MATERIAL WITNESS

Get knotted

Until the first protein with a knot in its native folded state was found in 1994, it was widely assumed that proteins avoid knots. Since then, several hundred proteins — around one percent of all known protein structures — have been found to contain knots. Yet the mystery is not why some proteins are knotted, but why more aren't. Compared with ordinary polymers, proteins have fewer knots than would be expected for a random distribution of conformations, suggesting that nature finds it expedient on the whole to eliminate knots. Yet apparently they are sometimes desirable, or at least not detrimental.

Why is it OK for some proteins to get knotted and not others? That's the question explored in two papers submitted for publication. Joachim Dzubiella at the Technical University of Munich has explored the size, shape and stability of protein knots using computer simulations (arxiv:0809.873; 2008); Matthias Rief, also at Munich, and his co-workers, have investigated a knotted protein experimentally using an atomic force microscope (AFM; T. Bornschlögl *et al.* arxiv:0809.1067; 2008).

One hypothetical role of protein knots is that they 'tie up' the native fold, making it more stable. But the results of Rief and colleagues challenge this notion. They have looked at the photoreceptor protein phytochrome of the bacterium *Deinococcus radiodurans*, which has a knotted figure-of-eight structure. This is a relatively unusual knot, denoted in mathematical notation as a 4_1-knot; most protein knots are the simpler trefoil or 3_1 type.

The researchers linked phytochromes into polymeric chains, which they attached at one end to the gold tip of an AFM cantilever. Pulling produced a jerky, sawtooth extension of the polymer chain, owing to successive unfolding of each compact polypeptide segment. Unfolding required a surprisingly low force — about 73 piconewtons for the protein with its chromophore, and rather less without the chromophore, showing that there is nothing especially stable about the knotted conformation. Pulling tightens the knots until they encompass just 17 amino acid residues and shorten the polypeptide chain by about 6.2 nm.

So what is the knot doing here? The researchers speculate that it might restrict the protein motions when excited by absorption of a photon, making sure that the energy is channelled towards the correct conformational change in the photoexcited molecule.

Dzubiella's calculations suggest some other possibilities. He finds a comparable length reduction of around 6.9 nm for 4_1 knots, but most adopt a pretzel rather than figure-of-eight shape. Both these and 3_1 knots create a 'lump' in the peptide chain that, even when pulled tight, would make the proteins too wide to slip through a pore narrower than around 2 nm. So perhaps some knots restrict protein transport.

Even more intriguingly, some knots seem able to bind a water molecule reversibly in their loops, which may be squeezed out by pulling. The binding is strongest for hydrophobic knots, because in this environment hydrogen bonds to the peptide backbone are less screened and thus stronger. Might this supply a means for mechanically controlling bound water, which can modify a protein's flexibility and catalytic action?

Philip Ball

ENERGY

Fuel for thought

The worlds of nanotechnology and energy meet to unveil a realm of functional materials for fuelling the challenge of low-carbon, sustainable energy.

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Increases in the price of oil, Earth's most visible energy source, create intense responses. Both the finite resources of fossil fuels and the threat of climate change have sensitized society and inspire innovation in the scientific community. In earlier oil crises, chemists reacted sensitively and provided, through catalysis, strategic technologies for non-nuclear alternative energies. This time, however, other scientific disciplines are rising to the energy challenge, creating an interdisciplinary wave of activity.

The properties of nanomaterials can be exploited for energy purposes: their surfaces have active sites, allowing heterogeneous catalysis, whereas the inner interfaces and global size control the charge and electron-transport properties for electronics (Fig. 1). Nanotechnology is therefore a major contributor to the resolution of the sustainable energy problem. An excellent insight into the state-of-the-art nanoscience-based alternative-energy technologies was provided at a European Science Foundation conference held in the Ötz Valley, Austria, in June 2008. The topics and applications discussed included photovoltaics, hydrogen production, fuel-cell batteries, thermoelectrics, environmental catalysis, and energy-saving applications such as organic light-emitting diodes (Fig. 1).

Despite the efforts spent on the physical aspects and metrology of nanoscience, there remains an enormous need for fundamental research into understanding nanoscale effects and hence realizing the rational design[1] of materials for energy applications. Intensive discussions illustrated this for the desired properties of titania[2]