in vitro treated with mitomycin C against chromosome breaks. Conversely, lysosome labilizers do not increase chromosome breakage.

B. R. Brinkley (Houston) presented the results of techniques recently developed for examining by high resolution electron microscopy specific chromosomal regions initially studied under light microscopy. Both sectioned and unsectioned, stained and unstained chromosomes were used. I. Bernard Weinstein (New York) presented evidence that the primary site of action of some carcinogens seems to be the transfer RNA. It was proposed that altering the pattern of transfer RNA molecules may well upset cell regulatory processes and so lead to neoplasia.

Mary C. Weiss (Seine et Oise) described somatic hybridization between mouse cells and SV40-transformed human cells. Such hybrids undergo rapid and preferential loss of human chromosomes. As the number of human chromosomes diminishes, clones arise which fail to show the presence of the virus antigen. Thus the virus seems to be stably integrated into the human chromosomes and not all chromosomes in a transformed cell may carry the virus.

Recent studies of neoplasia in allophenic mice were reported by Beatrice Mintz (Philadelphia). These mice are formed by fusion of blastocysts from two different strains, with subsequent implantation into a foster mother. The mice develop into normal looking, fertile animals but are really derived from four parents and are discrete mosaics of the two genotypes used to form them. Studies of strains with high and low susceptibility to mammary tumours and hepatomas indicate that the frequency of tumour appearance is similar to the high frequency parental strain. Furthermore, such tumours seem to arise primarily from cells of the high frequency strain, as indicated by various inherited cellular markers. Thus the basic susceptibility to tumour production seems to reside in the individual cells rather than in some general physiological state.

The annual Bertner Foundation Award for Outstanding Achievement in the Field of Cancer Research was presented (*in absentia*) to Professor Boris Ephrussi of Paris. The newly established Anderson Award for Scientific Creativity and Teaching was presented to Professor Theophilus S. Painter of the University of Texas at Austin.

COVALENT EQUILIBRIA

Enzymes and Inhibitors

from our Molecular Biology Correspondent

AN interesting covalent equilibrium, of a kind not hitherto observed, has been described by Niekamp, Hixson and Laskowski (*Biochemistry*, **8**, 16; 1969). This is a reversible proteolysis, and it occurs in the interaction of trypsin with soyabean trypsin inhibitor.

Laskowski and his associates had previously demonstrated that the association of the enzyme with its inhibitor is accompanied by the cleavage of a peptide bond in the latter. It was noted that the reaction never seemed to go fully to completion, and subsequently other workers found the same phenomenon with inhibitors from other sources. Niekamp *et al.* have now shown that this is the result of a true thermodynamic equilibrium; gel electrophoresis at pH 4 makes possible the separation of the pristine

inhibitor from the trypsin-modified form, the latter possessing in these conditions an extra positive charge from its additional α -amino group. With increasing incubation time, the enzyme-inhibitor complex shows progressively more of the modified component, and this approaches, but never exceeds, some 85 per cent of the total. If the modified protein is then isolated in homogeneous state from the gels, reincubated with trypsin and analysed electrophoretically, the band corresponding to native inhibitor reappears until equilibrium is again reached at the same proportion, 85 per cent, of the modified form. The position of the equilibrium was found to be independent of the trypsin concentration. From the rates of reaction, estimated by determining reactant and product concentrations from electrophoretic analyses at different times, forward and reverse rate constants were obtained, which agreed well with values derived from rates of proton uptake or release during incubation.

Such an equilibrium in proteolytic reactions does not seem to have been generally envisaged, and it would obviously be interesting to know whether and to what extent it obtains in other, more familiar, situations. Reversible hydrolysis of phosphodiester bonds in nucleic acids has by contrast been recognized for some time, and has been used to good advantage for synthesis of oligonucleotides by nucleolytic enzymes.

A remarkable situation, involving the making and breaking of disulphide bonds, has been discovered in bovine serum albumin by Foster and his group (Sogami *et al.*, *Biochemistry*, **8**, 49; 1969). This protein, which might well have been created solely for the delectation of protein chemists, possesses a large number of unusual and interesting properties, from which many lessons in protein chemistry have been drawn. It undergoes a conformational transition to an expanded form ($N \rightarrow F$) at pH 4-4.5, and Petersen and Foster showed that the pure, lipid-free, protein exhibits a microheterogeneity in respect of this transition. At high salt, the expanded, F , form is salted out, and the solubility profiles measure the breadth of the transition. Now it is possible to effect a fractionation on this basis, into components each giving a sharp transition at a characteristic pH mid-point within this range, and differing also in certain other physical properties. Sogami *et al.* have now found that the heterogeneity increases spontaneously on standing at pH 7-10, the rate of change being greater the higher the pH. The protein contains one thiol group in addition to the many disulphide bonds, and if this is chemically blocked, the growth of heterogeneity is fully inhibited. Because there is no dimerization during the reaction, it is concluded that the heterogeneity is caused by internal disulphide exchange. It may be noted that the presence of ligands, such as lipids, also strongly inhibits the reaction, presumably because they bind strongly to the initial isomeric state, which is therefore stabilized.

These results clearly have considerable bearing on the relation between sequence and conformation: Sogami *et al.* point out that whereas an enzyme must evolve in such a way as to possess a narrowly defined conformation with a deep potential energy well, the constraints on other proteins may be less severe, perhaps for positive physiological reasons; evidently albumin can exist in a range of states of comparable conformational energy.