

DNA as a kind of solid

Molecules with helical pretensions such as DNA may be the result of a phase transition, in the strict sense, from a more disordered state. But when will the process be calculable?

THE textbooks say that double-stranded DNA molecules make a double helix, and that large globular protein molecules contain well-ordered helical structures (pieces of alpha helix) which are held together by less well ordered structures. No doubt the textbooks are right, at least for much of the time. But it is also well known that DNA molecules cannot function as templates for transcription while they are tightly bound as helices. For some of the time, the DNA molecules must be partly unwound. So much is generally accepted (and taught), but on the understanding that the helix is the normal resting state.

There is naturally much more that might be said. The complementary strands of DNA molecules are held together specifically by well-identified hydrogen bonds; by contrast, the forces that hold together the successive turns in a helically twisted molecule are, to say the best of them, loosely defined. People tend to build molecular models that allow the closest packing compatible with the molecular geometry and arrive at structures which turn out to be not very different from those suggested by X-ray diffraction. The double-strandedness is energetically understandable, the helical packing less so for DNA (but it is a rather different tale with the stretches of alpha helix in globular protein molecules).

So why do double-stranded DNA molecules finish up as helices? At bottom, the answer cannot be very different from that which explains why molecules of water vapour will condense at zero degrees centigrade or thereabouts, into the molecular constituents of solid ice. The trade-off is that between the decreased potential energy of a molecule trapped by attractive forces and what might be called the heat of disorder, the absolute temperature multiplied by the entropy.

For many familiar kinds of phase transitions, that from a vapour to a solid for example, the basis for understanding and even calculating the transition is familiar. Calculate the free energy of the two phases as a function of the temperature, ideally in terms of the properties of the constituent atoms and molecules, whereupon the crossover (if any) will mark the point of the phase transition. Now, and not before time, there is an argument bearing on the question whether the formation of helical DNA is a phase transformation in this sense.

The good news is that there is a formal calculation of the transformation of a disordered polymer molecule into a helix in which, as it happens, none of the parameters has been calculated from first principles. The other side of the coin is that the calculation, due to Nigel Goldenfeld of the University of California at Santa Barbara and J.W. Halley of the University of Minneapolis (*Phys. Rev. Lett.* **55**, 730; 1985), while providing an ingenious framework within which to describe systems of polymer molecules which are helical in parts and differently constituted elsewhere, also shows in passing how far there is to go.

The objective is to calculate the thermodynamics of a system of molecules each of which can in principle exist in two quite different configurations. Individual molecules will then be found in which stretches of one configuration are separated from each other by stretches of the other. In general, the lengths of these alternating stretches will be random, and all possible permutations may exist. The thermodynamic properties of the system are accessible if it is possible to calculate the partition function Z , which is nothing but the sum of terms such as $\exp(-E/KT)$, where K is Boltzmann's constant, T the temperature and E the energy of some state of the molecule as a whole. But the sum must be expanded over all possible states of the molecule, and this is usually where the snags arise. Generalities such as these are of course familiar from the textbooks.

Goldenfeld and Halley have made the problem tractable by introducing the assumption that the energy of a particular molecular arrangement, with alternating random lengths of the two configurations, is simply the sum of the energies of the consecutive segments. Among other things, this entails the assumption that energy states of the molecule as a whole are of negligible importance. In particular, low-frequency vibrations involving a whole polymer are assumed not to matter. With these simplifications, the problem

then boils down to calculating the energy states of random lengths of polymer in the alternative configurations (and of being able to stomach the algebra that follows).

The outcome is nevertheless encouraging. Goldenfeld and Halley suppose that the alternative configurations are respectively helical and straight. Each chemical unit of polymer molecule in the second form is supposed to involve a certain potential energy penalty, perhaps made up for by the extra degrees of freedom that it enjoys. Apart from the potential energy penalty entailed, the energy states of the helical and straight configurations differ only in the vibrational energy states that are accessible to them.

For the sake of argument, the energy states of the helical sections are approximated by those of a rigid rod. The outcome is that the energy of the rod-like sections is determined linearly by a combination of the length and of its logarithm, but that the free energy of the remaining sections is simply proportional to length. The free energy curves will plainly cross each other if the coefficients, which depend on the temperature, have suitable values, so that there must be a set of circumstances in which the transition to a helical structure is a straightforward phase transition, with a latent heat and so on.

The calculation has the great virtue of showing clearly that phase transitions in polymers are just as real as some experiments suggest. But it also illustrates what needs to be done to fill out the model. At least for the polymers occurring in biological systems, water relations are evidently crucial, partly because they will affect the molecular configurations by hydrogen bonding, and partly because the vibrations of water molecules will modify the vibrational spectra of both the coiled and uncoiled versions as well as serving as a means of transferring heat from one place in the molecule to another. But getting even that far quickly will be a far from simple achievement for whoever is successful.

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Biological manuscripts

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