Analysis of a Model for Multiseptation in Bacteria

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The predictions of a model for multiseptation in bacteria recently proposed by Paulton are derived mathematically. It is shown that independent of the growth rate, the time between septum formation and cell division is constant, and the time interval between septum formation and the participation of the septum in cell division is a constant independent of the generation time of the cells. If the "waiting time" exceeds the generation time, multiple septa will be formed and the cells will aggregate in "chains." Paulton suggests that his model is analogous to the model of Helmstetter and Cooper (1-3) for multiforked deoxyribonucleic acid (DNA) replication in cells with generation times shorter than the DNA replication time.

The purpose of this note is to derive an exact mathematical formalism for the Paulton model which differs from the empirical expression suggested by Paulton.

Consider a bacterial culture which is growing exponentially with a doubling time (t) and neglect the distribution of interdivision times of individual cells. The number of cells at any time (t < t) is related to the number of cells at t = 0 by

\[ N(t) = N(0) \cdot 2^{t/t} \]  

The distribution of cells according to age is then given by

\[ n(t) = n(0) \cdot 2^{-1/t} \]  

where n(0) is the number of cells which have just divided (i.e., have age t = 0). For any arbitrary age (t), the culture may be divided into those cells which are younger than t and those cells which are older than t. The respective fractions of the culture are given by

\[ f_1(t) = \int_0^1 n(\theta) d\theta/ \int_0^1 n(\theta) d\theta = 2(1 - 2^{-1/t}) \]  

and

\[ f_2(t) = \int_1^\infty n(\theta) d\theta/ \int_0^1 n(\theta) d\theta = 2(2^{t/t} - 1/2) \]  

Of course, \( f_1(t) + f_2(t) = 1 \).

According to the Paulton model (4), there is a fixed-time interval \( t_k \) between the formation of the septum and the participation of that septum in cell division. The average number of septa per cell in an exponential culture may be directly computed as follows.

Suppose that \((s - 1)t < t_k < st\), where s is an integer. The average number of septa per cell (\( p \)) is given by

\[ p = f_1(st - t_k) \cdot (2^{st} - 1) + f_2(st - t_k) \cdot (2^s - 1) + 2(2^{2st/t} - 1) \]  

This result is independent of s and therefore is valid for all doubling times. Equation 5 may be rewritten in the form

\[ t_k/t = \log(p + 1)/\log(2) \]  

In deriving equations 5 and 6, it has been assumed that septum formation occurs symmetrically so that only \( p = 2^x - 1 = 0, 1, 3, 7, \ldots \) septa in each cell are observed.

The average number of successive division sites per cell (\( s \)) is obtained from the relation

\[ p = 2^x - 1 \]  

or

\[ s = \log(p + 1)/\log(2) \]  

A comparison of equations 6 and 8 yields the interesting result that the average number of successive division sites per cell is simply related to the growth rate \( R = 1/t \) by

\[ s = t_k/t = t_k \cdot R \]  

In Fig. 1, the data obtained by Paulton for the
average number of successive division sites per cell ($s$) as a function of the growth rate ($R = 1/t$) have been plotted on a linear scale (rather than a logarithmic scale). The data are fit very well by using the value of Paulton (t$_s$ = 138 min) to fix the slope of the line. The model appears to give excellent agreement except for very short doubling times.

Paulton has fitted his data by using the empirical equation

$$ s = 2.1 + 2.9 \log(R) \quad (10) $$

when $R \to 0$, $s \to -\infty$, which is clearly incorrect. Also, for $s = 0$, $\log(R) = -2.1/2.9 = -0.73$ or $R = 0.24$ is obtained. Equation 10 predicts that a culture of Bacillus subtilis growing at a slower rate than $R = 0.24$, i.e., a doubling time of 250 minutes, cannot be observed.

Thus, the model for multiseptation suggested by Paulton appears to give a valid description of the growth of bacterial cultures. An exact mathematical expression for the relation between the average number of septa per cell and the growth rate has been obtained in this note.

The Paulton model may prove to be a useful complement to the model of Helmstetter and Cooper (1-3) for multiforked-DNA replication. However, the latter model has been applied only to strains of Escherichia coli which do not form multiple septa. It would be of great interest to determine whether the septation and DNA cycles are correlated in multiseptate bacteria.

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