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A Combination Formula of Michaelis-Menten-Monod Type

E. BERTOLAZZI
Dip. Ingegneria Meccanica e Strutturale
Università di Trento
via Mesiano 77, Trento, Italy

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Abstract—The purpose of this paper is to present a general formula for the growth rate of unicellular microorganisms A generalization of the Michaelis-Menten-Monod formula for the growth rate of microorganisms is derived and discussed If nutrients and inhibitors are considered as limiting substances and assumed to be noninteracting, this generalized formula works for more than one limiting substance Both competitive and noncompetitive inhibitors are included This general form of Michaelis-Menten law is analytically derived from a few basic hypotheses, it yields both multiplicative and minimum formulas as limiting cases © 2005 Elsevier Ltd All rights reserved

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1. INTRODUCTION

The growth of microorganisms may be described by differential equations of the form [1–3]

$$\frac{\mathrm{d}P}{\mathrm{d}t} = G_{\max} G P + (\text{other terms}),$$

where $P = P(t)$ stands for the microorganisms mass and the function $G = G(S_1, \dots, S_n)$, $(0 \le G \le 1)$ describes the effects of generic limiting substrates. This formulation is the well-known extension to microorganisms growth of Michaelis-Menten enzyme kinetic [4]. Mathematically the effect of a single nutrient substrate $A = S_1$ is expressed by the Michaelis-Menten-Monod law (shortened as MMM)

$$G(A) = \frac{A}{K + A}. \tag{1}$$

Similarly, the effect of a single inhibitor substrate, $B = S_1$, is expressed by

$$G(B) = \frac{L}{L + B}, \tag{2}$$

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where K and L are the half-saturation and inhibition constant, respectively. Formulas (1) and (2) may be used only when the limiting function G depends on a single substrate, but there is not a unique generalization when G depends on multiple substrate. Possible interactions for substrates are usually described by combination law. For example, common generalizations for formula (1) in presence of two substrates A_1 and A_2 fall into one of these formulations [1,5].

(I) Minimum

$$G^{\mathrm{I}}(A_1, A_2) = \min\left\{\frac{A_1}{K_1 + A_1}, \frac{A_2}{K_2 + A_2}\right\}.$$

(II) Multiplicative

$$G^{\mathrm{II}}(A_1, A_2) = \frac{A_1}{K_1 + A_1} \times \frac{A_2}{K_2 + A_2}.$$

(III) Harmonic mean

$$G^{\mathrm{III}}(A_1, A_2) = 2\left(\frac{K_1 + A_1}{A_1} + \frac{K_2 + A_2}{A_2}\right)^{-1} = 2\left(2 + \frac{K_1}{A_1} + \frac{K_2}{A_2}\right)^{-1}.$$

(IV) Simple average

$$G^{\mathrm{IV}}(A_1, A_2) = \frac{1}{2}\left(\frac{A_1}{K_1 + A_1} + \frac{A_2}{K_2 + A_2}\right).$$

Similar generalizations correspond to formula (2).

Evidence for the multiplicative model has been brought forward by Baule [6] and O'Brian [7], while the minimum or threshold model better described the experimental results of Droop [8] and Rhee [9]

Formulations (I)–(IV) are derived by some intuitive approach; for example (I) reflects the well-known Liebig's minimum principle. The adoption of one of these formulations instead of the other clearly depends on the type of system under investigation The multiplicative model is more appropriate when dealing with microbiological population exhibiting age structure and physiological conditions changing in function of the growth stage [10]. The minimum model better reflects instead the growth features for specialized synchronous populations.

Formulations (I)–(IV) share some properties. First, if the concentration of substrates A_1 and A_2 saturates, i.e., they take the limit value ∞, then all the growth rates (I)–(IV) are maximum, i.e., take the value 1 This property shared by all (I)–(IV) will be referred to as *Property a* in what follows.

Second, if the concentration of nutrient A_2 takes the limit value ∞, then the single substrate limitation due to A_1 takes the form

$$G^{\mathrm{I}}(A_1, \infty) = G^{\mathrm{II}}(A_1, \infty) = \frac{A_1}{K_1 + A_1} \tag{3}$$

only for (I) and (II), while for (III) one has

$$G^{\mathrm{III}}(A_1, \infty) = \frac{A_1}{K_1/2 + A_1}$$

and for (IV) one has

$$G^{\mathrm{IV}}(A_1, \infty) = \frac{1}{2}\left(\frac{A_1}{K_1 + A_1} + 1\right)$$

This means that in (III) the half-saturation constant changes, while (IV) does not follow the MMM law any more. The property expressed by formula (3) will be referred to as *Property b*.

Third, if the concentration of A_2 is kept fixed, (II) becomes

$$G^{\mathrm{II}}(A_1, A_2) = G^{\mathrm{II}}_{\max}(A_2)\frac{A_1}{K_1 + A_1}, \qquad G^{\mathrm{II}}_{\max}(A_2) = \frac{A_2}{K_2 + A_2}, \tag{4}$$