other arginines in ubiquitin, but further study is warranted to fully understand the process.

As the reaction proceeds, ADPR-Ub is processed by the PDE domain and PR-Ub is attached to a serine residue on a substrate protein. In addition to their studies of SdeA, Akturk *et al.* present the structure of ADPR-Ub in complex with SdeD, a member of the SidE family that contains only a PDE domain. Kalayil *et al.* used mass spectrometry techniques to study the SdeA catalytic intermediates at this stage. Both groups propose a two-step reaction mechanism for SdeA on the basis of studies of SdeA or SdeD.

First, the Glu340 amino-acid residue of SdeA binds ADPR-Ub. The His277 residue of SdeA interacts with a phosphate group on ADPR-Ub, resulting in the release of a molecule of AMP. Second, His407 activates the hydroxyl group of a serine residue on the target protein, which enables the attachment of PR-Ub to the serine. Using a mutated version of SdeA in which the histidine residue at position 407 was replaced with asparagine to trap a catalytic intermediate, Kalayil *et al.* captured PR-Ub bound to His277 of SdeA (Fig. 1), confirming the catalytic mechanism. Wang *et al.* report the structures of related complexes of ADPR and ubiquitin with SidE.

If a water molecule enters the PDE domain's active site instead of a serine amino-acid residue, the reaction product released is unbound PR-Ub. PR-Ub can inhibit host E1-dependent ubiquitination because the PR modification prevents this form of ubiquitin from being a substrate for eukaryotic ubiquitination enzymes[7]. Kalayil *et al.* answered the question of whether the pathogenicity associated with SdeA arises from the generation of unbound PR-Ub or from the ubiquitination of host proteins. The authors tested bacterial mutants lacking SidE proteins that were engineered to express either wild-type SdeA or a mutant version of SdeA that generates only unbound PR-Ub. The authors observed that the bacteria that express mutant SdeA were unable to grow in host cells, indicating that the enzyme's key role is ubiquitination of host proteins.

The role of PR-Ub is an emerging topic in the field of ubiquitin research. These structures of SidE family members now pave the way for more questions to be answered. For example, how is ADPR-Ub shuffled between the PDE and mART domains? The active sites of the PDE and mART domains are far apart (55 ångströms) and do not face each other. There is conflicting evidence as to whether SidE proteins exist as monomers or dimers, and, as a result, there are different models of how the gap between the domains might be bridged.

And what range of functions does the enzyme's C-terminal domain have? The C-terminal domain stabilizes the catalytic core in SdeA but mediates protein dimerization in SidE. Dong *et al.* observed that ubiquitin molecules bind to the C-terminal domain of SdeA and induce a large conformational change in the enzyme, which suggests a possible regulatory role for this domain.

How many host proteins are ubiquitinated by SidE-family ligases? So far, only a few SdeA substrates have been identified[6,8,9]; these include the GTPase enzymes Rab and Rag, as well as the protein RTN4. From analysis of the ubiquitination sites in host proteins, Kalayil *et al.* and Wang *et al.* propose that the ligase enzyme specifically targets serine residues in disordered protein regions.

Finally, perhaps the most exciting question still to be answered is this: do enzymes that mediate this type of ubiquitination process also exist in eukaryotes? ■

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QUANTUM MATERIALS

Spinning on the edge of graphene

Long-sought evidence has been found of magnetism at the edges of graphene, a two-dimensional form of carbon. The findings might enable the development of the logic gates needed for quantum computers. SEE LETTER P.691

FERNANDO LUIS & EUGENIO CORONADO

The 2D form of carbon known as graphene has many potentially useful properties, but is usually not magnetic when pristine. However, theoretical predictions suggest that the edges of graphene sheets should become magnetic when they have a zigzag arrangement of carbon atoms[1]. Observing this effect has been challenging because of the difficulties of detecting the predicted minute magnetic signal and because it is hard to fabricate defect-free edges that have the required shape. On page 691, Slota *et al.*[2] report a method for making nanometre-wide graphene ribbons in solution, and thereby for producing nanoribbons with well-defined zigzag edges 'decorated' with organic radical molecules that bear electron spins — a quantum property of electrons that is associated with magnetism. The authors' results provide solid evidence of magnetism at graphene edges, and show that edge spins have potentially useful quantum dynamics.

Magnetic forms of graphene would be useful for spintronics, a technology that forms the basis of today's magnetic data storage[3,4]. But the main interest in generating magnetic edge states in graphene is for quantum technologies. Electron spins can adopt two orientations relative to an external magnetic field, and these could be used to encode the '0' and '1' states of a quantum bit (qubit), the basic information unit of future quantum computers and quantum-simulation devices.

The quantum states of a qubit must be strongly coupled to external control stimuli that drive the qubit's operation, but they must also be isolated from random external perturbations that can irreversibly upset the 'coherent' evolution of such quantum states (coherence is the existence of non-classical correlations between quantum states). In these respects, graphene has potential advantages[5] over other materials that are being investigated as hosts for spin qubits, such as gallium arsenide or silicon: electric currents flowing through a graphene sheet provide a means of coupling and manipulating spins; and the two main sources of decoherence are minimal in graphene. These sources of decoherence are the coupling between an electron's spin and its orbital motion (which is weak in graphene), and interactions of electron spins with atoms that have nuclear spins (the concentration of which is low in graphene).

Why has it been so difficult to observe magnetic edge states experimentally? The electronic and magnetic properties of graphene nanoribbons correlate closely with the structures of their edges, and are sensitive to even minute numbers of defects. Isolating a sufficient number of nanoribbons that have perfect zigzag edges to enable their magnetic characterization is extremely challenging, and so the data from such studies[6] are scarce and inconclusive. Experiments performed on single graphene layers prepared *in situ* under a high vacuum have revealed the formation of local electronic states at edges, but did not provide any evidence of magnetism[7].

By expanding a previously developed

50 Years Ago

One of the best ways to spread plant diseases is through the sale and shipment of seed. In some cases, such as celery leaf rust, only one infected plant in 10,000 is needed to cause an epidemic in the crop. Particularly critical are fungal diseases lodged within the seed … The problem in dealing with these diseases has been to kill the fungus but not the seed. This type of disease can now be completely eliminated by a process developed at the National Vegetable Research Station … The treatment is first to soak seed for twenty-four hours in a solution containing 0.2 per cent of the fungicide 'Thiram' at 30 °C. The seed is then dried by driving air through it for several hours. So far this treatment has been found to give complete control in eleven commercially important plant species with infections involving eighteen different seed-borne diseases.

From *Nature* 1 June 1968

100 Years Ago

The trustees of the British Museum have published a report on an investigation carried out … to ascertain how and when the infestation of Army biscuits by flour-moths takes place, and whether any steps can be taken to prevent this. A list is given of eight species of beetles and four Pyralid moths that were actually found in the tins of biscuits examined. But by far the most serious pest was the moth *Ephestia kühniella* … Evidence is adduced indicating that Central America is probably the original home of *E. kühniella*, the so-called Mediterranean flour-moth. The examination of various intact airtight tins showed that the biscuits contained in them were infested, thus indicating that the moths had gained access to them in the factory prior to packing.

From *Nature* 30 May 1918

chemical method[7], Slota *et al.* synthesized graphene nanoribbons in solution that have uniform widths and zigzag edges. The authors attached nitronyl nitroxide molecules — chemically robust organic radicals, which are magnetic because they carry an unpaired electron — to specific edge sites (Fig. 1). This method produces large amounts (milligram quantities) of chemically stable graphene nanoribbons that can be studied using conventional spectroscopic techniques. The authors show that the electron spins at the radicals induce a spin density at the edge carbon sites where the radicals are bonded, and therefore induce magnetic edge states. This trick is akin to moving a row of corks on a string up and down on the surface of a pool to induce ordered water oscillations at the pool's edge; not only do the corks induce waves, but they also make them easier to visualize.

Besides proving the existence of magnetic edge states, Slota and colleagues' experiments provide the first direct determination of the strength of the tiny spin–orbit coupling in their system. These findings will help to validate theoretical models of the electronic structure of graphene and its edge states[8].

The authors also measured the characteristic rates at which spins relax (reach equilibrium with the graphene lattice) and the time taken for them to lose coherence. The measured decoherence times are roughly one microsecond at room temperature — which is promising, because it means that spin coherence is preserved for much longer than has previously been measured in graphene electronic devices. A plausible explanation for this is that the graphene nanoribbons are free from the structural randomness and extrinsic effects (such as spin scattering caused by connecting graphene to electrodes) that have suppressed spin coherence in other systems[9]. Slota *et al.* find that decoherence in their nanoribbons seems to be mainly associated with interactions of the electron spins with nuclear spins in the radical molecule. This is good news, because chemical methods are available to reduce the concentration of nuclear spins, or to make spin qubits insensitive to the magnetic noise generated by nuclear spins[10].

Finally, the authors showed that unpaired electrons at the radicals interact with the edge spins. These interactions might allow graphene to be used as a coherent communication channel between different radical spins, and might therefore serve as the basis of the two-qubit logic gates necessary for a quantum computer.

Slota *et al.* show that the attachment of magnetic molecules to graphene creates coherent magnetic states on it, nicely complementing previously reported experiments[11] that showed how graphene influences the electron spins on molecules deposited on it. However, in the authors' system, electron spin is 'injected' into the nanoribbons from the radical molecules — so the intrinsic magnetism of graphene edges remains to be investigated.

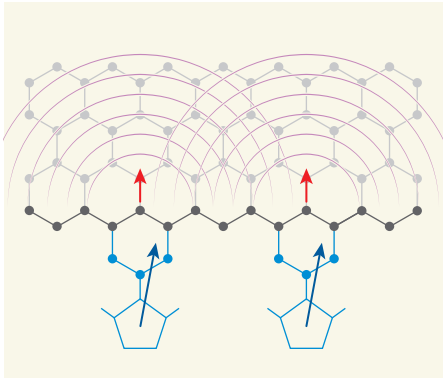

Figure 1 | Electron spins at graphene edges. Slota *et al.*[2] have made ribbons of graphene (grey) that have zigzag edges (black), and free-radical molecules (blue) attached at specific sites. Each molecule has an unpaired electron, which has an associated quantum property known as spin (blue arrows). The molecules stabilize the carbon nanoribbons and perturb electrons in the graphene at the edges (purple ripples), generating electron spins at the edges (red arrows).

One way to explore this would be to attach non-magnetic molecules, rather than free radicals, to the graphene edges.

A formidable challenge in the development of the reported nanoribbons for quantum computers will be to design a system that can manipulate and read out each qubit in a nanoribbon, and that can switch interactions between qubits on and off, in a way that also allows the computer to expand to incorporate more qubits without losing control of them. This will probably require graphene nanosheets to be coupled to a solid-state device, so it remains to be seen how the effects of coupling to the device will affect spin coherence.

Moreover, if the strength of the spin–orbit coupling of edge-modified graphene nanoribbons can be increased, then the spin at the attached molecules could be manipulated using an electric field. Such strengthening might be achieved by replacing the organic radicals with molecular metal complexes — which would require new chemical methods. It therefore seems that chemists hold the key to technologies and scientific discoveries involving magnetic graphene. ■

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SYNTHETIC BIOLOGY

Yeast shuffles towards a diverse future

A redesigned yeast genome is being constructed to allow it to be extensively rearranged on demand. A suite of studies reveals the versatility of the genome-shuffling system, and shows how it could be used for biotechnology applications.

JEE LOON FOO & MATTHEW WOOK CHANG

A global consortium of scientists is well on the way to making a synthetic genome for the yeast *Saccharomyces cerevisiae*[1] — the first synthetic genome for a member of the group of organisms known as eukaryotes, which includes plants, animals and fungi. Embedded within the extensively redesigned 'version 2.0' genome of *S. cerevisiae* (Sc2.0) are DNA sequences that form part of a system known as Synthetic Chromosome Rearrangement and Modification by LoxP-mediated Evolution (SCRaMbLE). This system allows extensive reorganization of the genome to be triggered on demand, generating Sc2.0 variants that have diverse genetic make-ups and characteristics. Sc2.0 is therefore a versatile platform that can be easily modified and evolved to produce yeasts that have desired attributes[2]. A collection of seven papers[3–9] published in *Nature Communications* demonstrates the immense potential of Sc2.0 for engineering and understanding yeast.

To enable SCRaMbLE, a palindromic DNA sequence known as *loxPsym* is inserted after every non-essential gene in the synthetic genome. In the presence of the enzyme Cre recombinase, the *loxPsym* sites undergo recombination with each other — that is, the *loxPsym* sequences break in the middle, and the broken ends can then join up with any other available *loxPsym* ends. This process results in genes being randomly deleted, inverted, relocated and duplicated.

In the original design of the SCRaMbLE system[10], Cre recombinase was produced only once during the lifetime of a cell, and was fused to a protein domain that binds oestradiol molecules — which allowed the enzyme to be activated by adding oestradiol to the yeast's growth medium, providing an on–off switch for genome rearrangement (Fig. 1). However, some 'background' genome rearrangement occurred even without oestradiol activation. This version of SCRaMbLE was functional[11,12], but four of the new papers now report improvements to the system.

Shen *et al.*[3] have modified SCRaMbLE to produce multiple pulses of Cre recombinase (instead of just one per lifetime) to increase rearrangement events while reducing background Cre recombinase activity. Jia *et al.*[4] have developed a SCRaMbLE variant in which both oestradiol and galactose molecules are required to activate rearrangement, also reducing background rearrangement. Hochrein *et al.*[5] have engineered Cre recombinase so that it is activated by red light, providing a new way to control SCRaMbLE. And Luo *et al.*[6] have introduced a reporter DNA sequence into a synthetic yeast strain, which allows cells that have undergone SCRaMbLE-induced genome rearrangement to be easily distinguished from those that have not. All four improvements facilitate effective and efficient implementation of SCRaMbLE.

An important application of SCRaMbLE is to generate genetically diverse pools of yeast mutants from which strains that have industrially valuable characteristics can be isolated. For example, yeasts can be genetically engineered to produce useful compounds, and Blount *et al.*[7] show that SCRaMbLE can generate yeast strains that produce antibiotics (violacein or penicillin) in greater quantities than could be achieved without SCRaMbLE. Blount and colleagues also used the system to produce yeast strains that use the sugar xylose for growth more effectively than strains produced without SCRaMbLE; xylose is poorly used by wild-type yeast, but is abundant in biomass and is therefore an attractive alternative to the sugars normally used to feed yeast in industrial applications. And Luo *et al.* have used their SCRaMbLE variant to accelerate the isolation of yeast strains that are tolerant to various stress factors, such as ethanol, heat and acetic acid.

Jia and co-workers report that production of β-carotene molecules can be drastically increased if SCRaMbLE is used in diploid yeasts, which have two copies of the genome, instead of haploids, which have a single copy. Similarly, Shen *et al.* used SCRaMbLE in diploids to improve the heat or caffeine tolerance of hybrid yeasts (organisms produced by crossing two different yeast species or subspecies).

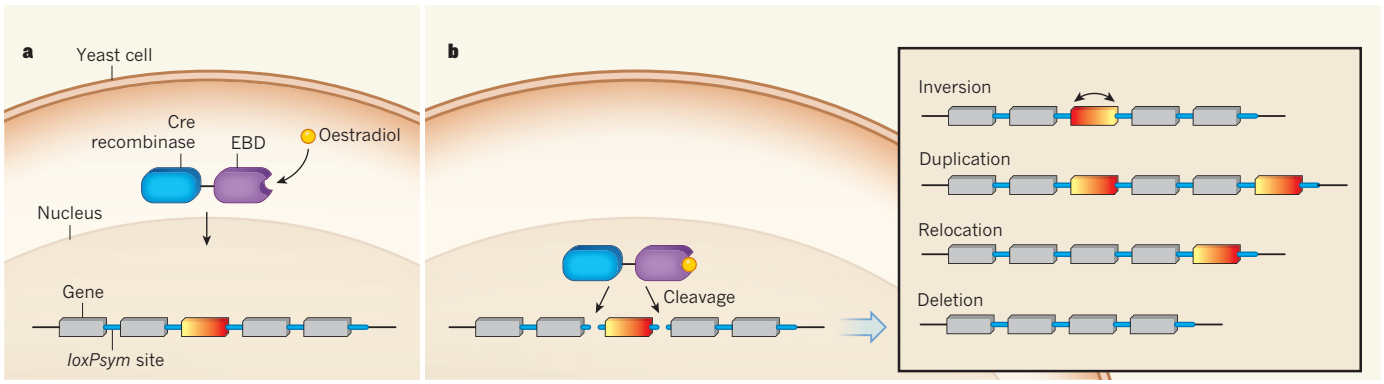

Figure 1 | Genome rearrangement on demand. A synthetic genome of the yeast *Saccharomyces cerevisiae* is being constructed that allows the genome to be rearranged using a system known as Synthetic Chromosome Rearrangement and Modification by LoxP-mediated Evolution (SCRaMbLE). In the first version of this system, a palindromic DNA sequence known as *loxPsym* is inserted after every non-essential gene, and a protein consisting of the enzyme Cre recombinase attached to an oestradiol-binding domain (EBD) resides in the yeast cytoplasm. When the protein is activated by the binding of an oestradiol molecule, it moves into the nucleus (**a**) where it cleaves the *loxPsym* sequences (**b**). The broken ends of *loxPsym* can then join up with any other available *loxPsym* ends, rearranging the genome. This process results in genes (such as the coloured rectangle) being randomly inverted, duplicated, relocated or deleted. Seven papers[3–9] now report improvements and applications of the SCRaMbLE system.