RÉSUMÉ

Joint proposal

UNUSUALLY high joint flexibility (hypermobility) can be a good thing and a bad thing for a performing musician, depending on which joints are especially flexible and which instrument is played. L.-G. Larsson *et al.* (*New Engl. J. Med.* **329**, 1079–1082; 1993) have analysed data on 660 staff and students at a school of music in New York state. The authors find that hypermobility of joints undergoing repetitive motion is an asset in reducing adverse effects in those joints. For instance, it may well benefit violinists to have highly flexible joints in the left hand in particular (as was said to be the case for Paganini). The downside is that over-flexibility in areas that provide support, such as the spine or knees, is associated with a higher incidence of musculoskeletal problems in such places. Violent conductors may pose a more serious risk of injury to a career musician — but it helps to have the right joints.

Light fantastic

FULLERENES from sunlight? It sounds like a physicist's pipe-dream, but two reports in the *Journal of Physical Chemistry* (**97**, 8696–8700 and 8701–8702; 1993) suggest that direct evaporation of a graphite target by concentrated sunlight will be a commercially useful way of generating large amounts of the smaller fullerenes. L. P. F. Chibante and colleagues use a small parabolic mirror on a tracking mount, whereas C. L. Fields and collaborators employ a 10-kW solar furnace. In both cases, argon flowing past the target sweeps the vaporized carbon away to condense in a darker region. The advantage of this, say Chibante *et al.*, is that it avoids the photochemical destruction of newborn fullerenes that is the bugbear of carbon-arc generators.

Back transmission

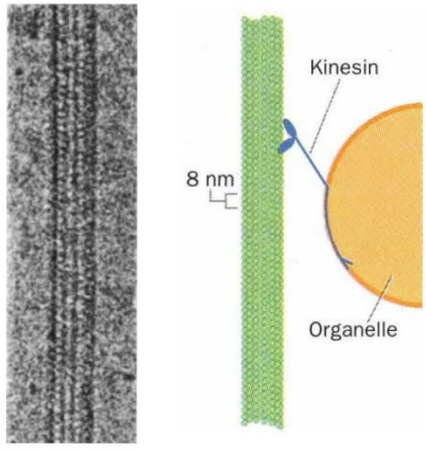
BOVINE spongiform encephalopathy (BSE) is thought to have been initially transmitted to cows through feed contaminated with scrapie, a sheep disease. J. D. Foster *et al.* now present the first report of experimental transmission of BSE back to the supposed source (*Vet. Rec.* **133**, 339–341; 1993). Foster and co-workers used 'positive' and 'negative' lines of Cheviot sheep, so named for their genetic differences in susceptibility to the SSBP/1 strain of scrapie; Anglo-Nubian goats were also included in the experiments because of their uniform response to several different scrapie isolates. The results with the goats were as expected, and consistent with other studies. Surprisingly, however, both lines of sheep developed the disease with an unpredictable and sporadic incidence, meaning that the link between genetics and susceptibility may well be more complex than previously indicated.

MOLECULAR MOTORS

One giant step for kinesin

Jonathon Howard

ON page 721 of this issue[1], Svoboda *et al.* report the first glimpse of a biological engine turning over: by recording the movement of a single kinesin molecule with extraordinary precision, they have directly observed the stepwise motion of this motor protein along the surface of a microtubule. An 8-nanometre step is small compared to the length of a microtubule (up to 100,000 nm). But it is a giant step for kinesin, the motor domain of which is only 10 nm across, and it is a huge step in our understanding of how biological motors work.



a, Electron cryo-micrograph of an unfixed 13-protofilament microtubule in ice (courtesy of R. H. Wade). The vertical striations correspond to the protofilaments. The individual tubulin monomers that make up each protofilament are just visible. *b*, Model of the microtubule in which the monomers are depicted as spheres of diameter 4 nm. The 8-nm steps made by a two-headed kinesin molecule as it carries an organelle along the microtubule correspond to the spacing of the tubulin dimer.

Motor proteins such as myosin, dynein and kinesin are enzymes that convert the chemical energy derived from hydrolysis of the γ-phosphate bond of ATP into mechanical work used to power cellular motility. Myosin drives muscle contraction; dynein propels the beating of sperm and cilia; and kinesin transports organelles from one part of the cell to another along microtubules. The motor reaction is far more complex than simple catalysis, traditionally thought of as the job of proteins. Rather than just accelerating an already energetically favourable reaction, the motor protein is a mechanical device which undergoes a sequence of conformational changes coupled to the sequential chemical steps in the hydrolysis of a molecule of ATP. Energy-transducing reactions are also performed by ion pumps which use the energy of ATP to do electrical work, and G-proteins which use the energy of GTP to do informational work by controlling the timing of signalling reactions. These proteins are examples of the molecular machines that distinguish cells from inanimate objects, and there is great interest from biologists, physicists and chemists in understanding the way in which they work.

Up to now, the elementary motor reaction has been obscured by the sheer numbers of motor molecules in active tissues and cells such as muscle and sperm. Svoboda *et al.* have now been able to see this reaction — the hydrolysis of a single molecule of ATP by a single motor protein — by using purified proteins in a cell-free system. By combining a laser interferometer with optical tweezers, they have made an instrument that can detect displacement with nanometre precision and millisecond temporal resolution. This feat ranks with that of Neher and Sakmann in developing the patch-clamp technique for recording the current flowing through single ion-channel molecules[2]. Indeed, in many ways the mechanical recordings are even more difficult: in the 10 milliseconds or so during which a motor protein hydrolyses a molecule of ATP, the flow of ions through an open sodium channel will have dissipated an energy equivalent to the hydrolysis of some 10,000 molecules of ATP.

The irregular, stepwise motion of kinesin along the microtubule is evident from the time traces recorded by Svoboda *et al.* at low ATP concentration or at high force (the statistical analysis of the noisy records obtained at high ATP concentration and low force is less convincing). The spatial periodicity of about 8 nm is consistent with kinesin taking steps of 8 nm, a distance which makes a lot of sense from a structural and biochemical point of view.

The microtubule is a polymer of the heterodimeric protein tubulin. The dimers are arranged head-to-tail to form a protofilament; and the lateral association of typically 13 protofilaments forms a sheet, closure of which defines the cylinder that is the microtubule. Kinesin moves parallel to the long, protofilament axis of the 13-protofilament microtubule. The distance between consecutive kinesin-binding sites is therefore either 4 nm (the intermonomer spacing) or 8 nm (the interdimer spacing)[3]. The 8-nm steps are consistent with biochemical studies which show just one kinesin-binding site per dimer[4].

As ATP concentration is decreased, the time interval between each consecutive step gets longer. So it seems that there is at most one step for each molecule of ATP