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A systematic derivation of the Monod equation for multi-substrate conditions

Una derivación sistemática de la ecuación de Monod para condiciones de múltiples sustratos

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Abstract

A simple kinetics scheme was considered for the systematic derivation of the Monod equation for multi-substrate conditions. The model derivation is based on a series expansion of the system solution in terms of a characteristic time constant. The multi-substrate Monod equation is structurally similar to the single-substrate Monod equation, containing terms that reflect the competitive interactions between the different substrates. Biodegradation of phenol-toluene was used to illustrate the ability of the Monod model for describing experimental data.

Keywords: Monod equation, multi-substrate; kinetics scheme; series expansion.

Resumen

Se consideró un esquema cinético simple para la derivación sistemática de la ecuación de Monod para condiciones de sustratos múltiples. La derivación del modelo se basa en una expansión en serie de la solución del sistema en términos de una constante de tiempo característica. La ecuación de Monod de sustrato múltiple es estructuralmente similar a la ecuación de Monod de sustrato único, y contiene términos que reflejan las interacciones competitivas entre los diferentes sustratos. Se utilizó la biodegradación de fenol-tolueno para ilustrar la capacidad del modelo de Monod para describir datos experimentales.

Palabras clave: ecuación de Monod, multisustrato; esquema cinético; expansión en serie.

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1 Introduction

The Monod equation is widely used to describe cell growth under single nutrient-limiting conditions. Models based on the Monod equation have found sound applications for the modeling and design of bioreacting systems in physiology, biotechnology and bioengineering (Bailey and Ollis, 1986). The attractiveness of the Monod equation relies on its simplicity, physical appeal and reasonable fitting of experimental data (Gaudy and Gaudy, 1980). The equation depends only on two parameters representing the maximum specific growth rate ($\mu_{\max}$) and the half-saturation constant (K_S), and can be written as follows:

$$\mu_X(X,S) = \frac{\mu_{\max}}{K_S + S} \tag{1}$$

As usual, S and X denote substrate and biomass concentrations, respectively. The parameters $\mu_{\max}$ and K_S are commonly used for the interpretation of kinetics mechanisms from experimental data. Many extensions to the Monod equation have been proposed in the past decades, mostly departing from heuristic grounds. For instance, Xu (2020) proposed a hybrid Monod-logistic model where the logistic factor accounts for the carrying capacity of the medium. Remarkably, the equation exhibits an implicit analytical solution in terms of transcendental functions.

Even though the Monod equation is widely used, it lacks some biochemical aspects, e.g., the microbial growth takes place under a mixture of several substrates and the limiting factor is not just one compound as the Monod equation supposes. In some instances, the growth of a single microbial species takes place under a mixture of several substrates. The biodegradation of naphthalene, phenanthrene, and pyrene mixtures (Guha *et al*., 1999), and the simultaneous degradation of chlorophenol mixtures by *Pseudomonas aeruginosa* (Durruty *et al*., 2011) are instances of microbial growth under multi-substrate conditions. Also, biodegradation of mixtures of benzene, toluene, and phenol by *Pseudomonas putida* has been studied (Reardon *et al*., 2000). Some efforts have been taken for extending the Monod equation for multi-substrate conditions. Guha *et al*. (1999) proposed that microbial growth is due to the utilization of all the compounds, such as the total specific growth rate is given by

$$\mu_T = \sum_{i=1}^{N} \mu_i \tag{2}$$

Here, μ_T is the total specific growth rate, and μ_i is the specific growth rate on the substrate S_i. It was proposed that the specific growth rate can be given as

$$\mu_i = \frac{\mu_{\max,i} S_i}{K_{S,i} + \sum_{j=1}^{N} \frac{K_{S,i}}{K_{S,j}} S_j} \tag{3}$$

where $\mu_{\max,i}$ and $K_{S,i}$ are respectively the maximum specific growth rate and half saturation constant from substrate S_i. It should be emphasized that the derivation of Eq. (3) was made under the hypothesis that all substrates are simultaneously utilized. Presumably, the ratio $K_{S,i}/K_{S,j}$ reflects the competitive interaction between the substrate S_i and the substrate S_j. Other studies proposed that specific growth rates are simply the sum of the traditional Monod equation (1) for individual substrates (Reardon *et al*., 2000; Akermann *et al*., 2021; Miri *et al*., 2021).

Although reported expressions like Eq. (3) provided acceptable fitting of experimental kinetics, they were proposed from heuristic grounds without a theoretical basis for justifying their functional structure. A detailed derivation of the Monod model for the multi-substrate condition would provide a tool to interpret experimental data and accurately describe the dynamics and operation of bioreacting systems. Motivated by this, the present note departs from a kinetics scheme to derive systematically a Monod equation for multi-substrate conditions. The resulting multi-substrate model can be reduced to the traditional Monod equation for single substrates.

2 Multi-substrate Monod equation

The Monod equation was proposed to model the specific microbial growth in a single substrate environment. The process can be seen as auto-catalytic where the activity of the existing microbial population leads to the production of more microbial units. In general, biomass growth involves a complex network of endogenous metabolic processes. A microbial unit can be seen as a body of enzymes required for sustaining microbial survival and reproduction. The substrate is in general dispersed in a continuous phase

surrounding the microbial surface. Once the substrate reaches the microbial bulk via transport mechanisms, the metabolic processes lead to the formation of new microbial cells via reproduction mechanisms. Moser (1983) departed from Langmuir adsorption and enzyme kinetics ideas to postulate a Monod mechanism where substrate molecules are adsorbed on the surface of the microbial before the reaction afterward. In this regard, Moser proposed a simple view of the microbial growth process reflected by the following kinetics scheme:

$$X + aS \xrightarrow{k_C} C \xrightarrow{k_X} (1+b)X \tag{4}$$

Here, X represents the microbial population, S is the substrate, and C is a complex formed between the absorbed substrate and the enzymes contained in the microbial bulk. On the other hand, k_C is the rate constant of complex formation, and k_X is the rate constant of microbial formation. The parameters $a > 0$ and b are stoichiometric coefficients. It is noted that $Y_{X/S} = b/a$ can be seen as the yield ratio between the consumed substrate and the formed microbial units. That is, $Y_{X/S}$ units of microbial cells are formed from one unit of a consumed substrate. Although the kinetics scheme is a simple view of the involved mechanism in the growth of microbial cells from a consumed substrate, the scheme provides a base for the systematic derivation of the Monod equation. The kinetics scheme can be seen as a lumped representation of physical and biochemical processes taking place outside and inside the microbial cells. The first kinetics step in the scheme (4) denotes the overall transport of the substrate from the bulk of the solution to the microbial cells surface/bulk where a substrate/enzyme complex is formed. On the other hand, the second kinetics step involves the metabolic processes taking place in the microbial cells and leading to the formation of new microbial units from the substrate consumption.

Microbial growth kinetics with multiple substrates in real systems involves complex cellular genetics and transport mechanisms. However, the derivation of models for fitting experimental data requires unavoidable simplifications. The mathematical derivation reported in our study departed from parallel utilization of each substrate, an assumption that is tacitly followed by the reported Monod models (Guha *et al.*, 1999). By assuming that N different substrates are available for simultaneous consumption by microbial cells, the simple scheme (4) can be extended as follows:

$$X + a_i S_i \xrightarrow{k_{C,i}} C_i \xrightarrow{k_{X,i}} (1+b_i)X, \quad i = 1,\ldots,N \tag{5}$$

where the subindex i in kinetics parameters refers to the ith-substrate. The derivation of the differential equations governing the substrate kinetics is carried out by means of the law of mass action. In this way, the mass balances from the kinetics scheme (5) leads to the following set of differential equations:

$$\begin{aligned}
\frac{dX}{dt} &= -\left(\sum_{j=1}^{N} k_{C,j} S_j\right) X + \sum_{j=1}^{N} (1+b_j) k_{X,j} C_j \\
\frac{dC_i}{dt} &= k_{C,i} S_i X - k_{X,i} C_i, \quad i = 1,\ldots,N \\
\frac{dS_i}{dt} &= -a_i k_{C,i} S_i X, \quad i = 1,\ldots,N
\end{aligned} \tag{6}$$

The derivation of a Monod equation involves the elimination of the intermediate species $C_i s$, such that the growth rate of microbial cells depends only on itself and substrate concentrations. To achieve this end, let us consider the new variables

$$Z_i = a_i C_i + S_i \tag{7}$$

It is noted that the variable Z_i reflects the total number of i-th substrate units that has not been converted to microbial units. Hence, the system (6) can be expressed as follows:

$$\frac{dX}{dt} = -\left(\sum_{j=1}^{N} k_{C,j} S_j\right) X + \sum_{j=1}^{N} \left(\frac{1+b_j}{a_j}\right) k_{X,j} (Z_j - S_j) \tag{8a}$$

$$\frac{dZ_i}{dt} = -k_{X,i}(Z_i - S_i), \quad i = 1,\ldots,N \tag{8b}$$

$$\frac{dS_i}{dt} = -a_i k_{C,i} S_i X, \quad i = 1,\ldots,N \tag{8c}$$

The equation (8b) governing the behavior of the intermediate variables Z_i has the advantage that is linear, and so offers some advantages for mathematical handling. First, note that the parameter $k_{X,i}^{-1}$, $i = 1,\ldots,N$ reflects the characteristic time-scale of the formation of microbial cells from the i-th substrate S_i. On the other hand, the parameter $(k_{C,i} S_{0,i})^{-1}, i = 1,\ldots,N$, where $S_{0,i}$ is the initial substrate concentration, can be seen as the characteristic time scale for the formation of the intermediate complex C_i (see Eq. (5)). Introduce the dimensionless parameters

$$\varepsilon_i = (k_{C,i} S_{0,i})/k_{X,i}, \quad i = 1,\ldots,N \tag{9}$$

The set of differential equations (8) can be re-written in the following form:

$$\frac{dX}{dt} = -\left(\sum_{j=1}^{N} k_{C,j} S_j\right) X + \sum_{j=1}^{N} \frac{k_{C,j} S_{0,j}}{\varepsilon_j} \left(\frac{1+b_j}{a_j}\right)(Z_j - S_j) \tag{10a}$$

$$\varepsilon_i \frac{dZ_i}{dt} = (k_{C,j} S_{0,j})(-Z_i + S_i), \quad i = 1,\ldots,N \tag{10b}$$

$$\frac{dS_i}{dt} = -a_i k_{C,i} S_i X, \quad i = 1,\ldots,N \tag{10c}$$

Consider the following series expansion for the variable Z_i:

$$Z_i = Z_i^{(0)} + \varepsilon_i Z_i^{(1)} + \varepsilon_i^2 Z_i^{(2)} + \mathbf{O}(\varepsilon_i^3), \quad i = 1,\ldots,N \tag{11}$$

Here, $Z_i^{(0)}$, $Z_i^{(1)}$ and $Z_i^{(2)}$ are functions that should be determined by the method of variation of parameters. Here, we assume that the parameters ε_i, $i = 1,\ldots,N$ are sufficiently small, such that the expansion (11) is valid up to $\mathbf{O}(\varepsilon_i^2)$. Such assumption implies that the rate of complex formation is much slower than the rate of cellular production. That is, the formation of the intermediate complex dominates the dynamics of the substrate consumption. It should be mentioned that the above assumption was taken as instrumental for the derivation of an expression with a structure similar to that of the single-substrate Mond equation. By substituting in the above expression in Eq. (10b), one obtains the equality

$$\varepsilon_i^3 \frac{dZ_i^{(2)}}{dt} + \varepsilon_i^2 \left(\frac{dZ_i^{(1)}}{dt} + k_{C,j} S_{0,j} Z_i^{(2)}\right) + \varepsilon_i^1 \left(\frac{dZ_i^{(0)}}{dt} + k_{C,j} S_{0,j} Z_i^{(1)}\right) + \varepsilon_i^0 \left(Z_i^{(0)} - S_i\right) = 0, \quad i = 1,\ldots,N \tag{12}$$

The matching condition implies the following equalities:

$$Z_i^{(0)} - S_i = 0 \tag{13a}$$

$$\frac{dZ_i^{(0)}}{dt} + (k_{C,j} S_{0,j}) Z_i^{(1)} = 0 \tag{13b}$$

$$\frac{dZ_i^{(1)}}{dt} + (k_{C,j} S_{0,j}) Z_i^{(2)} = 0 \tag{13c}$$

By considering Eq. (9), it can be shown that the approximate solution up to $\mathbf{O}(\varepsilon_i^2)$ terms is given by

$$Z_i = S_i - \left(\frac{1}{k_{X,i}}\right)\frac{dS_i}{dt} + \left(\frac{1}{k_{X,i}}\right)^2 \frac{d^2 S_i}{dt^2} + \mathbf{O}(\varepsilon_i^3), \quad i = 1,\ldots,N \tag{14}$$

One can use the expression given by Eq. (8c) to obtain the following expression:

$$Z_i = S_i + \left(\frac{1}{k_{X,i}}\right) a_i k_{C,i} S_i X + \left(\frac{1}{k_{X,i}}\right)^2 \left(a_i^2 k_{C,i}^2 X^2 S_i - a_i k_{C,i} S_i \frac{dX}{dt}\right) + \mathbf{O}(\varepsilon_i^3), \quad i = 1,\ldots,N \tag{15}$$

The above equation can be used in Eq. (10a) to give

$$\frac{dX}{dt} = -\left(\sum_{j=1}^{N} k_{C,j} S_j\right) X + \sum_{j=1}^{N} \left(\frac{1+b_j}{a_j}\right)\left[a_j k_{C,j} S_j X + \left(\frac{1}{k_{X,j}}\right)\left(a_j^2 k_{C,j}^2 X^2 S_j - a_j k_{C,j} S_j \frac{dX}{dt}\right) + \mathbf{O}\left(\varepsilon_j^3\right)\right] \tag{16}$$

As required, it is noted that the dynamics of the microbial concentration in the above equation depends only on microbial and substrate concentrations. By solving for the time-derivative of the microbial concentration, the following expression is obtained:

$$\frac{dX}{dt} = \frac{\left(\sum_{j=1}^{N} b_j k_{C,j} S_j\right) X + \sum_{j=1}^{N} \left(\frac{1}{k_{X,j}}\right)(1+b_j) a_j k_{C,j}^2 X^2 S_j}{1 + \sum_{j=1}^{N} \left(\frac{1}{k_{X,j}}\right)(1+b_j) k_{C,j} S_j} \tag{17}$$

In order to set the above equation in terms of the Monod's traditional parameters (i.e., maximum specific growth rate and half saturation constant), let us analyze Eq. (17) for a single substrate. In this case,

$$\frac{dX}{dt} = \frac{b k_C S X + \left(\frac{1}{k_X}\right)(1+b) a k_C^2 X^2 S}{1 + \left(\frac{1}{k_X}\right)(1+b) k_C S} \tag{18}$$

which can be re-written as follows:

$$\frac{dX}{dt} = \frac{\mu_{\max S}}{K_S + S} X + \frac{a k_C S}{K_S + S} X^2 \tag{19}$$

The first term in the right-hand side has the structure of a Monod model with the maximum specific growth rate and half-saturation constant are respectively given by

$$\mu_{\max} = \left(\frac{b}{1+b}\right) k_X \tag{20a}$$

$$K_S = \frac{k_X}{(1+b) k_C} \tag{20b}$$

Eq. (19) shows that the kinetics scheme (4) leads to the traditional Monod equation with an additional

second-order term $ak_C S X^2$, which reflects the self-catalytic effect of the produced biomass. Following the definitions given by Eq. (20), the rate of multi-substrate biomass generation given by Eq. (17) can be expressed as follows:

$$\frac{dX}{dt} = \frac{\left(\sum_{j=1}^{N} \mu_{\max,j} \frac{S_j}{K_{S,j}}\right) X + \left(\sum_{j=1}^{N} a_j k_{C,j} \frac{S_j}{K_{S,j}}\right) X^2}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{21}$$

Here, the parameters $\mu_{\max,i}$ and $K_{S,i}$ are given according to Eq. (20). The dynamics of the microbial growth rate governed by Eq. (21) is the result of two contributions. The second-order term

$$\frac{\left(\sum_{j=1}^{N} a_j k_{C,j} S_j / K_{S,j}\right) X^2}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{22}$$

reflects the formation of substrate/microbial complex units as specified by the first step in the kinetics scheme (5). On the other hand, the term

$$\frac{\left(\sum_{j=1}^{N} \mu_{\max,j} \frac{S_j}{K_{S,j}}\right) X}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{23}$$

is linked to the second step in the kinetics scheme (5) and corresponds to the generation of new microbial cells from the substrate/microbial substrate complex. The limiting step in the kinetics scheme (5) determines the relative dominance of either term in Eq. (21). In this way, the second-order term (22) can be discarded from Eq. (21) when the generation of new microbial units is the limiting step in the kinetics scheme (5). In such a case, Eq. (21) can be reduced to the following multi-substrate Monod equation:

$$\frac{dX}{dt} = \frac{\left(\sum_{j=1}^{N} \mu_{\max,j} S_j / K_{S,j}\right) X}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{24}$$

For single-substrate conditions, Eq. (24) becomes the traditional Monod equation. In this way, the specific growth rate is given by the sum of individual specific growth rates

$$\mu_T = \sum_{j=1}^{N} \mu_j \tag{25}$$

where

$$\mu_i = \frac{\mu_{\max,i} S_i / K_{S,i}}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{26}$$

It is noted that the specific growth rate is given as a function of the "normalized" substrate concentration $S_i/K_{S,i}$. Besides, Eq. (26) describes the individual contribution of the i-th substrate to cell growth. Overall, the above results suggest that the Monod equation can be accepted as an accurate model for microbial growth rate when the formation of microbial/substrate complexes (via, e.g., external and adsorption mechanisms) is faster than the internal biochemical processes leading to the formation of new microbial cells.

In terms of the microbial and substrate concentrations, the dynamics of the multi-substrate/biomass system is governed by the following set of differential equations:

$$\frac{dX}{dt} = \frac{\left(\sum_{j=1}^{N} \mu_{\max,j} S_j / K_{S,j}\right) X + \left(\sum_{j=1}^{N} a_j k_{C,j} S_j / K_{S,j}\right) X^2}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{27a}$$

$$\frac{dS_i}{dt} = -k_{C,i} S_i X, \quad i = 1, \ldots, N \tag{27b}$$

As done above, the discarding of the second-order term in Eq. (27) leads to the multi-substrate Monod model

$$\frac{dX}{dt} = \frac{\left(\sum_{j=1}^{N} \mu_{\max,j} S_j / K_{S,j}\right) X}{1 + \sum_{j=1}^{N} S_j / K_{S,j}} \tag{28a}$$

$$\frac{dS_i}{dt} = -k_{C,i} S_i X, \quad i = 1, \ldots, N \tag{28b}$$

In principle, this model suffices to describe the behavior of the biomass growth subjected to simultaneous multi-substrate consumption. Interestingly, the system (28) reduces to

$$\frac{dX}{dt} = \frac{\mu_{\max}}{K_S + S} \tag{29a}$$

$$\frac{dS}{dt} = -k_C S X \tag{29b}$$

for single-substrate conditions.

3 Example

The biodegradation of phenol and toluene by *Pseudomonas putida* as reported by Reardon *et al.* (2000) was considered for illustrating the viability of the system (28) in describing experimental data. Firstly, figures 1.a and 1.b present respectively the biodegradation of individual (i.e., single-substrate) phenol and toluene substrates. For each case, the system (28) was used for fitting the experimental data. The estimated parameters were $\mu_{\max}$ mg/L.h, K_S=422.25±8.26 mg/L, and k_C=2.10±0.03×10^{-3} 1/h for phenol, and $\mu_{\max}$ mg/L.h, K_S=73.25±2.26 mg/L, and k_C=1.73±0.02×10^{2} 1/h for toluene. The rate of biodegradation, reflected by the kinetics constant k_C, is one magnitude order higher for toluene as compared with the respective rate for phenol. The results in Figure 1 showed that the Monod model given by Eq. (28) provides an accurate description of the single-substrate experimental data. The second case considers the simultaneous biodegradation of phenol and toluene. The experimental data borrowed from Reardon *et al.* (1999) is displayed by Figure 2. The continuous lines depict the least-squares fitting by the multi-substrate model given by Eq. (28). The estimated parameters were $\mu_{\max,1}$ =0.82±0.02 mg/L.h, $K_{S,1}$=385.52±7.28 mg/L, and $k_{C,1}$=3.02±0.04×10^{-3} 1/h, $\mu_{\max,2}$ =2.98±0.12 mg/L.h, $K_{S,2}$=89.65±2.19 mg/L, and $k_{C,2}$=2.21±0.02×10^{2} 1/h, where the subindices "1" and "2" stand for phenol and toluene substrates, respectively. Notice that the values of the estimated parameters from the multi-substrate model are similar to the values of the parameters obtained from single-substrate models. The differences can be attributed to the competitive interaction between the binding sites of the individual substrate. This example is a common practical situation where hydrocarbon dispersed in contaminated soils is present in recalcitrant blends. A viable strategy to enhance the bioremediation efficiency is the addition of an easily assimilable substrate for carbon and energy sources, such as molasses. The presence of molasses promotes the microbial growth and co-metabolic degradation of hydrocarbon (Reardon *et al.*, 2000; García-Rivero *et al.*, 2008) and fermentation processes (González-Figueredo *et al.*, 2021). The multi-substrate Monod equation derived in this work is a useful tool for the systematic design of remediation strategies for contaminated sites. The case of bioreactors is also a potential application where multi-substrate conditions are commonly found in practice (Miramontes-Martínez *et al.*, 2019).

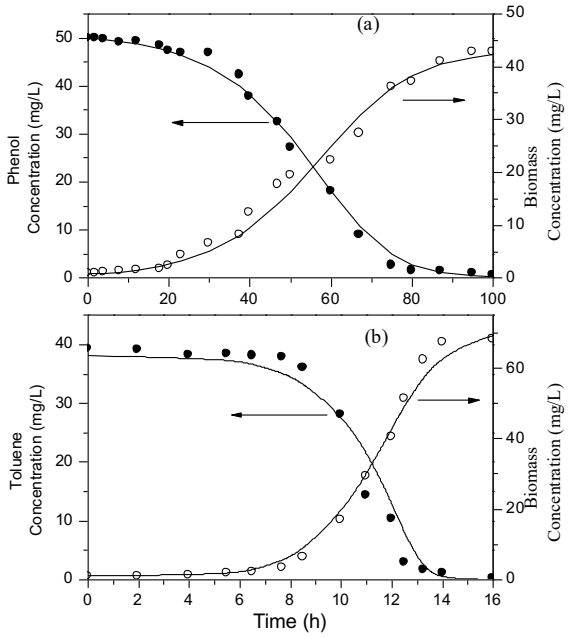

Figure 1. (a) Biodegradation of individual (a) phenol, and (b) toluene by *Pseudomonas putida*. The continuous lines denote the least-square fittings by single-substrate Monod model given by Eq. (28).

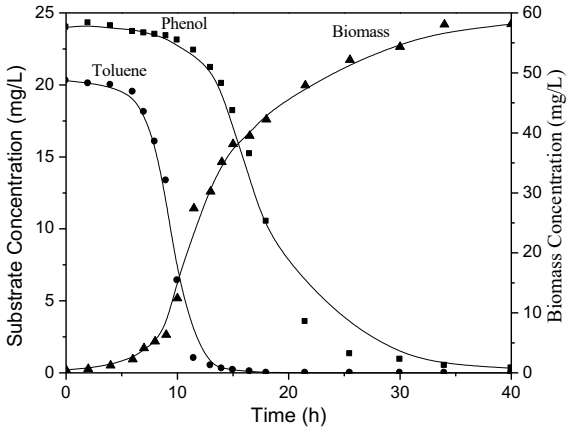

Figure 2. Simultaneous biodegradation of phenol and toluene by *Pseudomonas putida*. The continuous lines denote the least-square fittings by multi-substrate Monod model given by Eq. (28).

Conclusions

This work showed that the dynamics of biomass growth can be described by a Monod equation systematically derived from a kinetics scheme. The resulting Monod equation has the structure of a traditional Monod equation, where individual substrates are normalized by the corresponding half-saturation constant. By doing this, the multi-substrate Monod equation is simple in structure and affordable for the use and interpretation of experimental data by practitioners. The derived model would be useful to estimate parameters from experimental runs, describe the dynamics of multi-substrate bioreactors and derive optimal strategies to achieve selective substrate degradation and consumption.

Nomenclature

a,b	stoichiometric parameters
C	complex concentration
k_C	complex formation rate constant
k_X	biomass formation rate constant
K_S	half-saturation constant
S	substrate concentration
$Y_{X/S}$	substrate-to-biomass yield
X	biomass concentration
Greek letters	
ε	small perturbation parameter
$\mu_{\max}$	maximum specific growth rate

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Appendix. Order of magnitude analysis

The reduction of Eq. (21) to a Monod-type expression (see Eq. (24)) involves the discarding of the second-order term $\left(\sum_{j=1}^{N} \frac{a_j k_{C,j} S_j}{K_{S,j}}\right) X^2$. Establishing strict conditions under which the second-order term has marginal contributions to the biomass growth kinetics is a hard mathematical problem that is out of the scope of the present study. In the following, we describe an order of magnitude analysis proposed by Professor F.J. Valdés-Parada to gain insights on the contribution of the second-order term in the numerator of Eq. (21). To this end, starting with Eq. (17) one can propose the following orders of magnitude estimates:

$$\left(\sum_{j=1}^{N} b_j k_{C,j} S_j\right) X = \mathbf{O}\left(b_j k_{C,j} S_j X\right) \tag{A.1}$$

and

$$\sum_{j=1}^{N}\left(\frac{1}{k_{X,j}}\right)(1+b_j) a_j k_{C,j}^2 X^2 S_j = \mathbf{O}\left(\frac{k_{C,j}^2 S_j a_j (1+b_j)}{k_{X,j}} X^2\right) \tag{A.2}$$

The reduction of Eq. (17) to Eq. (24) implies assuming that

$$\sum_{j=1}^{N}\left(\frac{1}{k_{X,j}}\right)(1+b_j) a_j k_{C,j}^2 X^2 S_j \ll \left(\sum_{j=1}^{N} b_j k_{C,j} S_j\right) X \tag{A.3}$$

which is satisfied under the constraint

$$\frac{k_{C,j} X}{k_{X,j}} \ll \left(\frac{b_j}{a_j (1+b_j)}\right) \tag{A.4}$$

Assume that $X = \mathbf{O}(S_{0,j}/a_j)$. From Eq. (9), one obtains

$$\varepsilon_j \ll \left(\frac{b_j}{(1+b_j)}\right) \tag{A.5}$$

It is physically reliable assume that $b_j = \mathbf{O}(1)$, meaning that the biomass growth is basically a cellular duplication process (see Eq. (4)). In this way, the above inequality can be reduced to the following one:

$$\varepsilon_j \ll b_j \tag{A.6}$$

Finally, using Eq. (9) in Eq. (A.6) one obtains the inequality

$$(k_{C,j} S_{0,j})/k_{X,i} \ll 1 \tag{A.7}$$

That is, Eq. (17) can be reduced to a Mond-type equation when the rate of complex formation is the dominant kinetics step relative to the complex decomposition to form biomass.