say that significant advances may not be made by making a number of more limited, less ambitious assaults. Thus it may never be possible to compare the complete pre-Mesozoic polar wandering paths for several continental masses; but if it can be convincingly demonstrated that one or two pairs of such masses have moved relative to each other, albeit over limited intervals of time, the existence of some type of pre-Wegenerian drift will have been established—and that in itself will not have been an insignificant achievement.

Basically, this is the approach taken by both Spall and Irving *et al.* Thus Spall, although admitting the possibility of deficient data, has compared

the palaeomagnetic results from North America and southern Africa (the only two regions from which sufficient data of any quality are available) for the period 2,000–1,000 million years ago, and concludes tentatively that Precambrian drift did, in fact, occur. Likewise, Irving and his colleagues use palaeomagnetic data to show that the Grenville Province, which forms the younger, most south-westerly part of the Canadian Shield, was once displaced by several thousand kilometres with respect to the rest of the (older) Shield. Two swallows may not make a summer; but the evidence for pre-Mesozoic drift nevertheless begins to look more impressive as time goes by.—P. J. S.

Frame Shift Hot Spots

THE existence of the aptly named hot spots—regions in bacteriophage genes which mutate at very much higher frequencies than neighbouring regions of the same gene—was revealed as long ago as 1961 by Benzer during his classic analysis of the r_{II} A and r_{II} B cistrons of bacteriophage T4. As Benzer reported, the location of point mutations in the r_{II} region is very far from random; for example, of 1,612 spontaneous mutants mapping at 251 sites in this region, more than 500 mapped at a hot spot in the r_{II} B cistron and a further 300 mapped at a hot spot in the r_{II} A cistron, and, further, mutations induced by a variety of chemical mutagens were found not to cluster in these two spontaneous mutation hot spots.

Clearly, in at least some phage genes certain segments of DNA are more readily mutated than others, but clues to explain this have been very hard to come by and it is small exaggeration to say that for the past decade the molecular basis of the phenomenon of hot spots has remained almost totally obscure. The recent work of Streisinger and his colleagues on frame shift mutants of the lysozyme gene of phage T4 has, however, at last provided a chink of light. On page 338 of this issue of *Nature* Okada, Streisinger and their colleagues report a set of experiments which lead them to conclude that the high frequency of frame shift mutation and reverse mutation in the lysozyme gene may stem from the occurrence of sequences of five or more consecutive and identical base pairs.

The mutation they have chiefly worked with, $eJD11$, reverts to wild type at a frequency more than a hundred times greater than that of any other site in the lysozyme gene so far examined, and revertants “appeared identical to e^+ phage in every respect”. Furthermore, recombination tests proved that the reversion of the $eJD11$ mutation is a true reversion and does not result from the occurrence of a second compensatory mutation which might give rise to pseudowild type phage. And an accurate determination of the rate of reversion of the double mutant $eJD10$ - $eJD11$ to the single mutant $eJD10$ indicates that reversion frequency at the $eJD11$ site exceeds the summed total forward mutation frequency at all other sites in the gene. In short, the $eJD11$ mutation is very labile. But what is so special about the DNA at this site in the lysozyme gene?

In order to obtain information about the base sequence of the $eJD11$ site Okada, Streisinger and their colleagues analysed the amino-acid sequence of lysozyme specified by wild type e^+ phage, the double mutant $eJD10eJD11$ and that specified by a triple mutant designated $eJD10eJ17eJ42$ which is a pseudowild type. Their aim was to pin-point the changes in amino-acid sequence which result from these various mutations and by using accepted codon assignments thereby to arrive at the most probable base sequence of the $eJD11$ region. To cut a long and complex story short they were able to conclude, first, that although the $eJD10$ mutation consists of a single base deletion the $eJD11$

must consist of the addition of either an A or a G residue.

In the wild type lysozyme the amino-acids threonine, lysine and serine occur at the $eJD11$ site and there is good reason to believe that they are coded by the codons ACA, AAA, AGU, because fourteen of fifteen codons in the lysozyme gene have been identified in A or in U. Okada *et al.* favour therefore the idea that the mutation of e^+ wild type to $eJD11$ occurs when an additional A residue, rather than a G residue, is inserted in this sequence to give the sequence ACAAAAAGU with six instead of five consecutive A residues. Reversion of the $eJD11$ mutation would, of course, involve the deletion of the additional A residue and the restoration of the wild type sequence.

The striking feature of the base sequence of the wild type DNA at the $eJD11$ site is, of course, the presence of five consecutive A residues (AT base pairs in the double stranded DNA). Owen, one of the group, has apparently subsequently found that five other mutational sites in the lysozyme gene, all of which revert at unusually high frequencies, most probably also contain sequences of five identical base pairs.

It seems therefore that at least in this gene a high frequency of frame shift mutation and reversion (the insertion and deletion of a base pair) is associated with and perhaps caused by the presence of a sequence of consecutive identical base pairs in the wild type double stranded DNA. Whether, however, such runs of consecutive identical bases are associated with hot spots of the other class of mutations, which arise from the substitution of one base for another, rather than the deletion or insertion of a base, remains to be seen.—From our Cell Biology Correspondent.

PROTEINS

Energetic View

from our Molecular Biology Correspondent

THE appearance of yet another formulation for cooperative ligand binding by proteins may well cause many a reader to utter a cry of despair and turn to more congenial topics. But this is not merely another wrangle about concerted and sequential mechanisms, but an indictment of both as physically unrealistic and at times downright misleading. Weber (*Biochemistry*, **11**, 864; 1972) has produced a counterblast to the tacitly accepted notions of linked