

*in vitro* can be counted, however, is surely a favourable omen. The essential similarities with certain aspects of hormone action in animals also cannot be ignored, leading one to hope that a solution to the problem of the molecular nature of auxin action is not very far off.

#### DNA TUMOUR VIRUSES

### Replication *in vitro*

from our Cell Biology Correspondent

It scarcely needs saying that the biochemistry of DNA replication in mammalian cells has yet to be elucidated, and although several groups have shown that nuclei isolated from one sort of animal cell or another will support limited amounts of DNA synthesis such cell free systems and their products have not been thoroughly characterized. Not the least of the problems faced by those working with isolated cell nuclei is the characterization of the DNA that the nuclei make. Mammalian DNA is so complex and the amount of DNA per nucleus is so great that characterization of any DNA made *in vitro* is at present, as Winnacker *et al.* (*J. Mol. Biol.*, **72**, 523; 1972) comment, "an essentially hopeless task". It was to avoid attempting the hopeless that Winnacker and his colleagues decided to work with nuclei isolated from mouse 3T6 cells infected with polyoma virus. Polyoma virus DNA molecules, each weighing  $3.5 \times 10^6$  daltons, can at least be isolated and studied in some detail.

Last year Winnacker *et al.* (*Biochem. Biophys. Res. Comm.*, **44**, 952) reported that nuclei from such infected cells do incorporate deoxynucleotides into the replicative intermediate of polyoma virus DNA; now they have analysed this reaction more thoroughly. By centrifugation through neutral and alkaline gradients, by chromatography and by nucleic acid hybridization they have shown that a small amount of label is incorporated into covalently closed, superhelical duplex polyoma virus DNA when the nuclei are incubated in appropriate media.

The incorporation reaction depends on the presence of all four deoxynucleoside triphosphates and is stimulated by ATP,  $Mg^{2+}$  and monovalent cations. During 5 minute incubations  $^3HdTTP$  is incorporated into short chains of polyoma virus DNA, but after 30 minute incubations much of the label is found in linear polyoma virus DNA molecules of unit length. The rate of synthesis of the viral DNA varies with temperature; at 25°, 30°, and 35° C incorporation is non-linear and at all three temperatures incorporation

reaches much the same plateau level. These data suggest that viral DNA synthesis in these isolated 3T6 cell nuclei is restricted to the completion of daughter DNA chains, the synthesis of which had been initiated *in vivo*. This is not surprising because to date all mammalian cell free systems which support DNA synthesis do not apparently support new initiation events.

In a second report, the same group (Magnusson *et al.*, *ibid.*, 539) describe experiments in which they used a density label, dBrUTP, which replaces dTTP, to analyse the DNA synthesized *in vitro*; their data indicate that the synthesis of viral DNA *in vitro* is semi-conservative. And, by first labelling cells with  $^3H$ -thymidine, then extracting the nuclei and allowing them to incorporate dBrUTP and  $^{14}C$ -dATP and finally analysing by gradient centrifugation the distribution of the two radioactive labels and the density label, these authors have been able to conclude that the daughter chains of virtually every

partially replicated polyoma virus DNA molecule present in the nuclei are elongated *in vitro* at a rate at most only 20 per cent of that *in vivo*. Whether or not the daughter chains are synthesized discontinuously as a series of Okazaki-type pieces which are ligated remains an open question. The fact that after 5 minute incubations  $^3HdTTP$  is incorporated into short DNA chains whereas after 30 minute incubations label occurs in long chains is consistent with the idea that synthesis is discontinuous, but it can equally well be argued that the rate of addition of nucleotides decreases as the chain length increases.

This is one of the several questions that Winnacker and his colleagues may be able to solve using their cell free system, and whatever else they should find that replication of circular polyoma virus DNA is a bidirectional process. This would agree with the findings of Danna and Nathans (*Proc. US Nat. Acad. Sci.*, **69**, 3097; 1972) that repli-

### Building Structures from the Void

At a time when few scientists even know that "data" are plural and are given rather than taken, scientific etymology is out of fashion. Whoever pauses to ask how eutectics acquired their name? These are intimate mixtures of two or more phases, patterned in fine regular lamellae or rods, often as well ordered as a regiment on parade. The name simply means "well built". A eutectic grows when a molten alloy of the right composition is frozen. A liquid alloy is like the Earth before its formation: without form, and void-amorphous, in fact—and so the well-built structure emerges from the initial void.

Research on eutectics is in full spate: this is partly because of the intrinsic interest of the subject, and partly because of hopes of engineering applications. The interest lies in discovering what factors determine the spacing of the eutectic structure and the crystallographic relation between the phases, and the possible applications are centred on making strong and creep-resistant alloys.

In normal conditions fibre reinforced composites using glass or carbon fibres are manufactured by putting ready made fibres into a plastic, metal or glass matrix, and it has often proved very difficult by this means to get a uniform, regular and well-aligned composite, one which is literally eutectic. So a great deal of research has gone into directional solidification of molten alloys, in which heat is abstracted strictly in one direction so that the product is a single grain with one parallel set of lamellae

or rods, grown *in situ* (instead of the maze of winding lamellae or rods found in a normal ingot). By modifying composition in a ternary alloy, growth rate and temperature gradient, a variety of highly ordered eutectic structures can be designed. The technique builds on the earlier research on the basic features of eutectic solidification and is (*pace* the Manchester report) one of the more heartening examples of technology building on science.

The latest variant of the technique is to grow aligned eutectics not from liquids but from glasses, which are simply amorphous solids. Many melts can be turned into glasses, if not by slow cooling then by rapid quenching, and this method is most likely to be successful in congealing a liquid into a glass if it has a low freezing point: just this is a special feature of eutectic compositions.

In next week's *Nature Physical Science* (January 1) Carpay and Cense of Philips Research Laboratories in Eindhoven show how quenched glassy mixtures of certain salts or oxides can be turned into aligned eutectics by heat treatment in a temperature gradient well below the eutectic temperature: the gradient is best inverted so that the eutectic grows from cold to hot. Carpay and Cense have been working with model systems, not alloys, but perhaps their intriguing method can be extended to metallic systems. The most novel feature of their eutectics is the extremely fine lamellar spacing, often less than  $1 \mu m$ . The technique deserves to be followed up.