BIOCHEMISTRY

An Error in Model Building

ABOUT a year ago Dr. S. R. Pelc and Miss M. G. E. Welton claimed[1,2] that "it is possible to fit amino-acids stereochemically to their codons". They described how they built models using Courtauld space-filling components, but it was not possible to tell from their very brief descriptions whether their models were stereochemically acceptable. I therefore corresponded with Dr. Pelc and he was kind enough to show me some of their models.

Dr. Pelc produced several examples for me to examine, but I will comment here only on their model of lysine fitted to AAG, as illustrated in the photograph of Fig. 2 of the first of their two papers[1].

This model is stereochemically unacceptable for the following reasons. (1) The terminal $-NH_3^+$ group of the lysine was built as $-NH_2$. (2) In two places (one in the amino-acid, one in the triplet) adjacent methyl groups were in the eclipsed rather than the staggered configuration. (3) In two cases an >NH, which should either make a satisfactory hydrogen bond, or at least be free to make one to a water molecule, was pointing directly at a hydrophobic group.

Further inspection revealed that Dr. Pelc and Miss Welton had built all their polynucleotide sequences backwards*. Their AAG was in fact GAA (which codes glutamic acid). This mistake can be detected by a very careful study of Fig. 2 of ref. 1.

I conclude that the models of Pelc and Welton do not support their hypothesis.

F. H. C. CRICK

Medical Research Council,
Laboratory of Molecular Biology,
Hills Road, Cambridge.

Received January 19, modified January 23, 1967.

* For the standard convention see, for example, ref. 3. The triplet AAG can also be written as ApApG, the convention being that pG signifies a phosphate attached to the 5′-hydroxyl of the guanosine.

[1] Pelc, S. R., and Welton, M. G. E., *Nature*, **209**, 868 (1966).
[2] Welton, M. G. E., and Pelc, S. R., *Nature*, **209**, 870 (1966).
[3] "Abbreviated Instructions to Authors", *J. Biol. Chem.*, **241**, No. 23, iii (1966).

Sir John Randall, Director of the Medical Research Council Biophysics Research Unit at King's College, London, wishes to state that he has read Dr. Crick's letter in manuscript, that he agrees with its conclusion, and that he had so informed Dr. Pelc and Miss Welton at the time of their original publication.—EDITOR, *Nature*.

Adsorption of Octapeptide Hormones on to Lipid Monolayers

THE interaction between lipid monolayers spread on the surface of water, and oxytocin and vasotocin (arginine vasotocin) in the substrate, has been investigated, using a Langmuir surface trough, by studying the changes in pressure produced on injection of various quantities of the polypeptide solution under the film. This technique is similar to that used for the study of the interaction between protein in the substrate and lipid monolayers[1,2].

In order to avoid contamination the paraffin wax used to coat the trough was freed from surface active impurities by heating with hot 1 normal sodium hydroxide followed by hot 1 normal hydrochloric acid. After thorough washing the wax was recrystallized twice from light petroleum (40°–60°). The water was redistilled with alkaline permanganate, and nitrogen was passed over the covered trough during the experiments.

Samples of cholesterol, stearic acid and lauric acid were all recrystallized to constant melting point using light petroleum (40°–60°) which itself was 'AnalaR' reagent redistilled. The samples of oxytocin and vasotocin were used as supplied.

Solutions were made of cholesterol (19·3 mg/100 ml.) in benzene, stearic acid (14·4 mg/100 ml.) in light petroleum (40°–60°), lauric acid (10·0 mg/100 ml.) in light petroleum (40°–60°), oxytocin (16·0 mg/100 ml.) in water and vasotocin (10·0 mg/100 ml.) in water.

Using an 'Agla' microsyringe 12×10^{16} molecules of lipid were injected on to the water surface in the Langmuir surface trough, and the initial pressure of the film was adjusted to 10 dynes/cm in the case of cholesterol, and 2 dynes/cm in the case of the fatty acids. The polypeptide solution was injected through the lipid monolayer and the pressure of the film increased, reaching a maximum value after 50 min. This increase in pressure was measured by a horizontal torsion wire, which was sensitive to 0·02 dynes/cm, and was used to obtain isotherms for the adsorption of peptide on to the lipid monolayer (Fig. 1). All isotherms obtained were similar, showing two marked discontinuities which are believed to represent stable surface structures (Fig. 2). Details of the results obtained are listed in Table 1.

Structure *A*, which is proposed for the final structure of the adsorbed film, is based on the fact that the chemical structures of oxytocin and vasotocin contain rings with six peptide bonds:

Cys-Tyr-Ileu-Glu(NH_2)-Asp(NH_2)-Cys-Pro-Arg-Gly NH_2
Vasotocin

Cys-Tyr-Ileu-Glu(NH_2)-Asp(NH_2)-Cys-Pro-Leu-Gly NH_2
Oxytocin

Previous work[1,2] supports the idea that polar groups of the lipid associate with peptide links in protein. It is therefore reasonable to suppose that the final structure indicated by a 6 : 1 lipid to polypeptide ratio represents a ring of six lipid molecules adsorbed at each peptide link in the ring of the hormone—the ring structure being one of the essential structural features for physiological activity[3].

Structure *B* is proposed as the intermediate structure based on a 21 : 1 lipid to polypeptide ratio, found for both cholesterol and the fatty acids. Because these two types of lipid are very different in size, the association must

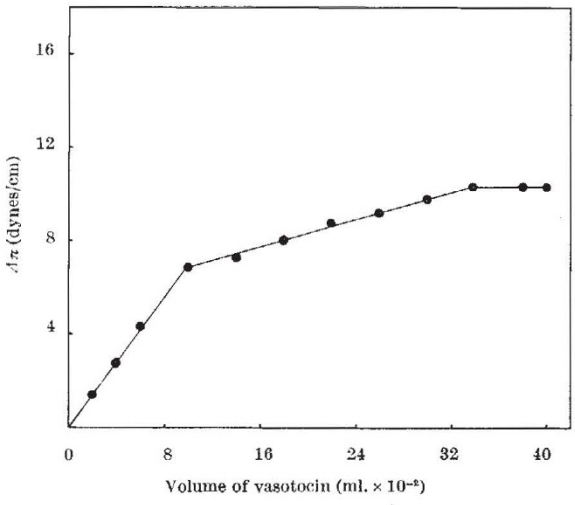

Fig. 1. The variation of surface pressure increase $\Delta\pi$, with volume of vasotocin solution injected through a monomolecular layer of cholesterol (12×10^{16} molecules) at a surface of water.