Quantum Computing for Drug Design

Where Quantum meets Chemistry:

Possibilities, Progress, and Practical Limits

qBraid

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Overview

Quantum computing holds immense promise for applications to large scale calculations in chemistry. Can the potential be tapped to improve the drug design process? What's real and what's hype? Join qBraid and SC Quantum to learn about this field. Beginning with the classical pipeline, this document examines where quantum technologies can improve the process, provides an overview of the state-of-the-art, and separates fact from fiction..

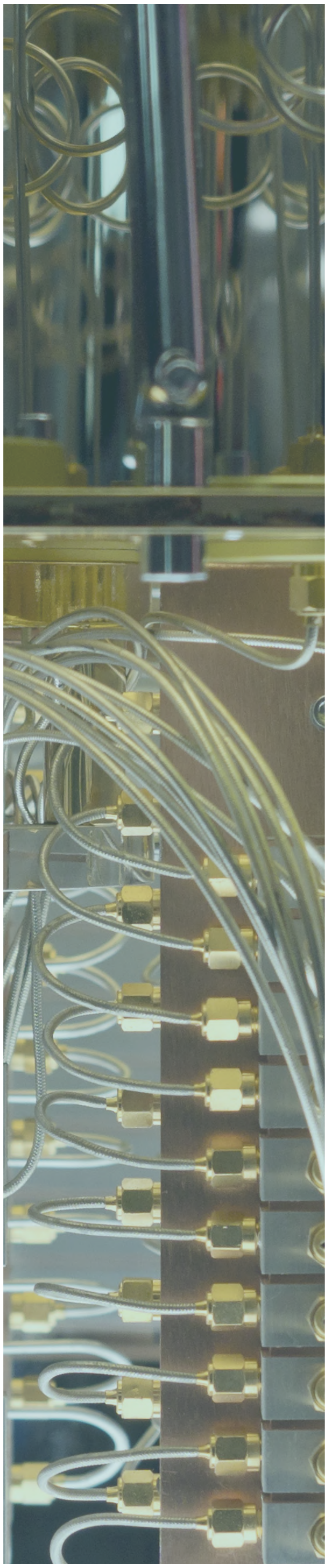
This white paper is part of a commissioned series from SC Quantum examining real-world case studies of quantum technologies deployed in industry. Developed in collaboration with qBraid, the series offers insight into how forward-looking organizations are integrating quantum solutions into their operations today. South Carolina Quantum (SC Quantum), a 501(c)(3) established in 2022, brings together academia, entrepreneurs, industry, and government to develop collaborative solutions that strengthen the state's position in a rapidly evolving field. https://qbraid.com | https://scquantum.org

01 - Classical Drug Design

Drug design is a long and complex process, sitting at the intersection of biochemistry, pharmacology, and manufacturing. Typically, it can take decades for a drug to reach the market after studies, human trials, and regulatory approval. The process starts with identifying the system of interest—for example, a protein that interacts incorrectly in the body or an enzyme that does not regulate function correctly. Then, the search begins for an ideal drug molecule that corrects the protein function. Of course, a lot is required of this molecule: it needs to be adsorbed, distributed, and metabolized by the body correctly, bind to the protein, and ultimately be excreted safely. This drug could emerge from many potential modalities such as small molecule, RNA, or gene therapy.

Suppose a drug is needed to fight Disease X. The first priority is to identify the causative pathology of the disease—for example, a specific protein (ABC) that is misbehaving. Next, the search begins for a small molecule (DEF) that inhibits this misbehavior. DEF must meet numerous criteria, often referred to as ADMET properties (absorption, distribution, metabolism, excretion, and toxicity). Typically, researchers identify this molecule by screening a large molecular library, gradually narrowing down candidates as selection criteria become more stringent. This rigorous process typically takes 7-10 years.

Once the lead candidate has passed these criteria, it is set to be tested in clinical settings. To ensure there are no delays in the process, it is crucial to thoroughly understand the mechanisms of pathology for the disease, protein-target interactions, and off-target interactions. How does protein ABC interact with DEF? How does ABC misbehave? Are alternative reactive pathways possible? Each of these questions is important, and requires significant chemistry and biophysics research.



02 - Quantum Computing: Why & How

Utilizing quantum algorithms can help the drug design process in two ways:

(1) Improving our understanding of binding, reactivity, and energetics with high accuracy calculations

(2) Exploring the space of molecules to access new molecules as potential targets

Algorithmically, these utilizations present two different approaches. The first involves hybrid chemistry algorithms where the goal is to get an accurate description of molecular interactions, electronic configurations, and ground and excited state energetics. These algorithms often evolve from classical chemistry methods and involve a classical component. Typically, they require using the Variational Quantum Eigensolver (VQE) or Quantum Phase Estimation (QPE) for the calculation, in conjunction with classical chemistry methods such as Density Functional Theory, Bootstrap Embedding, and Coupled Cluster. Quantum methods are required because higher accuracy classical methods (including quantum mechanical methods on classical computers) quickly become computationally intractable. The second approach is a search optimization problem. Finding the right molecule is like finding a needle in a haystack, and quantum algorithms can help in the search process. This family of search algorithms can also help with protein structure prediction for protein structures, where physics-inspired quantum search algorithms can help traverse the energy landscape, potentially provide more nuance and higher-stability structures than alternatives.

With these approaches, it is important to note that quantum computing is not being used as a replacement or alternative for the entire in-silico component of the drug discovery pipeline. That is neither feasible nor advisable. Instead, researchers are using quantum computing algorithms to target specific areas where classical methods have fallen short or are too expensive, to improve our understanding of protein interactions. In the long run, this improved mechanistic and energetic understanding can aid our search for target molecules, improve therapeutic modalities, and speed up the overall drug discovery process.

03 - Challenges

Utilizing quantum technologies for drug design has similar challenges to those faced by the broader quantum industry: shortage of qubits, noise and decoherence, and computational cost. For example, calculations on proteins, even with nuanced approximations, can easily require 100s of qubits, and with current noise and coherence times, obtaining meaningful results can be challenging. Active research is being pursued across all fronts: (1) improving algorithms to require shallower circuits, reduced weight terms (2) improving hardware to increase coherence times (3) improving error correction, detection, and suppression techniques to measure despite noise.

However, this field also faces some unique challenges, arising from the biochemical context of the problem. Proteins are large, often highly disordered, and to model them with correct physiological effects, one must include solvation effects. Practically, this means accounting for the presence of water molecules, explicitly or implicitly, around the protein, greatly increasing the size of the calculations. Furthermore, since we are focused on protein behavior within the human body, calculations must account for the effects of temperature, requiring extensive thermodynamic and kinetic calculations in addition to single-point energetics.

Despite these challenges, quantum computing for pharmaceutical applications certainly holds great promise, and increasingly more companies are investing in it. For example, Cleveland Clinic is working with IBM to have the first dedicated quantum computer for health care research.

04 - Current Landscape

Broadly, the landscape of quantum technologies for drug design is promising and rapidly evolving. Pharmaceutical companies, such as Genentech and Boeringer Ingelheim, have active quantum research programs. Conversely, quantum companies are also expanding research to pharmaceutical applications. Research programs like Wellcome Leap's Quantum4Bio are furthering research efforts in this direction, in addition to building a strong community of researchers from various fields. Established chemical companies are exploring this field too: Merck, in partnership with HQS Quantum Simulations, is developing more cost-effective drug discovery pipelines.

Quantum computing can have a significant impact on other rapidly developing methods as well, such as using Artificial Intelligence (AI) for predicting protein structure or Machine Learning (ML) for target identification. It is estimated by 2030 that of the $1.3 trillion valuation of the quantum industry, more than $180 billion will come from the life sciences, where R&D holds the most promise.

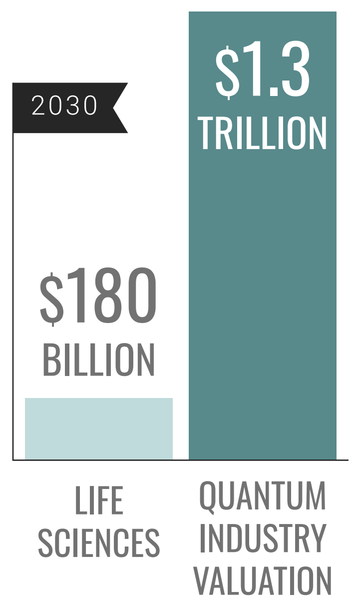


Figure: By 2030, $180B of the $1.3T quantum industry valuation will come from life sciences, where R&D holds the most promise.

05 - South Carolina Landscape

Pharmaceutical companies in South Carolina are incredibly well-positioned to introduce quantum computing to their research pipelines. For example, companies like Accellacare, Cosciens Pharmaceutical, Zylo Therapeutics, Senex Biotechnology, Alcami, and Ascenth are already at the forefront of cutting edge clinical, small molecule, and peptides research. Utilizing quantum computing to identify peptide APIs, improving property prediction for small molecules, optimizing drug delivery pathways, and refining diagnostics tools are all concrete possibilities for pharmaceutical companies to drive research breakthroughs.

06 - Use Case

At qBraid, researchers have explored how quantum algorithms can help our understanding of the pathogenesis of Alzheimer's Disease. Neurodegeneration in Alzheimer's is complex. Despite decades of in-silico and experimental research, we do not fully understand how amyloid-beta, a protein in the body, interacts with metal ions surrounding it. It has has been hypothesized that incorrect binding with metal ions is related to amyloid-beta aggregating and forming plaques in the brain, which has been linked to memory loss. We hope to better understand the mechanism of protein-metal binding using quantum algorithms.

qBraid has worked alongside researchers from the University of Chicago, Massachusetts Institute of Technology, Argonne National Laboratory, NVIDIA, North Carolina A&T, and the University of Wisconsin-Madison to develop a pipeline called Quanta-Bind. This pipeline starts with a protein, breaks it down into tractable smaller computational fragments, and then studies binding with high accuracy quantum methods within each fragment. Quantum Bootstrap Embedding and Localized Active Space methods are used to treat electronic correlation, while Generalized Superfast Encoding is used to map molecules to qubits. While this work is ongoing, it provides excellent potential to deeply study the binding mechanisms of strongly correlated systems in the human body. Interestingly, this pipeline is highly generalizable, and can be used to study large, strongly correlated systems not limited to amyloid-beta. qBraid places a high value on collaborative research. While challenging, the work holds immense promise for advancing applications of quantum computing in the drug design process.

07 - Recommendations

With such a dynamic and rapidly growing landscape, it is important to invest in quantum technologies early. It can be daunting to start, but there are already steps that can be taken.

Here are a few recommendations, if you're on the business side:

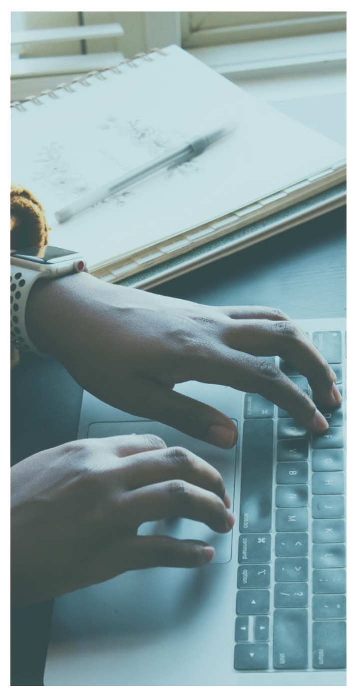
- Start early: Don't let caution be the enemy of growth. Foster broad awareness and engagement with quantum technologies among leadership teams and encourage all workers to explore quantum technologies.
- Build quantum expertise: Explore and implement training options to ensure your teams are quantum-literate and quantum-ready to create and maintain a competitive advantage through proper use cases.
- Identify concrete applications: Become proficient as an organization in evaluating how quantum techniques can help your company meet your goals. Focus on separating hype from reality, and identify clear use cases.

If you're on the technical side, here are a few recommendations to get started:

- Refresh and develop new skills: Refresh your quantum skills or upskill by taking courses in quantum mechanics, programming, and applications.
- Attend conferences: Quantum computing is a fast-evolving landscape, so meet fellow scientists, researchers, and engineers at conferences. Connect with them to explore collaborations and keep up with research.
- Connect with domain experts: Be aware of domain experts and existing work being done in your field. Keep abreast of technological advancements, papers, and patents in your domain.

08 - What's Next?

Whether you're building quantum expertise, identifying use cases, refreshing and developing skills, or connecting with domain experts, qBraid offers tools to help you take the next step through interactive courses, a cloud-based sandbox, and ready-to-use tutorials. They're designed to get you moving quickly. To learn more or schedule a conversation, visit qbraid.com. If you want to plug into quantum momentum in South Carolina and across the Southeast, visit scquantum.org. Getting started in quantum can feel complex, but with the right partners, the path forward becomes clear, more collaborative, and more rewarding than it might seem at first.



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