Exponential-like concentration distribution in modeling the specific consumption rate in substrate-limited microbial growth

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The specific consumption rate of substrate, as well as the associated specific growth rate, is an essential parameter in the mathematical description of substrate-limited microbial growth. In this communication we present a new model of substrate transport [1], based on recent knowledge on the structural biology of transport proteins [2], which correctly describes very accurate experimental results at near-zero substrate concentration values found in the literature [3, 4], where the widespread Michaelis-Menten model fails.

In order to establish the model for the specific consumption rate, the following two assumptions are considered:

1. The local substrate concentration, in the immediate neighbourhood of the corresponding membrane transport protein, fluctuates around the mean concentration (bulk concentration) with high probability for concentration below the mean and with low probability for concentration above the mean.

2. The substrate penetrates cell membrane if and only if the local substrate concentration, in the immediate neighbourhood of the transport protein, reaches or exceeds certain concentration threshold which will be named as *activation concentration*. Then, the substrate penetrates cell membrane at constant rate.

The first assumption concerns the features of substrate solution in the neighbourhood of the corresponding transport protein. As is represented in Fig 1 (a), substrate at bulk concentration C is transported into the cell by the corresponding protein with rate q_t, so that local substrate concentration c in the immediate neighbourhood of the transport protein will decrease. Forced convection in the liquid medium would immediately restore bulk concentration, but the existence of the cell wall prevents forced convection, so that bulk concentration will be restored by means of diffusion. Since substrate diffusion is a very slow process, it seems reasonable that the local concentration is smaller than bulk concentration with high probability, and greater than bulk concentration with low probability. The exponential distribution is the simplest probability distribution with these features among other suitable features

$$\mathcal{P}(c) = \frac{1}{C}\exp\left(-\frac{c}{C}\right). \qquad (1)$$

However, since exponential distribution has its maximum probability density at the perhaps unrealistic value $c = 0$, in Ref. [1] the model was improved by using the more general Weibull distribution, which includes the exponential distribution as a particular case.

The second assumption concerns the features of the mechanism of transport. The latest research on this issue [2] shows the existence of *several binding sites*, which, when activated, would also induce conformational changes. As is well known, in this case the kinetics is described by Hill equation which, for a high number of binding sites, tends rapidly to a smoothed Heaviside step function.

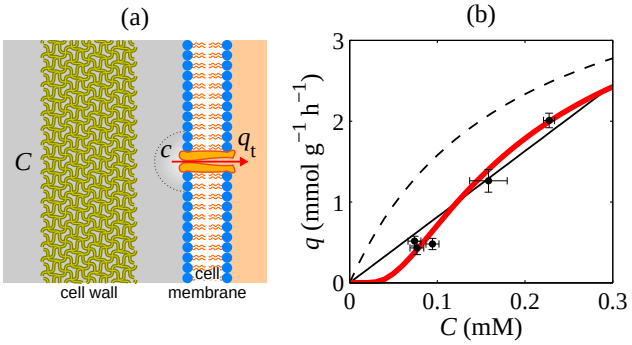

Fig. 1. (a) Schematic representation of the cell interface in the neighbourhood of a transport protein, with consumption rate q_t, showing the concept of local substrate concentration c *versus* bulk concentration C. (b) Experimental values of specific consumption rate q *versus* substrate concentration C for *S. cerevisiae*, taken from Boender *et al.* [4]. The fitted curve corresponding to the proposed model (red line) along with the fitted curve from the Michaelis-Menten based model (black line) are also depicted. Notice that Michaelis-Menten curve degenerates into a straight line. Additionally, the Michaelis-Menten curve corresponding to the fitting parameters from the proposed model, assuming Michaelis constant $K = c_{ac}$, has also been represented (dashed black line).

Thus, considering both assumptions jointly, if the substrate penetrates cell membrane through each transport protein at the constant rate q_t when the local concentration fulfills $c \geq c_{ac}$, and each cell has n transport proteins on average, then the statistically observable value of the specific consumption rate $q(C)$ will be given by

$$\begin{aligned} q(C) &= q_{max} \cdot \int_{c_{ac}}^{\infty} \mathcal{P}_\beta(c)\,\mathrm{d}c \\ &= q_{max} \cdot \exp\left(-\frac{c_{ac}}{C}\right), \end{aligned} \qquad (2)$$

with $q_{max} = nq_t$, resulting in the functional form for the specific consumption rate from the proposed model.

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