than any of the active antibiotics. The susceptibility of cells to these substances will, therefore, depend on the lipid composition of the cell membrane.

DNases Old and New

from our Molecular Biology Correspondent

AMONG the most important analytical weapons available for the study of both primary and secondary structure in nucleic acids is the increasingly wide range of nucleases. Nucleases are now known with specificities for different nucleotides, for single-stranded and double-stranded polymers, for long and short molecules and for the middles and the ends of chains. A considerable debt is therefore owed to the several groups of workers who have patiently searched for new nucleases and studied their function and specificity.

The latest of a series of studies by Bernardi and his associates concerns spleen exonuclease, which has now for the first time been obtained in uncontaminated form (Bernardi and Bernardi, *Biochim. Biophys. Acta*, **155**, 360; 1968). It is free from endonuclease, phosphomonoesterase and deaminase activity, and has good stability. It will degrade native as well as denatured DNA, but the latter, as usual, is much less susceptible (by a factor of 25). It also attacks RNA and synthetic polyribonucleotides (but not poly *C*). The enzyme should fill an important need, particularly in primary structure work.

The action of the endonuclease, pancreatic deoxyribonuclease (also called DNase I) has been studied by Hoard and Guild (*J. Mol. Biol.*, **31**, 595; 1968), with single-stranded polydeoxyribonucleotides as substrates. By introducing labelled segments into the substrates at the ends of the chain, it was shown that if the chain length is relatively short (some 40 nucleotides or less), the residues near the ends of the chain are less susceptible to hydrolysis by an order of magnitude than those near the middle. With long chains, however, this discrimination disappears. The results suggest the involvement of "subsites" in the activity, which interact with substrate residues not bound at the active centre. The factors which annul this effect when the substrate is long can at this stage only be guessed at.

A nice example of the use of a nuclease for the study of conformational phenomena comes from Wingert and Von Hippel (*Biochim. Biophys. Acta*, **157**, 114; 1968), who have extended earlier studies on hydrolysis of DNA by micrococcal nuclease. This enzyme shows the common strong preference for denatured over native DNA. With the latter, there is strong preferential attack on (A–T)-rich regions, the effect being greatly accentuated at reduced temperature. The digestion of denatured DNA, on the other hand, is associated with no such specificity, and the base-composition of acid-soluble product is that of the whole DNA. The authors use this as an argument to support the concept of a dynamic structure for two-stranded DNA, characterized by a "breathing" effect, or local opening and refolding of the structure. This is also supported by earlier evidence from hydrogen-exchange, and is of obvious importance in relation to the reactivity of the molecule towards agents which can interact only with accessible bases in a single strand. It is, of course, hard to prove that the preference of the enzyme for (A–T)-rich segments is indeed due to the lower stability of such regions, rather than to a direct recognition mechanism (such as has been demonstrated in the attachment of polylysine and some histones to DNA). The large increase in specificity at lower temperatures, however, and its complete elimination in the other direction, do suggest that the stability of different regions is important.

Sulkowski and M. Laskowski, sen. (*ibid.*, 207), have shown that the attachment of actinomycin D to DNA gives some protection against the same nuclease, and in particular that the (G–C)-rich parts, to which the antibiotic most strongly binds, are preferentially protected. Since actinomycin is known to stabilize the native DNA conformation, this observation is also consistent with Wingert and Von Hippel's conclusions.

Gas Chromatography

from a Correspondent

THE annual general meeting of the Gas Chromatography Discussion Group was held on Friday, March 29, at the Royal Institution, London. Of the activities of the group, the most important new departure was the formation of a liquid chromatography section which had held its first meeting the day before. It was hoped this will be repeated at irregular intervals of about a year.

The informal symposium which followed the meeting dealt with a cross-section of the whole gas chromatographic process. Professor Keulemans spoke of injecting samples into capillary columns. A well designed splitter was a satisfactory device but used a comparatively large sample. He described a method of dissolving a very small sample in silicone oil, and injecting, say, 1 μl. of the solution on to a small pre-column packed with dry support. The sample could then be flashed on to the capillary column and a perfect chromatogram obtained.

Dr D. R. Deans dealt with flow switching techniques for use in routine analyses. His circuits made possible back-flushing of unwanted high boilers, combinations of columns for certain difficult separations, and heart-cutting for peaks on tails. All these operations were performed by external gas switching. A punched card programmer could perform all the timed switchings automatically. The whole technique is most elegant and saves considerable analysis time.

Mr C. Narain described a simple d.c. discharge detector for determining traces of impurities such as carbon dioxide and the lower hydrocarbons in oxygen, air and other gases. The detector is robust, easily replaced when necessary and uses no amplifier. Sensitivity with a nitrogen carrier is about 5 ppm full scale. Mr R. Yeend described "interval programmed integration". This divides the chromatogram into a series of accurately timed periods with an integral printed out for each period. In this way drifting base lines or the tail of a large peak can be eliminated from the integral of a peak superimposed on them without the use of an expensive integrator with drift correction, which would not, in any case, deal with tails. By taking the integral in the period immediately before a peak and in the one immediately after it, the baseline contribution to the total integral can be calculated from the mean of the two and the number of periods in the peak. This is an ingenious way of getting the advantage of both digital and analogue integrators.

Mr E. S. Goodwin described the use of a quadrupole