The Road to Quantum Computing

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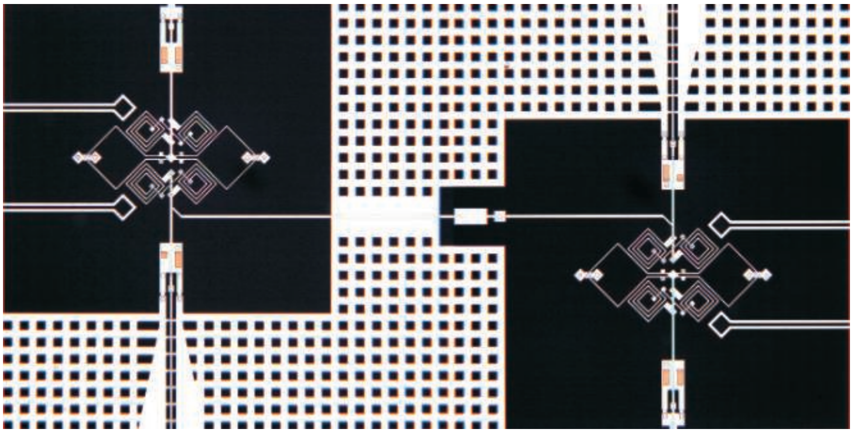
Quantum computers will be able to perform calculations that ordinary computers will never be able to, such as factorizing very large numbers (*1*). However, building a quantum computer is not easy. On page 1299 of this issue, McDermott *et al.* (*2*) report an important step toward a macroscopic version of such a computer.

The basic elements of the quantum computer are quantum bits (qubits) that, similar to ordinary bits, have two states. However, in contrast to ordinary bits, qubits can exist in combinations of states called quantum superpositions. To operate a quantum computer, one must be able to drive the qubits from any state to any other in a controlled manner. Also, one must be able to couple qubits in ways that lead to entanglement—an action-at-a-distance between quantum objects predicted by quantum theory that has been observed with photons and atoms.



Two fabricated quantum bits. The superconducting qubits with their control and measuring circuitry are situated at the left and right. They are coupled by a capacitor (white rectangle in the center). The qubits themselves are too small to be seen at this scale. The circuit is fabricated with standard semiconductor techniques.

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Photons and atoms are obvious candidates for qubits. But for large quantum computers, it may be advantageous to use macroscopic qubits that can be fabricated with the tools of the semiconductor industry. Superconducting systems are particularly promising. Using such a system, McDermott *et al.* (*2*) report the simultaneous readout of two coupled qubits, with tools that can in principle be scaled up to a large computer. The study is an important step toward the use of artificially made objects to realize two-qubit quantum gates that perform all the needed operations for the execution of any quantum algorithm.

The qubits in question consist of a superconducting Josephson tunnel junction through which a constant current is passed. In a Josephson junction, a thin insulator is sandwiched between two superconducting metal films. The current between the two films is controlled by the phase difference between them. If the phase difference varies in time, there is a voltage between the two films. Because the junction also acts as an electrical capacitance, this voltage leads to an electrical charging energy. A phase difference across the junction increases the energy, causing an oscillation with a frequency that is determined by the parameters of the junction. In such a quantum oscillator, the amplitude of oscillation is limited to a discrete set of values.

The potential well in which the oscillation takes place is a metastable energy minimum, which is separated from the global minimum by an energy barrier. The height of that barrier decreases with increasing current. To detect the state of the qubit, the current through the junction is suddenly increased slightly. If the qubit is in the excited state, the junction has just enough energy to cross the barrier. The crossing of the barrier induces an observable change in a secondary circuit, which behaves almost classically and can be read out at a later stage (*3*).

The qubits described above are known as phase qubits. Other types of superconducting qubits have also been reported (*4*); charge qubits are defined by the presence or absence of a single pair of electrons, whereas in flux qubits, a persistent circulating current runs clockwise or anticlockwise. With all three types, controlled, driven transitions of individual qubits have been demonstrated. However, further improvements are needed. All solid-state quantum bits can easily couple to noise from the outside world, particularly from circuit elements that are at a higher temperature than the qubit (which operates at a temperature of about 30 mK). Quantum information is lost after a "decoherence time" of typically 0.1 to 1 μs. Qubit operations take 1 to 10 ns (1 ns = 10^{-9} s). The ratio between the two time scales must be increased to get a usable quantum computer. The measurement procedure is especially important: Strong coupling to the measuring device brings in decoherence, whereas weak coupling makes it difficult to determine the qubit state unequivocally. The quantum engineer has to optimize both the contribution to decoherence and the expected quality of readout.

The main bottleneck for the further development of superconducting qubits is the quality of the thin insulator. In today's devices, the insulator is an oxide that is either amorphous or an imperfect crystal. It therefore contains defects that move with time and that become ionized and deionized. Because transport through the insulator depends exponentially on its thickness and materials properties, displacement of just one atom over microscopic distances can have far-reaching consequences. The rate of the resulting decoherence cannot be calculated. Epitaxial or other high-quality junctions may overcome these problems. Also, different types of defects have a different influence on the various types of qubits; which qubit will be used for particular applications may therefore depend on these materials-related noise sources.

To advance from a single qubit to a full quantum computer, one first has to realize a universal two-qubit gate, preferably a quantum controlled-not (C-NOT) gate. Superconducting qubits are not there yet, but with the new results of McDermott *et al.* (*2*), they are getting close. In classical electronic circuits (with ordinary bits that can be in the 0 or the 1 state), a C-NOT gate is a conditional two-bit gate: One bit flips from 0 to 1 or vice versa if and only if the other bit is in the 1 state. The quantum C-NOT gate is particularly desirable, because all quantum

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Published by AAAS

algorithms can be realized, at least on paper, by combining C-NOT gates with single-qubit operations.

A C-NOT gate has previously been realized with superconducting charge qubits (*5*). However, that gate could only start from specific positions (for example, with both qubits in the 0 state), did not provide the universal operations, and cannot easily be extended to provide them. It was therefore not suitable for building a large quantum computer. The qubits of McDermott *et al*. (*2*) have the potential to yield C-NOT or similar two-qubit gates for the universal quantum computer.

The experiments of McDermott *et al*. (*2*) have several special features. Particularly attractive is the well-controlled readout. Measuring one qubit does not, as in many other schemes, disturb the whole system. Measurement of the qubit yields an up/down digitized signal, which is first stored as a current in a superconducting loop situated on the chip next to the qubit. The transfer from the qubit to the secondary circuit has to be fast, because the relaxation time of the qubit is on the order of 100 ns. The initial transfer creates only a weak disturbance and can be performed in parallel on the two qubits. The readout of the secondary circuits takes place later. The up/down signals in the secondary loops are quite robust, and measurement of one signal does not influence the other. The whole process makes it possible to perform quantum operations on the coupled system and afterwards determine the state of both qubits simultaneously.

The new experiments (*2*) do not yet demonstrate the complete two-qubit gate that is required for a quantum computer. To do so, one would have to determine the outcome after a specific set of microwave pulses is applied to the qubits, starting from different initial conditions. Also, the amplitudes of the oscillations observed in (*2*) are smaller than is acceptable for applications. Nevertheless, the study is a substantial advance. The simultaneous measurement of two qubits opens the possibility of testing the concept of entanglement for artificially fabricated quantum objects. The results prove that two-qubit operations in which quantum information is shared and manipulated are possible in solid-state qubits that can, in principle, be used to build a large quantum computer.

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10.1126/science.1109554

MICROBIOLOGY

A Pathogen Attacks While Keeping Up Defense

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Many Gram-negative bacteria interact with human, animal, or plant hosts by injecting effector proteins into the cytosol of host cells through the so-called type III secretion system (injectisome) (*1*). The symptoms of infectious diseases, such as bubonic plague, shigellosis, salmonellosis, typhoid fever, and infantile diarrhea, largely depend on the repertoire of bacterial proteins injected by the type III secretion system, and what they do once inside eukaryotic host cells. The injectisome is remarkably well conserved among different bacterial pathogens (*2*). The multicomponent base structure spans the bacterial periplasm and is associated with both the inner and outer membranes of the bacterium (see the figure) (*3*). The filamentous needle, composed of a single protein, projects beyond the bacterial surface. For bacterial effector proteins to be translocated into host cells, the tip of the needle must make contact with the eukaryotic host cell membrane.

The enteric pathogen *Shigella flexneri* possesses a type III secretion system that enables invasion of the gut epithelial cells of mammalian hosts. Invasion provokes an extensive inflammatory reaction in the gut mucosa, a hallmark of shigellosis (bacterial dysentery) (*4*). To survive host inflammatory processes such as increased production of antibacterial peptides, *Shigella* is equipped with a lipolysaccharide structure in its outer membrane that contains protective repeat units of an O-antigen polysaccharide (see the figure). This O-antigen polymer extends beyond the bacterial cell surface and potentially could sterically impede the type III secretory apparatus. However, as West *et al.* (*5*) reveal on page 1313 of this issue, *Shigella* has developed an ingenious way of ensuring that its injectisome needle remains operational without compromising the ability of the O-antigen polymer to protect against host inflammatory mediators.

West *et al.* (*5*) used signature-tagged mutagenesis (*6*) to identify colonization-defective *S. flexneri* mutants in a rabbit model of shigellosis. From these attenuated mutants, they identified two genes residing on the *gtrA*, *gtrB*, *gtrV* operon of a resident bacteriophage (*7*). This operon directs the addition of a glucose residue to each O-antigen repeat unit; this glucosylation step imparts serotype specificity to different strains of *S. flexneri*. Substantially attenuated virulence was observed in glucosylation-defective *gtr* mutants of different serotypes; virulence could be restored by introducing a serotype-specific *gtr* operon. The *gtr* mutants could still produce lipopolysaccharide with the correct number of O-antigen repeats, and could withstand noxious conditions in the gut such as bile salts, complement-mediated lysis, and gut-specific antibacterial peptides. However, compared with wild-type *S. flexneri* carrying glucosylated O-antigen, the *gtr* mutants were considerably less invasive and were less able to provoke an inflammatory response, suggesting a defect in the type III secretion system. An IpaB monoclonal antibody, recognizing the tip of the needle complex, revealed a much lower exposure of the needle at the bacterial cell surface in the glucosylation-defective *gtr* mutants.

How does bacteriophage-mediated glucosylation of the O-antigen affect exposure of the type III secretion needle? West *et al.* used electron microscopy and three-dimensional molecular modeling to show that O-antigen glucosylation results in a conformational change, from a linear extended form of the repeating O-antigen polymer to a more compact structure (see the figure). This modification allows surface exposure of the protruding needle (which is roughly 60 nm long), without compromising the protective role of the O-antigen polymer.

Shigella species cause more than 1 million deaths per year from dysentery and diarrhea, and multidrug resistance of these bacteria is a rising problem. The type III secretion system of *Shigella* and other Gram-negative pathogens is an attractive target for development of new antivirulence drugs. Salicylanilides have been identified as potent inhibitors of type III secretion in the bacterium *Yersinia*, one species of which causes bubonic plague (*8*). The West

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