NUCLEIC ACIDS

Rules for Sequencing DNA

from a Correspondent

THE seemingly insurmountable problems involved in sequencing DNA molecules, or even substantial pieces of them, have always provoked stock responses about the necessity of finding specific deoxyribonucleases. This, however, is probably less important than choosing a promising DNA of modest size to work on (such as the reiterated sequences in some mammalian satellite DNAs being studied by Southern and Walker), and using adequate methods for fractionating fragments of it. Some of the technical foundations for the latter task have been laid down recently by K. Murray (*Biochem. J.*, **118**, 831; 1970) in a vast and painstaking study of oligodeoxynucleotide mapping procedures, lasting several years. He started with the methods devised by Sanger and his colleagues which have proved so successful in the sequence analysis of RNAs.

Murray used ^{32}P-labelled DNA prepared from *Escherichia coli* and the bacteriophages λ and fd as substrates. First, he fingerprinted digests of *E. coli* DNA carried out with pancreatic deoxyribonuclease and a deoxyribonuclease from the mould *Neurospora crassa*.

He used the standard method of electrophoresis on a strip of cellulose acetate at *p*H 3·5, followed by electrophoresis on DEAE-paper at *p*H 1·9. The fingerprints were qualitatively similar, and reproducible in defined conditions of digestion. Murray then analysed, fully or in part, about seventy spots ranging up to tetranucleotides in size. On the basis of his results, devotees can easily see that the oligodeoxyribonucleotides are fractionated in a similar way to oligoribonucleotides, falling into "graticules" according to their compositions, but the picture is complicated because of the lack of enzyme specificity, so that all the isomers of the smaller sequences arise as products of digestion. Many of these were separated from each other during subsequent fingerprinting, but the very complex mixtures of larger oligonucleotides were not fractionated by this system, and so Murray modified the fingerprinting procedure in two ways. This greatly improved the resolution of these larger products. In one case he carried out the first dimension of electrophoresis at *p*H 9·7 (5 per cent triethylamine carbonate) on DEAE-paper.

He also used a system in which DEAE-paper was replaced by AE-paper in the second dimension. He indefatigably constructed further maps, after examining about 120 products fractionated on the system using triethylamine carbonate, and another 110 products on fingerprints prepared on AE-paper.

There was, however, a rather unfortunate denouement when Murray attempted to compare the DNAs from *E. coli* and phages λ and fd. Pancreatic deoxyribonuclease fingerprints of these molecules gave essentially similar pictures, and it was not possible to ascribe any definite significance to the slight differences observed. The lesson must surely be that even these comparatively small DNAs are far too complex to be readily amenable to these methods. It will probably be several years before a roll of DEAE-paper and a strong constitution are all that is required to sequence λ DNA.

EARTHQUAKES

Why Chandler Wobble?

from our Geomagnetism Correspondent

ALTHOUGH the Chandler wobble, the precession of the Earth's axis of figure about the axis of rotation, was discovered in 1891, its cause is still a mystery. There are, in fact, two separate puzzles involved—the source of the excitations which produce the wobble of amplitude about 0·5", and the width of the spectral peak which indicates that the period of fourteen months varies within ± 4 per cent. The simplest explanation for the varying period is that it results from continuous excitation of a mechanical system whose natural period changes with time; but it is unlikely that physical changes in the Earth would produce the observed variations over times as short as a year. Alternatively, the Earth could have a fixed Chandler period produced by random excitations which are subject to damping. This is much more reasonable, especially as theoretical calculations of the period turn out to be about 1·20 years.

But what energy source maintains the random oscillations? During recent years it has become popular to imagine that this source is earthquakes; and this view has received considerable support from theoretical calculations which show that, given the right conditions, one large earthquake could produce 10 per cent or more of the observed Chandler wobble amplitude. If a single earthquake can do this, it seems intuitively likely that all earthquakes together could account for the whole of the Chandler wobble. Ben-Menahem and Israel (*Geophys. J.*, **19**, 367; 1970), however, are more pessimistic. They show that a single shallow earthquake of magnitude 8·5, occurring at a suitable latitude and with a favourable strike-azimuth, could maintain the Chandler wobble for about a year—and yet they conclude, paradoxically, that the total number of real earthquakes could account for only about 30 per cent of the observed wobble amplitude and corresponding secular polar shift.

The reason is, of course, that the secular polar shift produced by an earthquake is critically dependent not only on the shock's magnitude but on its position and its strike and source parameters. An earthquake of magnitude 8·5 may maintain the Chandler wobble for a year under optimum conditions; but an earthquake of that magnitude only occurs about once every 4 years, and when it does the conditions for Chandler excitation are far from optimum. If all the annual seismic energy were to be released in a single shallow strike-slip rupture on a meridional fault located at the equator, then again the resulting annual shock would be sufficient to drive the Chandler wobble for ever. In practice, circumstances are far less favourable.

It is important to realize, however, that Ben-Menahem and Israel have derived their conclusions from a mathematical model. It turns out to be a model which is considerably more favourable to the excitation of Chandler wobble by earthquakes than models previously used to describe the same effect—but it is a model none the less, and is therefore subject to simplifying assumptions. Thus Ben-Manahem and Israel have not proved conclusively that earthquakes do not account for Chandler wobble because some assumptions may not be valid and modifying conditions may remain to be discovered. For this reason, we have certainly not heard the last of earthquakes as the source of Chandler wobble.