

than have the less educated — and the latter find it hardest to abandon their cigarettes. If one is talking about cost-effective ways to keep even more old folk sprightly, then the best bet may be to improve the education of the poor and to persuade them to stop smoking. ■

Frances Cairncross is at Exeter College, University of Oxford, Oxford OX1 3DP, UK. e-mail: frances.cairncross@exeter.oxford.ac.uk

1. Manton, K. G., Lowrimore, G. R., Ullian, A. D., Gu, X. & Tolley, H. D. *Proc. Natl Acad. Sci. USA* **104**, 10802–10807 (2007).
2. Manton, K. G., Stallard, E. & Corder, L. *J. Gerontol. B* **50**, S194–S204 (1995).
3. Manton, K. G., Corder, L. & Stallard, E. *Proc. Natl Acad. Sci. USA* **94**, 2593–2598 (1997).
4. Cutler, D. M., Glaeser, E. L. & Rosen, A. B. *Is the US Population Behaving Healthier?* NBER working paper. 13013 (Nat. Bur. Econ. Res., Cambridge, Massachusetts, 2007).
5. Goldman, D. P. *et al. Health Status and Medical Treatment of the Future Elderly: Final Report* (Rand, Santa Monica, California, 2004).

MATERIALS SCIENCE

Stirring stuff

David J. Pine

Take silicon, soak in water, add acid — and stir. This simple new recipe for the self-assembly of complex microstructures belies an involved sequence of hydrophobic, electrostatic and van der Waals interactions.

In folding its proteins and constructing its complex membranes, nature uses self-assembly: bathed in water or another liquid, tiny building-blocks come together by virtue of their shape and interactions. As they report in the journal *Small*, Onoe *et al.*¹ adapt these natural processes for their own designs. They describe a method for assembling parts just 10 micrometres across into complex, three-dimensional objects, and go on to build up chains of interlocking rings. The research is another step towards the ultimate goal of building electrical or optical circuits, or even microscopic machines, from components at micrometre and smaller scales.

The folding of a protein molecule from a long, linear sequence of linked amino acids is one of nature's more spectacular demonstrations of self-assembly. In a watery environment, certain amino acids along the chain can attract each other by various means — van der Waals attraction, hydrogen bonding or hydrophobic interactions. Others might repel each other through their electrical charges or hydrophilic interactions. Geometrical constraints limit which amino acids along the chain can interact with each other, so which amino acid occupies a given position in the chain is crucial to the final topology and shape of the protein. Geometry thus conspires with attractive and repulsive forces to fold the amino-acid chain into the complex shape that gives a protein its particular function.

Simpler examples of self-assembly also abound. Soap molecules, or 'surfactants', are one. These consist of a water-loving (hydrophilic) head connected to a water-hating (hydrophobic) tail. When placed in water, the hydrophobic tails of different surfactant molecules bunch together to form the core of a sphere, with their hydrophilic heads at the surface. This way, both heads and tails get to live in their desired surroundings. While arranging themselves, the tails often corral a particle of dirt, isolating it so that it can be washed away.

Onoe and colleagues¹ exploit the same ideas of self-assembly, except that their building-blocks are not organic molecules, but particles of silicon formed into slightly tapered cylinders 10 μm in diameter at the wider end. This wider base is coated with a layer of hydrophobic molecules, whereas a thin layer of silicon dioxide (SiO_2) forms naturally through oxidation of the remaining surfaces in air. When placed in water with a nearly neutral pH of 6.5, the SiO_2 surfaces become negatively charged and repel each other when two particles come close. The hydrophobic bases of two cylinders, by contrast, can avoid contact with the water by pairing up flush against each other. And this is exactly what happens when the water is stirred to bring particles close to one another: the hydrophobic surfaces pair up to form barrel-shaped 'dimers' (Fig. 1a).

The authors then add a small drop of acid to the water. At the resulting lower pH of 2.0, the

SiO_2 surfaces lose their charge, and the barrel-shaped dimers no longer repel each other. In fact, when close together they experience an attractive van der Waals force, which is strongest between the exposed flat tops of the dimers, which provide the largest area of contact. (The authors also roughen the round sides of the dimers to diminish the attractive force between the already small contact area of the curved surfaces.) So, when the acid solution is gently agitated, the barrel-shaped dimers undergo a further stage of self-assembly into long, thin cylinders.

The next challenge, making a chain of linked rings, takes the process a significant step further. Starting this time with particles shaped like a wide squat U, with a square hydrophobic patch on the inside of the base, Onoe *et al.* follow the same procedure as before (Fig. 1b). The particles first link up at the hydrophobic patches, and then, when the pH is lowered, connect at their ends by van der Waals attraction to form rings. Only a couple of links are demonstrated, but the ability to form such topologically complex objects is intriguing.

This work follows on from the pioneering experiments of George Whitesides and his colleagues, who exploited hydrophobic and hydrophilic interactions, as well as capillary action, to build complex structures on scales of 10 μm and larger: rings, tetrahedra and tiny rugby balls²; chiral helices³; and stacked plates and three-dimensional crystals⁴. Here too, the geometry of the building-blocks largely determines the objects that are assembled. Particles can even be shaped to fit together in a lock-and-key manner². More recently, this mechanism has been exploited on length scales of a micrometre to build up an 'alphabet soup' of particle shapes⁵. These smaller particles are batted about naturally by thermal brownian motion, self-assembling with no external intervention, such as stirring, at all.

What is especially interesting about Onoe and

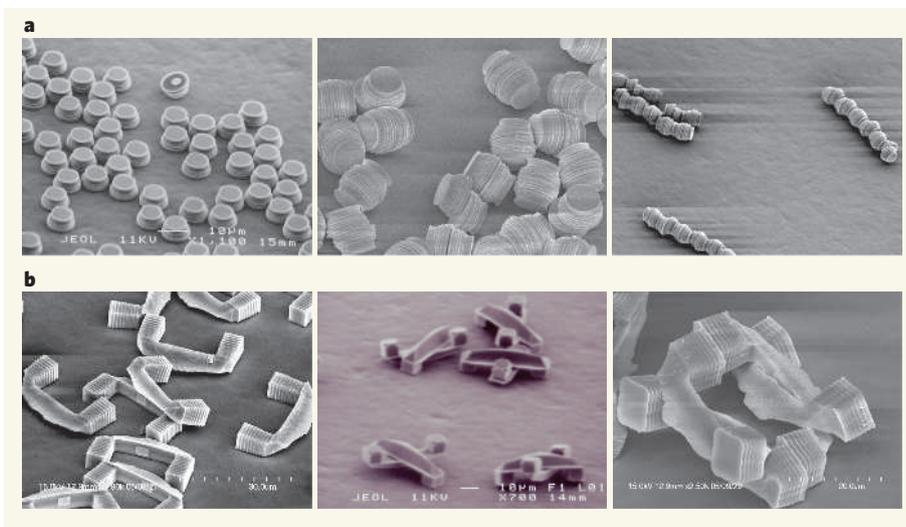


Figure 1 | Self assembly in action. Onoe and colleagues' processes seen under the microscope, starting from (a) tapered cylinders and (b) U-shaped particles. (Images reproduced, with permission, from ref. 1.)

colleagues' technique¹ is the sequential control over a self-assembly process that involves different interactions — first hydrophobic forces, then electrostatic repulsion and finally van der Waals attraction. Sequential self-assembly has been carried out before, most notably in beautiful experiments by Ned Seeman⁶ and Chad Mirkin⁷ and their colleagues using artificial sequences of DNA. But those experiments use the coding of DNA base pairs rather than different forces to control the sequence of self-assembly. Moreover, they are 'biokleptic' (Seeman's term): that is, they borrow heavily from biological processes. Onoe and colleagues' approach is more general and, at the current stage of development, much less powerful. It does, however, represent a useful addition to our toolbox.

To develop self-assembly into a practical technology, we will need to be even more ingenious than nature, exploiting all the interactions

at our disposal and creating yet-to-be envisaged pathways. The recent work¹ takes us a step further down that road. ■

David J. Pine is at the Center for Soft Matter Research, Department of Physics, New York University, 4 Washington Place, New York, New York 10003, USA.
e-mail: pine@nyu.edu

1. Onoe, H., Matsumoto, K. & Shimoyama, I. *Small* **3**, 1383–1389 (2007).
2. Terfort, A., Bowden, N. & Whitesides, G. M. *Nature* **386**, 162–164 (1997).
3. Breen, T. L., Tien, J., Oliver, S. R. J., Hadzic, T. & Whitesides, G. M. *Science* **284**, 948–951 (1999).
4. Clark, T. D., Tien, J., Duffy, D. C., Paul, K. E. & Whitesides, G. M. *J. Am. Chem. Soc.* **123**, 7677–7682 (2001).
5. Hernandez, C. J. & Mason, C. J. *J. Phys. Chem. C* **111**, 4477–4480 (2007).
6. Chen, J.-H., Kallenbach, N. R. & Seeman, N. C. *J. Am. Chem. Soc.* **111**, 6402–6407 (1989).
7. Taton, T. A., Mucic, R. C., Mirkin, C. A. & Letsinger, R. L. *J. Am. Chem. Soc.* **122**, 6305–6306 (2000).

EVOLUTIONARY BIOLOGY

Structure in mutualistic networks

Susanne S. Renner

Statistical analyses of the networks formed by plant–animal mutualisms can now take account of the relatedness of the players on either side. How helpful is this innovation for understanding network dynamics?

The mutually beneficial relationships between plants and animals take several forms. One example is pollination. Another is the process by which a fruit-eating creature, a frugivore, gets a meal and subsequently disperses a plant's seeds in its droppings.

In the context of a local ecological community, such relationships can be seen as networks in which the evolutionary dynamics of the partners may be mutually dependent, contributing to an array of coevolutionary processes¹.

On page 925 of this issue, Rezende *et al.*² report an analysis of plant–pollinator and plant–frugivore networks that includes information on the evolutionary history of the partners — that is, on the phylogenetic relatedness of each partner to other plants or animals in the network. Their aim was to determine whether relatedness affects network structure and whether it predicts 'cascades' of coextinction. This is the first such evolutionary network analysis, and it highlights both the power and the limitations of the approach. Two central concepts are those of species 'strength' and species 'degree' (as described in Box 1, overleaf, which gives the background to the method). Combining the two concepts has produced a boom in the analysis of plant–animal networks^{2–4}.

In mutualistic networks, optional interactions occurring among many species are common; most interactions are strongly asymmetric; and species interact with nested subsets of partners^{1,5,6}. Thus, a large number of species having few inter-

actions coexists with a relatively small number of super-generalists. Relatively rare plants and animals, as well as those with comparatively few partners, interact primarily with a core group of abundant generalist species.

Related participants in mutualisms are likely to have similar morphology, physiology and behaviour. These are traits that evolve as lineages diversify, so we would expect the structure of mutualistic networks to be influenced by the hierarchical phylogenetic relationships present in a particular community. This is the assumption Rezende *et al.*² set out to test. Statistical methods to estimate the role of phylogenies in explaining patterns of trophic (feeding) association are now available^{2,7}; these methods are based on established statistics for the phylogenetic comparative method^{8,9}. The basic approach is to structure the problem of pollinator–flower associations as a statistical model in which phylogenies are used to give the covariance structure of the 'error' terms.

Rezende *et al.* applied these methods to 59 plant–pollinator and plant–frugivore networks, which were compiled from the literature. Their approach involved obtaining phylogenies for the insects in 35 networks, birds (all frugivores) in 18, and flowering plants in 52. The number of interactions per species was significantly phylogenetically conservative in 25% of the phylogenies (26 of 105) and a third of the networks. Small phylogenies provide little power to detect phylogenetic effects, and when only the

22 phylogenies with more than 70 species were considered, this percentage increased to 55%. A correlation between phylogenetic relatedness and ecological similarity — the fraction of common interactors between two species — was detectable in 43% (50 of 103) of phylogenies.

For their ten largest communities (those with more than 40 animal and plant mutualists), Rezende *et al.* simulated coextinction cascades by removing pollinators systematically, starting with the least-linked (most specialized) partners and moving to the most-linked (most generalized). Species left without any local interaction were assumed to become extinct. The simulations show that related species do tend to become extinct together, although the effects were small.

Overall, given the modest percentage correlations cited above, Rezende and colleagues find that phylogenetic relationships do not have a marked effect on the degree and strength of interactions in local communities. This result will disappoint those who expect to find such a signal in every nook and cranny. One explanation may lie in the hugely varied temporal scales over which the hundreds of plant and animal species in the 59 local networks have been interacting. The networks encompass Mediterranean, tropical, temperate, subtropical and Arctic communities, which differ greatly in their stability and numbers of evolutionarily old or recent species. Also, some of the communities have comparatively few closely related species, and so lack a strong phylogenetic structure. Given the different temporal and spatial scales over which different pollinators (birds, bees, flies, beetles) and plants (tropical or temperate, woody or herbaceous) evolve, very large networks may be needed to discern phylogenetic signals in interaction strength and degree¹⁰.

However, even then, phylogeny might not predict numbers and kinds of mutualistic interactions. As has been shown¹¹ for a network involving many insects and one focal plant, broad-leaved lavender (*Lavandula latifolia*), having few or many visitors to a flower may not be a trait that is invariant at the species level, but instead may depend on research design (sampling effort) and biological phenomena (variation in absolute and relative pollinator abundance or visitation rates). If a large proportion of the interactions counted in pollination networks are not species-level traits, this would explain the absence of clear phylogenetic effects in insect–flower networks.

There is a risk that treating mutualistic networks as "coevolved structures rather than as diffuse multispecific interactions"⁵ could lead research on networks into a trap from which community ecology has long escaped¹². Instead of revealing coevolved interactions, Rezende and colleagues' results might be taken as showing that such interactions are not very important. And in terms of extinctions, the formation of associations between migrating or invading species and local generalist species