NATURE

100 YEARS AGO

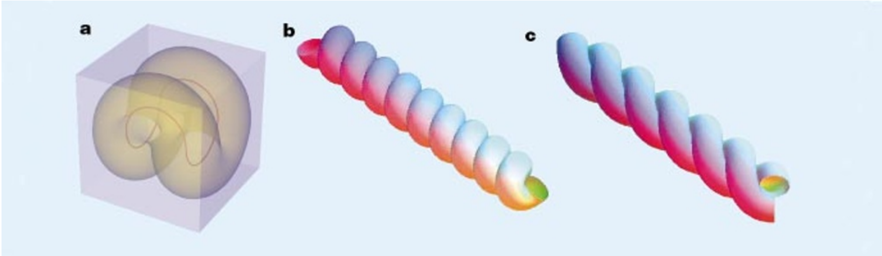
It is a remarkable sign of the times when the head of a firm principally distinguished for the introduction into this country of American methods of dealing with drugs, i.e. by putting them up in new and convenient shapes and doses, goes out of his way to fit up extensive research laboratories. This is what Mr. Wellcome has done... A well-built modern house has been secured at No. 6 King Street, Snow Hill, and has been converted into a series of three commodious and well-fitted laboratories, a library and office, and a store-room and workshop. Each laboratory is self-contained and each is connected with the other and with the directors' office by means of telephones… Mr. Wellcome intends to carry on his laboratories in no narrow spirit; this means, I presume, that he has other views then the conversion of his business into a chemical manufacturing concern. Though much work is done towards the perfection of the firm's preparations, time has been found for several researches which have been published, and other work of this kind is in hand… All interested in the advance of chemistry, whether pure or applied, will wish Mr. Wellcome success, and also that he may find imitators among the numbers of firms who are meditating an advance in the direction of a more scientific method of conducting their manufactures.

From *Nature* 19 July 1900.

50 YEARS AGO

Crystalline inclusion bodies in tobacco plants infected by tobacco mosaic virus have been known since 1903, and circumstantial evidence has made it appear likely that these crystals are composed largely of the virus protein. The present work makes it appear even more likely than before that the crystals are pure virus protein, and shows the crystals to be of considerable interest from several quite different but related points of view. On account of the exceptionally large dimension of the protein particle, it has been possible for the first time to make, in part at least, a structure analysis of the crystal using visible light in a manner analogous to that of X-ray diffraction. As a result, it has been possible to settle the controversial question of the length of the rod-shaped virus particle in the living plant. Also, the interpretation of the appearance of the crystals, as seen with the microscope, leads to a theory of the formation of images of three-dimensional objects. **M. H. F. Wilkins *et al.***

From *Nature* 22 July 1950.



P. PIERANSKI/A. DOBAY

Figure 1 **Tightly packed tubes.** a, **Packing of a tube into a box whose sides are four times the radius of the tube.** b, **A single helical tube whose centre line has the critical pitch/radius ratio of 2.512.** c, **Double-helical tubes in which the ratio between pitch and tube radius has the critical value 2π. Helices with parameters as in** b **closely resemble those observed in α-helical segments of proteins and are also obtained in numerical simulations of optimal packing of individual tubes by Maritan *et al.*[1], whereas the parameters of the double-helical tubes in** c **closely match those for DNA.**

spheres whose geometry is fixed, the optimal shape of the centre line of a deformable tube must be found. Consequently it is not a simple matter to find the optimal packing of even a single tube.

This modelling problem makes sense only if the tube, like any real rope or molecule, has a definite non-zero thickness. Figure 1a shows a way of packing (presumably optimally) a tube of length 4π and uniform thickness r (or radius r, but be aware that sometimes thickness means diameter) into a cubic box of side length $4r$. The centre line of the tube is a saddle-like trajectory that is built from four semi-circles. The point of this example is that, whenever the parameters of the tube and the box are less simply related, it is hard to even guess the optimal packing. This is the general topic addressed by Maritan *et al.*[1] in their numerical simulations.

The basic issue to be overcome in numerical simulations is that the idea of thickness is not quite as simple as it might first seem[4,5]. In the tube model a non-zero thickness has two possible effects: first, the centre line cannot be bent too sharply; and second, any two points that are far apart along the curve cannot be too close to each other in space. So, for a given centre line, the maximum possible thickness is governed by either local bending or by non-local points of closest approach, or, apparently exceptionally, by both conditions simultaneously. For the centre line of the tube shown in Fig. 1a, both of these conditions are simultaneously realized at every point along the red centre line.

Maritan *et al.* characterize the thickness of strings or tubes in terms of a quantity called global radius of curvature[6]. For any curve made up of discrete straight lines joining node points, the thickness is taken to be the minimal radius of all possible circles passing through any three nodes of the curve. If the smallest radius is achieved by three adjacent nodes, the thickness is controlled by local bending, whereas if the nodes on the minimal circle are not all adjacent, the thickness is governed by the non-local condition of closest approach.

Armed with this tool, Maritan *et al.* use a Monte Carlo algorithm to move the nodes of a centre line with a given length into an optimal shape, which maximizes thickness when subject to one of several compactness constraints. Perhaps the simplest compactness condition is that the centre line is completely contained in a given box. In spirit, their procedure is similar to that of earlier studies (see examples in ref. 7) but, with the exception of ref. 8, all previous work has looked at the optimal shapes of closed, knotted curves, much beloved of mathematicians. (A curve is closed if its two ends are joined or glued together to form a loop. A loop is knotted if it cannot be smoothly deformed to a simple circle without cutting.) Indeed, from a solely mathematical point of view, Maritan *et al.*'s contribution is the elegant, and in retrospect delightfully obvious, idea that the constraints of closure and knotting can usefully be replaced by one of several compactness conditions on the centre line. (In the absence of any compactness constraint at all, the optimal centre line is merely a straight line of infinite thickness.)

What about the physical implications of the simulations presented by Maritan *et al.*? Perhaps their most intriguing results arise when they impose local compactness conditions that are independent of external constraints such as a box. They state that, for "a broad class of local constraints", the optimal centre line is a particular helix in which the ratio of the pitch (or period) p to radius r is such that the bending and closest-approach constraints are realized everywhere simultaneously ($p/r = 2.512$). Maritan *et al.* then consider crystal structures of various α-helical polypeptides (one of the basic structural motifs of proteins), and show that the helices formed by the α-carbons in the polypeptide backbone have almost the same optimal shape as found in their simulations (Fig. 1b).

Are optimal packings of tubes related to other basic structural motifs in biology? For example, does the DNA double helix also involve optimally packed tubes? A related problem studied by Pieranski[8] involves finding the densest coiling of two identical

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