and the effects on cerebellar organization of the deletion of different cell populations by experimental or genetic means can be compared. These ongoing studies are providing invaluable insights into the mechanisms of brain development.

PROTEINS

Sifting the Subunits

from our Molecular Biology Correspondent

THIS week some *bonnes bouches* for collectors of the odd in the way of protein structures. Some proteins, on no very obvious teleological grounds, exist under physiological conditions in very large aggregates, containing many subunits. One of the first cases to be recognized was haptoglobin, a serum globulin, which has the function of absorbing any haemoglobin that is released into the plasma. There are three familiar genetic variants of human haptoglobin, one of which (Hp 1–1) is electrophoretically homogeneous, whereas the others, Hp 2–1 and Hp 2–2, take the form of an apparently limitless series of components of progressively lower mobility in the electrophoretic gels. More than a dozen zones can often be resolved, and these are now recognized as a set of linear polymers, which can be separated on denaturation and reduction into two types of chain, α and β, the α chain being characteristic of the haptoglobin type, the β chain common to all three. Just what the relation is between the members of the family of oligomers—for example, whether they are built up by successive addition of $\alpha\beta$ units, or of tetramers, or, as has been suggested, by repeated dimerization—has hitherto been in doubt. Now, however, Fuller *et al.* (*Biochemistry*, **12**, 253; 1973) seem to have settled the question.

Their preparation of haptoglobin 2–2 showed fourteen resolved zones in polyacrylamide gels and the first eight of these were isolated by preparative electrophoresis. In the absence of a reducing agent, the polymers do not dissociate in sodium dodecyl sulphate, and so detergent-gel electrophoresis could be used to give a first estimate of the molecular weights of the resolved members of the series. The first zone had a mobility corresponding to a molecular weight of some 200,000, which is consistent with an $\alpha_3\beta_3$ structure, the α chains with a molecular weight of 17,000 and the β chains 40,000. The apparent molecular weight increment between successive zones was constant, and corresponded to the addition of an $\alpha\beta$ unit at each step. The components from 2 to 5 were examined by sedimentation equilibrium, and the inferred molecular weights from the electrophoresis experiments were found nearly enough correct. The stoichiometry was more firmly established by amino-acid analysis and by end-group determination. Both confirmed that α and β chains were present in equimolar concentrations in all cases. Now it has been known for some time that the chains of the basic $\alpha\beta$ unit are united by disulphide bonds, and Fuller *et al.* now also show that disulphide bonds likewise secure these units to each other in the polymers, because electrophoresis in the presence of very low concentrations of mercaptoethanol reveals the progressive degradations of polymer 5, for example, to a mixture of components 2 to 5, number 4 being formed first. The $\alpha\beta$ subunits do not come apart, and the α-β disulphide bonds can, it seems, be reduced only under more drastic conditions. Evidently, therefore, the components of the polymerizable genetic haptoglobin forms are assembled by linear addition from a pool of $\alpha\beta$ units.

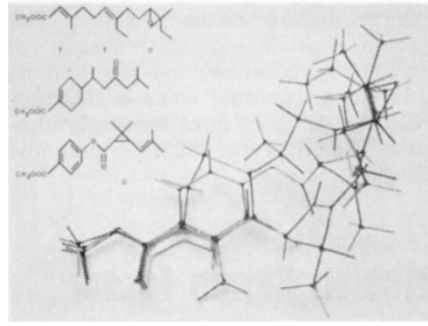
In unfolding the absorbing story of the enzymatic control of glycogen metabolism, Krebs and his colleagues have paused to examine the structural character of the phosphorylase kinase, which is responsible for the conversion by phosphorylation, of glycogen phosphorylase *b* to phosphorylase *a*. The activity of the phosphorylase kinase is itself controlled by cyclic AMP-dependent protein kinase, which catalyses its phosphorylation. The phosphorylase kinase emerges as a complicated enzyme with some curious properties. In the first of a set of three articles, Hayakawa *et al.* (*ibid.*, 567) describe the isolation of the protein in a high state of purity, having eliminated an aggregated fraction present in earlier preparations. The enzyme, when thus purified, has a sedimentation coefficient of 26S and a molecular weight, by sedimentation equilibrium, of 1.3×10^6. In sodium dodecyl sulphate it dissociates, and gives rise to three components with apparent molecular weights of 118,000, 108,000 and 41,000, which are termed the A, B and C chains. From the apparent concentrations of these components, the authors infer that the

Structure and Activity of Juvenile Hormone

MANY attempts have been made during the past few years to define the molecular characters that determine the juvenile hormone activity of the rather diverse chemicals which can produce these morphological effects (*Nature*, **221**, 190; 1969). In the first place the molecule must be neither too long nor too short: active substances have about fourteen carbon atoms in the chain length. They must not be too polar, nor must they be wholly paraffinic. General molecular configuration determined by *cis* or *trans* bonding along the chain is highly important, but no molecular shape that gives predictable effects has been defined.

The problem is complicated by the diverse effects of synthetics in different groups of insects. Although the natural juvenile hormone as originally isolated from the cecropia silkmoth seems to have universally high activity, even the simple straight chain compound dodecyl methyl ether is quite active in Lepidoptera, though very weak in activity in other groups; and "juvabione", the methyl ester of todomatuic acid from balsam fir, which is intensely active in plant bugs of the family Pyrrhocoridae, seems to be without effect in any other insects.

In next Wednesday's *Nature New Biology* (March 21), Punja, Ruscoe and Treadgold report on a new group of non-terpenoid compounds, esters of chrysanthemic acid, which possess a high order of juvenile hormone activity. These also were found to be active only in the pyrrhocorid bug *Dysdercus*; but the communication brings out clearly that activity is largely determined by the configuration at the C_1 end of the molecule where the most active mimics have a terminal carboxy alkyl or similar group conjugated with a double bond held *trans* to a long alkyl chain. As clearly shown in Dreiding molecular models the most active chrysanthemates, the principal cecropia hormone and juvabione all have closely similar configurations which are superimposable over this region (see figure). Extensive changes in other parts of the molecule seem to be much less significant.



These results do not explain changes in overall and species-related activity which are associated with small variations in structure. There is no indication as to why the effect of chrysanthemates is specific for Pyrrhocoridae, nor for the increased activity which is conferred by a methyl side-chain at C_3 and by methyl (as compared with ethyl) esters. But the molecular models demonstrate the importance of the spatial relationships in the terminal groups of juvenile hormone and its mimics.