Face to face with proteins

Stephen Mann

THE chemical and electronic properties of surfaces and interfaces are subtly influenced by the nature of adsorbed species, so controlling the way that molecules interact with a solid support is crucial if reproducible interfaces are to be fabricated for catalytic, electrical and sensory devices. This problem is becoming increasingly severe as micrometre-scale devices are replaced by systems of nanometre scale. In general, crystalline substrates can act as templates for the site-directed adsorption of small molecules and ions, but there are difficulties in achieving this level of specificity with species of higher molecular weight such as proteins and polysaccharides. A report by Douglas *et al.*¹ now shows how macromolecules can be assembled into periodic arrays on the surface of a thin (1.2-nm-thick) tantalum/tungsten film. The solution was to design a polycrystalline metal-oxide surface containing a regular lattice of holes 14 nm in cross-section. The protein molecules (12 nm in diameter) then slot into the surface indentations by preferential electrostatic bonding.

Although the idea is simple, engineering a metal surface on the nanometre scale to provide a molecular screen is a complicated business. First, a suitable template has to be found. For this, Douglas *et al.* exploited the natural ability of certain bacteria to produce thin protein films of mesh-like crystal structure. They used the crystalline glycoprotein (relative molecular mass 140–170 K) present in the surface layers of the cell wall of the thermophilic bacterium *Sulfolobus acidocaldarius*. This protein has a structure based on a triangular lattice that contains large (14 nm) channels of sixfold symmetry repeated at distances of 22 nm (ref. 2). Monolayer fragments of the protein were mounted onto amorphous carbon substrates and then coated in a fine-grained film of 3-nm tantalum/tungsten particles by evaporation. Regularly spaced holes in this alloy film were then introduced by bombarding the surface with argon atoms (argon-ion milling), which selectively removed metal atoms overlying the original holes of the protein lattice³.

Assembling macromolecules into this 'nanofabricated screen' is not just a matter of fitting the right size molecule into the right size hole. Proteins will adsorb on the metal surface as well as in the holes, and the resulting surface structure becomes ill-defined. To overcome this obstacle, Douglas *et al.* made the alloy surface negatively charged by oxidation of the metal in air over a period of several months. This 'primed' surface was exposed to an aqueous solution of the anionic

protein, ferritin. Protein molecules were electrostatically repelled from the oxide surface except at sites occupied by the holes of the screen. The resulting structure is a unique composite of biomolecules and metal-oxide particles organized at the nanometre level.

There are some problems with the technique. First, the dimensions of the metal lattice tend to fluctuate because of the presence of trace amounts of organic contamination and redeposition of metal atoms during the argon-ion milling process. Second, the number of adsorption sites filled by the macromolecules is low, often only 15 per cent. Douglas *et al.* suggest an intriguing strategy to improve on the efficiency. The approach is to increase the activity of the adsorption sites by adding functional groups to the carbon substrate located at the bottom of the holes so that these regions become selective in terms of molecular recognition. Possibilities include the attachment of organic residues through coupling agents (silanes for example) and chemical conjugation by adsorbed antibodies. Alternatively, it may be possible to isolate inorganic clusters in the holes to give an organized heterometallic surface. Islands of gold, for instance, could then serve as periodic sites for binding biological molecules.

The approach adopted by Douglas *et al.* highlights the possibility of designing interfaces with organized biological and

solid-state components. It is unclear what immediate applications could arise from their work, but it is undoubtedly of fundamental importance in the study of controlled interfacial phenomena.

It is interesting to speculate whether analogues of these nanoheterostructures exist in biological systems. For example, model systems of biological membranes such as phospholipid vesicles can be metallized by metal⁴ and semiconductor particles⁵ of nanometre size, and compressed surfactant monolayers can act as templates for orientated crystal nucleation⁶. Could similar inorganic nanoclusters exist on the membrane surfaces of cells and organelles? It would be difficult to identify these components because they are so small (and because of the enthusiasm of biochemists for purified biomolecules). Yet such structures could be involved in redox, photochemical and catalytic processes. Moreover, the question arises whether associations of mineral clusters and self-assembled macromolecules served as energy-capture and transformation devices in the early stages of life. □

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HUMAN EVOLUTION

The Y of human relationships

John Maynard Smith

WHEN, three years ago, Cann *et al.*¹ estimated that all human mitochondria are copies of the mitochondria in one woman living 200,000 years ago in Africa, it was perhaps inevitable that this should have been reported in the press as "Eve lived in Africa 200,000 years ago". Since then, I have been looking to the day when studies of the Y chromosome led to the conclusion that Adam lived in China at an earlier or later date. Two publications^{2,3} on the human Y, one of which appears on page 663 of this issue², raised my hopes, but it seems that, as yet, the Y chromosome is less informative than the mitochondrion.

I must first explain how data of this kind can be interpreted. Suppose we have a population of entities (Y chromosomes, mitochondria) that reproduce without recombination, then all the entities in the present generation must be descended, with or without mutation, from a single

entity in some past generation. If we assume that selection is weak, we can estimate how many generations ago that common ancestor lived. If family size is Poisson distributed — a reasonable assumption — then the expected time to a common ancestor is $2N$ generations, where N is the number of entities in a single generation: unfortunately, this estimate has a large standard error. If the variation in family size is greater than Poisson, the expected time to a common ancestor is shorter.

Cann *et al.* constructed a phylogenetic tree of the mitochondrial DNA from 147 humans, using 195 polymorphic restriction types. The average difference between unrelated humans was 0.57 per cent of nucleotide divergence. They estimated the rate of sequence divergence in mtDNA as 2–4 per cent for each million years: this estimate was based partly on data from other mammals, and partly on