.

106 R. V. Meter, W. J. Munro, K. Nemoto and K. M. Itoh, Arithmetic on a distributedmemory quantum multicomputer, *ACM J. Emerging Technol. Comput. Syst.*, 2008, **3**, 1–23.

107 S. DiAdamo, M. Ghibaudi and J. Cruise, Distributed Quantum Computing and Network Control for Accelerated VQE, *IEEE Trans. Quantum Eng.*, 2021, **2**, 1–21.

108 T. Häner, D. S. Steiger, T. Hoefler and M. Troyer, Distributed quantum computing with QMPI, Proceedings of the International Conference for High Performance Computing, Networking, Storage and Analysis. New York, NY, USA, 2021, pp. 1–13.

109 S. Niu and A. Todri-Sanial, How parallel circuit execution can be useful for NISQ com-puting? Proceedings of the 2022 Conference & Exhibition on Design, Automation & Test in Europe, Leuven, BEL, 2022, pp. 1065–1070.

110 L. Mineh and A. Montanaro, Accelerating the variational quantum eigensolver using parallelism, *Quantum Sci. Technol.*, 2023, **8**, 035012.

111 D. Claudino, B. Peng, K. Kowalski and T. S. Humble, Modeling singlet fission on a quantum computer, *J. Phys. Chem. Lett.*, 2023, **14**, 5511–5516.

112 D. Willsch, M. Willsch, F. Jin, K. Michielsen and H. De Raedt, GPU-accelerated simulations of quantum annealing and the quantum approximate optimization algorithm, *Comput. Phys. Commun.*, 2022, **278**, 108411.

113 T. Jones, A. Brown, I. Bush and S. C. Benjamin, QuEST and High Performance Simulation of Quantum Computers, *Sci. Rep.*, 2019, **9**, 10736.

114 G. G. Guerreschi, J. Hogaboam, F. Baruffa and N. P. D. Sawaya, Intel Quantum Simulator: a cloud-ready high-performance simulator of quantum circuits, *Quantum Sci. Technol.*, 2020, **5**, 034007.

115 H. Bayraktar, A. Charara, D. Clark, S. Cohen, T. Costa, Y.-L. L. Fang, Y. Gao, J. Guan, J. Gunnels, A. Haidar, A. Hehn, M. Hohnerbach, M. Jones, T. Lubowe, D. Lyakh, S. Morino, P. Springer, S. Stanwyck, I. Terentyev, S. Varadhan, J. Wong and T. Yamaguchi, cuQuantum SDK: A High-Performance Library for Accelerating Quantum Science, 2023 IEEE International Conference on Quantum Computing and Engineering (QCE), 2023, pp. 1050–1061.

116 W. Li, J. Allcock, L. Cheng, S.-X. Zhang, Y.-Q. Chen, J. P. Mailoa, Z. Shuai and S. Zhang, TenCirChem: An Efficient Quantum Computational Chemistry Package for the NISQ Era, *J. Chem. Theory Comput.*, 2023, **19**, 3966–3981.

117 T. Häner and D. Steiger S. 0.5 petabyte simulation of a 45-qubit quantum circuit, Proceedings of the International Conference for High Performance Computing, Networking, Storage and Analysis, New York, NY, USA, 2017.

118 V. Bergholm, J. Izaac, M. Schuld, C. Gogolin, S. Ahmed, V. Ajith, M. S. Alam, G. Alonso-Linaje, B. AkashNarayanan, A. Asadi, J. M. Arrazola, U. Azad, S. Banning, C. Blank, T. R. Bromley, B. A. Cordier, J. Ceroni, A. Delgado, O. D. Matteo, A. Dusko, T. Garg, D. Guala, A. Hayes, R. Hill, A. Ijaz, T. Isacsson, D. Ittah, S. Jahangiri, P. Jain, E. Jiang, A. Khandelwal, K. Kottmann, R. A. Lang, C. Lee, T. Loke, A. Lowe, K. McKiernan, J. J. Meyer, J. A. Montanez-Barrera, R. Moyard, Z. Niu, L. J. O'Riordan, S. Oud, A. Panigrahi, C.-Y. Park, D. Polatajko, N. Quesada, C. Roberts, N. Sá, I. Schoch, B. Shi, S. Shu, S. Sim, A. Singh, I. Strandberg, J. Soni, A. Száva, S. Thabet, R. A. Vargas-Hernández, T. Vincent, N. Vitucci, M. Weber, D. Wierichs, R. Wiersema, M. Willmann, V. Wong, S. Zhang and N. Killoran, PennyLane: Automatic differentiation of hybrid quantum-classical computations, *arXiv*, 2022, preprint, arXiv:1811.04968, DOI: **10.48550/arXiv.1811.04968**.

119 Y. Suzuki, Y. Kawase, Y. Masumura, Y. Hiraga and M. Nakadai, *et al.*, Qulacs: a fast and versatile quantum

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circuit simulator for research purpose, *Quantum*, 2021, **5**, 559.

120 J. Doi and H. Horii, Cache Blocking Technique to Large Scale Quantum Computing Simulation on Supercomputers, 2020 IEEE International Conference on Quantum Computing and Engineering (QCE), 2020, pp. 212–222.

121 S. Efthymiou, S. Ramos-Calderer, C. Bravo-Prieto, A. Pérez-Salinas, D. GarcíaMartín, A. Garcia-Saez, J. I. Latorre and S. Carrazza, Qibo: a framework for quantum simulation with hardware acceleration, *Quantum Sci. Technol.*, 2021, **7**, 015018.

122 R. S. Smith, M. J. Curtis and W. J. Zeng, A Practical Quantum Instruction Set Architecture, *arXiv*, 2017, preprint, arXiv:1608.03355, DOI: **10.48550/arXiv.1608.03355**.

123 E. Gustafson, B. Holzman, J. Kowalkowski, H. Lamm, A. C. Y. Li, G. Perdue, S. V. Isakov, O. Martin, R. Thomson, J. Beall, M. Ganahl, G. Vidal and E. Peters, Large scale multi-node simulations of Z2 gauge theory quantum circuits using Google Cloud Platform. 2021 IEEE/ACM Second International Workshop on Quantum Computing Software (QCS), 2021, pp. 72–79.

124 X.-Z. Luo, J.-G. Liu, P. Zhang and L. Wang, Yao.jl: Extensible, Efficient Framework for Quantum Algorithm Design, *Quantum*, 2020, **4**, 341.

125 K. De Raedt, K. Michielsen, H. De Raedt, B. Trieu, G. Arnold, M. Richter, T. Lippert, H. Watanabe and N. Ito, Massively parallel quantum computer simulator, *Comput. Phys. Commun.*, 2007, **176**, 121–136.

126 H. De Raedt, F. Jin, D. Willsch, M. Willsch, N. Yoshioka, N. Ito, S. Yuan and K. Michielsen, Massively parallel quantum computer simulator, eleven years later, *Comput. Phys. Commun.*, 2019, **237**, 47–61.

127 Qiskit contributors Qiskit: An Open-source Framework for Quantum Computing. 2023.

128 H. Shang, L. Shen, Y. Fan, Z. Xu, C. Guo, J. Liu, *et al.*, Large-Scale Simulation of Quantum Computational Chemistry on a New Sunway Supercomputer. Proceedings of the International Conference on High Performance Computing, Networking, Storage and Analysis, 2022.

129 Y. Fan, J. Liu, X. Zeng, Z. Xu, H. Shang and Z. Li, *et al.*, *J. Univ. Sci. Technol. China*, 2022, **52**, 2.

130 L. Noodleman, T. Lovell, T. Liu, F. Himo and R. A. Torres, Insights into properties and energetics of iron-sulfur proteins from simple clusters to nitrogenase, *Curr. Opin. Chem. Biol.*, 2002, **6**, 259–273.

131 Z. Li, J. Li, N. S. Dattani, C. J. Umrigar and G. K.-L. Chan, The electronic complexity of the ground-state of the FeMo cofactor of nitrogenase as relevant to quantum simulations, *J. Chem. Phys.*, 2019, **150**, 024302.

132 Y.-C. Cheng and G. R. Fleming, Dynamics of Light Harvesting in Photosynthesis, *Annu. Rev. Phys. Chem.*, 2009, **60**, 241–262.

133 T. Oka, Taming CH_5^+, the "enfant terrible" of chemical structures, *Science*, 2015, **347**, 1313–1314.

134 M. Qiu, Z. Ren, L. Che, D. Dai, S. A. Harich, X. Wang, X. Yang, C. Xu, D. Xie, M. Gustafsson, R. T. Skodje, Z. Sun and D. H. Zhang, Observation of Feshbach Resonances in the F + H_2 HF + H Reaction, *Science*, 2006, **311**, 1440–1443.