to the drugs' limited diffusion from those blood vessels[4].

Kurtova and colleagues add to these previous suppositions about cancer repopulation by providing evidence that there is selective repopulation from previously slowly proliferating bladder-tumour cells that have markers suggesting that they are tumour stem cells. Furthermore, they show that the release of PGE_2 by cells undergoing programmed apoptotic death as a result of chemotherapy directly stimulates these putative tumour stem cells to proliferate. The enzyme COX2, which mediates PGE_2 production, had previously been associated with inflammation and carcinogenesis in the urinary bladder[5]. Kurtova *et al.* demonstrate that inhibiting COX2 with celecoxib inhibits tumour-cell repopulation and improves the antitumour effects of chemotherapy in mice with tumours derived from human bladder-cancer cells.

These results emphasize the importance of studying drug resistance in solid tumours. Repopulation is just one of several factors limiting the relevance of investigations that use dispersed cells in culture; others include the steep gradients of drug concentration in solid tumours, which results in inadequate drug delivery to many tumour cells, and the influence of cellular contact on the response[4,6,7]. Kurtova and colleagues did not take these factors into account, and, indeed, PGE_2 production is probably only one of several mechanisms by which tumour-cell repopulation is induced during chemotherapy: in different tumours, other mechanisms, both specific (for example, the activity of growth factors) and nonspecific (such as improved nutrition in the tumour microenvironment), are probably involved.

Another possible limitation of Kurtova and colleagues' study is that they treated the mice continuously with celecoxib during cycles of chemotherapy. Celecoxib inhibits the production of PGE_2, thereby removing the proliferative stimulus for tumour stem cells. But to achieve maximum benefit, cell-cycle-inhibiting drugs such as celecoxib would need to be given between cycles of chemotherapy, and to be removed before the start of the next course of (cycle-dependent) chemotherapy. Surviving tumour cells are therefore then proliferating and sensitive to the anticancer drugs.

An obvious question is whether treatment with celecoxib can also improve the outcome of chemotherapy in patients. There have been several randomized clinical trials in which celecoxib has been added to chemotherapy (although probably not in an ideal schedule) for the treatment of various cancers, although I am not aware of such trials for patients with bladder cancer. A meta-analysis of these trials shows some increase in response rate, but no change in the more important endpoint of one-year survival[8]. Also, although inhibition of repopulation owing to PGE_2 might be expected to be specific to tumour cells, the addition of celecoxib led to increased cardiovascular toxicity and anaemia[8]. Despite these caveats, Kurtova and colleagues' findings establish the principle that treatment failure can be caused by mechanisms of drug resistance that operate only *in vivo*, but that it is possible to modify such mechanisms to improve therapeutic outcome. ■

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QUANTUM INFORMATION

Spin memories in for the long haul

Spin systems have now been found that have lifetimes of up to six hours. They could be used to build quantum-communication networks and, if optical transmission fails, could even be shipped as a 'quantum memory stick'. SEE LETTER P.177

JOHN J. L. MORTON & KLAUS MØLMER

It is just a little past the time of year when many children write letters to Father Christmas. While being typed, these electronic letters exist in their computers' dynamic memories, before being transmitted down optical fibres to the North Pole, where they are stored on hard disks and backed up using magnetic-tape storage (or so we are reliably informed). Quantum information offers the prospect of fundamentally secure communication, but constructing practical quantum networks relies on developing a similar set of interconnected, long-lived memories storing quantum bits (qubits; the smallest logical units of quantum information). On page 177 of this issue, Zhong *et al.*[1] show how qubits encoded in the magnetic moment (spin) of atomic nuclei in inorganic crystals can have lifetimes of up to six hours, and also offer a route to strong coupling with light. Six hours may seem short compared to storage times of conventional memories, but it should be plenty to develop quantum memories for the nodes that plug together quantum-communication networks. It is also striking that, using this technology, we could, rather straightforwardly, send a qubit from London to New York by air freight — something currently impossible using optical links.

Quantum cryptography is a way to communicate using information encoded in the states of quantum systems. It exploits the fact that measurements of quantum systems unavoidably affect their state, allowing communicating agents to validate that there is no eavesdropper on the line. Quantum states are notoriously fragile, and hence communication of qubits typically relies on using the states of nature's fastest and least-interacting particles: photons. However, even photons are eventually scattered or absorbed, which has so far limited quantum communication based on transmission of individual photons to distances of 200 kilometres in optical fibres[2] and 140 km through free space[3].

Extending such demonstrations to create a secure quantum network with global reach requires a quantum version of telecommunications signal repeaters to periodically boost the signal. Unfortunately, the same basic principles that make quantum cryptography resilient to eavesdropping forbid amplification of quantum signals without adding noise. Quantum repeaters therefore do not handle the actual data being transmitted — instead, their goal is to help to create high-quality quantum entanglement of two distant nodes of a network, which can be used to teleport information securely between them[4]. A quantum-repeater network consists of quantum memories, in the form of matter-based qubits, connected by short, low-loss optical channels[5]. Each quantum memory is first entangled with a light beam, and then pairs of these light beams are combined to entangle the memories, as was demonstrated in 2013 using 2 qubits encoded in the electron spin of nitrogen-based impurities in diamond crystals separated by 3 metres[6]. Pairs of entangled quantum memories can be

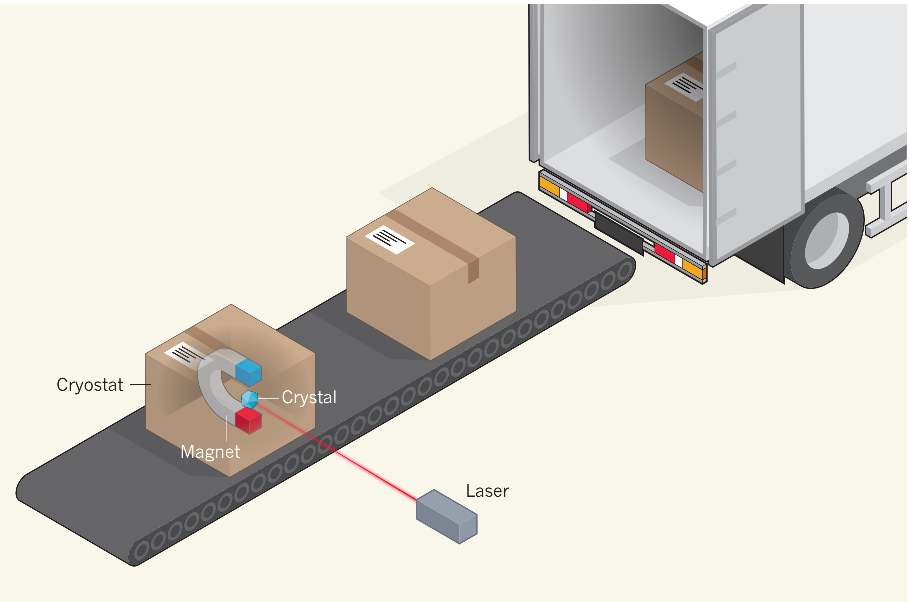

Figure 1 | Quantum postal service. Quantum bits (qubits) of information can be optically written, using laser light, into collective excitations of the nuclear magnetic moment (spin) of atomic ensembles in crystals such as yttrium orthosilicate (YSO). Zhong *et al.*[1] have shown that europium atoms in YSO can retain their nuclear spin states for as long as 6 hours at low temperatures (2 kelvin) and at a judiciously chosen magnetic field (around 1 tesla). Cryostats to keep systems at such low temperature, and magnets to produce such magnetic fields, are routinely shipped while operational, often by air, and are compact enough to fit in a modest van. On the basis of today's technology, the best way to send quantum information over long distances without loss could therefore be by post.

'daisy-chained' to form an extended quantum-repeater network, but practical quantum repeaters require the matter-based qubits to have stronger coupling to light and longer quantum lifetimes than have so far been achieved using diamond[6].

Rare-earth elements (those with atomic numbers 57 to 71) underpin today's optical communication technologies through devices such as optical-fibre amplifiers based on erbium impurities. They may well be just as crucial in quantum networks, as demonstrated by the entanglement between light and neodymium atoms in an yttrium orthosilicate (YSO) crystal[7]. Praseodymium nuclear spins in YSO have been placed in certain 'sweet spots' of an applied magnetic field, where the spins become insensitive, to first order, to fluctuations in magnetic field that would otherwise corrupt their state. When combined with dynamical decoupling — regularly flipping the spins to cancel out low-frequency noise — such nuclear spins showed quantum lifetimes of up to half a minute at cryogenic temperatures[8].

To go further, Zhong and colleagues turned to another rare-earth atom, europium, 'doped' in YSO, and identified conditions in which even the second-order sensitivity of the spins to magnetic-field fluctuations is suppressed, yielding predictions of quantum lifetimes of up to several minutes. The authors were in for a surprise, however, because, rather than minutes, they observed lifetimes extending up to 6 hours at temperatures of about 2 kelvin. This is because, in addition to securing the sweet-spot resilience to magnetic-field noise, the large applied magnetic field (1 tesla) also suppressed environmental fluctuations in the immediate vicinity of the europium atom, offering a double whammy of protection.

Although nuclear spins in YSO have extraordinary potential as quantum memories, more work is needed to 'write' qubits into them using optical means. There are many methods for this. In one scheme, an optical transition between two energy states in an ensemble of rare-earth atoms is driven with a laser beam, while a detector awaits the arrival of a single photon emitted by the ensemble at a wavelength or direction differing from that of the laser beam. When this happens, a particular pattern of quantum excitation becomes imprinted in the ensemble of nuclear spins (for example, imagine that the spins in the crystal adopt a striped pattern). Now, if we instead look for a photon in the interference pattern of light emitted from two such ensembles, it is possible to imprint entangled states across the two crystals (now the spins are striped in one crystal and plain in the other, and vice versa, like two pairs of Christmas socks that got mixed up before being wrapped).

Another challenge for quantum repeaters is dealing with errors, such as photon loss, which can be mitigated using a register of several coupled qubits located at each matter-based node. These allow multiple poor-quality, entangled states across distant nodes to be transformed into one high-quality, entangled state through a process known as entanglement distillation[9]. The nuclear spin 5/2 of the europium atom has 6 energy levels and so provides complexity beyond the two states of a simple qubit that could be used for such distillation.

In addition to laying the foundation for optical quantum repeaters, these long lifetimes raise the possibility of an intriguing alternative to qubit transmission: physically transporting the qubit-containing crystal instead of using optical fibres to send the qubits. Certainly, in 6 hours it is possible to travel much further than the 200 km that currently limits optical quantum communication — and sending such crystals by post would easily be the highest-fidelity qubit-transmission technology available today (Fig. 1). However, this is unlikely to become a widespread method for quantum communication once quantum repeaters become fully realized, for the same reasons of bandwidth and speed that underlie the popularity of e-mail over a posted letter. A more likely application of portable, spin-based quantum memories would be to fit them to vehicles and use them to hold on to quantum information for limited periods when an optical quantum-communication link becomes broken.

What about other memory applications, such as quantum money or quantum passports, whose serial numbers would exploit the 'unclonability' of quantum states to prevent forgeries? These uses typically require room-temperature operation and quantum lifetimes measured in months and years — but the longest room-temperature lifetimes observed so far have been around 40 minutes, for nuclear spins in silicon[10]. Border agencies may start worrying now about the international regulations (and taxation) for transporting quantum information between countries, but they are unlikely to need to search your hand luggage for qubits just yet. ■

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