EF-P and not from an initiation factor. Thus, the amino-acid sequence and function[1,2,7,8] of eEF1A, eEF2 and eIF5A are universally maintained. By contrast, the amino-acid sequence and function of many of the polypeptides associated with either the eukaryotic initiation or termination step shows that they have not evolved from equivalent bacterial factors (see table for details).

To directly probe the function of yeast eIF5A, Saini *et al.*[1] used a wide combination of molecular biological and biochemical assays. They find that depletion or inactivation of this factor leads to an increase in both the levels of polysomes — clusters of ribosomes bound to mRNA — and the time it takes ribosomes, after the initiation step, to read the mRNA code and release the nascent polypeptide. What's more, the effects of eIF5A inactivation are similar to those of sordarin, an inhibitor of eEF2.

These observations clearly indicate that eIF5A functions during the elongation step. But why does it also stimulate the initiation[3] and termination[1] steps? One possibility is that eIF5A is required for ribosomes to adopt the most reactive conformation for optimally interacting with factors and aminoacyl-tRNAs that are specifically involved in initiation, elongation and termination.

Two hypothetical models[9,10] — the reciprocating ratchet and the spring and ratchet — provide an account of how the mRNA and growing polypeptide chain are moved through the ribosome. According to these models, throughout the elongation step, the large and small ribosomal subunits move back and forth relative to one another, facilitating the movement of the mRNA and the growing polypeptide (peptidyl-tRNA) along the three consecutive sites on the ribosome — A (tRNA-binding), P (peptide-bond formation) and E (exit). Thus, faithful translation of the mRNA sequence into a polypeptide chain is ensured. As eIF5A also stimulates the initiation and termination steps, it is likely that this factor is bound to the ribosome while an initiator tRNA or the peptidyl-tRNA is bound to the P site, making the tRNA more reactive with an incoming aminoacyl-tRNA or termination factor at the A site.

Given that, at a relative molecular mass (M_r) of 15,000, eIF5A is much smaller than a ribosome — which has an M_r of roughly 4 million — it is unlikely that its effect on ribosome conformation can be detected experimentally. Nonetheless, data obtained through cryo-electron microscopy and three-dimensional reconstructions show[11] that, when bound to the 40S subunit of ribosomes, the initiation factors eIF1 and eIF1A (both about the same size as eIF5A) dramatically change the shape of this subunit, although the factors themselves cannot be visualized. So it might be possible to similarly investigate whether eIF5A alters the shape or subunit orientation of eukaryotic ribosomes, without necessarily visualizing it.

Saini and colleagues' results do not just establish a role for eIF5A as a major player during the elongation step. In eIF5A, they also add a useful tool to the experimental tool box, which should allow high-resolution probing of the alternating states that eukaryotic ribosomes might assume in order to accurately and efficiently catalyse the various steps of translation. ■

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MECHANOCHEMISTRY

Polymers react to stress

Christoph Weder

The latest polymers are chameleon-like: they change colour on deformation. The transduction mechanism underpinning this effect could be used to make polymers that respond in many other ways to mechanical stress.

Imagine a polymer that could send a warning signal if stressed close to the point of mechanical failure. Or one that actually becomes stronger under load. Or even one that heals itself after being damaged. On page 68 of this issue, Davis *et al.*[1] report a breakthrough that could enable all three possibilities: polymers in which the application of an external force activates preprogrammed chemical reactions, which in turn cause desired responses. The authors used this approach to make mechanochromic polymers — materials that change colour on deformation.

There is currently great interest in polymers whose properties change in response to stimuli such as chemicals, heat, light or electricity, because of their potential use in applications ranging from camouflage systems to artificial muscles to drug delivery[2]. Many such materials have been made, but comparably few polymers have been developed that respond in a useful way to mechanical stress[3]. These include materials that change their absorption or fluorescence colour on deformation, so providing visible warning signs before mechanical failure occurs[4–6]. The colour changes are caused by several mechanisms, including variations in the molecular interactions between dye molecules integrated into the polymers[4], or in the molecular conformations of integrated dyes[5]. Alternatively, in photonic-bandgap materials (through which only light of a specific wavelength can propagate), deformation of the sample changes the distance between particles in the material's lattice structure, which in turn changes the wavelength of light that passes through. But these mechanisms are fundamentally different from those of mechanically responsive materials found in nature, essentially all of which translate macroscopic forces into chemical reactions[7].

Davis *et al.*[1] set out to emulate nature's approach by making artificial polymers in which mechanical stress provides the activation energy for specific chemical reactions. The mechanochemically reactive unit — the mechanophore — used by the authors is a 'spiropyran' dye (see Fig. 1a on page 69). Spiropyrans change colour when exposed to light or heat, sometimes converting from colourless to highly coloured states, and they are used in applications such as self-darkening spectacles. These optical changes occur because light or heat activates a reaction in which a weak bond in the spiropyran is broken, causing the molecules to rearrange into a coloured product. The colour changes can also be triggered by grinding the compounds[8], demonstrating that such compounds have mechanochromic characteristics.

Seeking to make polymers that have mechanochemical properties, Moore and Sottos (the lead authors of the paper by Davis *et al.*[1]) have previously incorporated several mechanophores — including a spiropyran — into polymers[9,10]. Assuming that efficient force transfer between the macromolecules and the mechanophore would be essential, they developed several approaches for covalently connecting spiropyrans to polymers. One route involved attaching two chemical groups to a spiropyran core; the groups acted as initiation points from which polymer chains were grown. In this way, the authors prepared a polymer in which each molecule contains a spiropyran at its centre. They then showed that solutions of the polymer change from being colourless to pink on exposure to ultrasound[10]. This

happens because ultrasound-generated shear forces are funnelled through the polymer chains to the spiropyran, which responds by reacting as described previously. Other research groups have also shown that mechanoreceptors in polymers can break if the mechanophores contain sufficiently weak bonds. This was demonstrated recently by the reported ultrasound-induced activation of certain catalysts[11], for example.

So far, so good. But in most real-world situations, forces are not applied to polymer solutions by ultrasound; rather, they are applied to solids by stretching or compression. Furthermore, when solid polymers are exposed to excessive stress, the normal mechanochemical response is for the polymer molecules to break at random points along the chain[12]. A key question therefore remained: if solid spiropyran-containing polymers are placed under stress, does that stress break the mechanophores? Davis *et al.*[1] now show that it does. When they subjected spiropyran-containing polymers to stress, either by stretching a rubbery poly(methyl acrylate) polymer or by compressing a glassy poly(methyl methacrylate) polymer, the colour and fluorescence of the materials changed, indicating that the spiropyrans had reacted (Fig. 1).

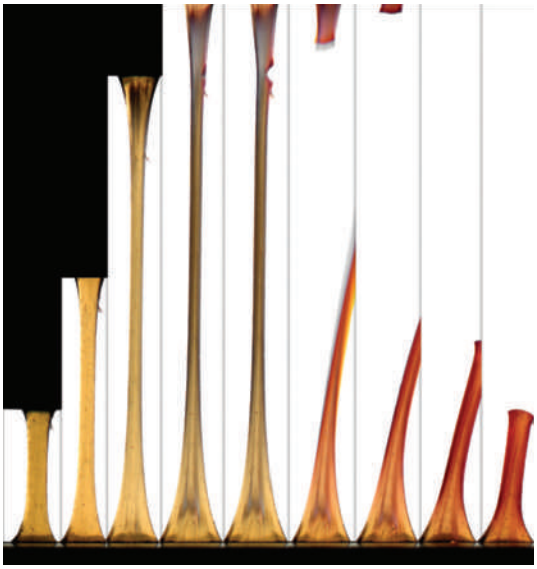

Figure 1 | Red for danger. Davis *et al.*[1] have prepared mechanochromic polymers that change colour under mechanical stress. When a sample of one of these polymers is stretched, the material turns red at the point where irreversible deformation (tearing) starts to occur, as shown in this sequence of pictures. Once the material snaps, the red colour is apparent throughout the sample. The sample on the left is 7.4 mm long.

Using a combination of experimental and theoretical models, Davis *et al.* showed that the underlying mechanism of the colour change is undeniably stress-induced reaction of the spiropyran upon irreversible deformation of the material. They further showed that the connectivity between the mechanophore and the polymer is important: placing two polymer chains on opposite sides of the spiropyran allows the maximum transfer of force from the polymer chains, whereas attaching chains to the same side of the spiropyran, or using only one polymer chain, prevents or limits transfer to the desired breaking point. The authors thus report the first set of guiding principles for the design of solid mechanochemical polymers. Nevertheless, further studies are required to work out just how selective the mechanochemical transduction really is. Although the authors' computational studies suggest that chain scission occurs only at the spiropyran, the possibility that rupture also occurs in other parts of the polymer chains cannot be ruled out.

Davis and colleagues' approach to making mechanochromic polymers should be readily adaptable to other polymer systems. But the development of materials that use spiropyran mechanophores as built-in strain sensors will require several practical problems to be solved. For example, the colour change in the polymers described[1] doesn't occur only in response to deformation; it also does so in response to heat and light. Furthermore, the ring-opening reaction of spiropyrans is reversed by exposure to light. The resulting loss of colour would clearly be a problem if the polymers are to be used as damage sensors.

The importance of Davis and colleagues' work goes far beyond the reported mechanochromic effect — it may become a milestone in polymer science, because the authors' general design concept can probably be adapted to make a plethora of materials that translate mechanical stress into all kinds of useful chemical reactions. The authors propose[1] that polymerization and molecular-crosslinking reactions could be triggered upon deformation. This could be achieved by mechanochemical processes that release reaction initiators or catalysts, and might be used to create self-healing materials. The reverse effect — cutting across molecules at predetermined breaking points — could be used to create polymers that have stress-activated fuses.

Other applications include materials that have stress-controlled drug-release properties, which could be used in tissues that are naturally subjected to mechanical stress; and substrates for cell culture that contain dimples in which cells won't grow, because the properties of those regions were mechanochemically altered when the dimples were stamped into the substrate. Scientists from many disciplines will be restricted only by their imaginations when it comes to finding ways of using mechanically responsive polymers for their specific needs. And studies of well-defined artificial systems might contribute to our often rather limited understanding of mechanochemical transduction in biological systems. ■

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CELL BIOLOGY

Arrest by ribosome

Sébastien Ferreira-Cerca and Ed Hurt

Impaired assembly of cells' protein-synthesis factories, the ribosomes, can cause cell-cycle arrest and disease. This finding emphasizes the close link between cell proliferation and ribosome formation.

Protein synthesis is mediated by complexes of RNA and protein known as ribosomes. Ribosome biogenesis is complicated, involving some 150 non-ribosomal factors and 100 small non-coding RNAs[1,2]. It is also the most energy-consuming process in growing cells, and so requires extensive regulation and coordination. Pressing questions are how ribosome synthesis is regulated, how it links to cell proliferation, and how it responds to environmental cues such as nutrient availability and stress. Writing in *Nature Cell Biology*, Fumagalli *et al.*[3] provide insight not only into the molecular mechanisms that connect ribosome biogenesis and cell proliferation, but also into underlying human diseases associated with defective ribosome synthesis — ribosomopathies[4,5].

Eukaryotic organisms (such as yeast, plants and animals) have two ribosomal subunits, 60S and 40S, which are assembled in the