protein. Sites of synthesis of the dysregulated version include fat, brain, liver and almost every other tissue. So agouti protein is one which can, when expressed in the wrong place and at the wrong time, cause obesity. The precise locus and mode of action of dysregulated agouti remains to be determined.

Between them the new studies raise as many questions as they answer. But obesity is a serious health issue, and the advent of the molecular era of research on the topic gives cause for optimism that those questions can be tackled — and even answered. □

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ELECTRON MICROSCOPY ——————————————————

The ultimate analysis

L. M. Brown

THE ultimate reductionist goal of the scientist engaged in unravelling the properties of solids is to locate and identify the component atoms, one by one; then to determine the possible electronic transitions which the electrons of those atoms can undergo. With the announcement by three groups — two elsewhere in this issue[1,2], and one in an earlier paper[3] — of atomic column-by-column imaging, accompanied by electron energy-loss spectrometry from a specified column, this goal has come within reach of many laboratories around the world. 'Columns' here means stacks of atoms, like grapefruit piled high in the supermarket.

The chain of evolution of the new techniques is ramified. The first single-atom images, accompanied by spectroscopy, were made many years ago by E. W. Muller; a modern review by Miller[4] tells the story. In this technique, the atomic mass of each atom can be established as the atoms are extracted from the specimen. But the electronic structure of the embedded atom is not accessible. Many years later, Crewe[5] managed to produce images of single atoms in a scanning transmission electron microscope incorporating a field emission electron gun to achieve enough current in his atomic-sized probe. His work demonstrated that the best way of getting the required contrast was to look at electrons scattered to large angles, in the 'annular dark-field detector'. Crewe's method was aimed at biological problems, where the atoms are generally not in crystalline arrays. But it rendered visible atoms embedded in their environment, and because it was a scanning technique, it opened the door, in principle, to the acquisition of electron energy-loss spectra from individual atoms. However, when it was applied to crystals, strong specular Bragg reflections confused the images.

It was Howie's suggestion[6] that much larger angles of collection should be used, so that only incoherent scattering contributed to the image. Armed with this technique, Pennycook and Boatner[7] were able five years ago to demonstrate incoherent imaging of atomic columns in thin films: a notable advance, because by conventional non-scanning methods the fringes of atomic spacing produced by coherent interference of Bragg beams depend treacherously upon foil thickness, defocusing the microscope, and the pre-
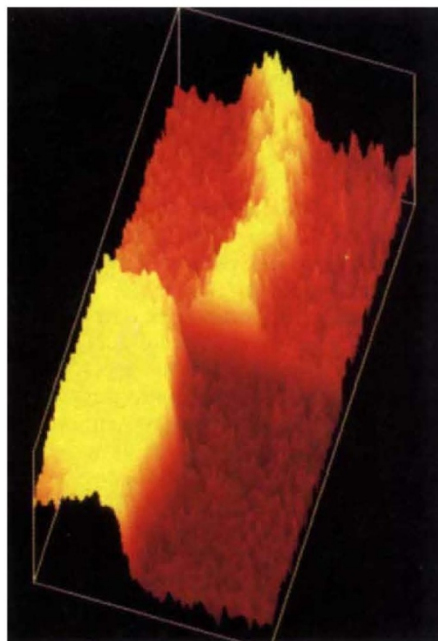
Interface between diamond film and silicon substrate (Muller et al.[1]). Top, bright band is threefold-coordinated amorphous carbon at the interface; bottom, bright region is fourfold-coordinated diamond film.

cise orientation of the atomic columns: delicate calculations are required to decide if atoms should be white or black!

While these developments were in train, considerable effort was put into improving electron spectrometers. Ideas were borrowed from the efficient β-particle spectrometers used by atomic physicists. Progress owes much to the advent of charge-coupled devices which permit digital acquisition of many channels of a spectrum at once, all under computer control and allowing fast numerical processing.

The two strands of development come together in the ability to image columns of a few tens of atoms, which show as light blobs in the dark-field image; then confidently to put the electron probe at the top of the column, directed down it, and to acquire a spectrum which indicates essentially the density of empty states available to the atomic electrons in the column, giving both the chemical species and the valence state, as well as vital information on the local coordination of neighbours. In this way, Batson[2] is able to see the different oxidation states of silicon in the neighbourhood of the interface with its oxides, and Muller et al.[1] to see atomic interlayers between a silicon substrate and a diamond film grown by chemical vapour deposition. These are applications of great importance, because they allow for the first time a robust view of the chemistry of the nucleation of thin films, on the scale of the initial nucleus.

What can we expect of the new technique? One limitation, as with all electron microscopy, is radiation damage: it will not be possible to study the interfaces between enzymes and their biological reaction products, nor any aliphatic compounds. The best spectral resolution achieved by Batson is 70 meV, so the infrared part of the spectrum is poorly covered. In fact, the uncertainty principle limits the spatial resolution obtainable at such low energy losses, so that only for losses of about 100 eV or higher does the technique really make sense.

On the other hand, the spectra obtainable at these energies are comparable to or superior to those from synchrotron sources, with the bonus of atomic spatial resolution. The cost of a machine to do this is about £400,000, which enables any well-equipped laboratory to carry out the experiments, and certainly compares very favourably with the cost of a synchrotron. So we must expect that in the world of inorganic thin films, where interfaces control the structure and properties of the product, these new techniques will be widely taken up and have a profound impact. In metals and ceramics, where grain boundaries act as chemically active interfaces, the techniques open up a whole new field of experimental grain-boundary chemistry which should lead at last to control and eradication, at the atomic level, of the chief causes of brittleness and failure of materials in service. □

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