Is Enough Too Much?

from our Cell Biology Correspondent

THE barons of biochemistry not infrequently these days publish sets of four, five or even six consecutive reports in one issue of this or that journal, but the thirteen articles from Khorana's group which comprise a complete issue of the *Journal of Molecular Biology* (**72**, 209–475; 1972) surely set something of a record. And it is a record that not everybody may wholeheartedly applaud as they return dyspeptic from midwinter festivities. The first report of the set is entitled "Studies on Polynucleotides" and has the subtitle "CIII. Total Synthesis of the Structural Gene for an Alanine Transfer Ribonucleic Acid from Yeast"; the final article is entitled "CXV. Total Synthesis of the Structural Gene for an Alanine Transfer RNA from Yeast. Enzymic Joining to Form the Total DNA Duplex".

Between these first and last reports Khorana and his thirteen colleagues, apparently virtuoso chemists to a man, describe in detail how they synthesized and ligated icosa, dodeca, undeca, deca, nona, hepta and hexadeoxynucleotides. (These reports provide a gentle test of familiarity with the arithmetic of the Ancients.) Every step of this synthesis has obviously been executed with consumate skill and the whole constitutes perhaps the greatest *tour de force* organic and biochemists have yet achieved. Like NASA with its Apollo programme, Khorana's group has shown it can be done, and both feats may well never be repeated.

Khorana has climbed his Everest, much of value has been learnt on the way up and maps of the route have been safely interred in the literature. That a description of the final assault on the peak fills a complete issue of the *Journal of Molecular Biology* may at first glance seem a trifle extravagant, but on reflexion it is perhaps true to say that the number of publications per man year of hard and most skilled work is far from extravagant and probably even below average. What Khorana's group and the editors of the *Journal of Molecular Biology* have done by courageously publishing a set of thirteen long reports in one issue of the journal, instead of discretely spreading them, is draw attention to the chronic limitations (or are they already acute?) of the hallowed methods of disseminating information in the scientific community. The proportion of devotees of the *Journal of Molecular Biology* who will actually read every word in these articles must be minute indeed. But who among the vast majority that does nothing more than glance at the contents list of the journal before hastily putting it back on the library shelf with feelings ranging from vexation to open-mouthed admiration has the audacity to suggest that publication of this work in this manner is inappropriate or unnecessary when it is increasingly the fate of most scientific reports to go unread and even unnoticed? Everybody knows the problem but nobody has yet provided a workable answer.

TECHNIQUES

Tips for Scanners

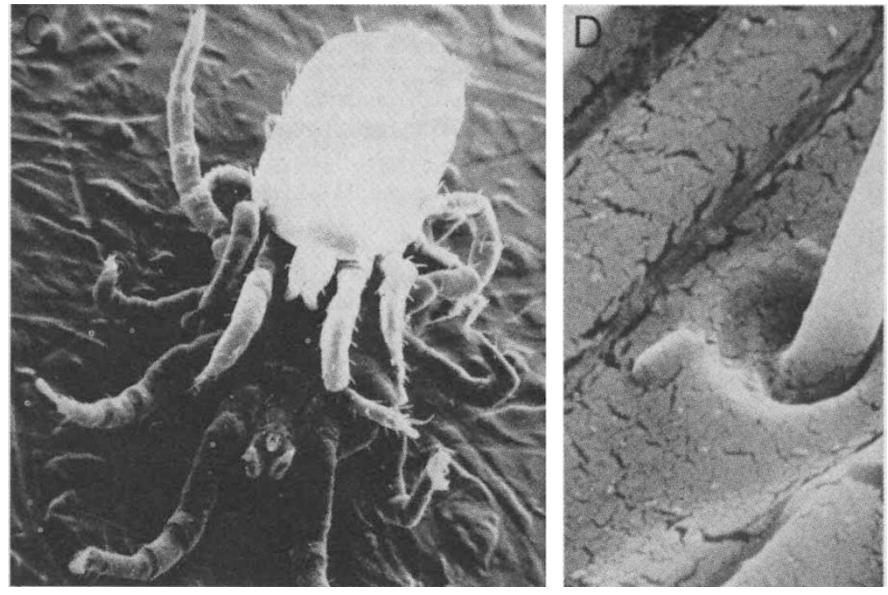
TUCKED away at the back of a collection of miscellanea in the latest issue of the *Bulletin of the British Museum (Natural History) Zoology* (**24**, 223; 1972) is a note which scanning electron microscopists may well find useful. Three members of the Electron Microscope Unit at the museum—R. H. Harris, B. S. Martin and C. G. Ogden—pass on their experience of the best techniques for preparing different natural history specimens; it would seem that conventional methods for dealing with some material are far from ideal.

Harris *et al.* recommend, for example, using chemical fixatives before freeze drying of fresh material such as blood cells, which are difficult to separate from the plasma surrounding them. They have found that the conventional transmission electron microscopy fixatives, glutaraldehyde and osmium tetroxide, both suitably buffered, are usually satisfactory, but with human blood cells better results are obtained with neutral Kaeserling I fixative.

Some specimens need narcotizing before fixation; for example, some oligochaetes and platyhelminthes not only contract violently if plunged directly into fixatives, but also secrete quantities of mucus which is often dispersed so finely that it is detected only on examination at magnifications outside the range of the optical microscope.

After describing some methods of freeze drying, Harris *et al.* turn to the disadvantages of some adhesives. A point often overlooked when specimens are being mounted is the part played by the adhesive in the background of the intended micrograph. Double-sided adhesive tape and 'Silver Dag', for example, can produce a confusing appearance and the specimen stub is scored with machine marks and small pits (see left-hand figure). A clean, clear background can be obtained by using 'Silver Dag' to stick a 10 mm diameter, circular, glass cover-slip on the stub surface.

The next step is the coating of specimens with a conductive layer, usually an evaporated metal. Without the coating the specimen becomes charged (see left-hand figure); there is loss of resolution and bright patches obscure detail. A coating of between 10 and 15 nm thick is considered satisfactory for most specimens. Harris *et al.* describe the advantages of some metals over others and provide formulae for determining the thickness of the coating. It seems that the coating on the surface of chitinous materials, such as hair and insect cuticle, often has a crazed appearance (see right-hand figure), but Harris *et al.*, with all their experience, have not yet found a way of eliminating this effect although they have found that prolonged air drying before mounting can reduce it to an acceptable level.



Left: Two mites (*Dermanyssus gallinae*) (×64); the upper of the two shows typical charging; the background pattern is caused by double-sided adhesive tape. Right: the cuticle of a mite showing the crazing effect associated with chitinous surfaces (×63,750). From Harris *et al.*, *Bull. Brit. Mus. (Nat. Hist.) Zool.*, **24**, 223; 1972.)

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