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Steady state thermodynamics for population growth in fluctuating environment

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We report that population dynamics in fluctuating environments is characterized by a mathematically equivalent structure to steady state thermodynamics. By employing the structure, population growth in fluctuating environments is decomposed into housekeeping and excess parts. The housekeeping part represents the integral of the stationary growth rate for each condition during a history of the environmental change. The excess part accounts for the excess growth induced by environmental fluctuations. Focusing on the excess growth, we obtain a Clausius inequality, which gives the upper bound of the excess growth. The equality is shown to be achieved in quasistatic environmental changes. We also clarify that this bound can be evaluated by the “lineage fitness”, which is an experimentally observable quantity.

I. INTRODUCTION

Steady state thermodynamics (SST) was established for understanding a “thermodynamics” of transitions between nonequilibrium steady states (NESS) [1–10]. The core of this theory was proposed by Oono and Paniconi [1] in a phenomenological sense as a decomposition of total heat during transitions into housekeeping and excess parts. The housekeeping heat represents the heat dissipated to maintain NESS, whereas the excess heat is the heat generated due to relaxation to NESS. Based on this decomposition, a Clausius inequality is reformulated in nonequilibrium situations. Although it was formulated in physics, we clarify here that this decomposition also contributes to evaluation of population growth in fluctuating environments.

In this paper, we deal with a heterogeneous population of organisms whose type (e.g. geno- and pheno- types) switches stochastically over time [11–18]. The long term expansion rate of population size (population growth) is the major observable in population dynamics that characterizes the competitive power of the population in evolution. In a fixed environment, this quantity converges to a stationary growth rate and can be evaluated by the largest eigenvalue of the time-evolution operator of the population dynamics [17]. However, fluctuations of environment disturb this convergence, and the population growth deviates from the simple integral of the stationary growth rates for each environmental state. This deviation is the major impact of environmental fluctuations [19–21]. By employing the same mathematical framework as SST [22], we show that the total population growth in a fluctuating environment can be generally decomposed into house-keeping and excess parts. The house-keeping growth is the integral of the stationary growth rate for each environmental state, and the excess part is the difference between the total growth and the house-keeping growth. If the type switching of individuals follows the detailed balance condition (DBC), the excess growth is shown to satisfy a Clausius inequality in

which the entropy function is defined by the stationary probability of the type switching, together with a “lineage fitness”, which quantifies the prosperity of each type in future. Moreover, Clausius *equality* is proved for quasistatic cases, and thereby excess growth can be exactly calculated from the lineage fitnesses at the boundaries of a history of an environmental change. In addition, in the SST framework, a loss of population growth from the upper bound is interpreted as “entropy production”, which is evaluated by employing a mathematically similar method to that used in deriving the fluctuation theorem in nonequilibrium physics. These results clarify the underlying constraints and the thermodynamic structure of the population dynamics and thereby pave the way for further understanding and controlling of the population growth (fitness) under fluctuating environments.

This paper is organized as follows. In the next section, we provide a concrete setup of a population dynamics and show a significance of Clausius inequality without its mathematical derivation. After presenting the main claim of this paper in Sec. II, we prove Clausius inequality in Sec. III and IV. In Sec. III, we consider quasistatic cases, i.e., we derive Clausius *equality*; in Sec. IV, we deal with non-quasistatic cases by proving Clausius *inequality*. Finally, we summarize this study in Sec. V.

II. SETUP AND CLAUSIUS INEQUALITY

We consider a simple but general population dynamics that consists of two processes, type switching and duplication. Let $x \in \mathcal{S}_x$ be a type of individual in a population, and its switching dynamics is given by a continuous-time ergodic Markov jump process generated by a transition rate matrix $T(x|x')$. Here, $\mathcal{S}_x$ denotes a finite set of geno- or pheno- type, and off-diagonal and diagonal elements of $T(x|x')$ represent a jump rate from x' to x , $\omega(x|x')$, and an exit rate from x , $\omega(x) = \sum_{x'} \omega(x'|x)$, respectively. The duplication rate of the individuals with type x in an environmental condition $y \in \mathcal{S}_y$ is denoted

by $\mu_y(x)$, where $\mathcal{S}_y$ is a finite-dimensional space. For instance, if we choose temperature and density of carbon dioxide as the environmental condition, then y represents a two-dimensional vector. From the above two processes, the time evolution of the population is described by

$$\frac{\partial N(x, t)}{\partial t} = \sum_{x'} \{ \mu_{y_t}(x) \delta_{x, x'} + T(x|x') \} N(x', t), \quad (1)$$

where $N(x, t)$ denotes the number of individuals with type x and $\delta_{\cdot, \cdot}$ is the Kronecker delta.

Under this setup, we consider population growth during time interval $[0, \tau]$, which is defined as

$$\Psi[Y] \equiv \log \{ N_\tau^{\text{tot}}[Y] / N_0^{\text{tot}} \}. \quad (2)$$

Here, Y denotes a history of the environmental change $Y = \{y_0, y_{\Delta t}, \dots, y_{\tau - \Delta t}, y_\tau\}$, where Δt is an infinitesimal time interval $\Delta t = \tau/M (M \rightarrow \infty)$ and N_t^{tot} represents the total number of individuals in the population at time t , which is evaluated as $N_t^{\text{tot}} = \sum_x N(x, t)$. According to the SST framework, we decompose the population growth as

$$\Psi[Y] = \Psi^{\text{hk}}[Y] + \Psi^{\text{ex}}[Y], \quad (3)$$

where Ψ^{hk} and Ψ^{ex} denote the housekeeping and the excess growth, respectively. Here, the housekeeping growth is defined as the integral of the stationary growth rate for each condition during a history Y , that is

$$\Psi^{\text{hk}}[Y] \equiv \int_0^\tau \lambda_0(y_t) dt, \quad (4)$$

where $\lambda_0(y)$ is the stationary growth rate in an environmental condition y . From Eq. (1), the stationary growth rate is equal to the largest eigenvalue of the time-evolution matrix $H_y(\cdot|\cdot') \equiv \mu_y(\cdot) \delta_{\cdot, \cdot'} + T(\cdot|\cdot')$ [17]. To be more precise, for any eigenvalue $\lambda_i(y)$ of $H_y(\cdot|\cdot')$, $\lambda_0(y) > \lambda_i(y)$ has to hold for $i \neq 0$. In addition, the right eigenvector corresponding to the largest eigenvalue (say $v_y(x)$) with a normalization condition $\sum_x v_y(x) = 1$ expresses the occupation probability of type x in the stationary growing population in environmental condition y . On the other hand, the excess growth is defined by

$$\Psi^{\text{ex}}[Y] \equiv \Psi[Y] - \int_0^\tau \lambda_0(y_t) dt, \quad (5)$$

which represents the deviation from the integral of the stationary growth rate. That is, this growth represents the growth generated when environment is switched. In this study, we assume that the type-switching rate $T(\cdot|\cdot')$ satisfies the detailed balance condition (DBC) [23],

$$T(x|x') P_T^{\text{st}}(x') = T(x'|x) P_T^{\text{st}}(x), \quad (6)$$

where P_T^{st} denotes the stationary probability of the type-switching rate $T(\cdot|\cdot')$. This assumption is not so restrictive biologically since geno- and pheno- type switching dynamics are often described with this condition [15, 24]. (We also discuss non-DBC cases in Sec. V). Note that the DBC condition here applies only to the type-switching dynamics rather than the whole growing system. Since population dynamics (growing systems) is different from ordinary stochastic processes, we can no longer consider the simple DBC for the whole process due to the duplication rate $\mu_y(x)$. In this paper, we argue that the SST framework plays an essential role even for such growing situations. As shown in the following sections, by employing the DBC, we obtain Clausius inequality,

$$\Psi^{\text{ex}}[Y] \leq S(y_\tau) - S(y_0), \quad (7)$$

where $S(y)$ represents “entropy” in the population dynamics [25], which is given by

$$S(y) = \frac{1}{2} \log \sum_x P_T^{\text{st}}(x) u_y(x). \quad (8)$$

Here, $u_y(x)$ denotes the left eigenvector corresponding to the largest eigenvalue $\lambda_0(y)$ with a normalization condition $\sum_x u_y(x) v_y(x) = 1$. In the context of population dynamics, $u_y(x)$ also represents the “lineage fitness” of type x in environmental condition y , which quantifies the future prosperity of each type [13–16] (also see FIG. 1 and a detailed explanation of “lineage fitness” is given in Appendix A). Corresponding to Clausius *equality* in thermodynamics, which holds for quasistatic protocols, the *equality* of Eq. (7) is achieved in quasistatic environmental changes. In addition, we can prove that $S(y) \leq 0$ for arbitrary y and $S(y) = 0$ if y is a no selection situation, i.e. $\mu_y(x) = \text{const.}$ for arbitrary x . (Proof is shown in Appendix B.) Therefore, the “entropy” $S(y)$ may represent a kind of selection strength for the environmental condition y . Furthermore, this entropy can be experimentally observed as follows.

Here, we show an experimental method to evaluate the entropy (8) without detail mathematical definitions and calculations. (Mathematical details are shown in Sec. III and IV.) Suppose that a population is in the stationary growing state with a fixed environmental condition y , that is, the population has converged to the stationary occupation probability v_y . If we track the offspring of individuals with type x at initial time $t = 0$, the offspring will change their types and grow in the population. The fraction of the offspring (irrespective of their types) in the population changes over time but finally converges to some value as $t \rightarrow \infty$ (say $P_{R_y}^{\text{st}}(x)$). Then, the lineage fitness of type x is given as $u_y(x) = P_{R_y}^{\text{st}}(x) / v_y(x)$, see FIG. 1. Accordingly, if we employ a labeling technique with which individuals with specific types can be labeled and their offspring inherit the label, we can estimate the lineage fitness experimentally by measuring the fraction

of the labeled offspring in the population. DNA barcoding may work for such labeling techniques. Furthermore, it is known that the convergence fraction $P_{R_y}^{\text{st}}(x)$ [26] is given by the stationary probability of the retrospective processes R_y [13–18] (see Sec. IV, B). Thus, we can also calculate the lineage fitness by tracing the lineage of the growing population time-backwardly. Next, we consider how to observe $P_T^{\text{st}}(x)$ in experiments. Since P_T^{st} is the stationary probability of the type-switching process T , we can obtain it by tracing the lineage of the population time-forwardly (see Appendix C). Taking these facts into account, we find that the entropy (8) can be evaluated experimentally.

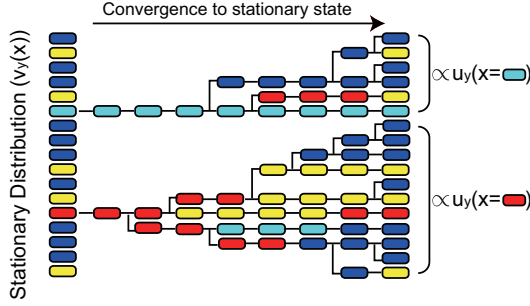


FIG. 1. (color online). Types of individuals are represented by colors. In experiments, we can calculate the lineage fitness by the following steps: (i) we observe the fraction of individuals with type x at initial time, that is the occupation probability $v_y(x)$; (ii) we culture the population in a fixed environmental condition y for a sufficiently long time; (iii) we finally observe the fraction of the offspring of the individuals with type x at initial time, which is denoted as $P_{R_y}^{\text{st}}(x)$; (iv) we obtain the lineage fitness of type x , $u_y(x)$, by the ratio, $u_y(x) = P_{R_y}^{\text{st}}(x)/v_y(x)$.

Before working on the derivation of Clausius inequality (7), we consider both the quasistatic and the non-quasistatic situations. In quasistatic environmental changes, Clausius *equality*, $\Psi^{\text{ex}}[Y] = S(y_\tau) - S(y_0)$, is achieved. Therefore, the excess growth can be exactly evaluated by observing entropies at the boundaries of an environment-switching history Y , although it is a functional of the history Y . On the other hand, in non-quasistatic situations, a loss of population growth from the upper bound occurs as

$$\sigma[Y] \equiv \{S(y_\tau) - S(y_0)\} - \Psi^{\text{ex}}[Y]. \quad (9)$$

By using the analogy with the second law of thermodynamics, this loss mathematically corresponds to “entropy production”. As shown in the following sections, this entropy production is evaluated with a mathematically similar form to the Kawai-Parrondo-Van den Broeck type fluctuation theorem (work theorem) [27],

$$\sigma[Y] = D^{\text{sym}}[Y] + \sum_x v_{y_\tau}(x) \log u_{y_\tau}(x), \quad (10)$$

where D^{sym} represents the symmetrized Kullback-Leibler divergence,

$$D^{\text{sym}}[Y] \equiv \sum_X P_B[X|Y] \log \frac{P_B[X|Y]}{P_R^{1/2}[X|Y] P_{\tilde{R}}^{1/2}[\tilde{X}|\tilde{Y}]}. \quad (11)$$

The definition and meaning of path probabilities, P_B , P_R and $P_{\tilde{R}}$, are shown in Sec. IV. Here, X represents a type-switching history $X = \{x_0, x_{\Delta t}, \dots, x_{\tau-\Delta t}, x_\tau\}$; $\tilde{X}$ and $\tilde{Y}$ represent time reversal of X and Y , respectively.

III. DERIVATION OF CLAUSIUS EQUALITY

Let us begin with derivation of the Clausius *equality*, i.e. we consider quasistatic environmental change. For simplicity, we rewrite Eq. (1) by using bra-ket notation as

$$\frac{\partial}{\partial t} |N(t)\rangle = \hat{H}_{y_t} |N(t)\rangle, \quad (12)$$

where $\hat{H}_y$ represents the time-evolution operator, $\hat{H}_y = \hat{\mu}_y + \hat{T}$ that satisfies $\langle x|\hat{H}_y|x'\rangle = H_y(x|x')$; $|N(t)\rangle$ denotes the population vector: $\langle x|N(t)\rangle = N(x, t)$. In this notation, the population growth Ψ is expressed by

$$e^{\Psi[Y]} = \left\langle \mathcal{P} \left| T \exp \left[\int_0^\tau \hat{H}_{y_t} dt \right] \right| N(0) \right\rangle / \langle \mathcal{P}|N(0)\rangle, \quad (13)$$

where $T \exp[\cdot]$ denotes the time-ordered exponential and $\langle \mathcal{P}|$ is defined as $\langle \mathcal{P}|x\rangle = 1$ for any $|x\rangle$; thus, $\langle \mathcal{P}|N(0)\rangle = N_0^{\text{tot}}$. We write eigenvalues of $\hat{H}_y$ as $\lambda_i(y)$, where $i=0$ indicates the largest eigenvalue. In addition, we denote left and right eigenvectors as $\langle \lambda_i(y)|$ and $|\lambda_i(y)\rangle$, respectively. These vectors are normalized as $\langle \lambda_i(y)|\lambda_j(y)\rangle = \delta_{i,j}$ and $\langle \mathcal{P}|\lambda_0(y)\rangle = 1$. Thus, we can write the stationary occupation probability v_y and lineage fitness u_y as $v_y(x) = \langle x|\lambda_0(y)\rangle$ and $u_y(x) = \langle \lambda_0(y)|x\rangle$, respectively. By inserting the completeness relation for eigenvectors $\sum_i |\lambda_i(y)\rangle \langle \lambda_i(y)| = 1$ into all time slices of Eq. (13), we have

$$\begin{aligned} e^{\Psi[Y]} &= \sum_{i_\tau, i_{\tau-\Delta t}, \dots, i_0} \langle \mathcal{P}|\lambda_{i_\tau}(y_\tau)\rangle \\ &\times \langle \lambda_{i_\tau}(y_\tau)|e^{\hat{H}_{y_\tau}\Delta t}|\lambda_{i_{\tau-\Delta t}}(y_{\tau-\Delta t})\rangle \times \dots \\ &\times \langle \lambda_{i_{\Delta t}}(y_{\Delta t})|e^{\hat{H}_{y_{\Delta t}}\Delta t}|\lambda_{i_0}(y_0)\rangle \langle \lambda_{i_0}(y_0)|N(0)\rangle / N_0^{\text{tot}}. \end{aligned} \quad (14)$$

By assuming that the initial population is stationary, that is $|N(0)\rangle = N_0^{\text{tot}}|\lambda_0(y_0)\rangle$, and by taking into account that the environmental changes are quasistatic, we reach

$$\begin{aligned} e^{\Psi[Y]} &= \langle \lambda_0(y_\tau)|e^{\hat{H}_{y_\tau}\Delta t}|\lambda_0(y_{\tau-\Delta t})\rangle \times \dots \\ &\times \langle \lambda_0(y_{\Delta t})|e^{\hat{H}_{y_{\Delta t}}\Delta t}|\lambda_0(y_0)\rangle. \end{aligned} \quad (15)$$

Here, we employ the adiabatic approximation in which the summation in Eq. (14) is dominated by the eigenvectors corresponding to the largest eigenvalue λ_0 , because, in quasistatic cases, the system is always in stationary growing states for each environmental condition. By taking the logarithm of both sides of Eq. (15), we obtain the population growth,

$$\Psi[Y] = \int_0^\tau \lambda_0(y_t) dt - \int_0^\tau dt \langle \lambda_0(y) | \nabla_y | \lambda_0(y) \rangle \cdot \dot{y}, \quad (16)$$

where we use $\langle \lambda_0(y_{t+\Delta t}) | \lambda_0(y_t) \rangle = e^{-\langle \lambda_0(y) | \nabla_y | \lambda_0(y) \rangle \cdot \dot{y} \Delta t}$ and ∇_y denotes differentiation with respect to y . The dots $\cdot$ and $\dot{y}$ represent inner product and time differentiation, respectively, and thus $\dot{y} \cdot \nabla_y = \Sigma_i (dy_i/dt) (\partial/\partial y_i)$ where i expresses the dimension of the environment. Taking into account the definition of the housekeeping growth, Eq. (4), we can evaluate the excess growth by the second term of Eq. (16): $\Psi^{\text{ex}}[Y] = -\int_0^\tau dt \langle \lambda_0(y) | \nabla_y | \lambda_0(y) \rangle \cdot \dot{y}$. This representation implies that the excess growth can be given by the geometric phase (Berry phase) [21, 28–30]. By using the completeness relation $\Sigma_x |x\rangle \langle x| = 1$, we find a more familiar form without bra-ket notation:

$$\Psi^{\text{ex}}[Y] = -\int_0^\tau dt \dot{y} \cdot \sum_x u_y(x) \nabla_y v_y(x). \quad (17)$$

Next, by using the DBC assumption for the type-switching operator $\hat{T}$, we calculate a potential of the integrand in Eq. (17). From the DBC, we can obtain a relation between the stationary occupation probability v_y and the lineage fitness u_y as

$$C(y) v_y(x) = P_T^{\text{st}}(x) u_y(x), \quad (18)$$

where the constant $C(y)$ is given by $C(y) = \Sigma_x P_T^{\text{st}}(x) u_y(x) = \Sigma_x P_T^{\text{st}}(x) u_y^2(x)$. (Derivation of Eq. (18) is described in Appendix D.) This representation, $C(y) = \Sigma_x P_T^{\text{st}}(x) u_y^2(x)$, leads to

$$-\nabla_y \left\{ \frac{1}{2} \log C(y) \right\} = -\sum_x \frac{P_T^{\text{st}}(x) u_y(x)}{C(y)} \nabla_y u_y(x). \quad (19)$$

By using Eq. (18), we have

$$-\sum_x \frac{P_T^{\text{st}}(x) u_y(x)}{C(y)} \nabla_y u_y(x) = -\sum_x v_y(x) \nabla_y u_y(x). \quad (20)$$

From $\Sigma_x v_y(x) \nabla_y u_y(x) = -\Sigma_x u_y(x) \nabla_y v_y(x)$ [31], we finally get

$$-\nabla_y \left\{ \frac{1}{2} \log C(y) \right\} = \sum_x u_y(x) \nabla_y v_y(x). \quad (21)$$

By substituting Eq. (21) into Eq. (17), we obtain Clausius equality:

$$\Psi^{\text{ex}}[Y] = S(y_\tau) - S(y_0), \quad (22)$$

where $S(y)$ denotes “entropy” defined in Eq. (8), because

$$S(y) = \frac{1}{2} \log C(y) = \frac{1}{2} \log \sum_x P_T^{\text{st}}(x) u_y(x), \quad (23)$$

where we use $C(y) = \Sigma_x P_T^{\text{st}}(x) u_y(x)$.

IV. DERIVATION OF CLAUSIUS INEQUALITY

In the following part, we derive Clausius *inequality*, i.e. we prove that the right hand side of Eq. (22) gives the upper bound of the excess growth. To derive the inequality, we need three kinds of path probabilities. Therefore, before proceeding with the main derivation, we introduce them briefly.

A. Time-backward process

We define a time-backward path probability [18] as

$$P_B[X|Y] = e^{-\Psi[Y]} \langle x_\tau | e^{\hat{H}_{y_\tau} \Delta t} | x_{\tau-\Delta t} \rangle \times \cdots \times \langle x_{\Delta t} | e^{\hat{H}_{y_{\Delta t}} \Delta t} | x_0 \rangle v_{y_0}(x_0). \quad (24)$$

where $\hat{H}_y$ denotes the time-evolution operator of the population dynamics and $\Psi[Y]$ represents total population growth for time interval $[0, \tau]$. Here, we assumed that initial condition is the stationary occupation probability in an environmental condition y_0 , $v_{y_0}(\cdot)$. The meaning of this path probability is as follows. The number of individuals at time $t = \tau$ who have undergone a type-switching history $X = \{x_0, x_{\Delta t}, \dots, x_{\tau-\Delta t}, x_\tau\}$ is represented as

$$N_\tau^{\text{tot}}[X|Y] = \langle x_\tau | e^{\hat{H}_{y_\tau} \Delta t} | x_{\tau-\Delta t} \rangle \times \cdots \times \langle x_{\Delta t} | e^{\hat{H}_{y_{\Delta t}} \Delta t} | x_0 \rangle v_{y_0}(x_0) N_0^{\text{tot}}, \quad (25)$$

where we assume that the initial state is a stationary growing state. By dividing both sides of Eq. (25) by the total population size $N_\tau^{\text{tot}}[Y] = \Sigma_X N_\tau^{\text{tot}}[X|Y]$ and using the definition of population growth $\Psi[Y] \equiv \log \{N_\tau^{\text{tot}}[Y]/N_0^{\text{tot}}\}$, we get

$$P_B[X|Y] = N_\tau^{\text{tot}}[X|Y]/N_\tau^{\text{tot}}[Y]. \quad (26)$$

Accordingly, we find that the time-backward path probability Eq. (24) implies the fraction of individuals at time $t = \tau$ who have undergone the type-switching history X in the environmental change Y . In other words, the time-backward path probability represents the probability to observe a type switching history X when we randomly sample an individual from the final population at time $t = \tau$ and track it back retrospectively. In addition, we note that, in fixed-environment cases $Y = \{y, y, \dots, y, y\}$, the stationary occupation probability v_y is evaluated as $v_y(x_\tau) = \Sigma_{x_{\tau-\Delta t}, \dots, x_{\Delta t}, x_0} P_B[X|Y]$.

We also note that $v_y(x_0) \neq \Sigma_{x_\tau, x_{\tau-\Delta t}, \dots, x_{\Delta t}} P_B[X|Y]$, since $\langle x_t | e^{\hat{H}_{y_t} \Delta t} | x_{t-\Delta t} \rangle$ in $P_B[X|Y]$ is not stochastic matrix.

B. Retrospective process

In fixed-environment cases, $Y = \{y, y, \dots, y, y\}$, the time-backward path probability with sufficiently long history X (i.e. $\tau \rightarrow \infty$) is well approximated by a Markov process in terms of large deviation theory [17, 32], and this Markov process is called a retrospective process [13–18], that is,

$$P_B[X|Y] \approx \langle x_\tau | e^{\hat{R}_y \Delta t} | x_{\tau-\Delta t} \rangle \times \dots \times \langle x_{\Delta t} | e^{\hat{R}_y \Delta t} | x_0 \rangle P_{R_y}^{\text{st}}(x_0), \quad (27)$$

where $\hat{R}_y$ denotes time-evolution operator of the retrospective process in an environmental condition y , which is given by

$$R_y(x|x') = u_y(x) \{H_y(x|x') - \lambda_0(y) \delta_{x,x'}\} / u_y(x'), \quad (28)$$

where $R_y(x|x') = \langle x | \hat{R}_y | x' \rangle$ [17]. $u_y(x)$ denotes the lineage fitness of a type x in an environmental condition y . $\lambda_0(y)$ is the stationary growth rate, which is calculated by the largest eigenvalue of $H_y(\cdot|\cdot')$. $P_{R_y}^{\text{st}}$ in Eq. (27) represents the stationary probability of the retrospective process R_y . In this study, we use the time-inhomogeneous retrospective process $P_R[X|Y]$ in the derivation of Clausius inequality;

$$P_R[X|Y] = \langle x_\tau | e^{\hat{R}_{y_\tau} \Delta t} | x_{\tau-\Delta t} \rangle \times \dots \times \langle x_{\Delta t} | e^{\hat{R}_{y_0} \Delta t} | x_0 \rangle P_{R_{y_0}}^{\text{st}}(x_0), \quad (29)$$

where Y is a fluctuated environmental history $Y = \{y_0, y_{\Delta t}, \dots, y_{\tau-\Delta t}, y_\tau\}$. Here, we note that the time-inhomogeneous retrospective process does not perfectly mimic the time-backward process $P_B[X|Y]$; only in time-homogeneous cases (i.e., fixed environment cases), the retrospective process describes the time-backward process.

Finally, we comment on the properties of the stationary probability of the retrospective process with a fixed environmental condition y , $P_{R_y}^{\text{st}}$. This is called ancestral distribution [13–18] and is related with $u_y(x)$ and $v_y(x)$ as $P_{R_y}^{\text{st}}(x) = u_y(x) v_y(x)$, since $\Sigma_{x'} R_y(x|x') u_y(x') v_y(x') = 0$. Owing to the law of large numbers, $P_{R_y}^{\text{st}}$ is also evaluated by an empirical probability on the retrospective process with a sufficiently large time interval, i.e., $P_{R_y}^{\text{st}}(x) = \lim_{\tau \rightarrow \infty} (1/\tau) \int_0^\tau \delta_{x,x_t} dt$, where the history $X = \{x_0, x_{\Delta t}, \dots, x_{\tau-\Delta t}, x_\tau\}$ is generated by $\hat{R}_y$. As in Eq. (27), in the fixed environment cases, the retrospective process with a sufficiently long history can be approximated by the time-backward path probability $P_B[X|Y]$. Therefore, we can obtain $P_{R_y}^{\text{st}}$ by

time-backwardly tracing the lineage of the population as mentioned in Sec. II. To be more precise, we can consider the following experimental protocol: (i) we culture population in a fixed-environmental condition y for a sufficiently long time; (ii) we choose an arbitrary individual in the population at final time and trace its ancestors; (iii) we time-backwardly trace the lineage sufficiently long time and obtain a very long single history X of the ancestors, which is generated by $\hat{R}_y$; (iv) from the history X , we calculate the empirical probability $P_{R_y}^{\text{st}}$.

C. Dual process

In addition, we need the dual process of the retrospective process to derive Clausius inequality. We define the dual process of $P_R[X|Y]$ as a Markov process generated by $\tilde{R}_y(x'|x) \equiv R_y(x|x') P_{R_y}^{\text{st}}(x') / P_{R_y}^{\text{st}}(x)$ with the time-reversal type switching and environmental history; here, the Markov generator $\tilde{R}_y$ is also written as

$$\tilde{R}_y(x|x') = \frac{1}{v_y(x')} \{H_y(x'|x) - \lambda_0(y) \delta_{x,x'}\} v_y(x). \quad (30)$$

Therefore, the path probability of the dual process is represented as

$$P_{\tilde{R}}[\tilde{X}|\tilde{Y}] = \langle x_0 | e^{\hat{\tilde{R}}_{y_{\Delta t}} \Delta t} | x_{\Delta t} \rangle \times \dots \times \langle x_{\tau-\Delta t} | e^{\hat{\tilde{R}}_{y_\tau} \Delta t} | x_\tau \rangle P_{R_{y_\tau}}^{\text{st}}(x_\tau), \quad (31)$$

where $\langle x | \hat{\tilde{R}}_y | x' \rangle = \tilde{R}_y(x|x')$; $\tilde{X}$ and $\tilde{Y}$ represent time reversal of X and Y , respectively, that is, $\tilde{X} = \{x_\tau, x_{\tau-\Delta t}, \dots, x_{\Delta t}, x_0\}$ and $\tilde{Y} = \{y_\tau, y_{\tau-\Delta t}, \dots, y_{\Delta t}, y_0\}$.

D. Fluctuation relations

By using the above three path probabilities, we construct two kinds of relations, FR-I and FR-II, which are mathematically similar to the detailed fluctuation relation developed in nonequilibrium physics. By expanding the exponential function in $\langle x_t | e^{\hat{R}_{y_t} \Delta t} | x_{t-\Delta t} \rangle$ in Eq. (29), we obtain

$$\begin{aligned} \langle x_t | e^{\hat{R}_{y_t} \Delta t} | x_{t-\Delta t} \rangle &= \langle x_t | \left(1 + \hat{R}_{y_t} \Delta t + O(\Delta t)\right) | x_{t-\Delta t} \rangle \\ &= e^{-\lambda_0(y_t) \Delta t} \frac{u_{y_t}(x_t)}{u_{y_t}(x_{t-\Delta t})} \langle x_t | e^{\hat{H}_{y_t} \Delta t} | x_{t-\Delta t} \rangle, \end{aligned} \quad (32)$$

where we use the definition of R_y , Eq. (28). From Eq. (30), with the same calculation as Eq. (32), we also have

$$\begin{aligned} \langle x_{t-\Delta t} | e^{\hat{\tilde{R}}_{y_t} \Delta t} | x_t \rangle \\ = e^{-\lambda_0(y_t) \Delta t} \frac{v_{y_t}(x_{t-\Delta t})}{v_{y_t}(x_t)} \langle x_t | e^{\hat{H}_{y_t} \Delta t} | x_{t-\Delta t} \rangle. \end{aligned} \quad (33)$$

By substituting Eqs. (32) and (33) into Eqs. (29) and (31), respectively, we can rewrite the retrospective processes as

$$P_R[X|Y] = e^{-\{\lambda_0(y_\tau) + \lambda_0(y_{\tau-\Delta t}) + \dots + \lambda_0(y_{\Delta t})\}\Delta t} \times \frac{u_{y_\tau}(x_\tau) u_{y_{\tau-\Delta t}}(x_{\tau-\Delta t}) \times \dots \times u_{y_{\Delta t}}(x_{\Delta t})}{u_{y_\tau}(x_{\tau-\Delta t}) u_{y_{\tau-\Delta t}}(x_{\tau-2\Delta t}) \times \dots \times u_{y_{\Delta t}}(x_0)} P_{R_{y_0}}^{\text{st}}(x_0) \times \langle x_\tau | e^{\hat{H}_{y_\tau} \Delta t} | x_{\tau-\Delta t} \rangle \times \dots \times \langle x_{\Delta t} | e^{\hat{H}_{y_{\Delta t}} \Delta t} | x_0 \rangle, \quad (34)$$

and

$$P_{\tilde{R}}[\tilde{X}|\tilde{Y}] = e^{-\{\lambda_0(y_\tau) + \lambda_0(y_{\tau-\Delta t}) + \dots + \lambda_0(y_{\Delta t})\}\Delta t} \times \frac{v_{y_{\Delta t}}(x_0) \times \dots \times v_{y_{\tau-\Delta t}}(x_{\tau-2\Delta t}) v_{y_\tau}(x_{\tau-\Delta t})}{v_{y_{\Delta t}}(x_{\Delta t}) \times \dots \times v_{y_{\tau-\Delta t}}(x_{\tau-\Delta t}) v_{y_\tau}(x_\tau)} P_{R_{y_\tau}}^{\text{st}}(x_\tau) \times \langle x_\tau | e^{\hat{H}_{y_\tau} \Delta t} | x_{\tau-\Delta t} \rangle \times \dots \times \langle x_{\Delta t} | e^{\hat{H}_{y_{\Delta t}} \Delta t} | x_0 \rangle. \quad (35)$$

By inserting equalities $u_{y_0}(x_0)/u_{y_0}(x_0) = 1$ and $v_{y_0}(x_0)/v_{y_0}(x_0) = 1$ into Eqs. (34) and (35), respectively, and by using the integral symbol, we obtain

$$P_R[X|Y] = \exp \left[- \int_0^\tau \lambda_0(y_t) dt - \int_0^\tau dt \dot{y} \cdot \nabla_y \log u_y(x) \right] \times \exp \left[\log \frac{u_{y_\tau}(x_\tau)}{u_{y_0}(x_0)} + \log \frac{P_{R_{y_0}}^{\text{st}}(x_0)}{v_{y_0}(x_0)} \right] e^{\Psi[Y]} P_B[X|Y], \quad (36)$$

and

$$P_{\tilde{R}}[\tilde{X}|\tilde{Y}] = \exp \left[- \int_0^\tau \lambda_0(y_t) dt + \int_0^\tau dt \dot{y} \cdot \nabla_y \log v_y(x) \right] \times \exp \left[\log \frac{v_{y_0}(x_0)}{v_{y_\tau}(x_\tau)} + \log \frac{P_{R_{y_0}}^{\text{st}}(x_0)}{v_{y_0}(x_0)} \right] e^{\Psi[Y]} P_B[X|Y], \quad (37)$$

where we use Eq. (24). Equations (36) and (37) lead to FR-I and FR-II as

$$\log \frac{P_B[X|Y]}{P_R[X|Y]} = -\Psi^{\text{ex}}[Y] + \int_0^\tau dt \dot{y} \cdot \nabla_y \log u_y(x) - \log \frac{u_{y_\tau}(x_\tau)}{u_{y_0}(x_0)} + \log \frac{v_{y_0}(x_0)}{P_{R_{y_0}}^{\text{st}}(x_0)}, \quad (38)$$

and

$$\log \frac{P_B[X|Y]}{P_{\tilde{R}}[\tilde{X}|\tilde{Y}]} = -\Psi^{\text{ex}}[Y] - \int_0^\tau dt \dot{y} \cdot \nabla_y \log v_y(x) - \log \frac{v_{y_0}(x_0)}{v_{y_\tau}(x_\tau)} + \log \frac{v_{y_0}(x_0)}{P_{R_{y_\tau}}^{\text{st}}(x_\tau)}. \quad (39)$$

Here, we divided both sides of Eqs. (36) and (37) by $P_B[X|Y]$ and took the logarithm.

Next, by taking the arithmetic mean of Eq. (38) and Eq. (39), we obtain

$$\log \frac{P_B[X|Y]}{P_R^{1/2}[X|Y] P_{\tilde{R}}^{1/2}[\tilde{X}|\tilde{Y}]} = -\Psi^{\text{ex}}[Y] + \frac{1}{2} \int_0^\tau dt \dot{y} \cdot \nabla_y \log \frac{u_y(x)}{v_y(x)} - \log u_{y_\tau}(x_\tau), \quad (40)$$

where we use $P_{R_y}^{\text{st}}(x) = u_y(x) v_y(x)$. By substituting Eq. (18), which describes the relation between u_y and v_y , into Eq. (40), we have

$$\begin{aligned} & \log \frac{P_B[X|Y]}{P_R^{1/2}[X|Y] P_{\tilde{R}}^{1/2}[\tilde{X}|\tilde{Y}]} \\ &= -\Psi^{\text{ex}}[Y] + \frac{1}{2} \int_0^\tau dt \dot{y} \cdot \nabla_y \log \frac{C(y)}{P_T^{\text{st}}(x)} - \log u_{y_\tau}(x_\tau), \\ &= -\Psi^{\text{ex}}[Y] + \frac{1}{2} \{ \log C(y_\tau) - \log C(y_0) \} - \log u_{y_\tau}(x_\tau) \end{aligned} \quad (41)$$

By taking the average with respect to $P_B[X|Y]$, we find

$$\begin{aligned} D^{\text{sym}}[Y] &\equiv \sum_X P_B[X|Y] \log \frac{P_B[X|Y]}{P_R^{1/2}[X|Y] P_{\tilde{R}}^{1/2}[\tilde{X}|\tilde{Y}]} \\ &= -\Psi^{\text{ex}}[Y] + \{ S(y_\tau) - S(y_0) \} \\ &\quad - \sum_X P_B[X|Y] \log u_{y_\tau}(x_\tau), \end{aligned} \quad (42)$$

where we use $S(y) = (1/2) \log C(y)$. Here, we note that we employ the DBC assumption for the type switching T , because Eq. (18) holds only under the DBC (see Appendix D).

E. Derivation of Clausius inequality

Now, we are in a position to prove Clausius inequality. Consider a transition between stationary growing states in the environmental condition y_0 to y_τ . We also assume that a history of environmental change Y is non-quasistatic during this transition. From Eq. (42), we obtain

$$\begin{aligned} & \Psi^{\text{ex}}[Y] + D^{\text{sym}}[Y] + \sum_x v_{y_\tau}(x) \log u_{y_\tau}(x) \\ &= S(y_\tau) - S(y_0), \end{aligned} \quad (43)$$

where $D^{\text{sym}}[Y]$ is the symmetrized Kullback-Leibler divergence defined in Eq. (11) and we use $\sum_X P_B[X|Y] \log u_{y_\tau}(x_\tau) = \sum_{x_\tau} v_{y_\tau}(x_\tau) \log u_{y_\tau}(x_\tau)$ [33]. Therefore, if the following inequality:

$$D^{\text{sym}}[Y] + \sum_x v_{y_\tau}(x) \log u_{y_\tau}(x) \geq 0, \quad (44)$$

is proved, we can obtain Clausius inequality (7). To prove the inequality (44), we suppose the transition from the environmental condition y_0 to y_F ; here, we assume that the environmental condition y_F corresponds to no selection situation, i.e., $\mu_{y_F}(x) = \text{const.}$ and thus $u_{y_F}(x) = 1$ (see Appendix B). We note that $y_\tau \neq y_F$ and therefore y_F is just an arbitrary environmental condition describing no selection situation, which is introduced to mathematically prove the inequality (44). By taking an arbitrary intermediate environmental condition y_M (finally,

y_M is set to be y_τ), we consider maximum excess growths within intervals, y_0 to y_M , y_M to y_F , and y_0 to y_F , see also FIG. 2; we denote these maximum growths as $\Psi^{\text{ex}}[Y_{0 \rightarrow M}^*]$, $\Psi^{\text{ex}}[Y_{M \rightarrow F}^*]$, and $\Psi^{\text{ex}}[Y_{0 \rightarrow F}^*]$, where $Y_{i \rightarrow j}^*$ represents the history that maximizes the excess growth functional $\Psi^{\text{ex}}[\cdot]$ in an interval $[y_i, y_j]$. From Eq. (43),

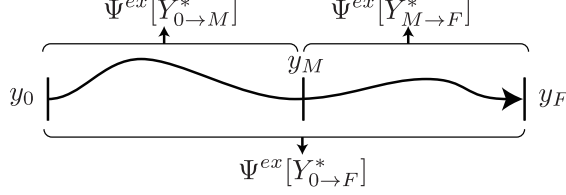


FIG. 2. Three maximum excess growths.

we can evaluate the excess growth for the interval from y_0 to y_M as

$$\Psi^{\text{ex}}[Y_{0 \rightarrow M}^*] = \{S(y_M) - S(y_0)\} - \left\{ D^{\text{sym}}[Y_{0 \rightarrow M}^*] + \sum_x v_{y_M}(x) \log u_{y_M}(x) \right\}. \quad (45)$$

By using $\sum_x v_{y_F}(x) \log u_{y_F}(x) = 0$ and $S(y_F) = 0$, we can calculate other two excess growths as

$$\Psi^{\text{ex}}[Y_{M \rightarrow F}^*] = -D^{\text{sym}}[Y_{M \rightarrow F}^*] - S(y_M), \quad (46)$$

$$\Psi^{\text{ex}}[Y_{0 \rightarrow F}^*] = -D^{\text{sym}}[Y_{0 \rightarrow F}^*] - S(y_0). \quad (47)$$

We recall the fact that, for quasistatic environmental changes $Y_{M \rightarrow F}^{\text{qs}}$ and $Y_{0 \rightarrow F}^{\text{qs}}$, $\Psi^{\text{ex}}[Y_{M \rightarrow F}^{\text{qs}}] = -S(y_M)$ and $\Psi^{\text{ex}}[Y_{0 \rightarrow F}^{\text{qs}}] = -S(y_0)$ hold, where we use Clausius *equality* (22). From $D^{\text{sym}}[Y] \geq 0$ for any Y , we obtain

$$\Psi^{\text{ex}}[Y_{M \rightarrow F}^*] = -S(y_M), \quad (48)$$

$$\Psi^{\text{ex}}[Y_{0 \rightarrow F}^*] = -S(y_0); \quad (49)$$

we also get the fact that quasistatic environmental changes $Y_{M \rightarrow F}^{\text{qs}}$ and $Y_{0 \rightarrow F}^{\text{qs}}$ respectively maximize the excess growth $\Psi^{\text{ex}}[\cdot]$ in intervals $[y_M, y_F]$ and $[y_0, y_F]$. Furthermore, the following inequality:

$$\Psi^{\text{ex}}[Y_{0 \rightarrow M}^*] + \Psi^{\text{ex}}[Y_{M \rightarrow F}^*] \leq \Psi^{\text{ex}}[Y_{0 \rightarrow F}^*], \quad (50)$$

is satisfied, because the intermediate environmental condition y_M works as a constraint of maximization of $\Psi^{\text{ex}}[\cdot]$ in the interval $[y_0, y_F]$. By substituting Eqs. (45), (48) and (49) into the inequality (50), we obtain

$$D^{\text{sym}}[Y_{0 \rightarrow M}^*] + \sum_x v_{y_M}(x) \log u_{y_M}(x) \geq 0. \quad (51)$$

Since $Y_{0 \rightarrow M}^*$ gives the maximum of $\Psi^{\text{ex}}[\cdot]$ in the interval $[y_0, y_M]$, $Y_{0 \rightarrow M}^*$ also yields the minimum of the functional $D^{\text{sym}}[\cdot] + \sum_x v_{y_M}(x) \log u_{y_M}(x)$ in the interval $[y_0, y_M]$, where we use Eq. (45). Accordingly, for

an arbitrary history Y with boundaries y_0 and y_M , the following inequality is satisfied:

$$D^{\text{sym}}[Y] + \sum_x v_{y_M}(x) \log u_{y_M}(x) \geq 0. \quad (52)$$

If we choose $y_M = y_\tau$, we have Eq. (44). As a result, from Eq. (43), we find Clausius inequality,

$$\Psi^{\text{ex}}[Y] = -\sigma[Y] + \{S(y_\tau) - S(y_0)\} \leq S(y_\tau) - S(y_0), \quad (53)$$

where $\sigma[Y]$ denotes the entropy production defined in Eq. (10).

V. DISCUSSION

We have established SST structure in population dynamics. Owing to Clausius inequality, the upper bound of excess growth is evaluated by the lineage fitnesses of initial and final environmental conditions. However, we must recall that DBC is assumed in our theory. When we deal with non-DBC type switching (e.g. metabolic switching and circadian rhythm), Clausius inequality is no longer available, because the potential condition Eq. (21) is broken down in these cases. Even for quasistatic environmental change, we need to directly calculate the geometric phase (17) in the similar manner as Tănase-Nicolafs study [21], because excess growth can not be evaluated by the potential as in Clausius equality (22). Furthermore, in non-DBC situations, it is still uncertain whether or not the geometric phase (17) gives an upper bound of the excess growth. These problems also arise in original SST. According to Ref. [10], even for quasistatic protocols, an excess heat does not have a potential like Eq. (22), and therefore a geometric phase (i.e., vector potential) plays an essential role. In addition, in the same way as our theory, it is uncertain whether or not this geometric phase gives an upper bound of the excess heat. Therefore, these are open problems not only in our study but also in the original SST.

In terms of its potential applications, it is expected that this decomposition can be exploited for designing effective external perturbation to suppress the population growth. Temporal (intermittent) therapies have recently been employed to suppress the growth of cancer cells, and their effectiveness was mathematically reported in Ref. [34]. Our theory may contribute to designing an optimal drug treatment for these therapies. Furthermore, methods to evaluate the cumulant generating function (as well as the large deviation function) by using population dynamics have been developed in nonequilibrium physics [35]. Since the population growth in our study mathematically corresponds to the cumulant generating function [17], our knowledge may facilitate designing a growing system to physically estimate the cumulant generating function of a given stochastic system.

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Appendix A

Here, we give a quantitative definition of “lineage fitness” and show that it is evaluated by the left eigenvector corresponding to the largest eigenvalue of $H_y(\cdot|\cdot)$. For convenience, we employ bra-ket notation as shown in Sec. III and IV. First, suppose that $N_y^\delta(\tau|a)$ is the size of a population at time $t = \tau$ in a fixed environmental condition y whose initial population distribution is given by $\delta_{x,a}$. In other words, we consider a population grown from one individual with type a at initial time $t = 0$ in the environmental condition y for a time interval $[0, \tau]$. Then, $N_y^\delta(\tau|a)$ is represented as

$$N_y^\delta(\tau|a) = \langle \mathcal{P} | e^{\hat{H}_y \tau} | a \rangle, \quad (54)$$

where $\langle \mathcal{P} |$ and $|a\rangle$ satisfy $\langle \mathcal{P} | x \rangle = 1$ and $\langle x | a \rangle = \delta_{x,a}$, respectively. Next, we evaluate the fraction of the population grown from the seed type a to the total population size N_τ^{tot} . Assuming that an initial population is given by a stationary growing state with environmental condition y : $N(x, 0) = N_0^{\text{tot}} v_y(x)$, we then evaluate the fraction as

$$\frac{N_y^\delta(\tau|a) N_0^{\text{tot}} v_y(a)}{N_\tau^{\text{tot}}}. \quad (55)$$

By dividing Eq. (55) by the initial fraction $v_y(a)$ and taking the limit $\tau \rightarrow \infty$, we obtain

$$\begin{aligned} g_y(a) &\equiv \lim_{\tau \rightarrow \infty} \left\{ \frac{N_y^\delta(\tau|a) N_0^{\text{tot}} v_y(a)}{N_\tau^{\text{tot}}} / v_y(a) \right\} \\ &= \lim_{\tau \rightarrow \infty} \left\{ \frac{N_y^\delta(\tau|a) N_0^{\text{tot}}}{N_\tau^{\text{tot}}} \right\}. \end{aligned} \quad (56)$$

This quantity is called “lineage fitness” of the type a in the environmental condition y . Obviously from the definition, the lineage fitness represents the prosperity of offsprings whose ancestors (i.e. seeds) had type a at time $t = 0$. By using $N_\tau^{\text{tot}} = \sum_x \langle \mathcal{P} | e^{\hat{H}_y \tau} | x \rangle N_0^{\text{tot}} \langle x | \lambda_0(y) \rangle$ and Eq. (54), we can rewrite the lineage fitness as

$$g_y(a) = \lim_{\tau \rightarrow \infty} \frac{\langle \mathcal{P} | e^{\hat{H}_y \tau} | a \rangle}{\sum_x \langle \mathcal{P} | e^{\hat{H}_y \tau} | x \rangle \langle x | \lambda_0(y) \rangle}, \quad (57)$$

where, as shown in Sec. III, $|\lambda_0(y)\rangle$ represents the right eigenvector corresponding to the largest eigenvalue $\lambda_0(y)$ and $\langle x | \lambda_0(y) \rangle = v_y(x)$.

Finally, we show that the lineage fitness $g_y(a)$ is evaluated by the left eigenvector corresponding to the largest eigenvalue. By inserting the completeness relation $\sum_i |\lambda_i(y)\rangle \langle \lambda_i(y)| = 1$ into the numerator of Eq. (57) and using another completeness relation $\sum_x |x\rangle \langle x| = 1$ for the denominator, we have

$$g_y(a) = \lim_{\tau \rightarrow \infty} \sum_i e^{(\lambda_i(y) - \lambda_0(y))\tau} \langle \mathcal{P} | \lambda_i(y) \rangle \langle \lambda_i(y) | a \rangle, \quad (58)$$

where we use $\langle \mathcal{P} | e^{\hat{H}_y \tau} | \lambda_0(y) \rangle = e^{\lambda_0(y)\tau}$. From $\lambda_0(y) > \lambda_i(y)$ for all $i \neq 0$, the index $i = 0$ dominates the summation in Eq. (58) in $\tau \rightarrow \infty$: that is,

$$g_y(a) = \langle \mathcal{P} | \lambda_0(y) \rangle \langle \lambda_0(y) | a \rangle. \quad (59)$$

By using the normalization condition $\langle \mathcal{P} | \lambda_0(y) \rangle = 1$ and the notation $\langle \lambda_0(y) | a \rangle = u_y(a)$, we find that the lineage fitness can be represented by the left eigenvector corresponding to the largest eigenvalue: $g_y(a) = u_y(a)$

Appendix B

We prove that $S(y) \leq 0$ for arbitrary y and that $S(y) = 0$ if y corresponds to no selection situation, i.e. $\mu_y(x) = \text{const.}$ for arbitrary x . From Eqs. (18) and (23) in Sec. III, the entropy can be written as

$$S(y) = \frac{1}{2} \log C(y) = -\frac{1}{2} \log \frac{v_y(x)}{P_T^{\text{st}}(x)} + \frac{1}{2} \log u_y(x). \quad (60)$$

By taking the average with respect to $v_y(x)$, we have

$$S(y) = -\frac{1}{2} D_{KL}[v_y || P_T^{\text{st}}] + \frac{1}{2} \sum_x v_y(x) \log u_y(x), \quad (61)$$

where $D_{KL}[v_y || P_T^{\text{st}}]$ represents the Kullback-Leibler divergence between v_y and P_T^{st} , and thus the first term is not positive. Next, we show that $\sum_x v_y(x) \log u_y(x) \leq 0$. From the normalization condition $\sum_x u_y(x) v_y(x) = 1$, we obtain

$$\left\langle e^{\log u_y(x)} \right\rangle_{v_y} = 1. \quad (62)$$

By using Jensen’s inequality, we have $e^{\langle \log u_y(x) \rangle_{v_y}} \leq 1$, and thus $\sum_x v_y(x) \log u_y(x) \leq 0$. Accordingly, we obtain $S(y) \leq 0$. In addition, we can show that $S(y) = 0$ if $\mu_y(x) = \text{const.}$, as follows. Owing to the property of the Kullback-Leibler divergence, we obtain that $D_{KL}[v_y || P_T^{\text{st}}] = 0$ if and only if $v_y = P_T^{\text{st}}$, which is achieved when $\mu_y(x) = \text{const.}$ Furthermore, the lineage fitness u_y satisfies $u_y(x) = 1$ for any x , if $\mu_y(x) = \text{const.}$ (we here set this constant α). The reason is as follows.

All elements of the left eigenvector corresponding to the largest eigenvalue of the stochastic matrix $T(\cdot|\cdot')$ are 1. Since we have assumed $\mu_y(x) = \text{const.} = \alpha$, we get a time-evolution matrix as $H_y(\cdot|\cdot') = \alpha\delta_{\cdot,\cdot'} + T(\cdot|\cdot')$. This time-evolution matrix shares the same eigenvectors with the stochastic matrix $T(\cdot|\cdot')$, and therefore we obtain $u_y(x) = 1$. Accordingly, we have $\log u_y(x) = 0$, and we finally find that $S(y) = 0$ if $\mu_y(x) = \text{const.}$

Appendix C

We define the time-forward path probability of $X = \{x_0, x_{\Delta t}, \dots, x_{\tau-\Delta t}, x_\tau\}$ as

$$P_T[X] = \langle x_\tau | e^{\hat{T}\Delta t} | x_{\tau-\Delta t} \rangle \times \dots \times \langle x_{\Delta t} | e^{\hat{T}\Delta t} | x_0 \rangle P_T^{\text{st}}(x_0), \quad (63)$$

which is a Markov process generated by the type-switching operator $\hat{T}$. Here, P_T^{st} denotes the stationary probability of this process, and it is given by the right eigenvector corresponding to the largest eigenvalue of $T(\cdot|\cdot') = \langle \cdot | \hat{T} | \cdot' \rangle$. Owing to the law of large numbers, P_T^{st} also represents empirical probability on a sufficiently long type-switching history X that is generated by T , i.e. $P_T^{\text{st}}(x) = \lim_{\tau \rightarrow \infty} (1/\tau) \int_0^\tau \delta_{x,x_t} dt$. Therefore, we can obtain P_T^{st} by time-forwardly tracing the lineage of the population. To be more precise, we consider the following experimental protocol: (i) we choose an arbitrary individual in the population and trace its offsprings; (ii) when an individual duplicates two daughters, we focus on one daughter by ignoring the other daughter; (iii) we observe offspring for a sufficiently long time interval and obtain a very long single history X ; (iv) from the history X , we calculate the empirical probability P_T^{st} .

Appendix D

We derive the relation between the stationary occupation probability v_y and the lineage fitness u_y introduced as Eq. (18) in the main text. The stationary occupation probability v_y is given by the right eigenvector corresponding to the largest eigenvalue of the time-evolution matrix $H_y(\cdot|\cdot')$, i.e. $\sum_{x'} H_y(x|x') v_y(x') = \lambda_0(y) v_y(x)$. Thus, by using $H_y(\cdot|\cdot') \equiv \mu_y(\cdot) \delta_{\cdot,\cdot'} + T(\cdot|\cdot')$, we have

$$\mu_y(x) v_y(x) + \sum_{x'} T(x|x') v_y(x') = \lambda_0(y) v_y(x). \quad (64)$$

By substituting the DBC, $T(x|x') P_T^{\text{st}}(x') = T(x'|x) P_T^{\text{st}}(x)$, into Eq. (64), we obtain

$$\mu_y(x) \frac{v_y(x)}{P_T^{\text{st}}(x)} + \sum_{x'} T(x'|x) \frac{v_y(x')}{P_T^{\text{st}}(x')} = \lambda_0(y) \frac{v_y(x)}{P_T^{\text{st}}(x)}. \quad (65)$$

This equation indicates that the vector $v_y(\cdot)/P_T^{\text{st}}(\cdot)$ is the left eigenvector corresponding to the largest eigenvalue of H_y , because $\sum_{x'} \{v_y(x')/P_T^{\text{st}}(x')\} H_y(x|x') = \{v_y(x)/P_T^{\text{st}}(x)\} \lambda_0(y)$. Since the time-switching process is ergodic, i.e. H_y is irreducible, the left eigenvector corresponding to the largest eigenvalue is unique up to a constant, owing to the Perron-Frobenius theorem. Therefore, we obtain

$$u_y(x) = C(y) \frac{v_y(x)}{P_T^{\text{st}}(x)}, \quad (66)$$

where we use the fact that the lineage fitness u_y is the left eigenvector corresponding to the largest eigenvalue and $C(y)$ denotes the constant depending on y . Since v_y is normalized as $\sum_x v_y(x) = 1$, we obtain $C(y) = \sum_x P_T^{\text{st}}(x) u_y(x)$. From the normalization condition $\sum_x u_y(x) v_y(x) = 1$, we also have $C(y) = \sum_x P_T^{\text{st}}(x) u_y^2(x)$.

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