of up to 7 Å on oxygenation. The critical contacts have the form of cogs which mesh only in two positions, one corresponding to the deoxygenated, the other to the oxygenated, state. In terms of mechanistic models the results do not fit precisely into the allosteric or sequential schemes of cooperativity, for the conformational change arises by progressive diminution of the energy margin between the low and high affinity states in response to an "induced-fit" effect of the first ligand.

Perutz goes on (*ibid.*, 734) to consider the nature of the Bohr effect. The key lies once more in the expulsion of the tyrosines on oxygenation: in the deoxy form the adjoining terminal histidine (in the β-chain) makes an ion-pair with an α-chain lysine. This it is which fixes the position of the tyrosine in the haem crevice. Moreover, the imidazole of the same histidine is enabled to pair with asp-93 (β), with consequent elevation of its pK. In the α-chain, deoxygenation similarly disturbs ion-pairs formed between the α-amino group and the α-carboxyl group of the other α-chain, and between a histidine and an aspartate on the same chain, so normalizing the imidazole and the α-amino pK. Perutz also shows how in the deoxy-structure the cofactor, diphosphoglycerate, fits nicely into a single positively charged niche, involving the N-terminus of the β-chains. On oxygenation this binding site closes up, so that the characteristics of the haemoglobin–diphosphoglycerate interaction established by the Benesches are nicely accounted for. Although a few details of the chemistry of oxygenation, as Perutz has described it, remain to be clarified or confirmed, it veritably appears that the function of haemoglobin, one of the most venerable issues in all biology, is now substantially understood, and that Perutz has at last scaled this scientific Everest.

RIBOSOMES

Attachment of Proteins

from our Nucleic Acids Correspondent

THE 30S ribosomal subunit is probably the most complex biological structure of which a detailed overall picture can seriously be expected to emerge in the next few years. A further major step in that direction has been described recently by Bollen, Herzog, Favre, Thibault and Gros (*FEBS Letters*, **11**, 49, 1970). They have investigated the interior of the ribosomal particle, and demonstrated that the sites of attachment of some of the 30S ribosomal proteins to the 16S RNA must include double helical regions within the RNA. This result is completely at variance with the models of ribosome structure which have been proposed by Cox, Gratzer and others, in which ribosomal proteins are shown exclusively attached to single stranded portions of the RNAs, and it reinforces recent widespread disquiet about the adequacy of these models.

Bollen *et al.* formed a fluorescent complex between the 16S RNA and ethidium bromide, which intercalates into the double stranded regions of the molecule, and used it, together with ribosomal proteins, to reconstitute ribonucleoprotein particles, with the aid of the methods developed by Nomura and his colleagues. If the proteins interact with double helical areas, the ethidium bromide might be expected to be displaced, with a consequent loss of fluorescence.

This is exactly what is observed when a mixture of all the 30S ribosomal proteins is added to the ethidium bromide–16S RNA complex. The successive addition of further amounts of the ribosomal proteins causes further release of ethidium bromide, showing that the reaction has a definite stoichiometry. Bollen *et al.* performed the necessary controls and niceties—50S ribosomal proteins or nucleohistones do not chase out ethidium bromide, and the 30S proteins do not displace ethidium bromide from the ethidium bromide–23S RNA complex. These findings indicate that the displacement of the dye is a highly specific process of real structural significance.

When the total 30S proteins were added in excess, only partial displacement of the bound ethidium bromide could be obtained, relative to the level of fluorescence of 30S particles reconstituted in the absence of ethidium bromide, and exposed afterwards to the dye. Bollen *et al.* therefore deduce that the reconstitution between the proteins and the dye-RNA complex is not complete, being blocked by the ethidium bromide at some stage, so that a complex is formed between the 16S RNA and only certain of the proteins. They searched for such a complex, with the aim of identifying the proteins present. They easily isolated the complex (of sedimentation coefficient about 20S) by centrifugation, and recovered the proteins by treating it with RNAse. They found eight bands by polyacrylamide gel electrophoresis of these proteins, corresponding to eight or nine proteins. The proteins present were almost entirely the same as the proteins found in the 21S particles accumulated in some cold-sensitive mutant strains of *Escherischia coli*, found by Nomura. It can therefore be suggested not only that this class of proteins recognizes specifically regions of the RNA, including double helical portions, but that the reconstitution carried out in these experiments is really analogous to the *in vivo* assembly process. Bollen *et al.* rounded off these experiments by showing that only the core proteins of the 30S particle form complexes in which the ethidium bromide is displaced, and the split proteins do not. Of the core proteins, they showed, by using purified proteins, that four out of the six proteins identified by Nomura as primary binding proteins can chase out the ethidium bromide. One could not reasonably ask for more.

CONTRACEPTIVES

Pill Progress

from our Biological Chemistry Correspondent

EARLIER this year, when Carl Djerassi assessed critically the developmental problems for new birth control procedures (*Science*, **169**, 941; 1970), he concluded that a once-a-month female contraceptive pill was unlikely to be developed during the present decade. Nonetheless, recent advances in prostaglandin research suggest that two of the problems may be surmountable and herald imminent commercial developments.

Sultan M. Karim, of Makerere University, Kampala, has described to the New York Academy of Sciences how vaginally administered prostaglandin tablets induce abortions at one-tenth of the dose required for successful intravenous injection. He also found that in this way side effects are greatly diminished. These findings obviously raise the stakes for a com-