

the formation of a single nucleus. When BAF was first described, one key feature noted was its ability to bind and crosslink two segments of viral DNA⁷. BAF is not picky; it can bind any double-stranded DNA⁸. Intriguingly, this DNA-bridging capacity is built into the structure of BAF proteins, because they exist as pairs called dimers, with their DNA-binding sites located on opposite sides of the dimer⁸.

Samwer and colleagues hypothesized that BAF's ability to connect distant DNA segments might be relevant to its action in nuclear assembly. To test this, they replaced normal BAF in human cells with a mutant version that was deficient in the ability to form dimers. When cells that contained this mutant divided, the authors observed the formation of micronuclei. This indicated that DNA bridging by BAF dimers is needed to collect chromosomes together in one nucleus.

The author's calculations suggested that BAF dimers are spaced about 49 nanometres apart on the chromosomal surface, and might form a network of BAF–DNA bridges that prevent nuclear-envelope membranes (which are approximately 60–100 nm in diameter⁹) from infiltrating between neighbouring chromosomes. Previous analysis¹⁰ of high-resolution images captured using electron microscopy provided another clue — the addition of BAF compresses the outermost layer of chromosomal DNA, giving it the appearance of a dense shell surrounding less-dense DNA. Samwer and colleagues showed that a dimerization-defective version of BAF failed to compress chromosomes.

Intrigued by the possibility that BAF alters the physical properties of chromosomes, Samwer and colleagues placed purified human chromosomes on glass slides, with or without the addition of BAF, and carried out two key experiments. First, using a tiny cantilevered metal rod to poke the chromosomal surface, they discovered that BAF stiffens chromosomes (Fig. 1). Second, they added fluorescent molecules called dextrans, which had average diameters of either 4 or 49 nm. Using microscopy, the team was able to observe the smaller dextrans infiltrating the internal chromosomal space, whereas the larger dextrans could enter this space only in the absence of BAF. This exclusion of larger molecules correlated with the authors' estimate that BAF dimers are spaced approximately 49 nm apart.

These results might open additional avenues of investigation into the molecular nature of the BAF-dependent chromosomal 'shield' and the biomechanics of nuclear assembly. Many questions remain to be addressed. Do BAF dimers function alone¹¹, or do they self-associate or bind to DNA-binding histone proteins^{12,13} to increase the degree of chromosomal compression? Do they recruit other proteins involved in capturing chromosomes? Furthermore, how do the BAF dimers

preferentially coat the outermost surfaces of chromosomes and avoid being trapped on interior chromosomal surfaces?

It will be interesting to learn how BAF 'shields' are dismantled, and how BAF contributes to chromosome re-engagement with lamins and nuclear-membrane proteins^{6,14}, because these molecular connections are essential for customizing 3D genome organization in specific tissues and organs¹⁵. Further research might move beyond cell division, perhaps investigating the possibility of targeting BAF for anticancer therapies^{16,17}, or detailing the mechanisms whereby BAF influences genome integrity, gene regulation and virus infection. Future research might also investigate the proposed involvement of BAF in progeria, a human genetic condition associated with characteristics of premature ageing¹⁸. ■

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ATOMIC PHYSICS

Large quantum systems tamed

Quantum-computing devices can be more powerful than their classical counterparts, but controlling large quantum systems is difficult. Two studies report work that overcomes this challenge. SEE ARTICLE P.579 & LETTER P.601

CHRISTINE MUSCHIK

Predicting the behaviour of more than a few quantum particles is tricky. The problem is so difficult that, in general, it cannot be tackled using classical (non-quantum) computers, and this has motivated the quest to build quantum simulators — controlled quantum devices that provide us with answers to questions about the nature of quantum matter. Quantum simulators can address fundamental problems in physics, ranging from exotic quantum phases to open questions in high-energy physics. On the more applied side, they might even help chemists to create low-cost fertilizers and organic batteries (see go.nature.com/2jvwchw). In the long run, they could revolutionize our ability to design materials and drugs¹. Today, however, quantum simulators are still at an early stage of development. On pages 579 and 601, respectively, Bernien *et al.*² and Zhang *et al.*³ report advances in this exciting endeavour.

We are only beginning to understand how to build quantum simulators. One method is to

use digital simulations⁴, in which a sequence of logic operations is performed on a quantum computer. Another approach is to use analog simulations, in which a specific model is emulated. For example, a classical analog simulation was used to design the roof of Germany's Olympic Stadium in Munich, which consists of a tantalizing structure of membranes. To find such lightweight yet stable configurations, architect Frei Otto experimented with soap bubbles. The experiments of Bernien *et al.* and Zhang *et al.* are quantum versions of this scenario — the researchers used trapped particles instead of soap solution and studied quantum phase transitions rather than roof designs.

Bernien and colleagues trapped atoms using optical tweezers — laser fields that hold atoms in place. This technique has the advantage that large arrays of atoms with arbitrary patterns can be prepared quickly and deterministically. The authors used additional lasers to excite atoms from the ground state to a Rydberg state, in which one of the atom's electrons is far away from the nucleus. Rydberg atoms have a large electric dipole moment and are coupled by

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long-range dipole–dipole interactions. The use of such interactions for quantum computing⁵ has developed into an active field of research.

Although Bernien *et al.* trapped only ground-state atoms, they were able to observe the scientifically interesting effects associated with Rydberg states because these effects happen so quickly. When exciting the atoms, the authors temporarily switched off the optical tweezers. For the short time required for the dynamics of interest to occur, the atoms remained in place. The authors then switched the tweezers back on and detected the system's quantum state. This approach provides a promising route to realizing controllable quantum many-body systems that have strong long-range interactions. The authors worked with a chain of atoms, but, as demonstrated by a Paris-based research group⁶, this technique can be extended to two and even three dimensions.

Following similar studies^{6,7}, Bernien and colleagues created a programmable version of the Ising model of magnetism⁸ to explore quantum phase transitions, which are analogous to classical phase transitions such as water turning into ice. The authors observed transitions of atom chains into ordered structures known as Rydberg crystals. By changing the initial separation between the atoms, the authors were able to produce different crystals (Fig. 1a).

In another experiment, Bernien *et al.* applied a rapid parameter change (a quench) to their system and measured the system's response — a quantum analogue to striking a bell and observing the ringing. The authors performed these measurements using up to 51 atoms. After the quench, they detected oscillating quantum many-body dynamics (quantum ‘ringing’), which is an indicator of the quantum nature of the resulting correlations between the atoms.

By contrast, Zhang and colleagues trapped a string of ions using electric fields. Each ion encodes a qubit (the quantum version of a classical bit) in its atomic state. Trapped ion qubits offer great versatility in their ability to perform high-quality quantum logic operations, and building useful quantum computers based on such qubits is an active area of research. The authors induced strong, long-range interactions using a method proposed⁹ by physicists Ignacio Cirac and Peter Zoller. Using a clever modification of these interactions¹⁰, realizations of quantum phase transitions have progressed from early proof-of-concept experiments using two ions¹¹ to experiments involving up to 16 ions^{12–15}. Zhang and colleagues now extend the number of ions to an impressive 53.

The authors performed quench experiments by switching on the coupling between the qubits and observing the system's response in different parameter regimes. They not only directly observed correlations between

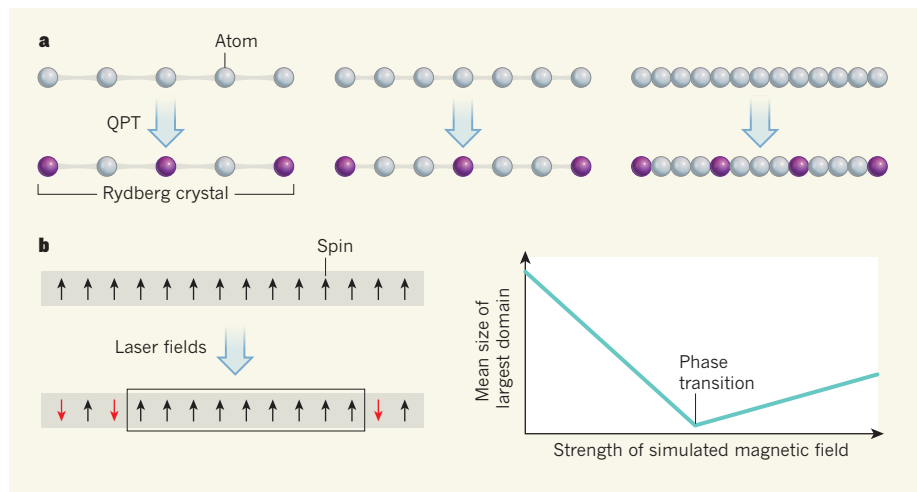


Figure 1 | Quantum simulators. Bernien *et al.*² and Zhang *et al.*³ present devices called quantum simulators that allow quantum matter to be investigated. **a**, Bernien and colleagues trapped chains of atoms, which were initially in the ground state (grey). They then observed quantum phase transitions (QPTs), in which some of the atoms were promoted to an excited (Rydberg) state (purple). The atoms formed ordered structures called Rydberg crystals. By varying the initial separation between the atoms, the authors produced different crystals. **b**, Zhang and colleagues trapped a string of ions whose magnetic moments (spins) initially pointed in the same direction (black). They then applied laser fields to the ions that induced interactions between the ions and mimicked a magnetic field, causing some of the spins to flip (red). Next, the authors measured the length of the largest domain in which spins were aligned (black box). By varying the strength of the simulated magnetic field, they identified a quantum phase transition.

pairs of qubits, but also evaluated higher-order quantum correlations. They used these measurements to characterize a dynamical phase transition, in which their system transitioned between differently ordered quantum states (Fig. 1b).

In strings involving fewer than ten ions, the ability to perform quantum simulations has already been demonstrated¹⁶. A complementary strategy is the maximization and automatization of control in few-qubit systems, such that long sequences of well-controlled, high-quality logic operations can be performed and different simulation concepts such as digital simulations can be realized^{17,18}. This approach has also been successfully pursued in solid-state systems¹⁹.

The experiments of Bernien *et al.* and Zhang *et al.* that used 51 and 53 particles, respectively, simulate models that are programmable but native — they use directly available couplings between pairs of particles. A much larger class of model could be realized (involving, for example, three- and four-body couplings) using digital rather than analog approaches. In the future, it will be useful to combine analog and digital elements in the demonstrated systems to expand the range of accessible problems.

Analog quantum simulations can also be realized using thousands of ultracold atoms in optical lattices²⁰. The short-range interactions between these atoms can be used to emulate theoretical models central to condensed-matter physics called Hubbard models, and involve particles called bosons and fermions, as opposed to qubits. As quantum

simulators grow, it will become increasingly important to develop tools for validation and error correction — in the case of the described analog demonstrations, it is not yet clear how this could be achieved. Methods to scale up quantum simulators include the intriguing possibility of combining simulation units in a quantum network.

Developing scalable, practical and useful quantum simulators is an ambitious task. We might find that different systems are suited for different problems and that different simulation concepts will be used for different physics questions. We are witnessing the first steps in this direction. Extending the size of controlled quantum systems is an exciting frontier, but progress in this area is not simply a matter of the size of a quantum register — it matters what we can do with it. ■

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MICROBIOTA

A high-pressure situation for bacteria

Analyses in mice suggest that dietary salt increases blood pressure partly by affecting some of the microbes that inhabit the gut. The implications of this work for hypertension warrant further study in humans. [SEE ARTICLE P.585](#)

DAVID A. RELMAN

High blood pressure is a leading cause of cardiovascular disease and hence preventable death in the United States¹, and is an increasingly prevalent and costly global health burden. Blood-pressure control in humans is inadequately understood — debate swirls around the contribution of dietary salt in particular. On page 585, Wilck *et al.*² draw connections between dietary salt, microorganisms in the gut, immune responses and blood pressure.

Processed foods and Western diets are packed with salt. Average daily sodium intake in the United States is more than 3.4 grams (equivalent to 8.5 g of table salt)³, despite the fact that guidelines⁴ recommend an intake of less than 2.3 g (5.8 g of salt). Most studies show that excess sodium consumption raises blood pressure in a dose-dependent manner⁴. But blood-pressure responses to salt are variable

and are generally detected in fewer than half of all subjects⁵. Known sources of such variability include genetics, dietary intake of other nutrients such as potassium, and kidney disease. In addition, responses to sodium intake are more pronounced if individuals have high blood pressure (hypertension)⁵.

Previous work⁶ has suggested that high salt intake increases the number and activity of immune cells called T lymphocytes, especially a pro-inflammatory subset called T_H17 cells. Activated T_H17 cells produce the immune-cell signalling factor interleukin-17, which not only promotes hypertension and inflammation in artery walls^{6,7}, but also induces autoimmune diseases⁸.

Wilck *et al.* sought to determine whether gut microbes (collectively known as the gut microbiota) have a role in mediating the effects of a high-salt diet (HSD). The authors fed mice an HSD for three weeks and analysed the composition of the animals' gut microbiota by

sequencing DNA from faecal samples. There were no major changes in composition; however, a machine-learning algorithm identified a DNA sequence that became less abundant in mice during HSD and more abundant when mice were returned to a normal diet. The sequence matched that of the bacterium *Lactobacillus murinus*.

The researchers recovered *L. murinus* from mouse faeces, and demonstrated *in vitro* that its growth was inhibited by salt concentrations equivalent to those found in the colons of mice fed an HSD. This bacterial species is not seen in humans, but the researchers found similar salt-sensitive growth in some human-associated *Lactobacillus* species. As expected, HSD caused hypertension in mice, but oral administration of *L. murinus* blunted this effect.

Wilck and colleagues found that *L. murinus* administration also prevented HSD-induced exacerbation of an autoimmune disease that can be experimentally generated in mice — actively induced experimental autoimmune encephalomyelitis (EAE). Administration of *L. murinus* was associated with a reduction in the numbers of T_H17 cells, which mediate EAE, in the intestinal wall, spleen and spinal cord (Fig. 1).

What links decreases in *L. murinus* to increased numbers of T_H17 cells? *Lactobacillus* species produce compounds called indoles from the dietary amino acid tryptophan, and treatment with indoles reduces the severity of actively induced EAE in mice⁹. The authors demonstrated that levels of indoles decreased when mice were fed an HSD, but were restored

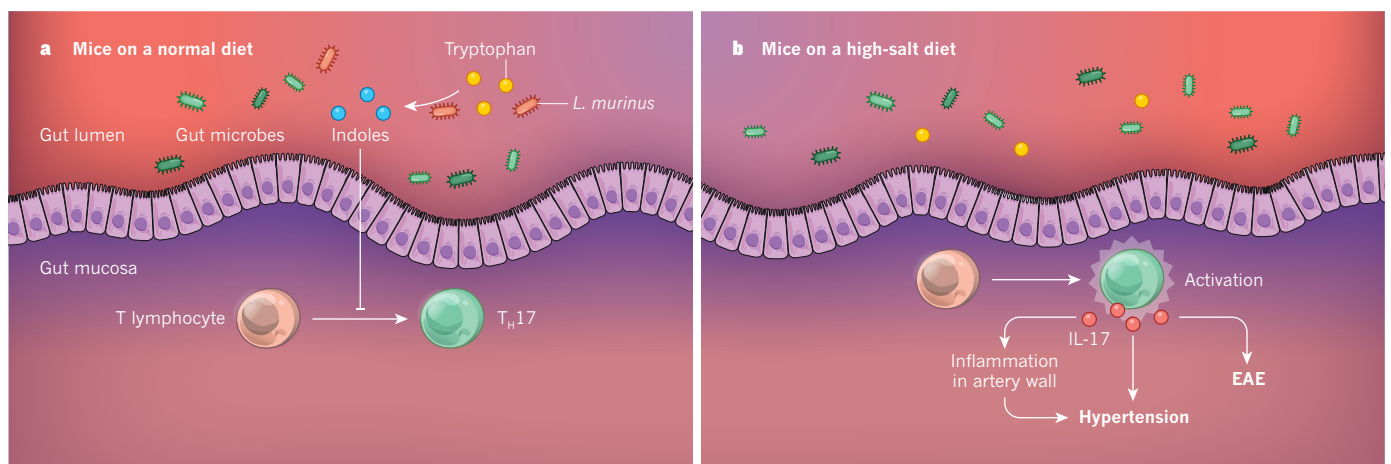


Figure 1 | A possible role for gut microbes in regulating blood pressure in mice. **a**, Bacteria of the genus *Lactobacillus*, such as *L. murinus*, convert the dietary amino acid tryptophan into compounds called indoles in the lumen region of the gut. Wilck *et al.*² have demonstrated in mice that one of these indoles prevents differentiation of immune cells called T lymphocytes into T_H17 cells in the gut mucosa. **b**, The authors showed that feeding mice a high-salt diet causes a decrease in the levels

of *L. murinus* in the gut. This diet and decrease in *L. murinus* was associated with an increase in the number and activation of T_H17 cells. These cells produce a pro-inflammatory molecule called interleukin-17 (IL-17), which is thought to promote high blood pressure (hypertension) and accompanying inflammation in artery walls, and exacerbate an autoimmune disease in mice dubbed actively induced experimental autoimmune encephalomyelitis (EAE).