auger well for this novel approach.

The classical approach to systematic drug design was described by C. R. Ganellin (Smith, Kline and French). The simple concepts of structure–activity relationships, such as Hansch analysis using linear free-energy relationships, have been widely used. The limitations of these methods are now well known; however, Ganellin showed that dynamic structure–activity relationships are capable of analysing quite complex situations, such as relative ionic populations in a prototropic equilibrium mixture, and hence identifying the ionisation sites of the pharmacologically active tautomer of, say histamine. The relevance of this approach (and indeed of most others) to the identification of active conformers and tautomers was questioned by W. G. Richards (University of Oxford), who reported on his recent quantum mechanical calculations on histamine. He also emphasised the importance of considering the topography of both nuclei and electrons of drug and receptor in an active environment, in order to determine the essential conformation of the drug. The active conformation of histamine, as determined from conformational probability maps, seems to be neither that determined in the solid state by X-ray crystallography, nor that present in solution, and furthermore there is no obvious positive charge centre in the active molecule. Although these results have to be treated with caution, their implications are of some importance.

Unsurprisingly, they provoked a lively discussion, during which some experimental support was suggested for essential conformations from structural studies on enzyme–substrate complexes. The audience, which consisted mostly of experimentalists, was doubtless relieved to hear that theoretical calculations of drug conformation are by no means infallible—indeed it is a characteristic experience that increasing sophistication in *ab initio* calculation often parallels increasingly poorer quality of results.

Magnetic resonance techniques for probing drug–receptor conformations in solution are currently enjoying a considerable vogue. Thus, J. Feeney (National Institute of Medical Research) showed how he has applied them to studies of hormonal peptides, such as oxytocin and gastrotetrapeptide. Although no direct information can be obtained about their conformations when bound to receptor sites, useful data indicating preferred modes of flexibility and intramolecular hydrogen-bonding organisation are more readily accessible. From this, Feeney and his associates have developed a "zipper" theory for the mechanism of receptor binding, whereby attachment is stepwise to a series of subsites, with each step giving a reorientation of the substrate conformation. G. C. K. Roberts (National Institute for Medical Research) presented a progress report on inhibitor bindings studied by NMR to the biosynthetically important enzyme dihydrofolate reductase. Although definitive conclusions must await an X-ray analysis, it is apparent that binding of, for example, the antileukaemic drug methotrexate (which is a competitive inhibitor for the natural substrate) is a complex process, which is accompanied by dynamic changes in the enzyme conformation.

Drug binding to nucleic acids, especially DNA, as receptors, has for long been a favoured field of study, doubtless partly because so much is known about the detailed structures of the nucleic acids. M. J. Waring (University of Cambridge) emphasised some of the challenging and unsolved problems in this area, particularly those concerned with binding to preferred lengths of sequence. Studies of binding with the antibiotic echinomycin, a cyclic octapeptide with two quinoxaline rings attached, have shown that this compound acts as a bifunctional intercalating agent. The two planar quinoxaline rings are believed to slot in between two base pairs, that is, with a gap of 10.2 Å. The problem of, *inter alia*, apparent violation of the neighbourhood exclusion principle at high binding levels has, however, hindered a detailed understanding of echinomycin binding to DNA so far.

It is not surprising that the complexity of membrane-bound receptor proteins has meant that knowledge of them at the molecular level is relatively sparse. Thus, the achievements of E. A. Barnard (State University of New York at Buffalo; now at Imperial College) and his associates in purifying the acetylcholine receptor (molecular weight 330,000) from denervated cat muscle, were the highlight of the session on these systems. It is worth remembering that the receptor, which was purified by binding to the snake venom α-bungarotoxin, exists in nanomolar concentrations in the tissue used. Results mentioned by Barnard from several laboratories have indicated the sites of receptor attachment to be the postjunctional membrane. The individual receptors are on the crest of the fold facing the presynaptic sites, and there appear to be roughly 20,000 individual molecules of protein per fold, arranged somehow within about 2,000 particles, as seen in freeze-etched electron micrographs. Clearly, this area of molecular pharmacology is destined for considerable advance in the near future. □

A hundred years ago

THE forty-seventh anniversary of the Zoological Society was held on Saturday last, Viscount Walden, F.R.S., the President, being in the chair. Mr. P. L. Sclater, F.R.S., the Secretary, read the report, which showed that the income (28,738*l.*) was greater than it had been in any previous year since the foundation of the Society. The total number of visitors in 1875 had been 699,918. The new lion house had been, as far as its main portions were concerned, completed and opened to the public. The building contains fourteen dens, the larger of which measure 20 ft. by 12 ft., the smaller being 12 ft. square. The out-door cages are to be completed by the end of July next; they will measure 44 ft. by 29 ft. Mr. Sclater desired it to be known that of the larger Felidae, the Ounce (*Felis uncia*) was a desideratum. The adoption of the report was moved by Prof. Huxley, seconded by Prof. Tennant, and carried unanimously.

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Solar system origin

from David W. Hughes

An advanced study institute on the Origin of the Solar System was held in the Institute of Lunar and Planetary Sciences of the University of Newcastle-upon-Tyne between March 29 and April 9, 1976 under the sponsorship of NATO.

COSMOGONY, the study of solar system origin processes is bedevilled by the fact that only one solar system is observable. The origin and evolution of stars (which are thousands of times further away and immeasurably less accessible than the planets) is much better understood simply because the sky is full of them—of different sizes and mass and at different stages in their evolution—and comparisons between them produce an abundance of clues to the physical processes responsible for their birth, life and death. The wavy paths of Barnard's star and Epsilon Eridani as they move across the celestial sphere indicate that they probably have planetary companions. Their remoteness, however, makes it completely impossible for us to measure the mass or orbits of the planets at