temperature at which $\Delta\epsilon_{277}$ finally started to fall coincided with the beginning of the second step in the biphasic E_{260} 'melting' curve (Henson & Walker, 1969).

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Molecular Models for Macromolecules: a New Concept for Teaching and Research

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X-ray crystallography is providing a rapidly increasing stream of accurate data for the construction of macromolecules of biological origin and simultaneously the chemist and the kinetic enzymologist are locating and studying active sites and clefts in such molecules. Models built so far have been based on skeletal or space-filled units, each of which represents an atom, but valuable as these are to those interested in a particular model or structure they are of little or no use for general purposes. The disadvantages of this type of model are the extreme cost, the tremendous amount of building time involved, the relatively large amount of superstructure necessary to support the model such that the model itself is often lost within its superstructure, and the size and weight, which make transport a problem such that the model often cannot easily be rotated even on its own axis.

For many workers and certainly for all students the amount of data inherent in such models is self-defeating as time is not available for the study of such models. We have therefore designed a new type of model with the intention of overcoming all these problems. The models to be described are extremely light in weight, flexible, free of visible superstructure and all have been built by students in 2-3 days (Smith & Smith, 1969; Smith, 1969; Smith, Smith & Roberts, 1970). The model 'bits' correspond to groups of atoms such as the various R groups of amino acids, nucleic acid bases etc., and are size- and colour-coded to draw out immediate similarities and differences in an easily recognizable manner. 'Backbones' of the proteins and nucleic acids are constructed from flexible tubing incorporating repeating units representing the amino acid or sugar phosphate monomer. Through the tube runs a plastic-coated wire, which helps to retain the model shape built from the X-ray data, and having built a section of 'backbone' the different R groups are inserted in holes placed circumferentially on each monomer unit to indicate the general direction in which the particular group points. The whole model is supported on a frame. The final

models readily show tertiary structures, including helical and non-helical regions, substrate 'pockets', active sites, codon-anticodon interactions etc., and the direct student participation in model building serves as a valuable aid to learning. Models of myoglobin, lysozyme, ribonuclease S, DNA and various tRNA species will be shown.

Because the 'backbone' can be readily cut and rejoined it is possible to demonstrate a variety of other chemical and genetic reactions. Thus a wall-board to illustrate the various enzymic and chemical digests of a protein will illustrate the current techniques useful in determining primary structure, and similar boards can illustrate genetic cross-reactions, transcription etc.

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Transport Pathway for Glycine Betaine in Rat Kidney Cortex *in vitro*

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Inhibition studies established that betaine (NNN-trimethylglycine) shares a transport pathway in the hamster small intestine in common with N-methylglycine (sarcosine) and NN-dimethylglycine. L-Proline and L-hydroxyproline had a greater affinity for the betaine carrier than for the neutral amino acid carrier (Hagihira, Wilson & Lin, 1962).

Uptake of ^{14}C -labelled compounds was studied with kidney-cortex slices from female albino Wistar rats. After washing in appropriate buffer solution (Robinson, 1949) kidney slices were incubated with test compound in buffer at 37°C in O_2 for 30 min. Uptake was related to the intracellular fluid and extracellular fluid of rat kidney cortex as determined with inulin (Rosenberg, Downing & Segal, 1962).

Recovery of ^{14}C -labelled betaine was >95% from the incubation media and 95% from the tissues. Hence there were negligible losses due to oxidation to CO_2 and incorporation into protein.

Betaine accumulated in kidney-cortex slices to give a concentration ratio (c.p.s. per ml of intracellular fluid/c.p.s. per ml of extracellular fluid) of 2.36 ± 0.09 and therefore did not occur by passive (physical) diffusion. 2,4-Dinitrophenol inhibited

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betaine transport to give a concentration ratio of 1.09 ± 0.06 . These results suggest that betaine accumulation by kidney slices is linked to oxidative metabolism. Glycine and L-lysine were non-competitive inhibitors of betaine uptake, with glycine being the more potent inhibitor. Betaine uptake was also inhibited, in increasing order of inhibition, by: L-valine, L-hydroxyproline, L-proline.

It may be concluded that small intestine and kidney both exhibit the betaine-imino acid transport pathway *in vitro*.

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Transport Pathway for Glycine Betaine in Rabbit Kidney *in vivo*

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A transport pathway for betaine and the imino acids can be demonstrated in rat kidney-cortex slices *in vitro* (Evered & Nunn, 1970). This pathway could not readily be demonstrated *in vivo* in the rat as the urine flow is low in this species. However, the rabbit has a very similar endogenous renal plasma clearance rate for glycine (Evered, 1967) and was chosen for studies *in vivo*.

Under chloralose anaesthesia a male rabbit was infused intravenously at 2 ml/min with 5% (w/v) mannitol, to induce diuresis, and 0.5% (w/v) creatinine in 0.9% NaCl solution. Subsequently 0.25 M-betaine hydrochloride (neutralized) was infused in addition. Appropriate urine and blood plasma samples were collected for each test period. Creatinine was determined colorimetrically. Ninhydrin-reacting compounds were determined with an automatic analyser (Technicon Instruments Co. Ltd., Chertsey, Surrey, U.K.) with L-norvaline as an internal standard.

Infused betaine did not alter the glomerular filtration rate determined from plasma clearances rates of creatinine. The infusion did increase the plasma clearance rates for all amino acids deter-

mined except arginine. Most increases were modest and below 3.5 times the control value. The clearance for glutamate was raised 4.7-fold and for glycine 8-fold, but the value for proline was 190 times the control value. An effect on hydroxyproline was also expected, but, owing to a mixed peak in chromatography, no analytical result was available.

Our interpretation is that betaine infusion specifically inhibited the renal reabsorption of proline. The slight glycinuria was a secondary effect of the prolinuria induced by betaine infusion. This hypothesis is consistent with the effect seen in familial hyperprolinaemia (Seriver, Efron & Schafer 1964).

Betainuria has been observed in children (Schirmer, Tieckelmann & Guthrie, 1965). Betain-aemia leading to prolinuria could be confused with a renal hyperiminoaciduria instead of a metabolic lesion. This could occur if only ninhydrin-reacting compounds were assayed, as is common in screening for human inborn errors of metabolism.

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The Effect of Circulating Lactose on Brain Metabolism in the Neonatal Rat

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Dietary lactose is normally hydrolysed to monosaccharides in the brush border of the small intestine, but the absorption of unhydrolysed lactose can occur in a variety of conditions in man (Arthur, 1966) and produces lactosuria. A number of findings have suggested that circulating lactose may have a deleterious effect in infants and young animals. The oral administration of lactose to young rats may cause retardation of growth with or without diarrhoea and also may lead to the development of cataracts (Koehler & Allen, 1934; Mitchell & Dodge, 1935). Infants with severe lactosuria may show aminoaciduria, proteinuria (Darling, Mortensen & Søndergaard, 1960) and a strong waxy pallor and are frequently irritable (Arthur, Clayton, Cottom, Seakins & Platt, 1966).

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