Supporting Text

Generalized Relative Variance. Here, we introduce the generalized relative variance as

$$\mathfrak{D} \equiv \frac{\frac{1}{S}\sum_{\mathbf{n}} P(\mathbf{n},t|\mathbf{n}_0,t_0)\sum_{i=1}^{S} n_i^2 - \left(\frac{1}{S}\sum_{\mathbf{n}} P(\mathbf{n},t|\mathbf{n}_0,t_0)\sum_{i=1}^{S} n_i\right)^2}{\left(\frac{1}{S}\sum_{\mathbf{n}} P(\mathbf{n},t|\mathbf{n}_0,t_0)\sum_{i=1}^{S} n_i\right)^2}, \tag{10}$$

where S is the number of cellular types within the community and $\mathbf{n} = (n_1, n_2, \ldots, n_S)$ is an S-dimensional vector whose elements, $n_i = n_i(t)$, represent the number of cells of type i at time t and $P(\mathbf{n},t|\mathbf{n}_0,t_0)$ is the probability that community has a composition $\mathbf{n}$ at time t given that it started with $\mathbf{n}_0$ at time t_0. We can rewrite Eq. 10 as

$$\begin{aligned}\mathfrak{D} &= \frac{\overline{\langle n_i^2\rangle} - \overline{\langle n_i\rangle^2}}{\left(\overline{\langle n_i\rangle}\right)^2} + \frac{\overline{\langle n_i\rangle^2} - \left(\overline{\langle n_i\rangle}\right)^2}{\left(\overline{\langle n_i\rangle}\right)^2} \\ &\equiv \mathfrak{D}_I + \mathfrak{D}_C, \end{aligned} \tag{11}$$

where the bracket operator, $\langle(\cdot)\rangle \equiv \frac{1}{S}\sum_{i=1}^{S}(\cdot)$, represents averaging over cell types within a given population; the bar operator, $\overline{(\cdot)} \equiv \sum_{\mathbf{n}} P(\mathbf{n},t|\mathbf{n}_0,t_0)(\cdot)$, is the ensemble average over the population distribution of all possible communities; and we have introduced $\mathfrak{D}_I$, the intracolony variance, and $\mathfrak{D}_C$, the cross-colony variance.

Because the two types of averaging commute, we may rewrite Eq. 11 as

$$\begin{aligned}\mathfrak{D} &= \frac{\frac{1}{S}\sum_i\left(\overline{n_i^2} - \overline{n}_i\right) - \frac{1}{S^2}\sum_{i,j}\left(\overline{n_i n_j} - \overline{n}_i\right)}{\frac{1}{S^2}\left(\sum_i \overline{n}_i\right)^2} + \frac{\frac{1}{S^2}\sum_{i,j}\left(\overline{n_i n_j} - \overline{n}_i\right) - \frac{1}{S^2}\left(\sum_i \overline{n}_i\right)^2}{\frac{1}{S^2}\left(\sum_i \overline{n}_i\right)^2} \\ &= \frac{S\sum_i \overline{n_i^2} - \sum_{i,j}\overline{n_i n_j}}{\left(\sum_i \overline{n}_i\right)^2} + \frac{\sum_{i,j}\overline{n_i n_j} - \left(\sum_i \overline{n}_i\right)^2}{\left(\sum_i \overline{n}_i\right)^2}. \end{aligned} \tag{12}$$

Note that the bar operator acts only on terms of the form n_i or $n_i n_j$. This means that, instead of the full probability distribution $P(\mathbf{n},t|\mathbf{n}_0,t_0)$, it is only necessary to calculate the first two moments of the distribution in order to calculate $\mathfrak{D}$.

Calculation of the First and Second Moments in Unbounded Growth Environments. The differential equation describing the evolution of the first and second moments of $P(\mathbf{n},t|\mathbf{n}_0,t_0)$ (Eq. 4 of the main text) can be decomposed into two sets of equations, one describing the first moments and the other the second moments. These equations can be solved exactly and for the first moments, $\mathbf{M}^{(1)}(t) = \left(\bar{n}_1(t), \bar{n}_2(t)\right)^T$, one obtains

$$\mathbf{M}^{(1)}(t) = \begin{bmatrix} \bar{n}_1(t) \\ \bar{n}_2(t) \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ \frac{\sigma_2-\sigma_1+\Delta}{2\tau_{12}} & \frac{\sigma_2-\sigma_1-\Delta}{2\tau_{12}} \end{bmatrix} \begin{bmatrix} \beta_1 e^{\theta t} \\ \beta_2 e^{\nu t} \end{bmatrix}, \tag{13}$$

where $\Delta = \sqrt{(\sigma_1-\sigma_2)^2 + 4\tau_{12}\tau_{21}}$, $\theta = \frac{1}{2}(\sigma_1+\sigma_2+\Delta)$, $\nu = \frac{1}{2}(\sigma_1+\sigma_2-\Delta)$, $\beta_1 = \frac{(\sigma_1-\sigma_2+\Delta)}{2\Delta}\bar{n}_1(0) + \frac{\tau_{12}}{\Delta}\bar{n}_2(0)$ and $\beta_2 = \frac{(\sigma_2-\sigma_1+\Delta)}{2\Delta}\bar{n}_1(0) - \frac{\tau_{12}}{\Delta}\bar{n}_2(0)$.

For the second moments, $\mathbf{M}^{(2)}(t) = \left(\overline{n_1^2}(t), \overline{n_2^2}(t), \overline{n_1 n_2}(t)\right)^T$, we obtain

$$\mathbf{M}^{(2)}(t) = \mathbf{Y}(t)\mathbf{C} + \mathbf{Y}(t)\int_0^t \mathbf{Y}^{-1}(t')\mathbf{H}(t')\mathrm{d}t' = \mathbf{Y}(t)\left[\mathbf{C} + \mathbf{F}(t) - \mathbf{F}(0)\right], \tag{14}$$

where $\mathbf{Y} = \mathbf{K}\mathbf{U}(t)$, $\mathbf{C} = \mathbf{K}^{-1}\mathbf{M}^{(2)}(0)$, $\mathbf{L} = \mathbf{K}^{-1}\mathbf{H}$, and

$$\mathbf{K} = \begin{bmatrix} \frac{(\sigma_1-\sigma_2+\Delta)}{2\tau_{21}} & \frac{(\sigma_1-\sigma_2-\Delta)}{2\tau_{21}} & \frac{2\tau_{12}}{\sigma_2-\sigma_1} \\ \frac{(\sigma_2-\sigma_1+\Delta)}{2\tau_{12}} & \frac{(\sigma_2-\sigma_1-\Delta)}{2\tau_{12}} & \frac{2\tau_{21}}{\sigma_1-\sigma_2} \\ 1 & 1 & 1 \end{bmatrix}, \mathbf{U}(t) = \begin{bmatrix} e^{2\theta t} & 0 & 0 \\ 0 & e^{2\nu t} & 0 \\ 0 & 0 & e^{(\theta+\nu)t} \end{bmatrix},$$

$$\mathbf{H} = \begin{bmatrix} \rho_1 + \frac{\sigma_2-\sigma_1+\Delta}{2} & \rho_1 + \frac{\sigma_2-\sigma_1-\Delta}{2} \\ \tau_{21} + \frac{\rho_2(\sigma_2-\sigma_1+\Delta)}{2\tau_{12}} & \tau_{21} + \frac{\rho_2(\sigma_2-\sigma_1-\Delta)}{2\tau_{12}} \\ -(\tau_{21} + \frac{\sigma_2-\sigma_1+\Delta}{2}) & -(\tau_{21} + \frac{\sigma_2-\sigma_1-\Delta}{2}) \end{bmatrix}, \mathbf{F}(t) = \begin{bmatrix} -\frac{\mathbf{L}_{11}\beta_1}{\theta}e^{\theta t} + \frac{\mathbf{L}_{12}\beta_2}{\nu-2\theta}e^{(\nu-2\theta)t} \\ \frac{\mathbf{L}_{21}\beta_1}{\theta-2\nu}e^{(\theta-2\nu)t} - \frac{\mathbf{L}_{22}\beta_2}{\nu}e^{-\nu t} \\ -\frac{\mathbf{L}_{31}\beta_1}{\nu}e^{-\nu t} - \frac{\mathbf{L}_{32}\beta_2}{\theta}e^{-\theta t} \end{bmatrix}.$$

With the above exact expressions of the first and second moments we can study the temporal behavior of $\mathfrak{D}(t)$, which can be expressed as a function of $\mathbf{M}(t)$

$$\mathfrak{D}(t) = \frac{M_1^{(2)} + M_2^{(2)} - 2M_3^{(2)}}{(M_1^{(1)} + M_2^{(1)})^2} + \frac{(M_1^{(2)} + M_2^{(2)} + 2M_3^{(2)}) - (M_1^{(1)} + M_2^{(1)})^2}{(M_1^{(1)} + M_2^{(1)})^2}. \tag{15}$$

For our two-phenotype community the behavior of the first and second moments is characterized by five exponents (θ, ν, $\theta+\nu$, 2θ, 2ν). In the long-time limit, the terms involving the largest exponent (2θ) will dominate, and the contributions of all other terms become negligible. The $t \rightarrow \infty$ expressions for $\mathfrak{D}_I$ and $\mathfrak{D}_C$ then become

$$
\begin{aligned}
\mathfrak{D}_I^{\infty} &= \frac{\left[C_1 - F_1(0)\right]\left(K_{11} + K_{21} - 2K_{31}\right)}{\beta_1^2\left[1 + \frac{\sigma_2 - \sigma_1 + \Delta}{2\tau_{12}}\right]^2} \\
\mathfrak{D}_C^{\infty} &= \frac{\left[C_1 - F_1(0)\right]\left(K_{11} + K_{21} + 2K_{31}\right)}{\beta_1^2\left[1 + \frac{\sigma_2 - \sigma_1 + \Delta}{2\tau_{12}}\right]^2} - 1.
\end{aligned}
\tag{16}
$$

Propagation of the Population Variation in an Unbounded Growth Environment for Different Initial States. SI Fig. 6 illustrates the propagation of the population variation in an unbounded growth environment for different initial states. Here the background colors represent different growth conditions, which correspond, perhaps, to growth media containing various levels of inducing agents that affect the various rates. The colors of the lines (red, orange, green, and blue) represent the initial states of the community ($(1,1)$, $(1,10)$, $(10,1)$, and $(100,100)$, respectively) and the style of those lines (dotted, dash, and solid) correspond to the contributions of the relative variance (intracolony, cross-colony, and overall variance, respectively). Both the intracolony and the cross-colony contributions, and therefore the overall variance, approach constant values in the long time limit in a constant unbounded growth environment (SI Fig. 6 Upper). When the growth medium is changed after a period of time, however, the variances are no longer at their equilibrium values and must again enter a transient phase before asymptotically approaching their new steady-state values (SI Fig. 6 Lower).

Two Symmetric Phenotypes. To better understand the physical meaning of the variability, we also examined a completely symmetric situation in which the growth, death and transitions rates were the same between the two phenotypes. Here we show the results of the symmetric setup in SI Fig. 7. In such a situation, the intracolony variability goes to zero in the long time limit, and the total variability is solely due to the cross-colony variability. In other words, because the rates are completely symmetric, the population within a given trial will eventually contain equal (but growing) numbers of the two phenotypes, making the intracolony variability zero. However, the total number of cells will vary from trial to trial, resulting in the non-zero cross colony variability. As the asymmetry of the rates grows, the long time limit of the intracolony variability will increase, since one phenotype will now have a majority within the total population.

The Single-Cell Initial Condition. We present the results with the initial condition of only one cell in the system. In SI Fig. 8, we show the dynamic profiles of the variance over time for the free growth environment. Notice that the final variability is highest for populations started from a single cell. In SI Fig. 9, we also show the corresponding properties of populations started from a single cell in the logistic growth environment.

Cellular Populations in Chemostat Environments. The cellular population in a chemostat environment is constrained by the corresponding container or chamber. Thus the dynamics are quite different from those cases of free environments. It can be described by the following Master equation

$$\begin{aligned}\tfrac{\partial}{\partial t}P(n_1,n_2,t) &= \beta_1 n_1^- P(n_1^-,n_2,t)[1-\Theta(n_1^-+n_2-N_{max})] + \delta_1 n_1^+ P(n_1^+,n_2,t)\\ &+\tau_{12} n_2^+ P(n_1^-,n_2^+,t) + \beta_2 n_2^- P(n_1,n_2^-,t)[1-\Theta(n_1+n_2^- - N_{max})]\\ &+\delta_2 n_2^+ P(n_1,n_2^+,t) + \tau_{21} n_1^+ P(n_1^+,n_2^-,t)\\ &+\beta_1 n_1^- \big(\tfrac{n_2^+}{n_1^-+n_2^+}\big) P(n_1^-,n_2^+,t)\Theta(n_1^-+n_2^+-N_{max})\\ &+\beta_2 n_2^- \big(\tfrac{n_1^+}{n_1^-+n_2^+}\big) P(n_1^+,n_2^-,t)\Theta(n_1^++n_2^--N_{max})\\ &-\Big[(\delta_1+\tau_{21})n_1 + (\delta_2+\tau_{12})n_2 + (\beta_1 n_1+\beta_2 n_2)[1-\Theta(n_1+n_2-N_{max})]\\ &+\tfrac{(\beta_1+\beta_2)n_1 n_2}{n_1+n_2}\Theta(n_1^-+n_2^+-N_{max})\Big] P(n_1,n_2,t), \end{aligned} \tag{17}$$

where N_{max} is the maximum population allowed by the environment, and $\Theta(x) = 1$ for $x \geq 0$ and is zero otherwise.

Although approximate solutions for $P(n_1, n_2, t)$ for any t can be obtained numerically, we are interested in two limits. First, we note that if the initial population is small ($n_1 + n_2 \ll N_{max}$) then for short times thereafter $P(n_1, n_2, t)$ is negligibly small at all points where $n_1 + n_2 \geq N_{max}$. In this case, all terms involving the product $P(n_1, n_2, t)\Theta(n_1^{\pm} + n_2^{\pm} - N_{max})$ are all vanishingly small in the short time limit. Eq. 22 then reduces to the master equation describing cells in an unbounded growth environment, given by Eq. 3 of the main text.

Second, as $t \to \infty$ the population will have grown such that $n_1 + n_2 \approx N_{max}$. Therefore the step function reduces to $\Theta(n_1^{\pm} + n_2^{\pm} - N_{max}) = 1$, and Eq. (22) becomes

$$\begin{aligned}\frac{\partial}{\partial t}P(n_1, t) = \left[\tau_{12}(N_{max} - n_1^-) + \beta_1 n_1^- \left(1 - \frac{n_1^-}{N_{max}}\right)\right] P(n_1^-, t) \\ + \left[\tau_{21} n_1^+ + \beta_2 n_1^+ \left(1 - \frac{n_1^-}{N_{max}}\right)\right] P(n_1^+, t) \\ + \left[\tau_{12}(N_{max} - n_1) + \tau_{21} n_1 + (\beta_1 + \beta_2) n_1 \left(1 - \frac{n_1}{N_{max}}\right)\right] P(n_1, t), \qquad (18)\end{aligned}$$

where we have suppressed the variable n_2 since $n_1 + n_2 = N_{max}$. Solving for the steady state distribution of the above equation (detailed balance) gives us

$$\frac{P(n_1)}{P(n_1 - 1)} = \frac{\tau_{12}[N_{max} - (n_1 - 1)] + \beta_1 (n_1 - 1)(1 - \frac{n_1 - 1}{N_{max}})}{\tau_{21} n_1 + \beta_2 n_1 (1 - \frac{n_1}{N_{max}})}, \qquad (19)$$

from which we have the steady state distribution:

$$P(n_1) = \prod_{i=1}^{n_1} \left[\frac{\tau_{12}[N_{max} - (i - 1)] + \beta_1 (i - 1)(1 - \frac{i-1}{N_{max}})}{\tau_{21} i + \beta_2 i (1 - \frac{i}{N_{max}})}\right] P(0), \qquad (20)$$

where $P(0)$ is the probability the $n_1 = 0$ (and hence $n_2 = N_{max}$) and is given by

$$P(0) = \left\{1 + \sum_{n_1=1}^{N_{max}} \prod_{i=1}^{n_1} \left[\frac{\tau_{12}[N_{max} - (i - 1)] + \beta_1 (i - 1)(1 - \frac{i-1}{N_{max}})}{\tau_{21} i + \beta_2 i (1 - \frac{i}{N_{max}})}\right]\right\}^{-1}. \qquad (21)$$

Cellular Populations in Logistic Environments. The dynamics of cellular population in a logistic environment can be described by the Master equation which is similar to that in chemostat environment

$$\begin{aligned}\frac{\partial}{\partial t}P(n_1, n_2, t) = \beta_1'\big(1 - \frac{n_1^- + n_2}{N_{equ}}\big) n_1^- P(n_1^-, n_2, t) + \delta_1 n_1^+ P(n_1^+, n_2, t) + \tau_{12} n_2^+ \\ P(n_1^-, n_2^+, t) + \beta_2'\big(1 - \frac{n_1 + n_2^-}{N_{equ}}\big) n_2^- P(n_1, n_2^-, t) + \delta_2 n_2^+ P(n_1, n_2^+, t) + \tau_{21} n_1^+ P(n_1^+, n_2^-, t) \\ -\Big[(\delta_1 + \tau_{21}) n_1 + (\delta_2 + \tau_{12}) n_2 + (\beta_1' n_1 + \beta_2' n_2)\big(1 - \frac{n_1 + n_2}{N_{equ}}\big)\Big] P(n_1, n_2, t), \qquad (22)\end{aligned}$$

where N_{equ} is the equilibrium population allowed by the logistic environment, and $\beta_1^{'}$ and $\beta_2^{'}$ are net growth coefficients for phenotypes 1 and 2 respectively.

Because of the population dependence of the growth rates for both phenotypes, the overall population $(N_1 + N_2)$ approaches to a steady state distribution with its mean around equilibrium population N_{equ} in the long time limit. We therefore have the analytical expression of the relative variance by employing an assumption that overall population is exactly the equilibrium population, i.e., $N_1 + N_2 = N_{equ}$.

Detailed balance of the system brings the following steady population distribution for phenotype 1:

$$P(n_1) = \prod_{i=1}^{n_1} \left[\frac{\tau_{12}[N_{max} - (i-1)]}{\tau_{21} i} \right] P(0), \tag{23}$$

where $P(0)$ is the probability the $n_1 = 0$ (and hence $n_2 = N_{equ}$) and is given by

$$P(0) = \left\{ 1 + \sum_{n_1=1}^{N_{max}} \prod_{i=1}^{n_1} \left[\frac{\tau_{12}[N_{max} - (i-1)]}{\tau_{21} i} \right] \right\}^{-1}. \tag{24}$$