NEWS AND VIEWS

Evergreen Enzyme

from our Molecular Biology Correspondent

OSCAR WILDE is said to have remarked that one must have a heart of stone to read of the death of Little Nell without laughing. The reports in last week's *Nature*, which show that the third version of the subunit structure of aspartate transcarbamylase is wrong, provoke the same guilty sensation. It is hard to see why this most interesting enzyme should have proved so treacherous. Gerhart and Schachman originally demonstrated that the catalytic and regulatory sites were situated on different subunits, but the number of each kind of subunit has only now been established.

It is interesting that a crystallographic study has provided an elegant demonstration of the structure. Wiley and Lipscomb (*Nature*, **218**, 1119; 1968) have examined two crystal forms of the enzyme, one octahedral, the other trigonal, and have determined the space groups, and also the water contents and densities of the crystals. The trigonal form, which is much the better ordered, results from crystallization in the presence of the inhibitor, CTP; from the volume of the unit cell, and the crystal density, it is found that the unit cell contains two molecules of protein, which, with the space group of this crystal, signifies the presence of a three-fold molecular symmetry axis. Consequently, the number of identical subunits must be three or a multiple of three. Repeating the same process for the tetragonal crystals, the unit cell is found to contain four molecules, which corresponds to a two-fold axis in the molecule. Thus the number of like subunits must also be a multiple of two, and the enzyme must possess six (or a multiple of six) each of the regulatory and catalytic species. This work represents again a nice example of how crystallography can yield information of the greatest relevance about proteins, without the need of high-resolution structure determination.

It is reassuring that revised chemical data produce the same answer. Weber (*ibid.*, 1116) in a careful study concludes that the molecular weights of the catalytic and regulatory chains are respectively 33,000 and 17,000. This emerges in the first place from the empirical method, involving gel electrophoresis, in the presence of detergent, devised by Maizel and his co-workers. The number of amino-acids released from either chain by carboxypeptidase *A* is consistent with these values. Weber has gone further, and has determined the complete amino-acid sequence of the regulatory chain. The formula weight for the 152 amino-acids is 17,000. The molecular weight of the intact enzyme of 310,000 remains unchallenged, and

corresponds well to six chains of each kind. The incompatibility of the new results with the previously reported sedimentation equilibria in 8 M urea suggests incomplete dissociation in this medium (and it may be noted in this connexion that by no means all proteins are denatured under these conditions).

Aspartate transcarbamylase is known to dissociate in the presence of the sulphhydryl reagent, *p*-chloromercuribenzoate, and if the molecular weight determinations are to be believed, the products of the dissociation are two catalytic fragments of three chains (C_3), and three regulatory of two chains (R_2). The mystery which remains is the discrepancy between the number of subunits and the number of binding sites, as determined by apparently straightforward methods. These binding sites will presumably now be reinvestigated. Meanwhile the relevant chapters in the elementary textbooks await revision.

WHO Comes of Age

THE World Health Organization is twenty years old this year. To mark this anniversary, in addition to the annual report of the director-general for 1967, another publication has been compiled, giving an account of the organization's work during the second ten years of its existence.

From 1958 to 1967 the organization's activities expanded considerably, not only in the continuation of previous projects, such as eradication of malaria and smallpox and prevention of cholera and plague, but also in newer undertakings. Membership of WHO has increased by nearly 50 per cent in this period—from 85 member states in 1957 to 126 in 1967—a reflexion of the emergence of many newly independent nations. As some of these new members have neither the minimum of essential health services nor people to run them, their problems have had a marked influence on the direction of the organization's growth.

REGULAR BUDGETS, 1958–1967

Year	Total budget US \$	Actual obligations US \$
1958	14,769,160	13,236,820
1959	16,028,026	14,654,981
1960	18,113,760	16,623,517
1961	21,114,348	19,201,885
1962	26,546,940	24,164,650
1963	32,543,670	29,783,550
1964	36,765,880	33,869,165
1965	42,028,370	38,346,067
1966	47,097,390	43,439,677
1967	55,523,640	51,339,664