FEATURE

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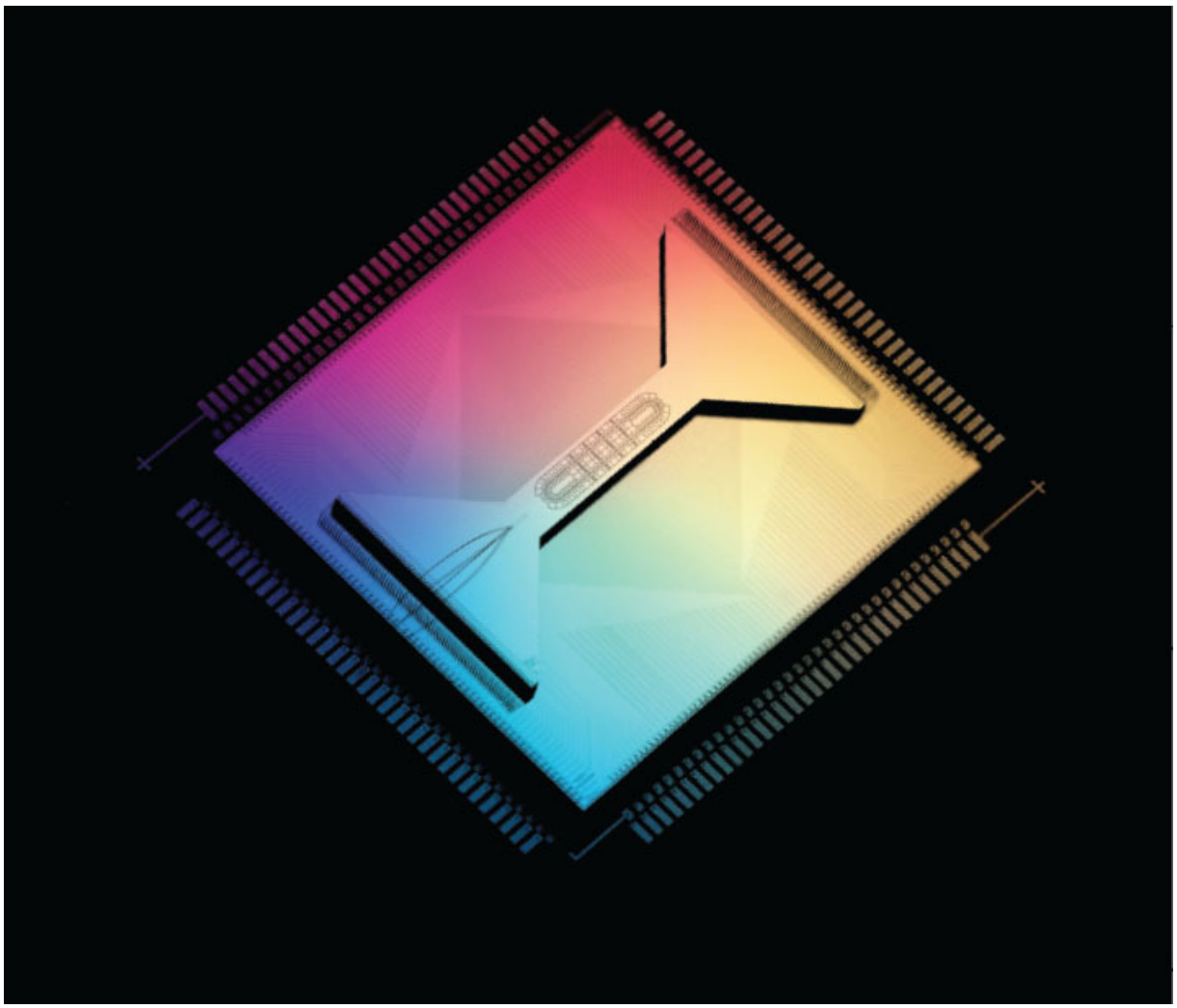
Compound interest

Practical uses for quantum computers are emerging in chemistry, promising to speed the development of materials, catalysts, and drugs

By Robert F. Service, in Broomfield, Colorado

Featured



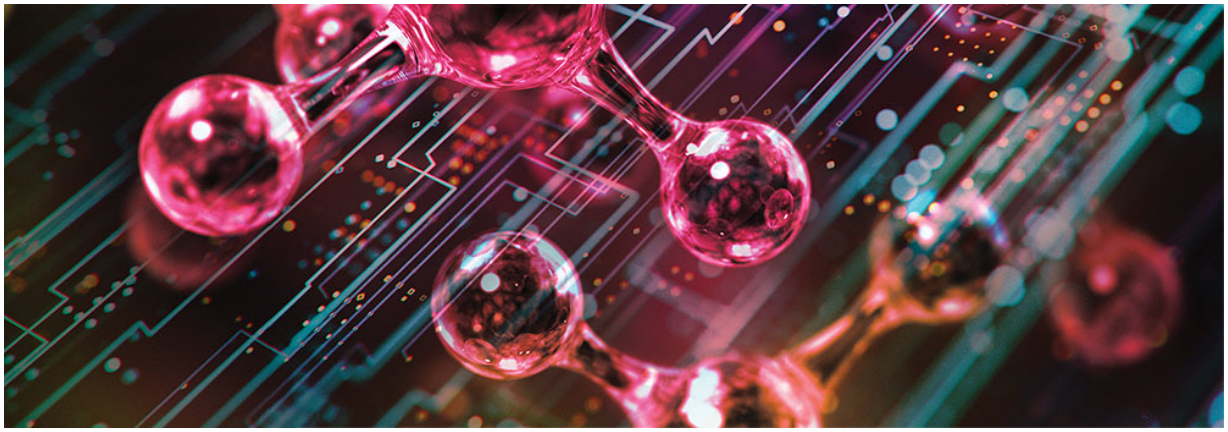
In Quantinuum's H2 chip, ions hovering above a tiny, central "racetrack" can compute molecular structures. IMAGE: QUANTINUUM

The core of this quantum computer looks familiar enough: a silicon chip the size of a stamp. But the resemblance to your laptop ends there. The chip, cocooned within a vacuum chamber and cooled nearly to absolute zero, is patterned with 198 gold electrodes, arranged like an oval racetrack.

Above the racetrack, a handful of ytterbium ions are trapped and levitated by a train of electrical, radiofrequency, and laser pulses. Subsequent manipulations impart specific amounts of energy to the ions and coax them to interact with one another to carry out a sequence of logical operations. A final burst of laser pulses nudges each ion to either fluoresce or not—a flash of binary code that detectors read out as the computation's solution.

Last year, researchers here at Quantinuum, a quantum computing startup, used a chip with eight ytterbium ions to compute the precise arrangement of a hydrogen molecule's two electrons in their most stable state, out of myriad possible configurations. In and of itself, that computational feat is barely worth noting; a typical laptop can manage it in seconds. But it marked the first demonstration of an advanced quantum simulation that's expected to perform better—and take on more complex molecules—as quantum computers grow more powerful.

The achievement shows how quantum computers are tentatively moving from the realm of mere promise to tackling real-world challenges. Quantinuum is one of many companies that believes applications in chemistry—particularly the hunt for novel drugs and catalysts—will be among the very first practical tasks for these new machines. They are ideally suited for predicting the structure and behavior of molecules, researchers say, because both the machines and the molecules are ruled by the counter-intuitive laws of quantum mechanics.



Molecules and quantum computers, both governed by the laws of quantum mechanics, are inherently aligned. IMAGE: BLACKJACK3D/ISTOCKPHOTO, KOTO FEJA/ISTOCKPHOTO, ADAPTED BY C. SMITH/*SCIENCE*

"We are currently using chemistry problems to advance quantum computing instead of using quantum computing to advance chemistry," says Quantinuum's head of strategy, Chad Edwards. "But there will be a tipping point," where those roles will be reversed. "There has been a clear speedup in the past year," agrees quantum physicist Louis-Paul Henry at PASQAL, a quantum computing startup based in Paris that is also focusing on chemistry. "More and more people are talking about applications and taking a look at harder problems relevant for real world uses."

Already, quantum computers are helping researchers zoom in on reaction pathways in fuel cell catalysts, simulate the infinitesimally brief interactions of light and matter, and reveal druggable pockets in proteins. Ashley Montanaro, a co-founder of Phasecraft, a quantum computing company, says today's quantum computers are almost good enough to make discoveries beyond the reach of classical systems. "It's a lot closer than people previously thought."

WHERE STANDARD computers manipulate bits of data as either 0s and 1s, quantum computers rely on "qubits," which can encode data as a 0, a 1, or any combination of the two states in a simultaneous "superposition." In the case of Quantinuum's computer, the qubits are the electrons in the ytterbium ions, which can hover in a superposition of two different energy levels. During a computation, multiple qubits are "entangled" so their energy states influence one another, making it possible to evaluate all their possible interactions simultaneously

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Quantinuum founder Ilyas Khan likens a classical computation to a mouse navigating a maze, taking one random turn after another in a trial-and-error search for the correct path through. A quantum computer, he says, has a bird's-eye view of the same maze, which makes it easier to see the optimum pathway all at once. And verifying the solution is as easy as testing the molecular structure or behavior revealed by the quantum computer. "You know you're at the end because you've got the piece of cheese," Khan says. Linking together even a few hundred qubits should enable fantastically complex calculations.

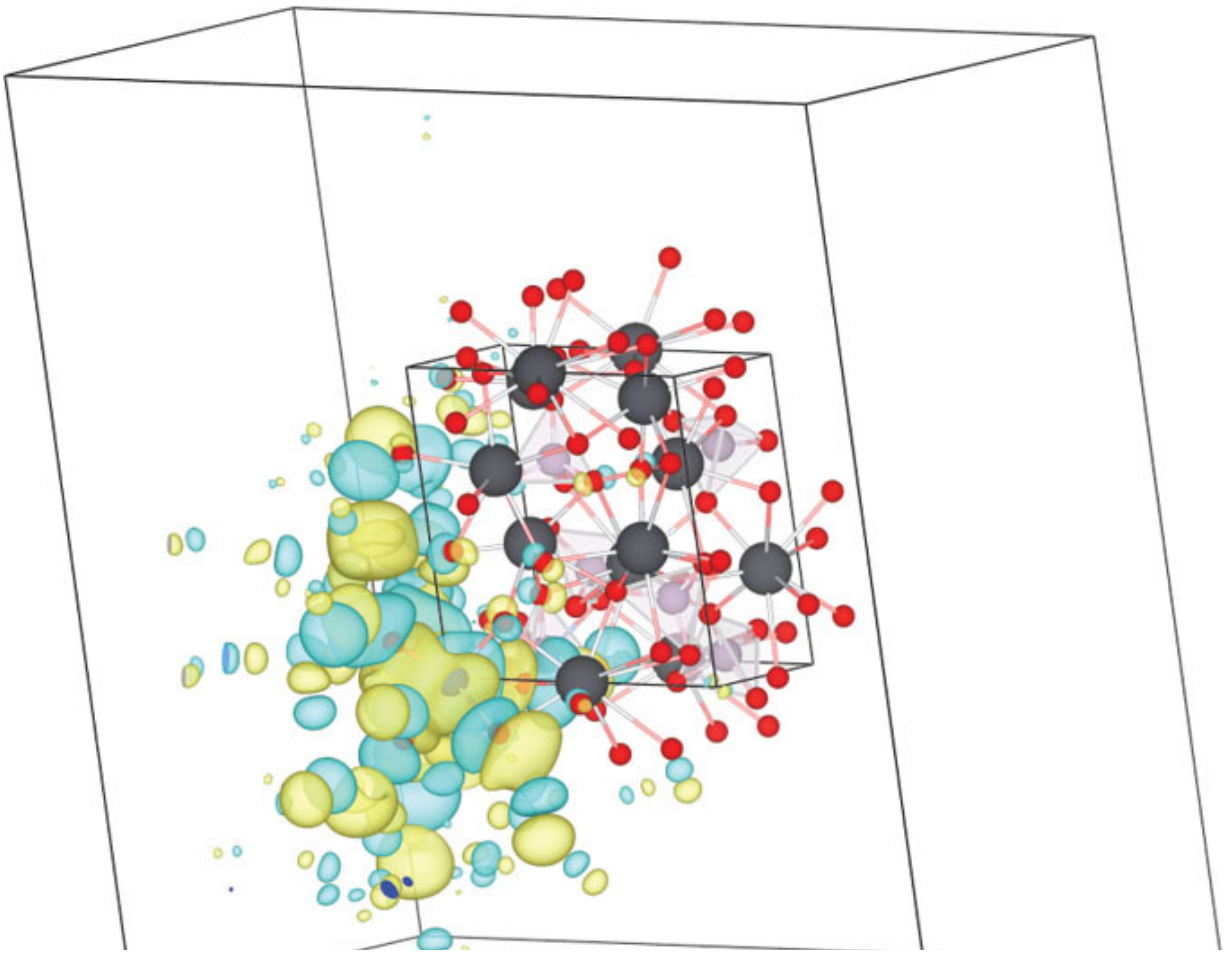
The challenge is that qubits are fragile: The slightest jostle by an air particle, a modicum of heat, or even a stray cosmic ray can upset a qubit's superposition state, creating an error that throws off the result. Researchers minimize these influences by chilling qubits and isolating them from their environment. They also build in redundancy. Even though today's quantum computers may link up dozens or hundreds of qubits, only a fraction of them perform logical operations, whereas the rest correct errors.

Even so, the machines are getting more powerful. Last year, IBM unveiled a computer with 1121 qubits based on tiny superconducting circuits, up from a 127-qubit version released in 2021. Atom Computing, a California startup, went one better, last year presenting a 1180-qubit computer that relies on the spins of neutral ytterbium atoms.

Others are striving for improved accuracy. In December 2023, researchers at Harvard University, working with a 280-qubit computer from QuEra, another neutral atom startup, reported that reduced error rates in their system enabled them to encode up to 48 logical qubits and faithfully carry out hundreds of operations before the quantum house of cards collapsed, a major improvement over prior setups. And last month, Quantinuum scientists reported that a new Microsoft algorithm dramatically improved their ability to detect and correct errors in their latest 32-qubit ion chip. "The hardware advances are [coming] fast enough that they could soon impact the number of applications achievable," says Prineha Narang, a quantum computing expert at the University of California, Los Angeles.

MANY RESEARCHERS expect those applications to emerge from chemistry. The properties of chemical compounds and materials are governed by the making and breaking of chemical bonds, the motion of electrons, and magnetic behaviors—all of which are dictated by quantum mechanics. Researchers can deduce the behavior of a molecule by solving its Schrödinger equation, which in part describes the probabilistic, wavelike behavior of electrons and their interactions with atomic nuclei, based on inputs such as electron energy levels and chemical bond lengths.

Classical computers have managed the calculation for molecules as large as pentacene, a chain of five hydrocarbon rings with 22 electrons in “pi” covalent bonds, which govern the molecule’s shape and reactivity. But the classical calculation relies on approximations, and for larger molecules inevitable errors compound, throwing off the results. Quantum computers, by contrast, need not use these fudge factors, and instead can directly map the interactions between electrons and nuclei onto qubits, using actual quantum systems to represent their kin. “There is an inherent alignment between quantum systems and quantum computing,” Edwards says.



Researchers at Phasecraft depicted what a quantum computer would need to simulate the behavior of electrons (yellow and blue) around atoms in a proposed superconductor (red and gray). IMAGE: PHASECRAFT

Another reason chemistry is a good match for quantum computing is that the problems can often be narrowly constrained, putting them within reach of the small quantum computers available today. A researcher may only need to focus on the interaction of a handful of electrons to understand how a drug molecule binds to its protein target. “The best problem for a quantum computer has a small problem size,” with many possible outcomes, says Brian Bilodeau, chief operating officer of Microsoft’s quantum group.

Given the still-modest capabilities of today’s quantum computers, researchers aren’t asking them to do all the computational lifting by themselves. Instead, most scientists pursue hybrid approaches that marry quantum and classical processors. “The reality is it will be a hybrid world,” Bilodeau says.

Today’s most popular hybrid, an algorithm known as a variational quantum eigensolver (VQE), uses classical computers to approximate a molecule’s stable ground state, the lowest energy configuration that is key to its structure and how it interacts with neighbors. Then a quantum computer takes over to find the ground state’s precise solution. But today’s error-prone quantum computers typically struggle with VQEs. The largest VQE simulation came in 2020, when Google researchers modeled the behavior of the 12 electrons in a molecular chain of 12 hydrogen atoms. That approaches but still falls short of the classically modeled pentacene and its 22 pi electrons.

But new and improved hybrid algorithms are gaining momentum. In 2022, Google scientists unveiled one that could compute ground states for up to 120 interacting electrons in substances such as molecular nitrogen and solid diamond. The algorithm used a classical computer to explore random variations in the electron interactions, and a quantum computer to guide the classical system to a precise result. But it did not achieve enough accuracy for the

researchers to claim a quantum advantage over classical approaches.

CHEMISTS ARE NOW pushing these hybrid setups toward the discovery of new materials and catalysts, and even understanding mysterious light-driven reactions. In a January report in *Nature Communications*, researchers at Phasecraft described yet another hybrid algorithm that harnesses a quantum computer to simulate the structure and electronic behavior of crystalline materials, whose repeating structures make them easier to model. In one such analysis, Phasecraft researchers found that their new algorithm should require 1 million–fold fewer computational steps than existing VQEs to accurately model strontium vanadate, a promising new battery electrode material. Although quantum computers are not yet good enough for Phasecraft to apply the algorithm, it could in theory reveal ways to tweak strontium vanadate's structure and improve batteries.

The reaction surfaces of catalysts, which speed up chemical reactions, are another target for this early work. In a July 2023 preprint on arXiv, Quantinuum researchers reported using a hybrid setup to explore the chemical reactivity of platinum-based catalysts, which are commonly used in fuel cells to generate electricity by converting hydrogen and oxygen into water. Platinum is expensive and rare, so researchers would love to ramp up its catalytic speed, allowing fuel cells to use less of the metal, or better yet replace it altogether with a cheaper substance.

To do so they need to understand how the platinum works—how oxygen and hydrogen adsorb to the catalyst, how they transfer electrons and protons through intermediate compounds, and how they finally react to form water molecules, which then dissociate from the catalyst. The computations have proved too tall a task for classical computers alone. So, researchers led by Quantinuum quantum chemist David Muñoz Ramo improved the accuracy of their simulations. First they used classical computers to model how molecules adsorb and desorb from catalyst particles; then they applied their quantum computer to identify the most likely reaction pathway of the electrons and protons involved. Although the approach hasn't yet discovered new fuel cell catalysts, Muñoz Ramo says the results of such simulations should only grow more powerful as quantum computing hardware improves.

Quantum algorithms also enable researchers to investigate basic questions in chemistry. Last year, for example, quantum researchers simulated how light and matter interact, a process central to vision and photosynthesis. They targeted a photochemical reaction in which molecules absorb energy from photons and transfer it to a neighbor. The energy transfer occurs in mere femto-seconds, or quadrillionths (1015) of a second, too fast to observe. Classical computers can simulate how multiple photons interact, but only a few at a time, because of the computational intensity.

So, Ting Rei Tan, a physicist at the University of Sydney, and colleagues used a trapped ion quantum computer to simulate how a single quantum "wave packet" of energy moves between neighboring molecules. That effectively slowed the process down 100 billion–fold and made it possible to simulate one of the events. With a more powerful quantum computer, the team should be able to model more of the reactions and surpass the classical technique. "We are approaching a quantum advantage," Tan says.

IN THE NEAR TERM, quantum computing could have its biggest impact in drug development. Today, developing a new drug takes an average of 12 years and costs more than $2 billion. Drug companies are looking for any advantage they can get in finding the next blockbuster, Edwards says. Already, Roche, Pfizer, Merck, Biogen, and other industry giants have formed early partnerships with quantum computing companies, hoping the new technology will accelerate discovery. "I'm absolutely convinced that it is coming," says Mark Fingerhuth, who heads R&D for drug developer ProteinQure.

> "Once quantum computing capabilities improve, it will become an integral part of drug discovery."
>
> Petrina Kamya, Insilico Medicine Canada

Some of those partnerships are starting to generate early results. In September 2023, researchers at PASQAL and Qubit Pharmaceuticals posted a preprint

describing a hybrid approach to tracking the water molecules that surround proteins, which can indicate the locations of drug-binding pockets. The researchers first narrowed the problem by using a classical algorithm to track the density of water molecules in and around a liver protein called major urinary protein-1 (MUP-1), which belongs to a class of proteins that has been considered undruggable. They then used PASQAL's quantum computer to pin down the specific location of water molecules in potential drug-binding pockets of MUP-1, setting the stage for using the same approach to identify druggable targets for proteins involved in diseases.

Meanwhile, in May 2023, researchers at Gero, another drug development company, reported in *Scientific Reports* that they used a quantum computer to more realistically simulate the electronic properties of likely drug targets, such as the distribution of positive and negative charges across molecules and the arrangement of weak chemical bonds called Van der Waals forces between neighboring atoms. They fed those constraints to artificial intelligence (AI) software running on classical computers, which came up with more than 2300 druglike molecules that could take aim at those targets. Although the results are just a proof of concept, Gero scientists noted how their quantum-AI hybrid showed its promise by homing in on chemical structures common to the best medicines. "If you solve the hard part with a quantum computer the other part becomes easy with classical AI," says Gero CEO Peter Fedichev.

A sharper picture of interactions between potential drug molecules and their protein targets is also the goal for drug developer Insilico Medicine. Insilico researchers reported in February that their hybrid algorithm, running on IBM's 16-qubit quantum computer, could help find new inhibitors of a cell-signaling protein called KRAS that's commonly mutated in cancers. After the algorithm had designed and ranked 1 million different potential KRAS inhibitors, the researchers synthesized 15 of the most promising candidates. Cell-based tests showed two of those compounds worked well, setting the stage for further testing.

Finding novel medicines isn't the only goal. Researchers at PASQAL also hope to forecast which drug candidates will fail. Even when would-be drugs excel in lab studies, many trigger toxic side effects when tested in people. Weeding out toxic drugs before human trials could save companies millions of dollars. In an initial

attempt, Henry and his PASQAL colleagues used their 32-qubit computer to predict the toxicity of 286 compounds by modeling their structure in high resolution and comparing them with 349 compounds known to cause cancer in mice. In an April 2023 paper in *Physical Review A*, they reported that their quantum algorithm gave results comparable to the best classical alternatives. “We are solving a real problem with a real biochemistry data set,” says Loïc Henriet, PASQAL’s chief technology officer.

The early work is just a taste of what may come with bigger and better machines. Google and IBM have road maps suggesting scientists will soon have hundreds of thousands of qubits at their disposal. And Quantinuum says it’s close to releasing a new quantum chip, trading in the racetrack for a larger 2D grid that can handle more of their high-fidelity ion qubits. Chemists have high hopes. “We think there is a lot of work to be done in this way to accelerate chemistry and drug discovery,” Bilodeau says. “We are just at the inflection point.”

The field of quantum computing itself stands to benefit, as researchers in other fields see that the exotic technology has down-to-earth payoffs. “Once quantum computing capabilities improve, it will become an integral part of drug discovery,” says Petrina Kamya, president of Insilico Medicine Canada. “It’s here to stay.”