are gathered into bundles, in a region of overlap midway between the two poles, forming a structure that is referred to variously as the spindle midzone, the spindle interzone or the central spindle (Fig. 1). This intriguing structure seems to be important late in mitosis, promoting the ingression of a membrane furrow that ultimately partitions the dividing cell into separate daughters — a process called cytokinesis[3].

Studies of both roundworm (*Caenorhabditis elegans*) and mammalian cells have shown that assembly of the central spindle requires a two-protein complex dubbed centralspindlin[4]. One of its protein constituents is a member of the kinesin family of motor proteins, called ZEN-4 in *C. elegans* and MKLP1 in humans. The other is a signalling protein of the Rho family — CYK-4 in *C. elegans*, MgcRacGap in mammals. These two proteins form a complex that crosslinks microtubules of opposite polarity. When functional centralspindlin is lost, the central spindle does not assemble and cytokinesis is defective.

Although the requirement for centralspindlin is well established, how its crosslinking activity is restricted to anaphase, and the functional significance of this restriction, has remained unknown. Mishima *et al.*[2] now present data suggesting that a cell-cycle regulator adds phosphate groups to (phosphorylates) centralspindlin to prevent assembly of the central spindle before anaphase. Dephosphorylation by another regulator then promotes assembly during anaphase.

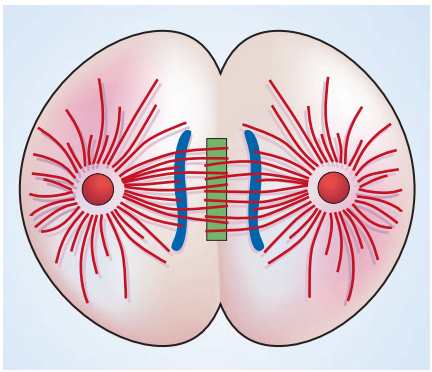

Figure 1 **The mechanics of cell division. The mitotic spindle in a dividing animal cell is composed of microtubules (red lines) projecting from each of two spindle poles (also known as centrosomes; red circles). Some microtubules capture sister chromatids (blue), shown separating during the anaphase period of the cell cycle. Some microtubules interdigitate midway between the two spindle poles, where they are cross-linked through the activity of the centralspindlin complex to form the central spindle (green box). Mishima *et al.*[2] have shown how the phosphorylation and dephosphorylation of a key component of centralspindlin ensures that the central spindle assembles at the correct time.**

Kinesins, such as ZEN-4 and MKLP1, are typically dimers that bind microtubules through two head regions, which can 'walk' along a single microtubule[5]. The head regions might also allow centralspindlin complexes to bundle microtubules, by binding to and crosslinking antiparallel microtubules. A kinesin's head regions are joined to neck regions, and Mishima *et al.* focus on amino acids that are found in the necks of both ZEN-4 and MKLP1 and that look like targets for phosphorylation.

The presence of these conserved potential phosphorylation sites, and the ability of the neck region to promote motor activity *in vitro*, compelled Mishima *et al.* to test the functional importance of neck phosphorylation. Their data show that a cell-cycle regulator called Cdk1–cyclin B phosphorylates the neck regions of both proteins. To examine the consequences of this phosphorylation, the authors performed both *in vitro* and *in vivo* tests. Kinesins use chemical energy obtained from the hydrolysis of adenosine triphosphate (ATP) molecules to power their movement on microtubules. Phosphorylation of the ZEN-4/MKLP1 neck greatly lowered this ATP hydrolysis activity *in vitro*, and reduced the affinity of the proteins for microtubules. So, as long as Cdk1–cyclin B is active, microtubule crosslinking is prevented. This would delay the assembly of the central spindle until anaphase, when Cdk1–cyclin B is known to be inactivated.

To address the functional significance of this phosphorylation *in vivo*, Mishima *et al.* expressed an altered MKLP1 in cultured mammalian cells. In this altered protein the amino acid alanine, which cannot be phosphorylated, replaces amino acids that would normally be targeted by Cdk1–cyclin B. This alteration resulted in premature bundling of microtubules before anaphase, and interfered with sister-chromatid segregation. So, neck phosphorylation does indeed seem to prevent premature assembly of the central spindle, and might thereby facilitate the proper capture and segregation of sister chromatids.

To complete their story, the authors also found that a cell-cycle phosphatase called CDC14 can dephosphorylate the ZEN-4/MKLP1 necks. In mutant *C. elegans* cells lacking functional CDC14, ZEN-4 failed to localize to the central spindle during anaphase, presumably because the protein's neck could not be dephosphorylated. In contrast, as would be expected if neck phosphorylation prevents central-spindle assembly, ZEN-4 that had been altered by alanine substitution to prevent neck phosphorylation did localize to the central spindle when CDC14 was not functional. Thus, by targeting the neck region of the centralspindlin kinesin, cell-cycle kinase and phosphatase activities can restrict assembly of the central spindle to anaphase.

100 YEARS AGO

Inaugural address by the Right Hon. A. J. Balfour: Reflections suggested by the New Theory of Matter.

If we jump over the century which separates 1804 from 1904, and attempt to give in outline the world-picture as it now presents itself to some leaders of contemporary speculation, we shall find that in the interval it has been modified, not merely by such far-reaching discoveries as the atomic and molecular composition of ordinary matter, the kinetic theory of gases, and the laws of the conservation and dissipation of energy, but by the more and more important part which electricity and the ether occupy in any representation of ultimate physical reality… But to-day there are those who regard gross matter, the matter of everyday experience, as the mere appearance of which electricity is the physical basis; who think that the elementary atom of the chemist, itself far beyond the limits of direct perception, is but a connected system of monads or sub-atoms which are not electrified matter, but are electricity itself… Surely we have here a very extraordinary revolution. Two centuries ago electricity seemed but a scientific toy. It is now thought by many to constitute the reality of which matter is but the sensible expression.

From *Nature* 18 August 1904.

50 YEARS AGO

Institution of Electronics Exhibition in Manchester. **The commercial section was impressive chiefly for its evidence of steady progress in the development of known techniques. Applications of television were prominent, and there were on view no fewer than three industrial closed-circuit television channels… The Institute of Cancer Research exhibited ultrasonic echo-locating equipment, used for the examination of brain structure. When the equipment is in use, a quartz transducer in acoustic contact with the head emits a narrow, pulsed beam of ultrasound. Any echoes incident on the transducer are transmitted as pulses through amplifier and display circuits, and appear on an oscillograph screen. The position of the pulse on the screen gives a measure of the distance of the source of the echo from the transducer. At present, observations are being compared with what is known of the 'normal' brain, with the view of the possible identification of abnormal structures.**

From *Nature* 21 August 1954.