

# Supplementary Text for ”Mathematical Modeling of Microbes: Metabolism, Gene Expression, and Growth”

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In the nonsegregated models used in the main text, all cells have been lumped into a single aggregated population, whereas in segregated models a distinction is made between the individual cells. In this supplementary text, we formulate conditions under which a nonsegregated model provides an accurate description of the dynamics of the individual cells making up the population.

Let  $n(t)$  be the number of cells in the population, varying with time  $t$ . Moreover,  $Vol_k(t)$  is the time-varying volume of cell  $k$ . In what follows, we simplify the notation by dropping the time-dependence of the variables. We define

$$Vol_{\bullet} = \sum_{k=1}^n Vol_k. \quad (1)$$

That is,  $Vol_{\bullet}$  represents the aggregated volume obtained by summing the volumes of the individual cells in the population. Moreover, analogously to Eq. 1 in the main text, the dynamics of  $Vol_k$  is given by the following differential equation:

$$\dot{Vol}_k = \mu_k \cdot Vol_k. \quad (2)$$

Under the assumption that  $\mu_k = \mu$  for all  $k$ , that is, all cells have the same growth rate, we find

$$\begin{aligned} \dot{Vol}_{\bullet} &= \sum_{k=1}^n \dot{Vol}_k = \sum_{k=1}^n \mu_k \cdot Vol_k \\ &= \mu \sum_{k=1}^n Vol_k = \mu \cdot Vol_{\bullet}. \end{aligned} \quad (3)$$

In other words, the assumption implies that the growth-rate dynamics of the individual cells and the population composed of these individual cells are the same.

Let  $c_{ik}$  denote the concentration of molecular constituent  $i$  in cell  $k$ . Moreover, define

$$c_{i\bullet} = \sum_{k=1}^n c_{ik} \cdot \frac{Vol_k}{Vol_{\bullet}}. \quad (4)$$

That is,  $c_{i\bullet}$  represents the aggregated concentration of constituent  $i$  in the population, obtained by summing its concentrations in the individual cells, weighed by the relative contribution of the volume of each cell to the total volume. Now, under the assumption that  $c_{ik} = c_i$  for all  $k$ , that is, the concentration of constituent  $i$  is the same in all cells  $k$ , we obtain

$$c_{i\bullet} = \sum_{k=1}^n \frac{c_{ik} \cdot Vol_k}{Vol_{\bullet}} = c_i \cdot \frac{\sum_{k=1}^n Vol_k}{Vol_{\bullet}} = c_i. \quad (5)$$

Under this assumption the concentration of constituent  $i$  in the population is thus the same as the concentration in the individual cells.

Furthermore, we define  $X_{i\bullet}$  as

$$X_{i\bullet} = \sum_{k=1}^n X_{ik} = \sum_{k=1}^n x_{ik} \cdot Vol_k, \quad (6)$$

where  $x_{ik}$  represents the concentration of constituent  $i$  in cell  $k$  in molar units. Moreover, let  $v_k$  be the vector of reaction rates in cell  $k$  and, analogously to Eq. 9 in the main text, define

$$\frac{\dot{X}_{ik}}{Vol_k} = N_i \cdot v_k. \quad (7)$$

We now write

$$\begin{aligned} \frac{\dot{X}_{i\bullet}}{Vol_{\bullet}} &= \frac{\sum_{k=1}^n \dot{X}_{ik}}{Vol_{\bullet}} = \frac{\sum_{k=1}^n (\dot{X}_{ik}/Vol_k) \cdot Vol_k}{Vol_{\bullet}} \\ &= \sum_{k=1}^n N_i \cdot v_k \cdot \frac{Vol_k}{Vol_{\bullet}}. \end{aligned} \quad (8)$$

We further make the assumption that  $v = v_k$  for all  $k$ , that is, the reaction rates in the individual cells are the same. This is justified under the above assumption that  $c_{ik} = c_i$ , and hence  $x_{ik} = x_i$ , since the reaction rates in the models considered here depend on the concentrations of the constituents involved in the reactions. As a consequence,

$$\frac{\dot{X}_{i\bullet}}{Vol_{\bullet}} = N_i \cdot v \cdot \frac{\sum_{k=1}^n Vol_k}{Vol_{\bullet}} = N_i \cdot v, \quad (9)$$

so that the reaction rates are the same in the individual cells and in the aggregate population composed of these individual cells.