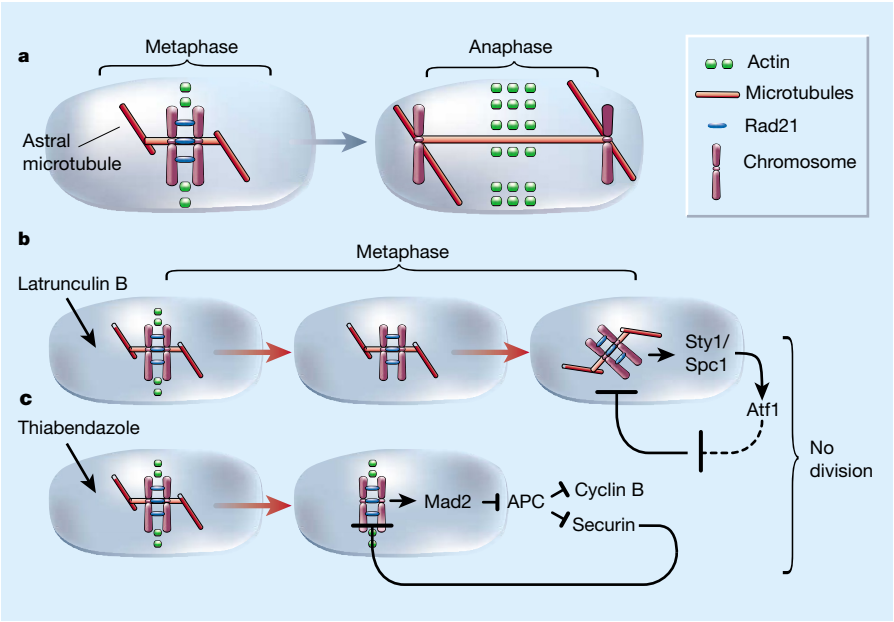

Figure 1 **Keeping a check on the cytoskeleton.** a, **During nuclear division, spindle microtubules attach to duplicated chromosomes (in metaphase) and pull them apart to opposite poles of the nucleus (in anaphase).** b, **As shown by Gachet *et al.*[3], when the actin-based cytoskeleton is damaged by treatment with a drug, latrunculin B, progression into anaphase is halted. The molecular details of this new cell-cycle checkpoint have not been fully worked out, but actin disorganization somehow results in the spindle being misorientated, which activates the proteins shown. The ultimate result is a failure to degrade Rad21 and to segregate duplicated chromosomes.** c, **The 'spindle-assembly' checkpoint can be triggered by thiabendazole, a drug that damages tubulin. When chromosomes detect that they are no longer attached to microtubules, the spindle-assembly checkpoint is activated. This involves different molecules from those in the actin checkpoint, except that one of the ultimate targets is also Rad21.**

tein kinase, which adds phosphate groups to Atf1, activating it. Atf1 is a transcription factor, working to control gene expression. Both Atf1 (ref. 8) and Sty1/Spc1 have counterparts in humans. The authors found that cells lacking Atf1 failed to arrest during mitosis in the presence of latrunculin B, and later died. The loss of actin polymerization (but not the addition of a tubulin poison) induced the phosphorylation and activation of Sty1/Spc1. Gachet *et al.* conclude that the 'stress-activated' protein kinase pathway, which includes Sty/Spc1, is a key part of the actin-dependent mitotic checkpoint.

To explain how actin affects spindle orientation, Gachet *et al.* propose that there is a functional connection between astral microtubules, which extend outwards from the spindle, and the ring of actin that forms in the cell cortex (the outermost layer of the cytoplasm) during mitosis. The actin ring might use the astral microtubules to orientate the spindle microtubules. If so, when the actin ring becomes disorganized, the spindle would be orientated incorrectly. The stress-activated pathway would then be switched on, so the sister chromatids would fail to separate. This is still hypothetical, particularly because the role of astral microtubules in organizing spindle microtubules is unclear. Nevertheless, it seems plausible: the interaction of microtubules with the cortex is known to be important in positioning dividing nuclei[9].

This work might have broad implications. For example, cells acquiring mutations that enable them to bypass this 'spindle-orientation' checkpoint might develop genomic instability — a feature of tumour cells. Moreover, spindle orientation is known to be important in determining the fate of many cell types during the early development of multicellular animals[10]. Specifically, the orientation of the spindle is involved in whether a cell divides symmetrically or asymmetrically. So the new checkpoint might also be linked to the control of cell fate. ■

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Daedalus

Unchemical chemistry

Chemistry is mainly about simple aggregates of just a few atoms. It deals more uneasily with polymers, huge molecules or bonded lattices, but even these redeem themselves by being composed of repeating simple units. Daedalus is now inventing an entirely different chemistry.

His inspiration was the strange yellow solid deposited from phosphine gas. This solid is apparently a random mass of phosphorus atoms bonded any which way, with any loose bonds terminated by hydrogen atoms. He reckons there must be a whole range of random atomic aggregates like this, with no repeating units. Indeed, chemists must have made them thousands of times — as the brown 'tar' of so many failed reactions, always thrown down the sink in disgust. Coal is perhaps the closest natural example. But Daedalus is now making them deliberately.

He is aiming a number of atomic beams *in vacuo* at a cryogenically cooled target. Each atom sticks where it lands, and bonds to other atoms nearby. The overall composition of the product can be varied by changing the intensity of the beams, but its short-range structure must be entirely random. It will not be a polymer or copolymer, but rather a random macromolecular structure, or 'randomer'.

When the deposit is warmed up, it may turn out to be unstable, and decompose to small molecules. But for certain ranges of composition, it will be stable. Stable randomers will probably contain a high proportion of atoms such as carbon, sulphur, silicon and phosphorus, which bond easily to each other. They will have less hydrogen, oxygen, nitrogen or halogens, although these will be useful for terminating spare valencies. Metals, especially transition metals of variable valency, may aid the incorporation of other atoms. They will also add variety to the range and properties of randomers.

When he has a sense of the most promising randomer compositions and their properties, Daedalus will make them in bulk, by adapting the most tar-like products of conventional reactions. It will be slow work, and even Daedalus cannot guess what use its products may be. As covalently bonded glasses, they may fill a gap in the polymer spectrum; as utterly unnatural substances, they may be ideal for inert surgical implants; as solid-state compositions, they may transform electronics. But new chemistry is always fertile. The field of randomers is bound to be good for something. David Jones