

## LETTERS TO THE EDITORS

*The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications*

## Terminology of Enzyme Formation

It has been recognized for many years that in micro-organisms the formation of a large variety of enzymes can be specifically induced by exposing cells to compounds which are substrates for the enzymes in question. Recently, the same phenomenon has been demonstrated in a mammal<sup>1</sup>, and it will probably prove to be a general property of biological systems. Since a change of this sort can occur against a constant genetic background, it must be distinguished from a change in enzymatic constitution that is primarily mutational. In order to distinguish between these two phenomena, microbiologists have for many years referred to the former type of enzymic variation as 'enzyme (or enzymatic) adaptation'. The term was, perhaps, an unfortunate choice<sup>2,3</sup> since the word 'adaptation' has an old and well-established biological meaning. In biological parlance, 'adaptation' denotes the modifications of either structure or function which increase fitness; mechanism is unspecified, and in fact both phenotypic and genotypic changes are included thereunder. Logically, therefore, 'enzymatic adaptation' should denote a modification of enzymatic constitution which increases fitness, irrespective of whether it involves genotypic or phenotypic change, and microbiologists have in fact often used it in this broader sense<sup>4,5</sup>.

The use of the term 'enzymatic adaptation' to describe the direct induction of enzyme formation is open to objection for a second reason: enzyme formation can be specifically induced under conditions which preclude function of the enzyme so formed<sup>3,6</sup>, a process which might be expected to have a negative effect (if any) on the fitness of the organism concerned.

It might prove unpractical to abandon the use of the term 'enzyme adaptation' altogether at this stage; but we should like to suggest that, in suitable cases where it is possible to be more precise as to the nature of the change underlying the increase in enzymic activity, a more accurate and significant terminology be employed. We therefore propose the following terms and designations; previously used terms are placed in parenthesis. A relative increase in the rate of synthesis of a specific apo-enzyme resulting from exposure to a chemical substance is an 'enzyme induction' (enzyme adaptation). Any substance thus inducing enzyme synthesis is an enzyme 'inducer'. An enzyme-forming system which can be so activated by an exogenous inducer is 'inducible', and the enzyme so formed is 'induced' (adaptive). Although many compounds can act both as inducer and substrate, the terms are not equivalent. Certain substrates for induced enzymes are not inducers, while some inducers cannot function as substrates of the enzymes the formation of which they elicit<sup>3</sup>.

Many enzymes are formed in considerable amounts in the absence of an exogenous inducer. Such enzyme formation is 'constitutive' (constitutive). The amount of a constitutively formed enzyme can frequently be increased by specific induction, and it is also possible to obtain mutants in which synthesis of a particular enzyme is wholly constitutive (that is, not increased by any known inducer), from a parental

type in which formation of the same enzyme is largely inducible<sup>7,8</sup>. Thus 'constitutivity' and 'inducibility' are properties of enzyme-forming systems, not of enzymes *per se*, and can be used as significant expressions only in a biological frame of reference, not in a chemical one. It should be stressed that the notions of constitutivity and inducibility are relative, not absolute; in any given biological system, a certain fraction of a particular enzyme-forming capacity may be constitutive, the remaining fraction inducible. For the sake of convenience, one may wish to refer to 'an induced enzyme' or to 'a constitutive enzyme'; but it should always be kept in mind that these are shorthand expressions for 'an enzyme the formation of which is largely or entirely inducible (or constitutive) in the particular organism concerned'.

The exposure of an organism to a single inducer which is also a substrate may result in the induction of a sequence of enzymes, since the metabolism of the primary, exogenous inducer gives rise to the formation of a succession of intermediary metabolites each of which in turn serves as an inducer for the enzyme which converts it into the next member of the metabolic chain. This phenomenon is termed 'sequential induction' (simultaneous or successive adaptation).

M. COHN  
J. MONOD

Service de Physiologie microbienne,  
Institut Pasteur, Paris.

M. R. POLLOCK  
National Institute for Medical Research,  
London.

S. SPIEGELMAN  
Department of Bacteriology,  
University of Illinois, Urbana.

R. Y. STANIER  
Department of Bacteriology,  
University of California, Berkeley.  
Oct. 8.

<sup>1</sup> Knox, W. E., *Brit. J. Exp. Path.*, **32**, 462 (1951).

<sup>2</sup> Stanier, R. Y., "Ann. Rev. Microbiol.", **5**, 35 (1951).

<sup>3</sup> Monod, J., and Cohn, M., *Adv. Enzymol.*, **13**, 67 (1952).

<sup>4</sup> Ryan, F. J., *J. Gen. Microb.*, **7**, 69 (1952).

<sup>5</sup> "Adaptation in Microorganisms", a symposium held by the Soc. for General Microbiology, London, 1953 (in the press).

<sup>6</sup> Bellamy, W. D., and Gunsalus, I. C., *J. Bact.*, **50**, 95 (1945).

<sup>7</sup> Lederberg, J., in "Genetics in the 20th Century" (Macmillan, New York, 1951).

<sup>8</sup> Cohen-Bazire, G., and Jolitt, M., *Ann. Inst. Pasteur*, **84**, 60 (1953).

## Nomenclature of cycloHexane Bonds

It was shown originally by X-ray and electron diffraction, and has been confirmed by other physical and by chemical means, that the most stable and permanent form of the cyclohexane ring is that particular strainless form which is sometimes likened to a chair or a staircase. Geometrically, its chief feature is a six-fold alternating axis of symmetry. Its twelve extracyclic bonds fall into two classes<sup>1</sup>: six lie parallel to the axis, while six extend radially outward at angles of  $\pm 109.5^\circ$  to the axis. The stereochemical properties of substituents bound by these two classes of bond are so different that a need has been felt for verbal and symbolic means of distinguishing the classes.

The first suggestion<sup>2</sup> to this end designated the six parallel bonds as 'ε' and the others as 'κ'. However, although these symbols have been considerably used,