Another important area of pharmacology concerns the actions of specific antagonists; H. P. Rang and J. M. Ritter (University of Oxford) communicated some unusual findings on the properties of a new irreversible acetylcholine antagonist. As well as behaving as an affinity label of the acetylcholine receptor, this ligand has the unexpected property of high affinity for receptors which have recently interacted with agonists. They called this action of agonists, of increasing the affinity of the receptor for antagonist, a "metaphilic" action. Their hypothesis is that the molecular basis for this metaphilic effect of agonists may be the conformational change in the receptor macromolecule which must underlie the process of stimulation: they propose that stimulus may correspond to a discrete event—the alteration of the receptor from one form to another. After the receptor has undergone this change it is supposed to be in a "desensitized" (refractory form, which has high affinity for their antagonist.

POLYMERS

Statistical Models

from a Correspondent

THE third Polymer Meeting Point, held by the Polymer Consortium at the University of Essex on March 19, had an audience of sixty-five, of whom about half came from industry and several from overseas.

Professor M. Gordon (University of Essex), reviewing cascade models, emphasized the power of probability generating functions (pgf) in simplifying combinatorial problems. Relatively simple formulae for molecular weight averages emerge—mean square radii, elastic and swelling parameters, gel points, sol fractions and the like. Substitution effects and ring-chain competition can also be included in the theory, which has given good agreement with experiments on various polymer systems. Recently the theory has been improved by adding a master theorem which abolishes the need for specifying redundant stoichiometric information, which should be generated by a self-contained statistical–mechanical treatment. This theorem provides necessary and sufficient conditions for the initial member of a cascade process to correspond to the random choice of vertex from a set of trees. When a questioner raised the technologically important subject of steric hindrance, it was pointed out that short-range hindrance is covered by the theory of substitution effects.

Professor P. Whittle (Statistical Laboratory, University of Cambridge) expounded his theory of clustering processes, which is more fundamental than the Flory–Stockmayer or the cascade approach in that it replaces deterministic by stochastic equations. By replacing rate constants by transition probability intensities, polymerization becomes a Markov process in continuous time. The function of the rate equations is taken over by a differential equation for the pgf which is consistent with the Gibbs distribution. Substitution effects are included in the theory. A generalization to a formal treatment of cyclization has led to operators with commutation properties analogous to certain quantum operators. Concrete solutions coincide with those of the Flory–Stockmayer or the cascade method. In the discussion, Dr G. Weiss (National Institutes of Health, Bethesda) hinted at the possibility of an even more fundamental approach based on Liouville's equation.

Professor C. Domb (Department of Physics, King's College, London) reviewed the lattice methods for treating excluded volume effects on the size and shape of polymer chains. Exact computer enumerations of self-avoiding walks for chains of up to about twenty segments can be used to infer asymptotic behaviour (of infinitely long chains). The effectiveness of the extrapolation procedure can be checked against exact two-dimensional solutions of the Ising problem, or against Monte Carlo calculations. The appearance of simple rational exponents in various power laws suggested by these methods has occasionally triggered off the construction of theoretical proofs confirming them. Long-range non-Gaussian behaviour is found to be satisfactorily independent of the postulated lattice structure.

PROTEINS

Enzymes and Sequences

from a Correspondent

WHEN the third meeting of the Chemical Society's Protein Group was held at Oxford on March 19, Professor Dorothy Hodgkin started the day by reviewing the development and achievements of protein X-ray crystallography. During the ensuing discussion Professor H. N. Rydon pointed out that all protein chemists need access to molecular models of proteins, and suggested that if several centres had "libraries" of such models, it would then be easier to make full use of the available structural information.

One of the chief difficulties of protein X-ray crystallography is the preparation of suitable heavy-atom derivatives, and two papers given at the meeting impinged on this problem. First, D. G. Lindsay and S. Shall (University of Sussex) described a study of the reaction of insulin with diketene, undertaken because the acetoacetyl groups thus introduced can be mercurated. Then P. J. Anderson, I. Gibbons and R. Perham (University of Cambridge) reported work on the amino-acid sequences of aldolases from various species. One conclusion of the aldolase work was that the bovine enzyme might be the most suitable for X-ray examination, for it contains a reactive cysteine residue which is absent from the other enzymes studied and therefore offers the best prospects for obtaining useful heavy-atom derivatives.

The isolation and sequential analysis of a decapeptide from gastric juice of normal fasting humans was described by J. G. Heathcote and R. J. Washington (University of Salford), who stimulated much discussion; no function can as yet be ascribed to this compound. The peptide has been synthesized by Professor G. W. Kenner and his colleagues. Some members of the Liverpool University group (G. Gawne, G. W. Kenner and R. C. Sheppard) reported on the mechanism and use of a new method of peptide synthesis involving direct conversion of the carboxyl component to an *o*-acyl derivative of hexamethylphosphoramide (that is, an acyloxyphosphonium salt) which can be smoothly aminolysed to give a peptide in high yield with little danger of racemization. The synthesis of a large fragment of calcitonin-M using this new method of coupling has been undertaken to test this original