Oak Ridge National Laboratory in Tennessee (see go.nature.com/35zfbuu). Summit is currently the world's leading supercomputer, capable of carrying out about 200 million billion operations per second. It comprises roughly 40,000 processor units, each of which contains billions of transistors (electronic switches), and has 250 million gigabytes of storage. Approximately 99% of Summit's resources were used to perform the classical sampling.

Verifying quantum supremacy for the sampling problem is challenging, because this is precisely the regime in which classical simulations are infeasible. To address this issue, Arute *et al.* first carried out experiments in a classically verifiable regime using three different circuits: the full circuit, the patch circuit and the elided circuit (Fig. 1). The full circuit used all n qubits and was the hardest to simulate. The patch circuit cut the full circuit into two patches that each had about $n/2$ qubits and were individually much easier to simulate. Finally, the elided circuit made limited two-qubit connections between the two patches, resulting in a level of computational difficulty that is intermediate between those of the full circuit and the patch circuit.

The authors selected a simplified set of two-qubit gates and a limited number of cycles (14) to produce full, patch and elided circuits that could be simulated in a reasonable amount of time. Crucially, the classical simulations for all three circuits yielded consistent XEB fidelities for up to $n = 53$ qubits, providing evidence that the patch and elided circuits serve as good proxies for the full circuit. The simulations of the full circuit also matched calculations that were based solely on the individual fidelities of the single-qubit and two-qubit gates. This finding indicates that errors remain well described by a simple, localized model, even as the number of qubits and operations increases.

Arute and colleagues' longest, directly verifiable measurement was performed on the full circuit (containing 53 qubits) over 14 cycles. The quantum processor took one million samples in 200 seconds to reach an XEB fidelity of 0.8% (with a sensitivity limit of roughly 0.1% owing to the sampling statistics). By comparison, performing the sampling task at 0.8% fidelity on a classical computer (containing about one million processor cores) took 130 seconds, and a precise classical verification (100% fidelity) took 5 hours. Given the immense disparity in physical resources, these results already show a clear advantage of quantum hardware over its classical counterpart.

The authors then extended the circuits into the not-directly-verifiable supremacy regime. They used a broader set of two-qubit gates to spread entanglement more widely across the full 53-qubit processor and increased the number of cycles from 14 to 20. The full circuit could not be simulated or directly verified in a reasonable amount of time, so Arute *et al.* simply archived these quantum data for future reference – in case extremely efficient classical algorithms are one day discovered that would enable verification. However, the patch-circuit, elided-circuit and calculated XEB fidelities all remained in agreement. When 53 qubits were operating over 20 cycles, the XEB fidelity calculated using these proxies remained greater than 0.1%. Sycamore sampled the solutions in a mere 200 seconds, whereas classical sampling at 0.1% fidelity would take 10,000 years, and full verification would take several million years.

This demonstration of quantum supremacy over today's leading classical algorithms on the world's fastest supercomputers is truly a remarkable achievement and a milestone for quantum computing. It experimentally suggests that quantum computers represent a model of computing that is fundamentally different from that of classical computers[4]. It also further combats criticisms[5,6] about the controllability and viability of quantum computation in an extraordinarily large computational space (containing at least the 2^{53} states used here).

However, much work is needed before quantum computers become a practical reality. In particular, algorithms will have to be developed that can be commercialized and operate on the noisy (error-prone) intermediate-scale quantum processors that will be available in the near term[1]. And researchers will need to demonstrate robust protocols for quantum error correction that will enable sustained, fault-tolerant operation in the longer term.

Arute and colleagues' demonstration is in many ways reminiscent of the Wright brothers' first flights. Their aeroplane, the *Wright Flyer*, wasn't the first airborne vehicle to fly, and it didn't solve any pressing transport problem. Nor did it herald the widespread adoption of planes or mark the beginning of the end for other modes of transport. Instead, the event is remembered for having shown a new operational regime – the self-propelled flight of an aircraft that was heavier than air. It is what the event represented, rather than what it practically accomplished, that was paramount. And so it is with this first report of quantum computational supremacy.

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Neuroscience

Gut microbes help mice forget their fear

Drew D. Kiraly

Microorganisms in the gut influence fear-related learning. The results of a study that reveals some of the mechanistic underpinnings of this phenomenon promise to boost our understanding of gut–brain communication. **See p.543**

The gut's resident bacteria, collectively called the gut microbiota, can have marked effects on brain function and on behaviour – but the mechanisms underlying this interplay remain largely unknown. On page 543, Chu *et al.*[1] define these mechanisms in unprecedented scope and detail. The authors report that mice lacking a complex microbiota exhibit altered fear-associated behaviour, changes in gene expression in cells in the brain, and alterations in the firing patterns and rewiring ability of neurons. The work represents a leap forward in our understanding of the interplay between the gut and brain.

Animals update their responses to environmental cues throughout their lives. This process of behavioural adaptation is driven by underlying cellular and molecular changes in the brain. Chu and colleagues analysed how changes in the gut microbiota affect one such adaptation: fear conditioning.

First, the authors trained mice to associate a tone with an electric shock, and measured how strongly that association was formed. The association developed normally both in control animals and in animals that had been treated with antibiotics to deplete their gut microbiota. The researchers then performed an extinction task, in which they repeatedly played the tone without an electric shock before measuring

the rate at which the animals updated their behaviour (such an update indicates that the fear response has been extinguished). The microbiota-deficient mice were unable to update their response, and showed persistent fearful behaviour long after control animals had adapted. Chu *et al.* found the same phenomenon in mice that had been raised germ-free in sterile isolators and so had never developed a gut microbiota.

The current study is not the first to examine the effects of the microbiota on fear conditioning — previous work has shown a decrease in the acquisition of this response in germ-free mice compared with controls[2,3]. But Chu and colleagues are the first to report a specific deficit in fear extinction (Fig. 1). What truly sets their work apart, however, is the breadth and depth of the mechanistic findings that they subsequently went on to gather.

Extinction of the fear response is heavily dependent on the function of the brain's prefrontal cortex[4]. Chu *et al.* performed *in vivo* imaging of this brain region in their animals to analyse both neuronal activity patterns and the formation and elimination of structures called dendritic spines, which are involved in the formation of synaptic connections between neurons. During the fear-extinction test, control animals showed less dendritic-spine elimination and more spine formation than did microbiota-deficient animals. The ability to create synapses and to maintain appropriate existing synapses is a key part of synaptic plasticity — a process crucial to learning and memory, in which the strength of synaptic connections changes in response to changes in neuronal activity. A higher ratio of spine formation to elimination might therefore partially explain why control animals were better able to appropriately extinguish the fearful stimulus.

Tight control of gene expression is also crucial for proper regulation of synaptic and behavioural plasticity. Previous work has indicated that changes in the microbiota alter the gene-expression profile of the prefrontal cortex as a whole[5], but Chu and colleagues performed RNA sequencing on single cells throughout the region, enabling them to identify gene-expression changes in individual cell types. These data show that microbiota depletion has a more pronounced effect on excitatory than on inhibitory neurons, setting the stage for future research in which the microbiota could be targeted to alter the characteristics of specific neuronal populations.

The authors' single-cell sequencing also reveals gene-expression changes in microglia, the brain's resident immune cells. Previous studies[6,7] have shown that altering the microbiota causes changes in microglial gene expression and function. Chu and colleagues found high expression of genes associated with an immature state in the microglia of their microbiota-deficient animals — a change that might affect the cells' ability to function normally.

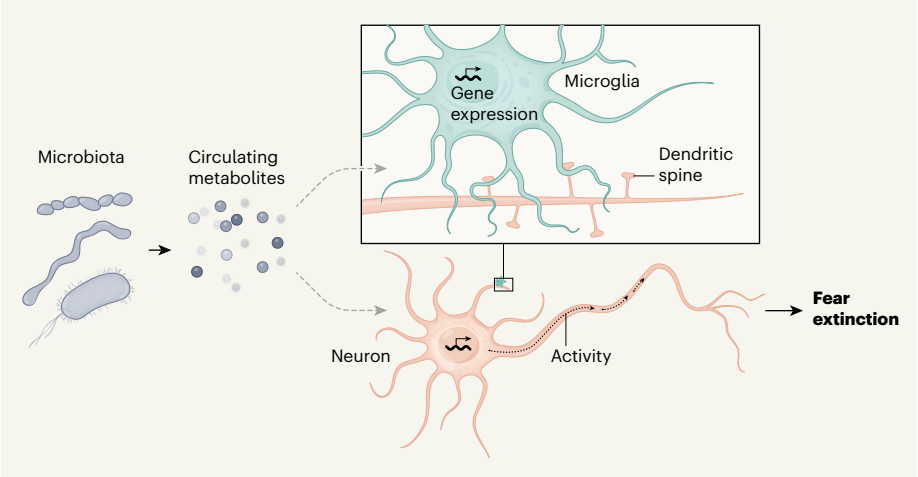

Figure 1 | Multiple effects of the gut microbiota on the brain. The gut's resident bacteria, the microbiota, can markedly affect the brain and behaviour. Chu *et al.*[1] provide evidence that the microbiota is needed for mice to update their behaviour in response to changing environmental cues — for example, to stop reacting to a once-frightening stimulus when it is no longer threatening (a phenomenon called fear extinction). The authors hypothesize that this role in behavioural adaptation involves metabolite molecules that are produced by the microbiota and circulate in the blood. They suggest that the metabolites modulate the ability of the brain's immune cells, microglia, to engulf and degrade structures called dendritic spines that form synaptic connections between neurons. In addition, microglia could affect neuronal activity directly — together, these activities would promote behavioural adaptation. In support of this idea, the researchers show that changes in the microbiota lead to altered gene expression in microglia and neurons, and to changes in dendritic-spine maintenance.

In the past decade, it has become clear that microglia have a crucial role in synaptic connectivity. By engulfing and degrading unwanted synapses, the cells ensure that neuronal connections are pruned or maintained as needed[8]. Changes in this process can alter neurodevelopment[9] and are implicated in psychiatric disease[10]. The researchers' RNA sequencing revealed changes in genes related to the role of the microglia in synapse organization and assembly. Although Chu *et al.* did not directly assess changes in the engulfment of synapses, their results lay the groundwork for future research into how interactions between the microbiota and microglia affect synapse density in the brain.

Finally, Chu and colleagues profiled gut metabolites (the molecules produced from metabolic processes) to identify molecules that might drive the gut–brain interactions they had observed. The authors found four metabolites that were significantly less abundant in microbiota-deficient mice than in controls. They therefore posit that the microbiota affects neurons and microglia in the brain through metabolites that are released into the circulation.

The gut microbiota is highly metabolically active, and the theory that the gut and brain communicate through circulating microbiota-derived metabolites is a popular one[11]. Manipulations of microbial metabolites have been shown to affect a range of behaviours, from autism-like actions[12] to those involving reward-seeking for drugs[13]. Experiments that manipulate levels of the metabolites identified by Chu *et al.* could improve our understanding of gut–brain communication.

Such research could also reveal a route to translating the current findings into clinical advances. The potential applications are wide-ranging, because alterations in cognition and synaptic plasticity are seen in nearly all neuropsychiatric disorders. Perhaps most germane to the current study would be the treatment of post-traumatic stress disorder, in which people cannot extinguish memories of frightening or traumatic experiences. Chu and colleagues' work raises the possibility of targeting the gut microbiota and its metabolites as a strategy for helping such individuals. Much remains to be done, but this study is an important step in our mechanistic understanding of the gut–brain axis.

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