Cooperation in the abstract

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Cooperativity Theory in Biochemistry: Steady-State and Equilibrium Systems. By Terrell L. Hill. *Springer-Verlag: 1985. Pp.459. DM 398.*

COOPERATIVITY is of central importance for the control of biochemical processes. Although most enzymes obey rate equations in which the rate of reaction shows a less than proportional dependence on the concentration of the substrate, and although this is quite satisfactory for many purposes, it does not allow for the possibility of a rapid switching from one metabolic state to another in response to a primary stimulus that may be quite small. As a result, certain proteins, not all of them enzymes, have evolved the property of cooperativity, whereby a large change in behaviour can result from a relatively small change in conditions.

The classic example is provided by the binding of oxygen to haemoglobin. Here, a cooperative response is needed to allow most of the binding sites to be filled when blood passes through the lungs and most of them to be vacated before it returns, despite a relatively small difference between the partial pressure of oxygen in the lungs and that in the tissues. This phenomenon has been known since the beginning of the century, and study of it has contributed in large part to our present understanding of cooperativity, not least because haemoglobin, a binding protein and not an enzyme, can properly be treated by equilibrium methods. When used to study enzyme cooperativity, by contrast, equilibrium theory is at best an approximation.

So far as most biochemists are concerned, the main developments in theories of cooperativity occurred about 20 years ago, with the publication in 1965 of the "allosteric model" of Monod, Wyman and Changeux, and in 1966 of the "sequential model" of Koshland, Némethy and Filmer. These models have dominated discussion ever since, despite the fact that they are both "quasi-equilibrium models" that seek to explain kinetic phenomena as if they did no more than mirror behaviour that one might observe if the system were at equilibrium. The allosteric model, in particular, has had wide intuitive appeal, although its central postulate of conformational symmetry has no foundation in physical principles.

Nonetheless, even if for many biochemists the field ceased to be interesting in about 1970, there have been a few people who have tried to place the properties of cooperative systems in biochemistry on a firmer basis of physics. One of the most notable of them has been Terrell Hill, who has spent some years showing that in addition to the traditional empirical approach to cooperativity it is possible to work from a much more fundamental molecular point of view, considering systems in terms of partition functions and, indeed, all of the concepts of statistical thermodynamics. As the author mentions in the preface to *Cooperativity Theory in Biochemistry,* his new book can be regarded as a continuation of his successful textbook *Introduction to Statistical Thermodynamics,* published in 1960. More specifically, it gathers together the material published by the author and a few collaborators between 1977 and 1982, in the hope that this will bring it to the attention of a wider audience.

For physicists already familiar with statistical thermodynamics, this book will provide a valuable introduction to the kinds of problem that exist in the biological sciences, and which will eventually need to be understood on a much more fundamental level. Biochemists on the other hand, despite the appeal of the title, will find that it is extremely demanding and makes few concessions to any lack of familiarity with statistical mechanics. The treatment throughout is abstract and mathematical, with little discussion of experimental systems. The most familiar examples — haemoglobin, aspartate carbamoyltransferase and so on — are barely mentioned. Instead, the main experimental system considered is cooperativity in muscle proteins, a very important example, certainly, but one that is rather too complicated to be approached as a first step.

The treatment presented in the book is very much the author's own creation, developed largely in isolation from others interested in similar problems. A high proportion of the references, both in the book and in his original papers, are to his own work. Hill's contribution to the field is widely recognized, though less widely studied, and to have it summarized in a single book is very useful. □

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