like *Sxr* mice. A bovine complementary DNA which hybridizes to three of the four conserved regions has now been obtained, so such an experiment may not be far off.

Two other aspects of the work are particularly interesting. First, there seems to be a similar gene on the X chromosome, both in man and in all the other mammals examined. Page *et al.* argue that this may be functionally related to TDF and that the high degree of conservation makes it unlikely that this is a pseudogene. They speculate that the X gene could act antagonistically to TDF or, alternatively, that the two gene products could act in concert as a heterodimer in males, whereas the X gene product alone would act in females. They also discuss a more radical possibility, which would unite the processes of X-chromosome inactivation and sex determination[8]. If X and Y genes perform identical functions, and are expressed at the same level, then X-chromosome inactivation would leave one active gene in XX and two in XY. This dosage difference, rather than the presence or absence of the Y gene, could act to direct to subsequent events. Dosage mechanisms of this type are involved in sex determination in some invertebrates, such as fruitflies[9] and nematode worms[10], but there is no reason to expect them to be universal.

Second, the putative TDF probe detects a related sequence in chicken DNA, although there are identical hybridization patterns for both roosters and hens. In birds, the female is the heterogametic sex (ZW), whereas males are ZZ, so the bird gene, if it is also male-determining, must be regulated in a different way from mammalian TDF. Furthermore, if the gene is present in birds, then it is probably also present in reptiles, which exhibit further variations in sex-determination mechanisms. In fact, ancestral tetrapod sex-determination may have been environmental rather than chromosomal: many turtles and crocodiles exhibit temprature-sensitive sex determination[11]. Perhaps the original TDF protein was temperature-sensitive in function, and came under different kinds of regulation with the evolution of homoiothermy in mammals and birds. In any event, the isolation of this key gene should unlock the door to the understanding (and exploitation) of primary sex determination in all mammals, and possibly in other vertebrates. □

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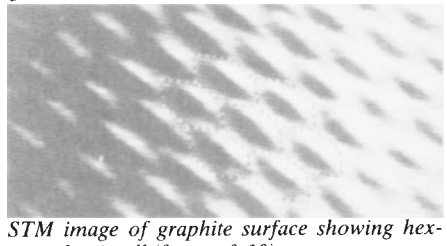
Scanning tunnelling microscopes

Atomic-scale engineering

J.B. Pethica

ATOMIC-RESOLUTION images of surfaces are now regularly obtained using the recently developed scanning tunnelling microscope (STM). Efforts have also been made to alter the structure of the surfaces using the STM as a high-resolution probe. It has thus become one of the principal *gedanken* tools for nanotechnology — the proposed direct manipulation of matter, especially biological, on the atomic scale. On page 324 of this issue[1], J.S. Foster and colleagues demonstrate the pinning of small organic molecules to a graphite surface, and the partial ability to dissect these molecules. These appear to be the smallest scale structures to be made and imaged by the STM to date.

Writing of near atomic scale structures was demonstrated[2] last year, and I discussed it in a News and Views article[3] at the time. Very small groups of germanium atoms were placed on an otherwise flat germanium surface by means of a voltage pulse; they were subsequently 'read' using the STM in its imaging mode. In the new work[1] of Foster *et al.*, graphite is the flat substrate onto which features are written. The graphite is covered with a small drop of di(2-ethylhexyl) phthalate and the STM tip brought to the graphite through this organic liquid. A voltage pulse is then applied, and immediately thereafter a feature about 1 nm across appears on the STM image of the graphite surface. The feature is attributed to an organic molecule becoming pinned on the graphite surface. The authors suggest that the molecule becomes pinned because the voltage pulse excites the molecules, giving charge transfer or bond breaking. This could also alter the unoccupied electronic levels of the graphite, allowing the molecule to be imaged. Under some circumstances it was possible to create structures only 0.4 nm across, the smallest deliberate structure yet made.



STM image of graphite surface showing hexagonal unit cell (from ref. 10).

Having created a feature on the graphite, it can be altered by applying a further voltage pulse when the tip is again over the feature. This results in enlargement, partial erasure or complete removal of the feature, at present unpredictably. The partial erasure reported by Foster *et al.* implies that molecules may have pieces deliberately removed, and in principle be atomically 'edited', thereby demonstrating one of the ideals of nanotechnology.

The work has a number of intriguing features. First, the type of molecule does not appear to be important, successful writing being obtained with a variety of organic species. This implies that the binding mechanism may be generic to organic materials, such as the hydrogen and oxygen binding to graphite that Foster *et al.* suggest. Second, writing and altering the structures requires about 3.5 V, similar to the C–C bond energy. This is also the voltage, around the value of the work function, near which field emission or evaporation, or dielectric breakdown may occur across the narrow tunnel gap. The polarity independence also suggests a field or impact effect rather than a bond specific mechanism. Last, it should be noted that the work is exclusively on graphite. This gives very clear-cut and elegant images of the graphite lattice, which are known, however, to have some rather unusual characteristics — excessively high image corrugation heights for the known charge density, and freedom from single-atom scale defects. Some models for these anomalous effects (applicable also to other layered materials) have been proposed[4-6] which may involve mechanical contact of the tip and graphite surface[6,7]. The tunnelling occurs over an area rather larger than a single atom (see figure). The features seen by writing could thus be caused by voltage-pulse induced alteration of the graphite itself; small features the size of the contact area would be produced and altered.

Progress is being made in a number of applications of surface alteration using the STM. Structures have been written on the 10-nm scale or greater in amorphous metals[8] and in standard electron-beam lithography resists[9]. The work[2] on germanium is closer to the atomic scale. The work of Foster *et al.*[1] represents a significant attempt at the much more important and difficult problem of the direct manipulation of the structure of biological materials. □

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