Overview of Industrial Wavefunction-based Quantum Chemistry

Jonathan Varghese

December 2025

Abstract

Wavefunction-based *ab initio* computational chemistry methods, though limited in the past, have been hypothesized to see dramatic speed ups in runtime with the usage of quantum algorithms and quantum processing units (QPUs). This article aims to provide an introduction to wavefunction-based WFT computational chemistry methods, as well as an overview on the quantum computing industry as to who is conducting such calculations using QPUs, and what strategies companies are exploring to overcome these expensive computation barriers.

1 Introduction

Computational chemistry has been used for drug development, understanding molecular structures, recording data on chemical compounds, and synthesizing materials for around the past 50 years [32][31] [14]. In this time, a variety of methods have been developed and improved on. Molecular Mechanics (MM) uses classical approximations like the harmonic oscillator to represent chemical bonds. Molecular Dynamics (MD) calculate forces according to Newtonian mechanics [40]. Monte Carlo methods conduct random sampling of molecule positions and configurations to find ground state energies [42]. The most commonly used Density Functional Theory (DFT) involves the creation of electron density functions that are used to calculate orbital interactions. However, there is only one type of computational chemistry method that uses true quantum mechanical calculations to determine the orbital dynamics of molecules; these are Wavefunction Theory (WFT) methods [10].

WFT methods involve writing out the wavefunctions for every electron in a molecule and accounting for every electron-nuclei and electron-electron interaction to determine ground states of molecules. As it may be imagined, these methods are more accurate but extremely computationally expensive, which is why they have been fairly limited in the past. But with the emergence of quantum computing, it has been hypothesized and observed that quantum computers will allow for far better runtimes than previously possible. In this article, we hope to provide an overview on who in industry is conducting WFT calculations using quantum computers, and showcase how companies are overcoming these expensive computation barriers using a variety of strategies.

This article is organized as follows: Motivations for WFT Methods will explain the limitations of DFT and why WFT methods are worth developing. Next will be an introduction to WFT methods, and how the electron wavefunctions are contracted and configured. Finally, there will be an overview as to which companies are exploring what methodologies to improve WFT runtimes on QPUs. Table 1 provides a concise summary of the research conducted.

2 Motivation for WFT Methods

2.1 The Limitations of Density Functional Theory

While density functional theory has become the most widely used electronic structure method in computational chemistry due to its favorable computational cost, DFT struggles with several important classes of chemical systems, including strongly correlated materials, charge transfer excitations, and transition states . The fundamental issue lies in the approximate nature of all practical exchange-correlation functionals. Unlike wavefunction methods, which have a clear hierarchy allowing systematic improvement, density functionals are not systematically improvable—there is no guarantee that using more sophisticated functionals will yield better results .

Modern state-of-the-art functionals have achieved near-chemical accuracy for many applications, but principal remaining limitations are associated with systems exhibiting significant self-interaction errors, delocalization errors, and strong correlation effects . The root cause is straightforward: both Hartree-Fock and Kohn-Sham DFT are single-determinant methods, and accurately describing multi-reference systems with strong correlation requires information from multiple determinants .

2.2 Strong Correlation: Where DFT Fails and WFT Succeeds

The distinction between weakly and strongly correlated systems is crucial for selecting an appropriate computational method. In weakly correlated systems, local functionals and hybrids with small exact exchange fractions perform acceptably, but addressing strong correlation within Kohn-Sham DFT remains the least solved problem among DFT's limitations . Strong correlation arises in several chemically important scenarios: molecules undergoing bond dissociation, transition metal complexes with multiple unpaired electrons, excited states, and systems with near-degenerate frontier orbitals.

For weakly correlated systems, DFT provides excellent results at modest computational cost—essentially offering Hartree-Fock-like efficiency while capturing electron correlation that would otherwise require expensive post-HF methods. However, this computational advantage disappears for strongly correlated systems, where the single-determinant framework becomes fundamentally inadequate. In such cases, multi-reference wavefunction methods become necessary. WFT approaches like CASSCF, MRCI, or coupled cluster variants explicitly construct multi-determinant wavefunctions that can properly describe the physics of strong correlation.

The challenge is that one cannot always predict *a priori* whether a system will exhibit weak or strong correlation, particularly for novel molecules or unexplored reaction pathways. This uncertainty motivated the development of diagnostic tools (such as the T_1 diagnostic in coupled cluster theory) to assess the multi-reference character of a wavefunction. When studying new chemical systems—such as those encountered in early characterization of novel viruses or drug candidates—the correlation regime is unknown, necessitating the use of WFT methods that can reliably treat both weakly and strongly correlated scenarios.

2.3 The Role of Experimental Validation

Computational predictions must ultimately be validated against experimental measurements. Traditional experimental techniques like electron spin resonance (ESR) spectroscopy have provided benchmarks for comparing DFT and WFT predictions of hyperfine coupling constants and other magnetic properties. However, classical ESR has fundamental sensitivity limitations.

Recent advances in quantum sensing have dramatically improved measurement precision. Bienfait and colleagues demonstrated that a Josephson junction-based quantum sensor achieved four orders of magnitude improvement in electron spin resonance sensitivity compared to classical ESR techniques [5]. Such quantum-enhanced measurements may provide superior benchmarks for validating computational predictions, potentially resolving discrepancies between different theoretical approaches that previously fell within experimental uncertainty.

As quantum sensing technologies mature and become more widely adopted in biomedicine and chemistry[1], the interplay between high-precision WFT calculations and quantum-enhanced experimental validation will become increasingly important for molecular characterization and drug discovery.

2.4 Computational Cost and the Quantum Computing Opportunity

The fundamental obstacle to widespread use of WFT methods is computational cost. While DFT scales approximately as $\mathcal{O}(N^3)$ for N basis functions, correlated wavefunction methods scale much more steeply: CCSD scales as $\mathcal{O}(N^6)$, CCSD(T) as $\mathcal{O}(N^7)$, and full CI grows exponentially as $\mathcal{O}(2^N)$ [43]. This severe scaling has historically confined accurate WFT calculations to small molecules.

Quantum computers offer a fundamentally different approach to this scaling problem. Because quantum hardware can natively represent superpositions of exponentially many determinants, quantum algorithms promise polynomial rather than exponential scaling for certain correlation problems. This potential motivates the industrial interest in quantum computing for chemistry—if quantum algorithms can achieve practical advantage over classical methods, the 5% of chemical problems that truly require multi-reference treatment could become as routine as the 95% currently handled by DFT [16].

The algorithmic developments discussed in subsequent sections represent efforts to realize this potential on near-term quantum hardware, despite the noise and limited qubit counts of current devices.

3 Introduction to Wavefunction-based *Ab-Initio* Chemistry

To understand wavefunction-based WFT chemistry, one must have a basic understanding of quantum mechanics. According to quantum physics, the exact state of any system is unknowable and undefinable, and instead is inherently probabilistic. The complete description of any quantum system is not determined by exact scalar values but instead can only be described by a complex-valued wavefunction.

The wavefunction can be loosely thought of as a probability distribution. If you asked someone the numerical value of a rolling dye, it's easy to understand the question is nonsensical. The best that one could give you as a description for the rolling dye is the probability mass function that describes the likelihoods of each value landing upwards. In a similar way, if you asked someone the x,y, and z coordinates of an electron within a hydrogen atom, the best you could receive as a description of that electron's position is the function that has assigned a probability to every possible x,y, and z coordinate possible. This probability distribution can be thought of (or more precisely derived from) the electron's wavefunction. It is a function that has assigned a probability to every possible configuration of a system.

For a system of N electrons in an atom, we use a many-electron wavefunction $\Psi(\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_N)$, where $\mathbf{x}_i(\mathbf{r}_i, s_i)$ denote both spatial and spin coordinates. This wavefunction encodes the probability amplitude of finding N electrons in a specific position and spin orientation. The probability is not the output of the wavefunction itself (since the output is a complex number), but

[1] See *Quantum Sensing in Biomedical Applications*, Quantum Economic Development Consortium (2024), available at `https://quantumconsortium.org/publication/biomedical2024/`

is instead the found by taking the square modulus of the output $|\Psi|^2$. Because of this, any wavefunction must be "normalized", satisfying the condition

$$\int |\Psi(\mathbf{x}_1, \ldots, \mathbf{x}_N)|^2 \, d\mathbf{x}_1 \cdots d\mathbf{x}_N = 1, \tag{1}$$

to ensure the probabilities of all possible electron configurations sum to 1[48].

3.1 One-Electron Basis Functions

What do these many-electron wavefunctions look like? First, we try to define a wavefunction describing a single electron in the simplest system possible, the hydrogen atom. The exact solution for this wavefunction is found by solving the Schrödinger equation, where we insert the electromagnetic energy function between a single proton and electron to generate our wavefunction solutions [21]. But these functions are complicated and difficult to work with, so we create approximations of the true solution.

Historically, *Slater-type orbitals* (STOs) were introduced as analytic approximations to the hydrogenic solutions of the Schrödinger equation,

$$\psi_{\text{STO}}(r, \theta, \phi) = N r^{n-1} e^{-\zeta r} Y_\ell^m(\theta, \phi), \tag{2}$$

where ζ is an orbital exponent, Y_ℓ^m are the spherical harmonics, and N is a normalization constant [44]. STOs possess the correct cusp behavior at the nucleus and decay exponentially at long distances, making them physically realistic. However, their products over multiple centers are expensive to integrate analytically.

To address this, the *Gaussian-type orbitals* (GTOs) were introduced [44]:

$$g(x, y, z) = N \, x^a y^b z^c e^{-\alpha r^2}. \tag{3}$$

Although less physically accurate than STOs (the Gaussian radial decay is too rapid) their advantage is the analytic integrability of all required one- and two-electron integrals. As shown by Boys and others, the product of two Gaussians remains a shifted Gaussian, dramatically simplifying molecular calculations [6].

3.2 Contractions and Basis Sets

Because individual primitive Gaussians do not reproduce the correct exponential behavior of atomic orbitals, they are often combined into *contracted Gaussian functions*:

$$\phi(\mathbf{r}) = \sum_{\mu=1}^{K} d_\mu \, g_\mu(\mathbf{r}), \tag{4}$$

where d_μ are contraction coefficients and g_μ are primitive GTOs [44]. The set of such contracted functions chosen to approximate the atomic orbitals of all atoms in a molecule constitute a *basis set*. There are many different basis sets, of various complexities, but they all serve the same purpose; describe how to sum up enough primitive functions to approximate the true orbital wavefunction solutions in an atom/molecule (most basis sets contract Gaussian functions as primitives, but sometimes other primitives can be used as well, i.e. plane waves.) Depending on which atomic/molecular orbital we are approximating, we solve for the best coefficient d_μ and GTO exponent α, for which exist archives of pre-solved basis sets for specific atoms like the Basis Set exchange[26].

Several widely used basis sets include [44]:

- **STO-nG**: minimal basis sets where each orbital is approximated by n Gaussians summed together(e.g. STO-3G).
- **Pople-style split-valence sets**: such as 6-21G, 6-31G, etc., offering flexibility by summing the core orbitals and valence shell orbitals differently.
- **Correlation-consistent sets**: e.g. cc-pVDZ, systematically improvable basis sets introduced by Dunning.

So using a basis function, we have a way of writing out the single-electron wavefunction in a specific orbital. But how do we add in other electrons?

3.3 Hartree–Fock Theory and the Slater Determinant

The Hartree–Fock (HF) method provides an approximate solution to the electronic Schrödinger equation by representing the many-electron wavefunction as a single *Slater determinant* of spin-orbitals:

$$\Phi_{\text{HF}} = \frac{1}{\sqrt{N!}} \begin{vmatrix} \chi_{1s^\uparrow}(\mathbf{x}_1) & \chi_{1s^\downarrow}(\mathbf{x}_1) & \chi_{2s^\uparrow}(\mathbf{x}_1) & \cdots & \chi_N(\mathbf{x}_1) \\ \chi_{1s^\uparrow}(\mathbf{x}_2) & \chi_{1s^\downarrow}(\mathbf{x}_2) & \chi_{2s^\uparrow}(\mathbf{x}_2) & \cdots & \chi_N(\mathbf{x}_2) \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \chi_{1s^\uparrow}(\mathbf{x}_N) & \chi_{1s^\downarrow}(\mathbf{x}_N) & \chi_{2s^\uparrow}(\mathbf{x}_N) & \cdots & \chi_N(\mathbf{x}_N) \end{vmatrix}. \tag{5}$$

Here, we take the orbital wavefunction ϕ defined by our basis sets and multiply by a spin function to get a spin-orbital χ.

By taking this determinant, we conveniently incorporate our Pauli-exclusion requirement that no two electrons within the same orbital share the same spin. However, all electrons are packed into the lowest possible orbitals, without any possibility of an excited electron.

3.4 Post-Hartree–Fock Correlation Methods

Since Hartree–Fock omits correlated electronic motions, post-HF methods introduce linear combinations of excited determinants to recover correlation energy. These methods include:

- Configuration Interaction with Doubles (CID)
- Configuration Interaction with Singles and Doubles (CISD)
- Coupled Cluster Singles and Doubles (CCSD)
- Coupled Cluster with perturbative Triples [CCSD(T)]
- Full Configuration Interaction (FCI), the exact solution within a finite basis

In these post-HF methods, we create excited Slater determinants by replacing 1 or more columns of occupied orbitals with a specific higher energy orbital. If we are creating a single excitation configuration, we choose one column to replace with one higher orbital, also known as a *virtual orbital*. If we are creating a double excitation configuration, we choose two occupied orbitals, and replace them with two possible virtual orbitals. We then sum across all possible combinations, a linear combination of all single excitations, double excitations, triple, and so on. Depending on the specific configuration we are using, we truncate this linear combination at singles, doubles, triples or so on[48]. The correlated molecular wavefunction is expressed as:

$$\Psi = c_0\Phi_0 + \sum_i c_i \Phi_i^{(1)} + \sum_{ij} c_{ij}\Phi_{ij}^{(2)} + \cdots, \tag{6}$$

where Φ_0 is the HF determinant and $\Phi_i^{(1)}$, $\Phi_{ij}^{(2)}$ denote singly and doubly excited determinants, respectively. This framework underlies much of modern WFT quantum chemistry.

4 WFT Quantum Chemistry in Industry

Although Quantum Computational Chemistry theories have existed since the 80s, implementing real simulations efficiently has been challenging due to the fact that exact quantum chemistry scales super-exponentially with system size. However, in the past decade, there has been a surge of industrial interest in applying quantum computing to ab-initio quantum chemistry, driven by both advances in quantum hardware and sophisticated algorithmic strategies to circumvent the prohibitive scaling of traditional methods. While fault-tolerant quantum computers remain years away, a diverse ecosystem of quantum startups, tech giants, and pharmaceutical companies are developing hybrid classical-quantum approaches that make near-term applications increasingly feasible.

4.1 Industrial Landscape

The quantum chemistry space is being pursued by three distinct categories of players. Quantum-native companies like Quantinuum, IonQ, Xanadu, QC Ware, and Rigetti are developing both hardware platforms and specialized software stacks optimized for chemical simulations. Tech giants including Google and IBM have leveraged their substantial R&D resources to advance both quantum processors and open-source software ecosystems for quantum chemistry. Finally, pharmaceutical companies like Boehringer Ingelheim (through QC Ware) and Chugai (with Deloitte) have begun direct investments in quantum chemistry research

This industrial activity has also catalyzed development of a robust software ecosystem. Open-source packages like PySCF and Psi4 provide classical quantum chemistry foundations that interface with quantum algorithms, while quantum-specific tools have proliferated: Google's OpenFermion for translating chemical problems into qubit operators, Xanadu's PennyLane for quantum machine learning and chemistry, Quantinuum's InQuanto for quantum computational chemistry workflows, and QC Ware's proprietary Promethium platform. This layered software architecture enables researchers to combine classical and quantum methods fluidly.

4.2 Methods for Industry Quantum Chemistry

To be able to push towards industry grade, scalable ab-intio quantum chemistry, companies have been focusing their research efforts into improvements of specific areas of quantum chemistry calculations and utilizing certain strategies to simplify and optimize the ab-intio chemistry workflow, shown in Figure 1.

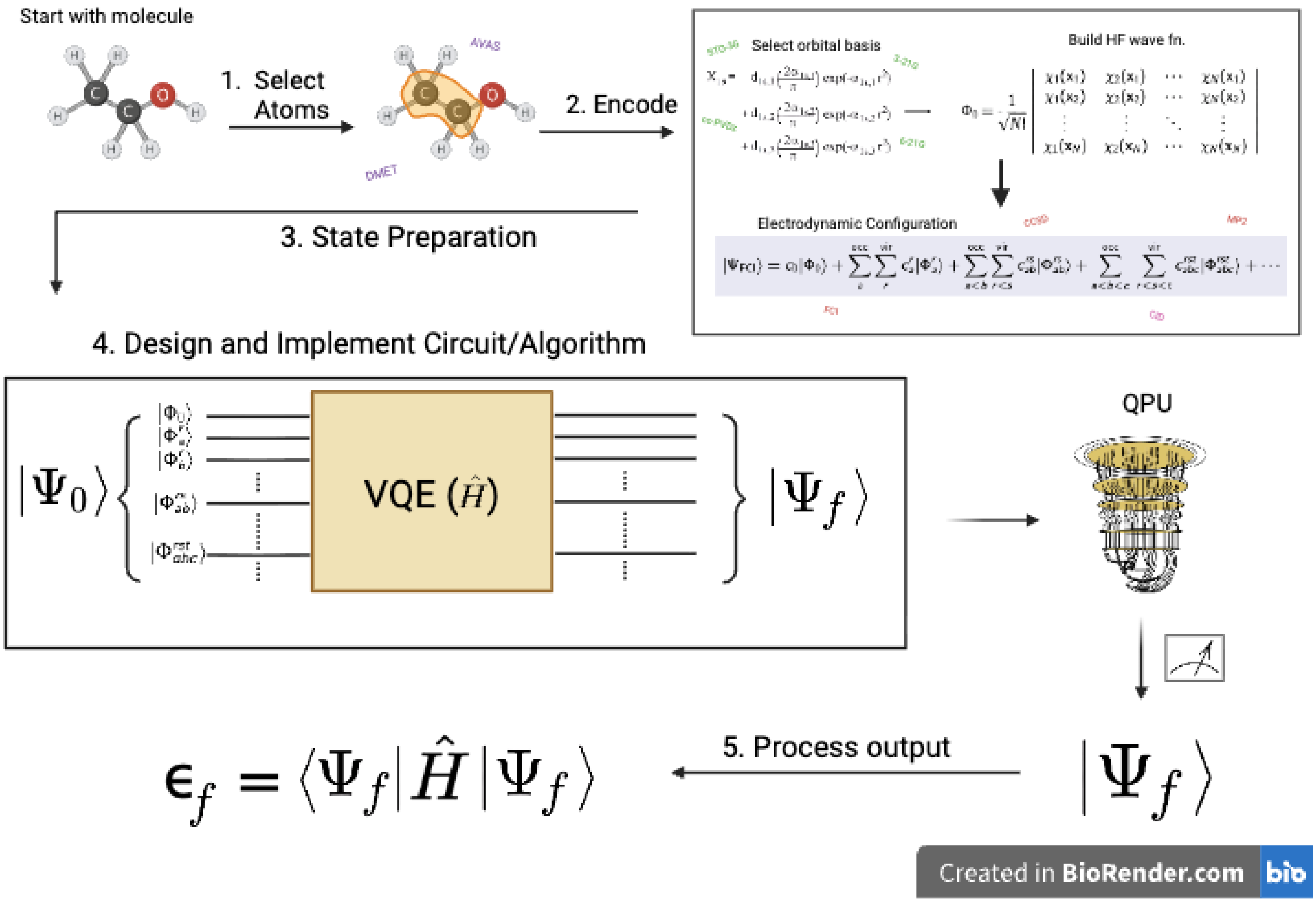

Figure 1: A diagram showcasing the general quantum chemistry workflow

4.2.1 Fragmentation and Active Space Methods

One way companies attempt to simply quantum chemistry simulations is by lowering the number of orbitals we are including in calculations. Quantinuum has been particularly prominent in demonstrating density matrix embedding theory (DMET), which fragments large molecular systems into smaller subsystems that can be treated accurately while capturing environmental effects through embedding. This approach transforms an intractable calculation on N orbitals into multiple tractable calculations on subsystems of size $n \ll N$, with spatial complexity reducing from exponential in N to exponential in n. Another way to simplify the simulated molecule is by a technique known as atomic valence active space (AVAS) methods. AVAS automatically selects a compact active space of orbitals expected to be chemically relevant—typically those involved in bond breaking, excited states, or other strongly correlated phenomena. By focusing quantum resources on the subset of orbitals where correlation is essential while treating the remainder at a mean-field level, AVAS reduces both the number of qubits required and the depth of quantum circuits needed, though it requires chemical intuition about which orbitals are likely to be important.

4.2.2 Circuit Optimization and Adaptive Algorithms

The second common approach for improving computations involve reducing the time complexity of the quantum algorithms used for simulations through circuit optimization. Traditionally, simulations are done by defining some ansätze circuit, that is then parameterized using a variational quantum eigensolver (VQE). A very typical ansätze for molecular simulations would be something like a UCCSD ansätze, where we take CCSD operators and reformat them to be unitary and therfore implementable using gates [13]. Using this as a starting point, some companies have tried creating spin-off ansätzes based on UCCSD to improve runtimes.

Another approach to optimizing circuit design will be by utilizing the ADAPT-VQE algorithm. VQE uses a fixed ansätze that may contain many unnecessary parameters, leading to deep circuits prone to noise and slow classical optimization. ADAPT-VQE, developed by Grimsley and colleagues and actively explored by Quantinuum and others, instead grows the quantum circuit iteratively by adding only operators that significantly reduce the energy [20]. This produces problem-tailored circuits with minimal depth and parameter count, directly addressing the time complexity bottleneck. While ADAPT-VQE requires multiple rounds of quantum-classical communication, the resulting circuits often achieve chemical accuracy with far fewer gates than fixed ansätze, a crucial advantage on noisy intermediate-scale quantum (NISQ) devices.

A related area of research conducted by companies like Google and Algorithmq was on devloping algorithms for efficient state-prearation. The idea behind state-preparation is to initialize our wavefunction as close to the desired final state as possible in order for the VQE to not need to run as many iterations. By doing so, the VQE would not need as many iterations, allowing for faster convergence towards a desired ground state.

4.2.3 Hybrid Classical-Quantum Approaches

A very pragmatic near-term strategy that many will use instead of pure ab-intio computation are hybrid apporaches that combine quantum and classical methods within a single calculation. Quantinuum and others have explored DFT+wavefunction schemes where density functional theory treats the bulk of weak electron correlation at polynomial cost, while quantum algorithms target the strongly correlated subsystem where DFT fails. This division of labor exploits the complementary strengths of each approach: DFT's efficiency for weakly correlated systems and quantum computing's ability to capture strong correlation. The spatial and time complexities become dominated by the quantum subsystem, which can be made substantially smaller than the full system.

4.2.4 Quantum Phase Estimation

While the near-term algorithmic strategies discussed above focus on NISQ-era approaches like VQE and its variants, quantum phase estimation represents a fundamentally different paradigm that can achieve exponential speedup in finding the eigenspectrum of unitary operators, provided an appropriate trial state with nonzero overlap with the true solution can be prepared . Unlike VQE, which relies on repeated classical optimization of variational parameters, QPE estimates eigenvalues through a purely quantum process involving controlled unitary evolution and inverse quantum Fourier transforms.

The algorithmic advantage of QPE is significant. QPE can achieve exponential speedup and is likely to demonstrate quantum advantage when the first sufficiently large fault-tolerant quantum computers are built, though it requires millions of qubits and gates even for relatively small systems—a requirement far beyond current NISQ hardware capabilities .

Recent work has explored resource-efficient implementations of QPE for chemistry applications. Tachi and colleagues demonstrated quantum phase estimation-based complete active space configuration interaction calculations for intermolecular interaction energies, using MP2-based active space selection with Boys localized orbitals to reduce system size, achieving interaction energy predictions with errors of only 0.02 kcal/mol relative to CASCI results using just 6 system and 6 ancilla qubits . This work illustrates how QPE can be combined with classical dimensionality reduction techniques—active space selection, orbital localization, and supramolecular fragmentation approaches—to make fault-tolerant chemistry calculations tractable.

The primary challenge for QPE remains circuit depth and resource requirements. The algorithm requires coherent application of controlled-unitary operations that scale with the desired precision, along with quantum Fourier transforms across ancilla registers. Statistical variants of QPE have emerged as promising alternatives, offering shorter circuit depths and natural resilience to noise, particularly after error mitigation, with demonstrated accuracy comparable to or better than VQE on current hardware

Company	**Hybrid Methods**	**Fragmentation**	**Space Selection**	**Basis Selection**	**State Preparation**	**VQE/ADAPT-VQE based**	**Other Ansatz Design**	**Error Mitigation**	**QPE**
Quantinuum		[17], [28]	[19], [9]		[27], [18]	[12], [9]			
Google				[3], [23]	[23]			[38], [2]	
Algorithmiq		[29]	[46]			[34],[15],[35] ,[22]	[30]		
QSimulate	[26]				[4]				
QC Ware	[37]				[36]	[39]			
IonQ						[33]	[51]		
Xanadu						[8],[11]	[25]		
Other		Rigetti/Astex[24]							Deloitte/Chugai[45]

Table 1: Quantum Chemistry Methods by Company: Papers looked at in this report, from which companies and focused on which areas.

. These statistical approaches sacrifice the deterministic readout of traditional QPE for probabilistic sampling strategies that reduce circuit depth at the cost of additional measurements.

4.3 Common Research Themes

In summary, industrial efforts to improve Quantum Chemistry simulations tend to focus onto certain areas. One is state preparation—efficiently initializing the quantum computer with a reasonable guess at the molecular wavefunction—has received substantial attention, as poor initial states lead to slow convergence and deeper circuits. Algorithm and circuit optimization work seeks to minimize both gate count (time complexity) and qubit requirements (space complexity) through improved ansätze, operator ordering, and measurement strategies. Several groups have developed comprehensive frameworks for quantum chemistry simulations that systematically explore tradeoffs between basis set size, correlation treatment, circuit design, and hardware constraints. Finally, there has been increasing emphasis on actual hardware demonstrations rather than purely classical simulations, testing whether algorithmic advances translate to noisy real devices.

Despite all these different strategies, there seems to be a consensus on what the pathway to industry grade ab-initio modeling should look like; wherein the primary obstacle stands the accurate characterization of noisy systems, which will be overcome through the developments of fault-tolerant computers. This current pathway is clearly guided by the premise that closed quantum systems are the best way to encode and model chemical systems. Upon conducting research for this article by parsing through dozens of companies and their listed publications, it became more and more apparent that there is far less focus in exploring open-system chemical modeling by utilizing noise as a type of bath environment. The only instances found were in one paper from IBM [41], where a noisy system was used to simulate thermal relaxation of spin chemistry systems, and another that we here at Iff collaborated on with UCLA, where noisy systems were used in the parameterization of a circuit used to simulate Hyperfine and Zeeman interactions for spin chemistry [7]. Despite these, it appears evident there exists an overall industry-wide sentiment that open-systems are not as viable of an option for developing industry grade *ab-initio* modeling and instead, the focus should remain on being well prepared for the eventual emergence of fault-tolerance.

4.4 Biopharmaceutical Applications and Metalloprotein Characterization

The pharmaceutical industry presents particularly compelling use cases for WFT quantum chemistry, for example in characterizing metalloproteins and metal-binding sites that are poorly described by classical methods. Zinc finger proteins are a specific case of this challenge: these ubiquitous transcription factors coordinate zinc ions through cysteine and histidine residues in geometries that classical force fields struggle to reproduce accurately. In 2017 Friedman and co-workers calculated the interaction energies between Zn2+ and its ligands in several representative complexes using both QM and MM methods. It was found that MM calculations that neglect or only approximate polarization could not reproduce even the relative order of the QM interaction energies of these complexes [1]. The fundamental challenge echoes the strong correlation problem discussed earlier: researchers often cannot predict whether a given metal-binding site will exhibit multi-reference character requiring correlated wavefunction methods, or whether DFT with an appropriate functional will suffice. This uncertainty is particularly acute for transition metal complexes with multiple unpaired electrons and for systems undergoing redox chemistry. Similarly, photosynthetic reaction centers—another target for biomimetic catalyst design—involve strongly correlated excited states that have historically required WFT methods for accurate characterization. Quantum chemistry has contributed substantially to understanding natural photosynthesis and informing artificial photosynthesis efforts, but these calculations remain at the limits of classical computational resources [47].

The intersection of WFT quantum chemistry and biopharmaceutical applications represents a growing employment sector, with recent workforce analyses of the Sacramento area identifying approximately 160 positions requiring expertise in both quantum computing and biotechnology [50]. However, a knowledge gap persists: many computational chemists in pharmaceutical settings lack exposure to modern WFT methods and cannot readily assess when such methods are necessary. Conversely, quantum computing specialists often lack the domain knowledge to identify high-value pharmaceutical targets. Educational initiatives emphasizing the complementary strengths of DFT and WFT approaches would better prepare the biopharmaceutical workforce to leverage quantum computing advances as they mature.

Furthermore, recent advances in quantum sensing offer new opportunities for validating WFT predictions in biological contexts. Quantum sensors can achieve orders-of-magnitude improvements in sensitivity for detecting metal coordination environments, radical pair intermediates, and other quantum phenomena in biological systems. As these sensing modalities become more accessible, the interplay between high-precision WFT calculations and quantum-enhanced experimental validation will become increasingly important for characterizing metalloprotein function and guiding rational drug design [49].

References

[1] E. Ahlstrand, K. Hermansson, and R. Friedman. Interaction energies in complexes of zn and amino acids: A comparison of ab initio and force field based calculations. *The Journal of Physical Chemistry A*, 121(13):2643–2654, 2017. PMID: 28272891.

[2] F. Arute, K. Arya, R. Babbush, D. Bacon, J. C. Bardin, R. Barends, S. Boixo, M. Broughton, B. B. Buckley, D. A. Buell, B. Burkett, N. Bushnell, Y. Chen, Z. Chen, B. Chiaro, R. Collins, W. Courtney, S. Demura, A. Dunsworth, E. Farhi, A. Fowler, B. Foxen, C. Gidney, M. Giustina, R. Graff, S. Habegger, M. P. Harrigan, A. Ho, S. Hong, T. Huang, W. J. Huggins, L. Ioffe, S. V. Isakov, E. Jeffrey, Z. Jiang, C. Jones, D. Kafri, K. Kechedzhi, J. Kelly, S. Kim, P. V. Klimov, A. Korotkov, F. Kostritsa, D. Landhuis, P. Laptev, M. Lindmark, E. Lucero, O. Martin, J. M. Martinis, J. R. McClean, M. McEwen, A. Megrant, X. Mi, M. Mohseni, W. Mruczkiewicz, J. Mutus, O. Naaman, M. Neeley, C. Neill, H. Neven, M. Y. Niu, T. E. O'Brien, E. Ostby, A. Petukhov, H. Putterman, C. Quintana, P. Roushan, N. C. Rubin, D. Sank, K. J. Satzinger, V. Smelyanskiy, D. Strain, K. J. Sung, M. Szalay, T. Y. Takeshita, A. Vainsencher, T. White, N. Wiebe, Z. J. Yao, P. Yeh, and A. Zalcman. Hartree-fock on a superconducting qubit quantum computer. *Science*, 369(6507):1084–1089, Aug. 2020.

[3] R. Babbush, D. W. Berry, J. R. McClean, and H. Neven. Quantum simulation of chemistry with sublinear scaling in basis size. *npj Quantum Information*, 5(1), Nov. 2019.

[4] D. W. Berry, Y. Tong, T. Khattar, A. White, T. I. Kim, G. H. Low, S. Boixo, Z. Ding, L. Lin, S. Lee, G. K.-L. Chan, R. Babbush, and N. C. Rubin. Rapid initial-state preparation for the quantum simulation of strongly correlated molecules. *PRX Quantum*, 6(2), May 2025.

[5] A. Bienfait, J. J. Pla, Y. Kubo, M. Stern, X. Zhou, C. C. Lo, C. D. Weis, T. Schenkel, M. L. W. Thewalt, D. Vion, D. Esteve, B. Julsgaard, K. Mølmer, J. J. L. Morton, and P. Bertet. Reaching the quantum limit of sensitivity in electron spin resonance. *Nature Nanotechnology*, 11(3):253–257, Dec. 2015.

[6] S. F. Boys. Electronic wave functions-i. a general method of calculation for the stationary states of any molecular system. *Proceedings of the Royal Society of London. Series A. Mathematical and Physical Sciences*, 200(1063):542–554, 1950.

[7] T. J. Brokowski, F. T. Chowdhury, L. D. Smith, P. Alvarez, S. Sandeep, and C. Aiello. Spin chemistry simulation via hybrid-quantum machine learning. In *2022 IEEE International Conference on Quantum Computing and Engineering (QCE)*, pages 867–868, 2022.

[8] D. Castaldo, S. Jahangiri, A. Delgado, and S. Corni. Quantum simulation of molecules in solution. *Journal of Chemical Theory and Computation*, 18(12):7457–7469, Nov. 2022.

[9] G. Christopoulou, C. D. Paola, F. E. Elzinga, A. Jallat, D. M. Ramo, and M. Krompiec. Quantum hardware calculations of the activation and dissociation of nitrogen on iron clusters and surfaces, 2023.

[10] F. De Proft, P. Geerlings, F. Heidar-Zadeh, and P. W. Ayers. Conceptual density functional theory. In M. Yáñez and R. J. Boyd, editors, *Comprehensive Computational Chemistry (First Edition)*, pages 306–321. Elsevier, Oxford, first edition edition, 2024.

[11] A. Delgado, J. M. Arrazola, S. Jahangiri, Z. Niu, J. Izaac, C. Roberts, and N. Killoran. Variational quantum algorithm for molecular geometry optimization. *Physical Review A*, 104(5), Nov. 2021.

[12] C. Di Paola, E. Plekhanov, M. Krompiec, C. Kumar, E. Marsili, F. Du, D. Weber, J. S. Krauser, E. Shishenina, and D. Muñoz Ramo. Platinum-based catalysts for oxygen reduction reaction simulated with a quantum computer. *npj Computational Materials*, 10(1), Dec. 2024.

[13] D. A. Fedorov, Y. Alexeev, S. K. Gray, and M. Otten. Unitary selective coupled-cluster method. *Quantum*, 6:703, May 2022.

[14] F. Feng, L. Lai, and J. Pei. Computational chemical synthesis analysis and pathway design. *Frontiers in Chemistry*, Volume 6 - 2018, 2018.

[15] A. Fitzpatrick, A. Nykänen, N. W. Talarico, A. Lunghi, S. Maniscalco, G. García-Pérez, and S. Knecht. Self-consistent field approach for the variational quantum eigensolver: Orbital optimization goes adaptive. *The Journal of Physical Chemistry A*, 128(14):2843–2856, Mar. 2024.

[16] M. H. Gordon. Computational quantum chemistry: Classical gaps, quantum opportunities, open questions. [`https://www.youtube.com/watch?v=WGu0O8aVmqA`], July 2025.

[17] G. Greene-Diniz, D. Z. Manrique, W. Sennane, Y. Magnin, E. Shishenina, P. Cordier, P. Llewellyn, M. Krompiec, M. J. Rančić, and D. M. Ramo. Modelling carbon capture on metal-organic frameworks with quantum computing, 2023.

[18] G. Greene-Diniz, G. Prokopiou, D. Z. Manrique, and D. M. Ramo. Quantum state preparation of multiconfigurational states for quantum chemistry, 2025.

[19] G. Greene-Diniz, C. N. Self, M. Krompiec, L. Coopmans, M. Benedetti, D. Muñoz Ramo, and M. Rosenkranz. Measuring correlation and entanglement between molecular orbitals on a trapped-ion quantum computer. *Scientific Reports*, 15(1), Aug. 2025.

[20] H. R. Grimsley, S. E. Economou, E. Barnes, and N. J. Mayhall. An adaptive variational algorithm for exact molecular simulations on a quantum computer. *Nature communications*, 10(1):3007, 2019.

[21] D. M. Hanson, E. Harvey, R. Sweeney, and T. J. Zielinski. The Schrödinger Wave Equation for the Hydrogen Atom, aug 16 2025. [Online; accessed 2026-01-09].

[22] M. Hassan, F. Pavošević, D. S. Wang, and J. Flick. Simulating polaritonic ground states on noisy quantum devices, 2023.

[23] W. J. Huggins, O. Leimkuhler, T. F. Stetina, and K. B. Whaley. Efficient state preparation for the quantum simulation of molecules in first quantization, 2025.

[24] 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. *Journal of Computational Chemistry*, 44(3):406–421, July 2022.

[25] S. Jahangiri, J. M. Arrazola, N. Quesada, and A. Delgado. Quantum algorithm for simulating molecular vibrational excitations. *Physical Chemistry Chemical Physics*, 22(44):25528–25537, 2020.

[26] J. Jung, K. Yagi, C. Tan, H. Oshima, T. Mori, I. Yu, Y. Matsunaga, C. Kobayashi, S. Ito, D. Ugarte La Torre, and Y. Sugita. Genesis 2.1: High-performance molecular dynamics software for enhanced sampling and free-energy calculations for atomistic, coarse-grained, and quantum mechanics/molecular mechanics models. *The Journal of Physical Chemistry B*, 128(25):6028–6048, 2024. PMID: 38876465.

[27] I. Khan, M. Tudorovskaya, J. Kirsopp, D. Muñoz Ramo, P. Warrier, D. Papanastasiou, and R. Singh. Chemically aware unitary coupled cluster with ab initio calculations on an ion trap quantum computer: A refrigerant chemicals' application. *The Journal of Chemical Physics*, 158(21), 2023.

[28] J. J. M. Kirsopp, C. Di Paola, D. Z. Manrique, M. Krompiec, G. Greene-Diniz, W. Guba, A. Meyder, D. Wolf, M. Strahm, and D. Muñoz Ramo. Quantum computational quantification of protein–ligand interactions. *International Journal of Quantum Chemistry*, 122(22), Aug. 2022.

[29] E. R. Kjellgren, P. Reinholdt, A. Fitzpatrick, W. N. Talarico, P. W. K. Jensen, S. P. A. Sauer, S. Coriani, S. Knecht, and J. Kongsted. The variational quantum eigensolver self-consistent field method within a polarizable embedded framework. *The Journal of Chemical Physics*, 160(12), Mar. 2024.

[30] E. Magnusson, A. Fitzpatrick, S. Knecht, M. Rahm, and W. Dobrautz. Towards efficient quantum computing for quantum chemistry: reducing circuit complexity with transcorrelated and adaptive ansatz techniques. *Faraday Discussions*, 254:402–428, 2024.

[31] S. Muresan, M. Sitzmann, and C. Southan. *Mapping Between Databases of Compounds and Protein Targets*, pages 145–164. Humana Press, Totowa, NJ, 2012.

[32] F. Musil, A. Grisafi, A. P. Bartók, C. Ortner, G. Csányi, and M. Ceriotti. Physics-inspired structural representations for molecules and materials. *Chemical Reviews*, 121(16):9759–9815, 2021. PMID: 34310133.

[33] Y. Nam, J.-S. Chen, N. C. Pisenti, K. Wright, C. Delaney, D. Maslov, K. R. Brown, S. Allen, J. M. Amini, J. Apisdorf, K. M. Beck, A. Blinov, V. Chaplin, M. Chmielewski, C. Collins, S. Debnath, A. M. Ducore, K. M. Hudek, M. Keesan, S. M. Kreikemeier, J. Mizrahi, P. Solomon, M. Williams, J. D. Wong-Campos, C. Monroe, and J. Kim. Ground-state energy estimation of the water molecule on a trapped ion quantum computer, 2019.

[34] A. Nykänen, A. Miller, W. Talarico, S. Knecht, A. Kovyrshin, M. Skogh, L. Tornberg, A. Broo, S. Mensa, B. C. B. Symons, E. Sahin, J. Crain, I. Tavernelli, and F. Pavošević. Toward accurate post-born-oppenheimer molecular simulations on quantum computers: An adaptive variational eigensolver with nuclear-electronic frozen natural orbitals, 2023.

[35] A. Nykänen, L. Thiessen, E.-M. Borrelli, V. Krishna, S. Knecht, and F. Pavošević. δadapt-vqe: Toward accurate calculation of excitation energies on quantum computers for bodipy molecules with application in photodynamic therapy, 2024.

[36] P. J. Ollitrault, C. L. Cortes, J. F. Gonthier, R. M. Parrish, D. Rocca, G.-L. Anselmetti, M. Degroote, N. Moll, R. Santagati, and M. Streif. Enhancing initial state overlap through orbital optimization for faster molecular electronic ground-state energy estimation, 2024.

[37] P. J. Ollitrault, M. Loipersberger, R. M. Parrish, A. Erhard, C. Maier, C. Sommer, J. Ulmanis, T. Monz, C. Gogolin, C. S. Tautermann, G.-L. R. Anselmetti, M. Degroote, N. Moll, R. Santagati, and M. Streif. Estimation of electrostatic interaction energies on a trapped-ion quantum computer. *ACS Central Science*, Mar. 2024.

[38] T. E. O'Brien, G. Anselmetti, F. Gkritsis, V. E. Elfving, S. Polla, W. J. Huggins, O. Oumarou, K. Kechedzhi, D. Abanin, R. Acharya, I. Aleiner, R. Allen, T. I. Andersen, K. Anderson, M. Ansmann, F. Arute, K. Arya, A. Asfaw, J. Atalaya, J. C. Bardin, A. Bengtsson, G. Bortoli, A. Bourassa, J. Bovaird, L. Brill, M. Broughton, B. Buckley, D. A. Buell, T. Burger, B. Burkett, N. Bushnell, J. Campero, Z. Chen, B. Chiaro, D. Chik, J. Cogan, R. Collins, P. Conner, W. Courtney, A. L. Crook, B. Curtin, D. M. Debroy, S. Demura, I. Drozdov, A. Dunsworth, C. Erickson, L. Faoro, E. Farhi, R. Fatemi, V. S. Ferreira, L. Flores Burgos, E. Forati, A. G. Fowler, B. Foxen, W. Giang, C. Gidney, D. Gilboa, M. Giustina, R. Gosula, A. Grajales Dau, J. A. Gross, S. Habegger, M. C. Hamilton, M. Hansen, M. P. Harrigan, S. D. Harrington, P. Heu, M. R. Hoffmann, S. Hong, T. Huang, A. Huff, L. B. Ioffe, S. V. Isakov, J. Iveland, E. Jeffrey, Z. Jiang, C. Jones, P. Juhas, D. Kafri, T. Khattar, M. Khezri, M. Kieferová, S. Kim, P. V. Klimov, A. R. Klots, A. N. Korotkov, F. Kostritsa, J. M. Kreikebaum, D. Landhuis, P. Laptev, K.-M. Lau, L. Laws, J. Lee, K. Lee, B. J. Lester, A. T. Lill, W. Liu, W. P. Livingston, A. Locharla, F. D. Malone, S. Mandrà, O. Martin, S. Martin, J. R. McClean, T. McCourt, M. McEwen, X. Mi, A. Mieszala, K. C. Miao, M. Mohseni, S. Montazeri, A. Morvan, R. Movassagh, W. Mruczkiewicz, O. Naaman, M. Neeley, C. Neill, A. Nersisyan, M. Newman, J. H. Ng, A. Nguyen, M. Nguyen, M. Y. Niu, S. Omonije, A. Opremcak, A. Petukhov, R. Potter, L. P. Pryadko, C. Quintana, C. Rocque, P. Roushan, N. Saei, D. Sank, K. Sankaragomathi, K. J. Satzinger, H. F. Schurkus, C. Schuster, M. J. Shearn, A. Shorter, N. Shutty, V. Shvarts, J. Skruzny, W. C. Smith, R. D. Somma, G. Sterling, D. Strain, M. Szalay, D. Thor, A. Torres, G. Vidal, B. Villalonga, C. Vollgraff Heidweiller, T. White, B. W. K. Woo, C. Xing, Z. J. Yao, P. Yeh, J. Yoo, G. Young, A. Zalcman, Y. Zhang, N. Zhu, N. Zobrist, D. Bacon, S. Boixo, Y. Chen, J. Hilton, J. Kelly, E. Lucero, A. Megrant, H. Neven, V. Smelyanskiy, C. Gogolin, R. Babbush, and N. C. Rubin. Purification-based quantum error mitigation of pair-correlated electron simulations. *Nature Physics*, 19(12):1787–1792, Oct. 2023.

[39] R. M. Parrish, E. G. Hohenstein, P. L. McMahon, and T. J. Martínez. Quantum computation of electronic transitions using a variational quantum eigensolver. *Physical Review Letters*, 122(23), June 2019.

[40] K. Ramachandran, G. Deepa, and K. Namboori. *Computational Chemistry and Molecular Modeling: Principles and Applications*. Springer Berlin Heidelberg, 2008.

[41] B. Rost, B. Jones, M. Vyushkova, A. Ali, C. Cullip, A. Vyushkov, and J. Nabrzyski. Simulation of thermal relaxation in spin chemistry systems on a quantum computer using inherent qubit decoherence. *arXiv preprint arXiv:2001.00794*, 2020.

[42] A. Satoh. Chapter 3 - monte carlo methods. In A. Satoh, editor, *Introduction to Molecular-Microsimulation of Colloidal Dispersions*, volume 17 of *Studies in Interface Science*, pages 19–63. Elsevier, 2003.

[43] A. Sengupta, R. O. Ramabhadran, and K. Raghavachari. Breaking a bottleneck: Accurate extrapolation to "gold standard" ccsd(t) energies for large open shell organic radicals at reduced computational cost. *Journal of Computational Chemistry*, 37(2):286–295, 2016.

[44] D. Sherrill. Basis sets in quantum chemistry[lecture notes]. Course CHEM 6485: School of Chemistry Biochemistry, Georgia Institute of Technology.

[45] Y. Tachi, A. Arakawa, T. Osawa, M. Terabe, and K. Sugisaki. Supramolecular approach-based intermolecular interaction energy calculations using quantum phase estimation algorithm, 2025.

[46] F. Tarocco, P. A. B. Haase, F. Pavošević, V. Krishna, L. Guidoni, S. Knecht, and M. Stella. Aegiss – atomic orbital and entropy-based guided inference for space selection – a novel semi-automated active space selection workflow for quantum chemistry and quantum computing applications, 2025.

[47] M. A. Thompson and G. K. Schenter. Excited states of the bacteriochlorophyll b dimer of rhodopseudomonas viridis: A qm/mm study of the photosynthetic reaction center that includes mm polarization. *The Journal of Physical Chemistry*, 99(17):6374–6386, 1995.

[48] J. Toulouse. Quantitative quantum chemistry: Introduction to wave-function methods[lecture notes]. Course Master 5C208: Laboratory of Theoretical Chemistry, Sobornne University, 2025.

[49] H. Yukawa, H. Kono, H. Ishiwata, R. Igarashi, Y. Takakusagi, S. Arai, Y. Hirano, T. Suhara, and Y. Baba. Quantum life science: biological nano quantum sensors, quantum technology-based hyperpolarized mri/nmr, quantum biology, and quantum biotechnology. *Chem. Soc. Rev.*, 54:3293–3322, 2025.

[50] S. S. Zainab Anwar and K. McGregor. The intersection of quantum and biopharmaceuticals jobs report 2025: A look into the industrial niche cross-section and the labor pool availability in the sacramento valley. November 2025.

[51] L. Zhao, J. Goings, K. Shin, W. Kyoung, J. I. Fuks, J.-K. Kevin Rhee, Y. M. Rhee, K. Wright, J. Nguyen, J. Kim, and S. Johri. Orbital-optimized pair-correlated electron simulations on trapped-ion quantum computers. *npj Quantum Information*, 9(1), June 2023.