dissimilarity, that is the factor by which the concentration of antiserum against a particular species of albumin has to be raised, in complement fixation experiments, to give a reaction with a heterologous albumin equal to that given with the homologous albumin. For example, the index of dissimilarity between human and chimpanzee albumins is 1·14.

The very similar antigenic properties of albumins of humans and African apes imply that these molecules have very similar structures. If Sarich and Wilson's previous conclusion—that albumin molecules of all the anthropoid lines have evolved at steady rates since they diverged from a common ancestor—is accepted, it follows that humans and African apes shared a common ancestor much more recently than is usually supposed.

But how can the index of dissimilarity be related to real time? The fossil record of primate evolution is too fragmentary to make a direct correlation, but Reichlin (1966) and Salthe and Kaplan (1966) have related the index of dissimilarity of various dehydrogenases of fish, amphibians, reptiles and birds with the fossil record which shows when these classes diverged. The logarithm of the index of dissimilarity, measured in immunological experiments, is approximately proportional to the time of divergence. Assuming this relationship holds for the serum albumins of primates, Sarich and Wilson calculate that humans and African apes had a common ancestor only five million years ago. Not every anthropologist who has studied the fossil record would argue against this date, but it will remain tentative until it has been proved that serum albumins evolve at much the same rates as other proteins. Sarich and Wilson suggest that an immunological study of the serum albumins of ungulates, for which there is an extensive fossil record, might settle this point.

Nucleases

from our Molecular Biology Correspondent

ONE of the most beguiling visions on the horizons of enzymology is the prospect of being able to compare the catalytic mechanisms of a range of endonucleases. The three-dimensional structure of one of these is already largely known, and others are being studied; sequences have been determined, and an enormous mass of enzymology and protein chemistry has accumulated. Some interesting new work on T1 ribonuclease and on staphylococcal nuclease has now been described.

T1 ribonuclease is remarkable because, although it binds to a highly negatively charged substrate, it is nonetheless a very acidic protein, with only five basic groups (three of them histidines). As a first step to defining the active centre, Takahashi, Stein and Moore (*J. Biol. Chem.*, **242**, 4682; 1967) have studied the inactivation of T1 ribonuclease by iodoacetate, a reagent which inactivates pancreatic ribonuclease by reacting with the histidine residues at the active centre. It is startling to find that in T1 the reaction occurs at a glutamic acid residue—an amino-acid not previously imagined to be capable of reacting with iodoacetate. The carboxyl group, identified as glu-58, is esterified to $-COOCH_2COO^-$. This involves a displacement of the charge by 4 Å, which is evidently sufficient to cause inactivation. That this unique reactivity is conferred upon glu-58 by its specific environment is shown by the loss of reactivity with iodoacetate on denaturation of the protein.

Staphylococcal nuclease has been completely sequenced by Anfinsen and his associates (Taniuchi *et al.*, *ibid.*, 4759). It has 149 residues, is basic and has no disulphide bridges. Its most striking feature lies in the physical changes which occur when it interacts with competitive inhibitors. Cuatrecasas *et al.* (*ibid.*, 4759) have found that binding of a nucleoside diphosphate in the presence of calcium ions (which are also required for activity) generates a sizable ultraviolet difference spectrum, arising from perturbation of tyrosine residues; moreover, spectrophotometric titrations show that their ionization is inhibited by the diphosphate, and finally a spectrophotometric method (solvent perturbation) shows that three or four of the seven tyrosines at the same time become effectively inaccessible. Although one cannot entirely rule out a direct interaction of all these tyrosines with the substrate, the observations are altogether consistent with a considerable convulsion in the conformation of the enzyme when the substrate binds.

Whether such a conformational change occurs, and its nature and extent, are, of course, general issues in enzymology. It is worth noting that the most direct evidence of such an effect emerges from preliminary X-ray data, just reported by Lipscomb's group on carboxypeptidase (Steitz *et al.*, *ibid.*, 4662). Here binding of a dipeptide generates quite considerable changes in electron density around the active site region. In lysozyme Phillips and his colleagues observed very small changes, whereas in pancreatic ribonuclease Richards' group found no significant changes at all in electron density of the enzyme when specific inhibitors were introduced. Their technique of diffusing substrates into the crystal in the diffractometer lends itself particularly well to precise determinations of small differences, and it must be concluded that in this case the conformation remains undisturbed. Evidently, therefore, generalizations about "induced fit" effects are not warranted at this stage.

Genetic Polarity

from our Cell Biology Correspondent

EARLIER this year, Imamato and Yanofsky found evidence that polar mutations in the lactose operon of *E. coli* cause a failure in transcription of the DNA beyond the mutation (see *Nature*, **215**, 1327; 1967). At the same time, there is strong evidence that polarity involves a failure in transcription. It is easy enough to reconcile these two sets of evidence because translation can control transcription by regulating the release of *m*RNA from the DNA template (see *Nature*, **214**, 228; 1967). So at least in organisms which have DNA as the genetic material, polarity seems to affect both transcription and translation.

Engelhardt, Webster and Zinder (*J. Mol. Biol.*, **29**, 45; 1967) and Capecchi (*J. Mol. Biol.*, **30**, 213; 1967) have now detected polarity *in vitro* with RNA from amber mutants of RNA bacteriophage. This result, together with Fink and Martin's work on polarity in the histidine operon of *S. typhimurium* (*J. Mol. Biol.*, **30**, 97; 1967), suggests that polarity is fundamentally a translational phenomenon which only incidentally involves transcription.

The RNA bacteriophages *f*2 and *R*17 are virtually identical. Both Zinder's group at the Rockefeller University and Watson's group at Harvard have