

## Quantitative Analysis of Metabolic Processes†

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### § 1. MODELS FOR ENZYME SYNTHESIS AND KINETICS OF ENZYME FORMATION

THE operation of a complex system can perhaps be understood on the basis of description. However, such knowledge about the system may often be illusory and quite inadequate to evaluate the relationships between the individual functional units. Furthermore, there may exist interaction patterns between the units which are not at all apparent in a superficial analysis, but only emerge when definite and formalized relationships are established in a quantitative manner. Metabolic systems can be considered to belong to such a category, and complex relations of the metabolic processes can only be understood when they can be formalized and made quantitative. This can be done perhaps only in the simplest of terms, but even an elementary formulation is significant. There is no need to emphasize the difficulties should such an attempt be made. However, it seems essential that formulation should be expressed in terms which can be analysed experimentally and vice versa.

Obviously mathematical formulation of a complex metabolic system is extremely difficult and in some respects may be quite impossible. At the present time a steady-state analysis has been applied for simpler transfer systems (Christiansen 1953, Haeron 1952). However, metabolic systems in a growing cell cannot be analysed with sufficient accuracy and understanding *via* a 'steady-state' approach. This is especially true in the case of cellular injury when one would be dealing with a 'transient-state' metabolism.

In recent years it has become apparent that when a cell is exposed to various physical or chemical agents an alteration and disorganization of normal cellular processes is produced. This may lead to conditions of altered growth or in extreme cases there is loss of cellular viability. There is also ample evidence that in multicellular organisms many diseases are caused by metabolic disorder (Snyder 1959). Since organizational patterns of cells are extremely complex, the degree of disorganization

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† Extensive part of this work was carried out at the Tumor Clinic, Michael Reese Hospital, Chicago, Illinois, U.S.A.

cannot be estimated by mere guessing or by observations. In order to obtain some quantitative criteria for disorganization it seems prerequisite that, at first, normal systems should be formulated as far as possible mathematically. However, before complex inter-related cellular processes can be analysed, it seems essential to formulate some basic processes independently. The purpose of this paper is to present some models for enzyme synthesis and to carry out some mathematical analysis of the latter.

We do not intend to review previous theories on enzyme synthesis. Induced enzyme synthesis has been thoroughly analysed by Mandelstam (1956) and enzyme formation in general and inter-related processes are extensively reviewed by Dixon and Webb (1958). Our purpose here is to introduce some new models of enzyme synthesis in which the operational units are of such character that the model system can be analysed theoretically as well as tested experimentally. It is expected that such models will induce more specific and definite experiments which in turn would result in the improvement or redesign of the models. The present attempt to formulate enzyme synthesis is based essentially on classical ideas and proposals for induced enzyme synthesis (Cohn and Monod 1953, Pollock 1953). Some recent experiments reveal (Pardee *et al.* 1958) that the rôle of the inducer may be more complex as anticipated on the basis of classical concepts of induced enzyme synthesis. In spite of the fact that available experimental data are limited and the rôle of the inducer has not been definitely established, it appears that an inducer may have a much more versatile function in enzyme synthesis than was postulated on the basis of classical schemes. However, more experimental data are required to elucidate this issue further. At the present time it seems that there is sufficient experimental evidence to show that enzyme synthesis can be analysed on the basis of classical concepts of induced enzyme synthesis. Especially significant experimental evidence in this respect is the phenomenon of sequential induction (Stanier 1951, 1954). This type of enzyme synthesis has been reviewed by Dixon and Webb (1958) and it seems definitely established that the inducer rôle here is a classical one, since addition of one substrate induces a whole series of enzymes, where intermediate substrates formed themselves act as inducers in respective enzyme synthesis and participate also in enzyme-substrate reactions with the formed enzyme. Dixon and Webb (1958) reviewed further experimental evidence which showed that sequential enzyme synthesis need not be induced externally and the phenomenon appears in natural conditions. Evidently many enzymes which appear to be constitutive are induced by intermediary metabolites. It appears that the distinction between 'induced enzyme' and 'constitutive enzyme' is quantitative rather than qualitative (Dixon and Webb 1958).

In view of the experimental evidence that a metabolite can act as an inducer for the enzyme synthesis as well as be the substrate for the formed enzyme, we will attempt to formulate some schemes and models for the enzyme synthesis. No attempt will be made to review some previous

models proposed in the past, since this has already been carried out (Dixon and Webb 1958, Mandelstam 1956). A number of postulates will be made concerning the basic operational units of the model system.

## § 2. ANALYSIS OF ENZYME SYNTHESIS ON THE BASIS OF A MODEL SYSTEM

Fundamental operational units for the enzyme synthesis are considered to be templates, pools (containing amino acids and co-factors), inducers, and substrates. A hypothetical scheme for enzyme synthesis is presented in fig. 1. Individual elements of the system will be postulated to have the following properties.

### 2.1. *Pretemplates and Templates*

The template is a basic structural unit for enzyme formation which determines the biological specificity of the enzyme. The pretemplate is synthesized from precursors by a series of condensation processes in which the pre-existing template system would act as the base for the formation of a new template. During the synthesis of the template the inducer is incorporated at one or several steps into the pretemplate and thereby lends to it an inducer specific configuration. The pretemplate surfaces have molecular configurations which make possible a competition between various inducers on particular interaction sites. Since the precursor pool for pretemplate formation is considered limited, there may, consequently, be a competition for the precursor pool between various template-forming systems. Precursor concentrations within the pool may be kept constant by feed-back control mechanisms.

### 2.2. *Inducers and Substrates*

Metabolites and some external molecules may act as the inducers for the template formation. Since no definite information is available concerning the alteration of internal substrates into an inducer, it is considered here that an internal substrate may act directly. The level of internal inducer depends, consequently, on the activity of particular enzymes in the metabolic pathways. Substrates as inducers are considered to produce only substrate specific templates.

In our calculations sometimes the term substrate is used. This is done to avoid confusion in terminology since in the present and in the subsequent calculations it is considered that an internal metabolite can be a substrate for an enzyme reaction as well as an inducer for the enzyme formation. Since in such a case a substrate has a double function, it is essential that in mathematical calculations only one symbol be used. For internal synthesis the term substrate facilitates the analysis. However, it should be kept in mind that an external inducer need not be a substrate.

### 2.3. *Pool*

In order to form an enzyme, a number of amino acids is required and certain co-factors must be available. The pool must contain all essential

units, otherwise the synthesis stops. The general steps of enzyme synthesis based on the scheme in fig. 1 can be described as follows.

Under the influence of the original template system ( $T_0$ ), various precursor components ( $x, y, z$ , etc.) form an incomplete template which will be called pretemplate ( $T$ ). When the pretemplate interacts with an inducer, an inducer specific template is formed. Here, the inducer-pretemplate

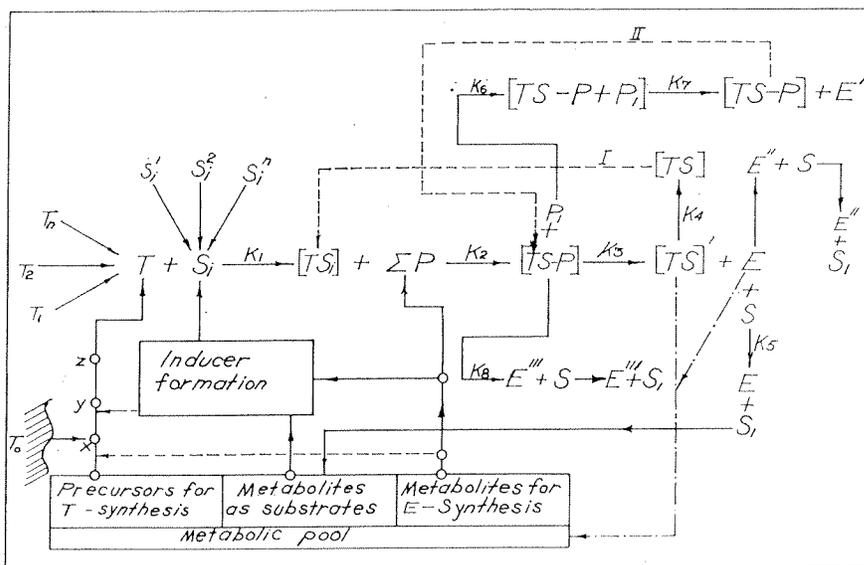


Fig. 1. A simplified scheme of enzyme synthesis

The following notations are used :

- $S, S_1, S_2 \dots S_n$  metabolic substrates or external molecules acting as inducers for the synthesis.  
 $T, T_1, T_2 \dots T_n$  pretemplates.  
 $(TS)$  'substrate specific' template.  
 $(EP)$  pool, which is an aggregate of amino acids and co-factors.  
 $(TS-P)$  a complex which can be a non-dissociable enzyme.  
 $E, E', E'', \text{etc.}$  various enzymes.  
 $X, Y, Z$  precursors for the pretemplate formation.  
 $T$  original template system.  
 $K_1, K_2 \dots K_n$  indicate the rate constants for various processes.

interaction is considered to occur as the final step in the template formation, since such an operational sequence can be analysed in mathematical terms. It is conceivable that a multiple type of interaction between the inducer and template can take place, as indicated symbolically in the scheme, but no further analysis of such a process is attempted. Various inducers and pretemplates having different molecular configurations may interact simultaneously, in general, which is symbolically indicated in fig. 1 by

various arrows and letters ( $S_1, S_2, \dots S_n$ , and  $T_1, T_2, \dots T_n$ ). Pretemplate (T) and inducer ( $S_i$ ) will interact at a definite rate. Theoretically this reaction can be reversible, but since the  $S_i$  concentration in sequential induction depends primarily on enzymatic reactions in the metabolic pathways, the reversible reaction step ( $K_{-1}$ ) can be neglected, as a first order approximation, and a continuously synthesizing system can be considered to be essentially a forward proceeding one. The next step represents a multiple process which is, in a comparative sense, very slow. Here, considerable time is required for the template to interact with a number of amino acids and cofactors. The reaction is considered to be finished when the last unit of the pool ( $\Sigma P$ ) has interacted with the template ( $TS_i$ ). The rate for the overall process is indicated by  $K_2$ . The template-pool complex ( $TS-P$ ) has several interesting properties:

(a) It can be considered to be a non-soluble enzyme; it could either function directly or it could become functional only after a specific activation process ( $E'''$ ).

(b) It may dissociate ( $K_3$ ) and liberate the original template ( $TS_i$ ) or a pseudo-original template (TS) (which may pass via a simple conversion process) and both may serve again as enzyme forming templates. An enzyme (E) is released in this process. This enzyme could function either directly or after an activation process ( $E''$ ); such an enzyme could be formed repeatedly from the same template, depending on thermal and proteolytic stability, and the enzyme formation would proceed, once initiated, without the new template synthesis. However, in a living cell where growth process takes place, the enzyme will be gradually diluted out, unless additional template formation occurs.

(c) As a third possibility ( $TS-P$ ) complex could act as a more complex type of template and, by further interaction with pool ( $P_1$ ), would follow essentially the same steps ( $K_6$ ) as already described. Such synthesis would be very complex and very difficult to formulate quantitatively; it could illustrate certain ideas on enzyme synthesis, i.e. template is composed of nucleo-protein.

As a general property, all functional units can be considered to have varying degrees of thermal and proteolytic stability. In the process of decomposition the products will return into various pools, where they can be re-utilized for the synthesis. The quantitative aspects of the enzyme synthesis, based on the scheme in fig. 1, depend largely on the values designated to the individual components of the systems.

It should be pointed out that the diffusion as such is not considered at the present time as a parameter in the cellular reactions since its effects cannot be evaluated and an arbitrary introduction would not serve any particular purpose except in making the mathematical treatment very complex. The difficulties of the diffusion problem have been pointed out previously in the analysis of chain reactions by Haeron (1952).

Enzyme-substrate reactions are usually considered to be reversible. However, in our analysis mostly unidirectional schemes (for example, inducer-template reaction) are considered, because in many processes the

forward reactions are quantitatively much larger than the reverse reactions, and the former will be the principal feature of the system; e.g. during the growth of bacterial cells, synthetic processes are relatively rapid and the system is essentially expanding. The significance of overbearing unidirectional flow of metabolic reactions has been pointed out by Krebs (1947). In view of such evidence it is considered that in normal processes, often only unidirectional reactions can be considered. However, in the case of cellular injury, where functional processes are disorganized and abnormally high substrate concentrations may appear, reversible reactions may be significant.

#### 2.4. Repressor Problem

A rôle of a repressor has been proposed for the inducer in enzyme synthesis (Pardee *et al.* 1958). However, at present the experimental data is so limited that no evaluation for the kinetics of enzyme formation can be made in a repressed system. Basic mathematical treatment for the repressed and a classical induced system may be considered to be similar on the basis of the following premises.

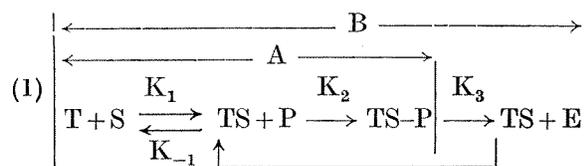
(a) In a classical induced system a pretemplate is incomplete and only after interaction with an inducer is an active substrate-specific template formed in (fig. 1 [TS]).

(b) In a repressed system one can consider that the pretemplate is in a repressed state and the repression is removed only after interaction with the inducer, yielding an active template.

Both systems could be used for the evaluation of kinetics of enzyme formation using the basic scheme in fig. 1. However, a difference may appear when quantitative restrictions are placed in scheme components. In order to avoid confusion in the following mathematical treatment, only the classical system is analysed.

### § 3. MATHEMATICAL FORMULATION OF ENZYME SYNTHESIS

In fig. 1 a scheme was proposed with the purpose of describing the process of enzyme synthesis on the basis of a model system. This scheme is simplified in order to carry out a formalization. Operative entities are designated to be in the following inter-relationships:



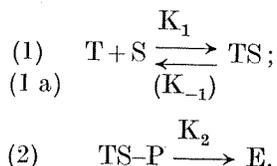
Notation (symbolic):

- T—pretemplate;
- S—substrate (acts as an inducer);
- P—pool for the synthesis;
- E—dissociable enzyme;
- TS—P—complex or non-dissociable enzyme;
- TS—substrate specific template.

The complex enzyme (CE) would be formed by the processes designated as the region 'A' and dissociable enzyme (DE) would be formed according to the scheme in the region 'B'. At first we will consider CE formation. An analysis of dissociable enzyme formation has also been carried out, but it is not a subject of this paper (Heinmets and Herschman 1959).

### 3.1. *Synthesis of Complex-enzyme (CE)*

Symbolic scheme for this process is as follows:



Reaction rate constants are indicated as follows:

- $K_1$  } substrate—pretemplate complex formation and dissociation;  
 $K_{-1}$  }  
 $K_2$  multiple step complex formation; it is the average rate for the process when the last component of the pool has interacted with the template.

The reaction in the first step can be considered to be reversible. However, since the substrate concentration in the cell is determined primarily by corresponding enzyme-substrate reactions and not by the take-up of the template, the reversible step can be considered to be not essential. Calculations can be carried out in which the reversible step is included, but derived expressions are too complex and too clumsy for demonstration of inter-relationship between various operational parameters. The primary aim in deriving the equations is to have simplest possible formulations, so that an analysis and graphical presentation is possible. Here some accuracy of final values may be lost, but for the demonstration purpose these are accurate enough when compared with the results which are obtainable by the experimental methods.

Molecular weights for enzymes vary in a wide range from about 10 000 to a million (Dixon and Webb 1958). Synthesis of enzymes requires a number of amino acids, and depending on the size of the enzyme the number of amino acids may range perhaps from a few dozen to several hundred. Consequently, when it is assumed that interaction coefficients between substrate-pretemplate are of the same order of magnitude as between the individual amino acids and the template, then it is apparent that the value of  $K_2$  is *much smaller* than that of  $K_1$ . We are going to consider two general kinds of enzyme synthesis.

(a) First, where the pool concentration is maintained at a constant level during the synthesis; for example, this could be accomplished by a control mechanism, such as a feed-back process. Such a condition can also exist in the case when the pool is very large, when compared to the quantity of product being produced by the synthesis.

(b) Second, the pool content is finite and it is reduced during the synthesis as a function of time. This type of synthesis seems to be a more natural type of process especially in cases where many enzymes are synthesized and they compete for the pool. During the cellular growth and division this type of competitive synthesis can be considered to take place.

The following symbols will be used to designate the concentrations of the components of the synthetic scheme :

- $a_1$ —pretemplate (T) concentration ;
- $a_2$ —template (TS)                   ,,
- $a$ —substrate (S)                   ,,
- $b_1$ —pool (P)                       ,,
- $b_2$ —enzyme (TS-P)               ,,

### 3.2. Synthesis with Infinite Pool

According to the scheme (1 a), the following relationships may be derived on the basis of mass-action law :

$$\frac{da_1}{dt} = -k_1 a_1 s; \quad . . . . . (1)$$

$$\frac{da_2}{dt} = k_1 a_1 s - k_2 a_2 b_1; \quad . . . . . (2)$$

$$\frac{db_2}{dt} = k_2 a_2 b_1. \quad . . . . . (3)$$

Conditions for synthesis are :

$$a_0 = a_1 + a_2 + b_2 = \text{constant, and } \frac{ds}{dt} = 0, \frac{db_1}{dt} = 0. \quad . . (4)$$

At time  $t = 0$ ;                     $a_1 = a_0$ ;  $a_2 = 0$ ;  $b_2 = 0$ ;  $k_{-1} = 0$ .

Conditions:                         $k_1 s \gg k_2 b_1$ .

At time  $t$ ,                          $a_1 \cong a_0 \exp(-k_1 s t). \quad . . . . . (1 a)$

Combining eqns. (1 a), (3) and (4) yields:

$$\frac{db_2}{dt} \cdot \frac{1}{k_2 b_1} + b_2 = a_0 - a_0 \exp(-k_1 s t).$$

Solution of this differential equation is the following :

$$b_2 = a_0 [1 - \exp(-k_2 b_1 t)] + \frac{a_0 [\exp(-k_1 s t) - \exp(-k_2 b_1 t)]}{\left(\frac{k_1 s}{k_2 b_1} - 1\right)}. \quad (3 a)$$

From eqn. (4) we obtain:

$$a_2 = a_0 - a_1 - b_2,$$

and after the substitutions:

$$a_2 = \frac{a_0 [-\exp(k_1st) + \exp(-k_2b_1t)]}{\left(\frac{k_1s}{k_2b_1} - 1\right)} \quad \dots \quad (2a)$$

On the basis of derived equations, the loss of pretemplate (T), and the formation of substrate specific template (TS) and enzyme (TS-P), are presented in fig. 2. The entity 'X' is proportional to the time and the ordinate represents relative values of concentrations. In order to demonstrate the time dependence of various components graphically, a logarithmic scale has to be used for the time unit. Pretemplate decay is very rapid,

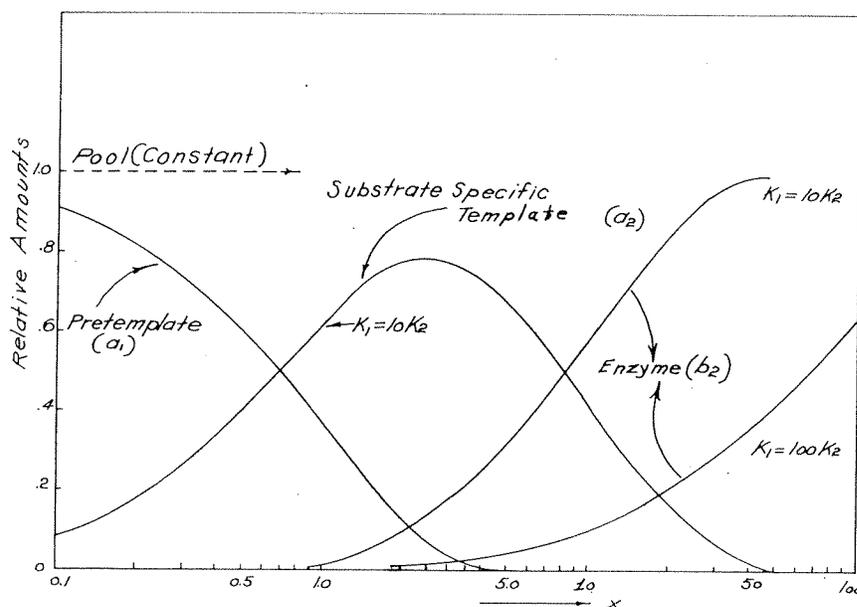


Fig. 2. Decay of pretemplate (T), and formation of substrate specific template (TS) and enzyme (TS-P) as function of time. Entity (X) is equivalent to time ( $x = k_1st$ ) and is plotted in log scale.

and it has practically disappeared before enzyme formation starts. Observation of pretemplate decay in such a hypothetical system would be possible only if rapid methods of measurements were used. Substrate specific template (TS) formation passes through a maximum and it is exhausted when the enzyme formation is completed. Since in the experimental work the enzyme formation is usually presented in linear time scale, in order to make visual comparisons, theoretical curves calculated on the basis of postulated scheme (1a) are again presented in the linear time scale in fig. 3. The curve forms, of course, depend on the relative values of

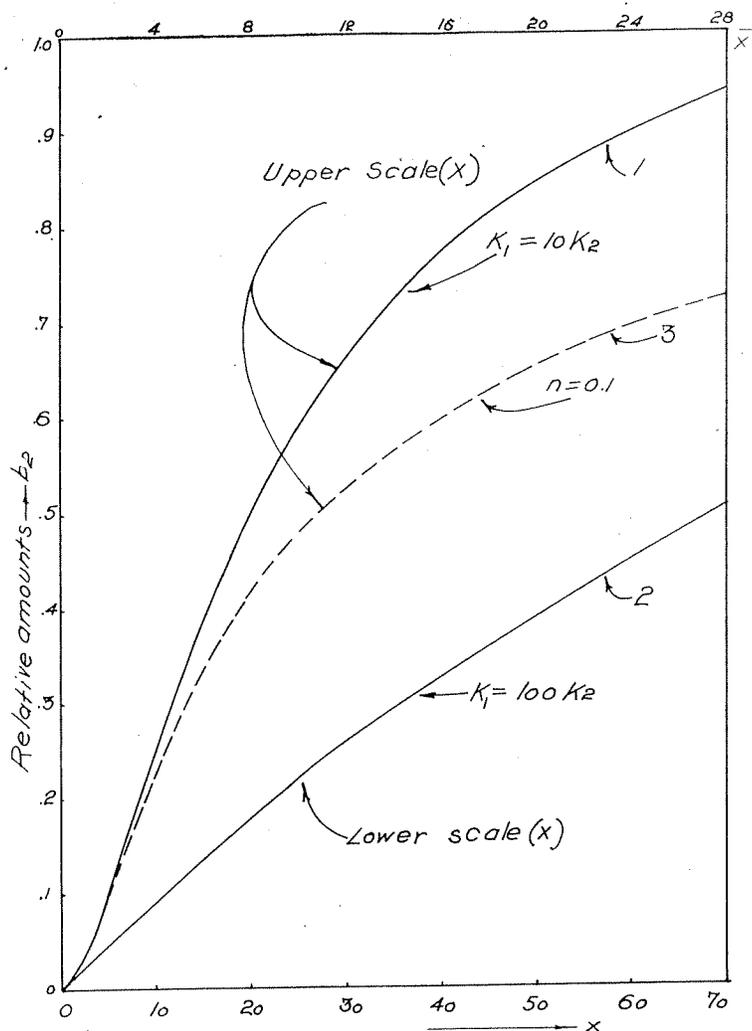


Fig. 3. Formation of enzyme as a function of time (linear scale) at two relative rate constant values (curves 1 and 2). Conditions for the synthesis are : Curves 1 and 2 for the constant pool ( $db_1/dt=0$ ). Curve 3 indicates enzyme formation in the case of finite pool (derivation in § 3.3). Time scale ( $X$ ) for the curve 2 is lower and for the curves 1 and 3 upper abscissa.

rate constants. It is evident from this that in order to represent enzyme formation in linear time scale the initial phase of enzyme formation cannot be properly resolved. Furthermore, when conventional experimental methods are used for the measurement of enzyme formation, these are not rapid enough to resolve time dependence of enzyme formation in the initial period. The relative shape of the curves can be altered when different values are designated for the rate constants, as seen in fig. 3, when curves 1 and 2 are compared.

This particular example of enzyme formation has been derived on the postulate that the pool for the synthesis is not exhausted, but pre-temple system is reduced as a function of time. If pretemple in this scheme is considered to be essentially a nucleic acid, then enzyme formation in such a hypothetical system would depend on the ability of the system to form nucleic acids. It has to be pointed out that enzyme synthesis 'appears' to be in certain phases a steady-state process (fig. 3) but the relationships between individual operational units, demonstrated in fig. 2 indicate that we are dealing with time dependent events.

Since we are interested in studying enzyme synthesis in various conditions of cellular metabolism, it is desirable to analyse a hypothetical synthetic system where concentrations of several operational units would be variable. The difficulties of formalizing enzyme synthesis in such conditions are considerable, and it will be attempted only by setting certain limiting conditions.

### 3.3. Enzyme Synthesis with the Finite Pool

The conditions for the enzyme synthesis (Scheme 1a) with the finite pool are the following:

$$(1a) \quad a_1 + a_2 + b_2 = a_0;$$

$$(2a) \quad b_1 + b_2 = b_0;$$

$$(3a) \quad \text{At time } t=0; \quad a_1 = a_0; \quad a_2 = 0; \quad b_2 = 0; \quad b_1 = b_0,$$

in addition  $k_{-1} = 0$ .

Pretemple ( $a_1$ ) concentration is reduced as function of time again as previously (eqn. 1a)

$$a_1 \cong a_0 \exp(-k_1 st).$$

The rate of change of the pool concentration is:

$$\frac{db_1}{dt} = -k_2 a_2 b_1. \quad \dots \dots \dots (5)$$

Combining eqns. (1a), (2a) and (5), the following equation is obtained:

$$\frac{1}{k_2 b_1} \cdot \frac{db_1}{dt} + b_1 \cong b_0 - a_0 + a_1 \cong b_0 - a_0 + a_0 \exp(-k_1 st). \quad \dots \dots (6)$$

The solution of (6) gives (approximately):

$$b_1 \cong \frac{b_0 \exp[k_2(b_0 - a_0)t]}{1 + \frac{b_0}{b_0 - a_0} [\exp(k_2(b_0 - a_0)t - 1)]};$$

$$\cong \frac{b_0}{\frac{b_0}{b_0 - a_0} - \frac{a_0}{b_0 - a_0} \cdot \exp[k_2(a_0 - b_0)t]} \quad \dots \dots \dots (7)$$

$$b_1 \cong \frac{(b_0 - a_0)}{1 - \frac{a_0}{b_0} \cdot \exp [k_2(a_0 - b_0)t]} \quad \dots \dots \dots (8)$$

The enzyme formation can be evaluated from eqns. (2 a) and (8), yielding

$$\left. \begin{aligned} b_2 &\cong \frac{a_0 [1 - \exp (k_2(a_0 - b_0)t)]}{1 - \frac{a_0}{b_0} \exp [k_2(a_0 - b_0)t]} ; \\ b_2 &\cong \frac{a_0 b_0 [\exp (k_2 b_0 t) - \exp (k_2 a_0 t)]}{b_0 \exp (k_2 b_0 t) - a_0 \exp (k_2 a_0 t)} \end{aligned} \right\} \dots \dots \dots (9)$$

It is evident that the smaller of the  $a_0$  or  $b_0$  will determine the enzyme formation rate at the conditions of asymptosis. In the case when  $a_0 = b_0$  the mathematical expressions can be simplified and will lend themselves more readily to graphical analysis. Since this is desirable, we will evaluate the time dependent behaviour of the operational units at these conditions.

For this case the eqn. (6) reduces to :

$$\frac{1}{b_1 k_2} \cdot \frac{db_1}{dt} + b_1 = a_0 \exp (-k_1 s t),$$

and

$$b_1 = \frac{a_0 \exp \left( \frac{k_2 a_0}{k_1 s} \right) \left( 1 - \frac{k_2 a_0}{k_1 s} \exp (-k_1 s t) + \dots \right)}{1 + k_2 a_0 \exp \left( \frac{k_2 a_0}{k_1 s} \right) \left[ t - \frac{k_2 a_0}{(k_1 s)^2} \left( 1 - \exp (-k_1 s t) \right) + \dots \right]} \quad (10)$$

The enzyme formation is determined by

$$b_2 = a_0 - b_1 \quad \dots \dots \dots (11)$$

and

$$a_2 = b_1 - a_1.$$

In order to simplify the calculations for graphical presentation, we will take the normal case where  $k_1 s$  is very large. We then have for  $t \gg 1/k_1 s$ , the asymptotic behaviour :

$$\begin{aligned} b_1 &\cong \frac{a_0}{1 + k_2 a_0 t} ; \\ b_2 &\cong a_0 - b_1 \cong \frac{k_2 a_0^2 t}{1 + k_2 a_0 t} \quad \dots \dots \dots (12) \end{aligned}$$

$$a_2 \sim b_1.$$

For

$$t \ll \frac{1}{k_2 a_0}$$

$$\begin{aligned}
 a_1 &\cong a_0 \exp(-k_1st) \\
 b_1 &\cong \frac{a_0 \left[ 1 + \frac{k_2 a_0}{k_1 s} [1 - \exp(-k_1st)] + \dots \right]}{1 + k_2 a_0 t \left( 1 + \frac{k_2 a_0}{k_1 s} + \dots \right)}; \quad (13a) \\
 b_2 &\cong a_0 - b_1; \\
 a_2 &\cong b_1 - a_1.
 \end{aligned}$$

In order to demonstrate the time dependence of the operational units, an example will be used for the illustration. Following will designate:

$$k_1st = X;$$

$$\frac{k_2 a_0}{k_1 s} = n$$

Then eqn. (13a) can be expressed as,

$$b_1 = \frac{a_0(1 + n - ne^{-x})}{1 + nx + n^2x} \dots \dots \dots (13b)$$

Using eqns. (13a) (13b) time dependent (x) concentrations for various operational units have been calculated. These are presented in fig. 4 which is self-explanatory.

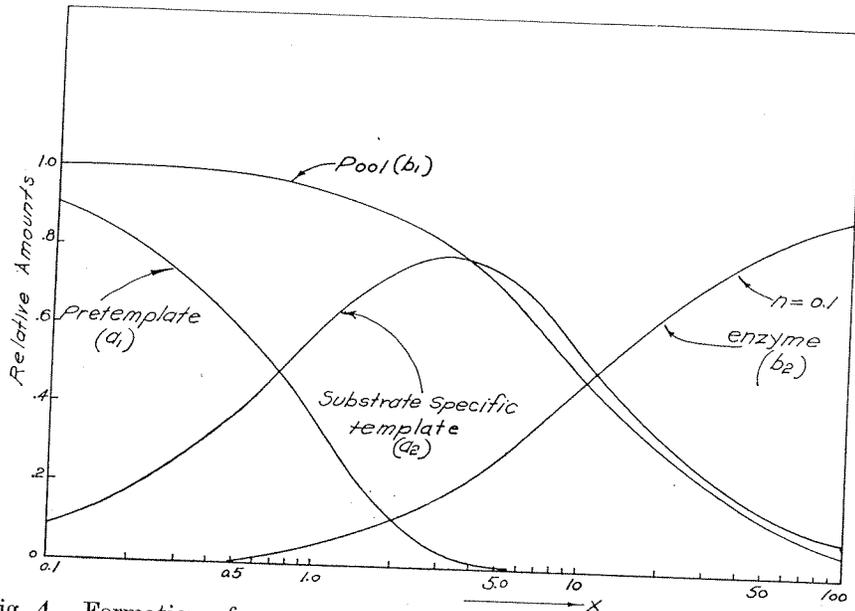


Fig. 4. Formation of enzyme and other components of synthetic system as functions of time (x is equivalent to time). Conditions: pretemplate and pool concentrations are finite; substrate is constant.

It should be pointed out here that enzyme formation is slower with the finite pool when compared with the rate of formation obtained with the infinite pool. Figure 3, curve 3, illustrates the hypothetical synthesis as a function of time (in linear scale) with the finite pool.

## ACKNOWLEDGMENT

We would like to thank Dr. Selig Starr for carefully checking the mathematical solutions in the manuscript and for his suggestions.

## SUMMARY

A model system for induced enzyme synthesis has been proposed and some mathematical calculations have been carried out. It is not attempted at the present time to compare the kinetics of enzyme formation between experimental and theoretical systems since experimental data in the literature do not duplicate exactly the conditions used for theoretical calculations. For such purpose, specific experiments have to be designed. These would permit to test the validity of the model system or perhaps could help to improve the system. However, it has to be pointed out that general kinetic characteristics of enzyme formation of the model system seem similar to kinetics of enzyme formations in many experimental systems published in the literature.

## RÉSUMÉ

On a proposé un système modèle pour la synthèse induite de l'enzyme, et quelques calculations mathématiques ont été exécutées. On n'essaie pas à présent de comparer les systèmes expérimentaux et théoriques de la cinétique de la formation de l'enzyme, puisque les résultats des expériences, trouvées dans la littérature, ne se rapportent pas exactement aux conditions employées pour les calculations théoriques. Des expériences spéciales doivent être préparées pour ce but. Ces expériences permettraient de vérifier la validité du système modèle, ou bien elles pourraient aider à le perfectionner. Néanmoins, on doit indiquer que les caractéristiques générales de cinétique du système modèle de formation de l'enzyme paraissent être semblables à la cinétique de la formation de l'enzyme dans beaucoup de systèmes expérimentaux publiés dans la littérature.

## ZUSAMMENFASSUNG

Es ist ein Modellsystem für induzierte Enzymsynthese vorgeschlagen worden und es sind einige mathematische Berechnungen ausgeführt worden. Es wird gegenwärtig nicht versucht, die Kinetik der Enzymbildung in experimentellen und theoretischen Systemen zu vergleichen, da die in Literatur zur Verfügung stehenden Versuchsergebnisse den für die theoretischen Berechnungen verwendeten Bedingungen nicht ganz genau entsprechen. Besondere Versuche müssten für diesen Zweck angestellt werden. Diese Versuche würden es ermöglichen, die Gültigkeit des Systems zu untersuchen; sie könnten vielleicht auch von Nutzen sein, um das System zu verbessern. Doch muss es darauf hingewiesen werden, dass die Hauptmerkmale der Kinetik der Enzymbildung für das Modellsystem denjenigen der Kinetik der Enzymbildung in vielen in der Literatur veröffentlichten experimentellen Systemen ähnlich zu sein scheinen.

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