Bet Hedging against Demographic Fluctuations

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Biological organisms have to cope with stochastic variations in both the external environment and the internal population dynamics. Theoretical studies and laboratory experiments suggest that population diversification could be an effective bet-hedging strategy for adaptation to varying environments. Here we show that bet hedging can also be effective against demographic fluctuations that pose a trade-off between growth and survival for populations even in a constant environment. A species can maximize its overall abundance in the long term by diversifying into coexisting subpopulations of both "fast-growing" and "better-surviving" individuals. Our model generalizes statistical physics models of birth-death processes to incorporate dispersal, during which new populations are founded, and can further incorporate variations of local environments. In this way, we unify different bet-hedging strategies against demographic and environmental variations as a general means of adaptation to both types of uncertainties in population growth.

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Growth of biological populations is a stochastic process subject to various types of uncertainties. In particular, environmental variations change the growth rate of a population by affecting the physical condition of individual organisms, whereas demographic variations cause the population size to fluctuate due to intrinsic noise in birth and death processes. Such processes have been vigorously studied using statistical physics models [1,2].

When considering the evolutionary success of a species, it is often assumed that a faster growth rate on average would help a species to achieve greater abundance in the long term. Thus, for example, in a fluctuating environment, a population that has the largest long-term average growth rate is supposed to be the most favored by natural selection. Under some circumstances, the maximum long-term growth rate of a population can be achieved by diversifying into subpopulations of different phenotypes, a mixed strategy known as "bet hedging" [3,4]. Many studies have focused on bet hedging in temporally or spatially varying environments [5–9] or under stochastic ecological interactions [10].

Another factor in population dynamics which has been less studied is the extinction risk of local populations. If all individuals in a population happen to die before producing new offspring, the population will go extinct and never recover. The probability that such an extinction event happens can be significant for small populations. This extinction risk is uniquely caused by demographic fluctuations, which exists even in the absence of environmental variations.

The growth rate and the extinction risk of a population may depend differently on the phenotype of individuals. Consider an asexual population whose individuals have a birth rate β and a death rate δ. The growth rate of the population is given by $r = \beta - \delta$, while the extinction risk is associated with the factor $q = \delta/\beta$ (it is the probability that a population founded by one individual goes extinct [1]; see [11]). Apparently, a large growth rate r does not guarantee a low extinction risk q. Intuitively, the growth rate represents the mean of population size change, while the extinction risk is due to fluctuations around that mean. Since it is common to have a trade-off between maximizing the mean and minimizing the fluctuations, one may expect a similar trade-off between growth and survival. Such trade-offs have been studied in many fields including ecology [14–19], economics [20], and engineering [21].

What consequences may this kind of trade-off have on biological populations? One situation where the trade-off between growth and survival will be important is during biological dispersal [14–19]. Indeed, natural resources are often limited in a local environment, which can support only a finite population size. A successful species would gain abundance by spreading to more locations. During range expansion, new colonies are typically founded by a small number of individuals. In such circumstances, the survival of new populations may be a more important factor than the growth of already established populations. For example, microbes can be dispersed through interactions between their hosts and may infect new hosts if they successfully establish large growing populations.

Here, we quantitatively analyze the trade-off between growth and survival using a simple statistical physics model. In this model, individuals can grow within local "patches" or disperse to new patches. We show that, depending on the dispersal rate, natural selection may favor either a fast growth rate or a low extinction risk of

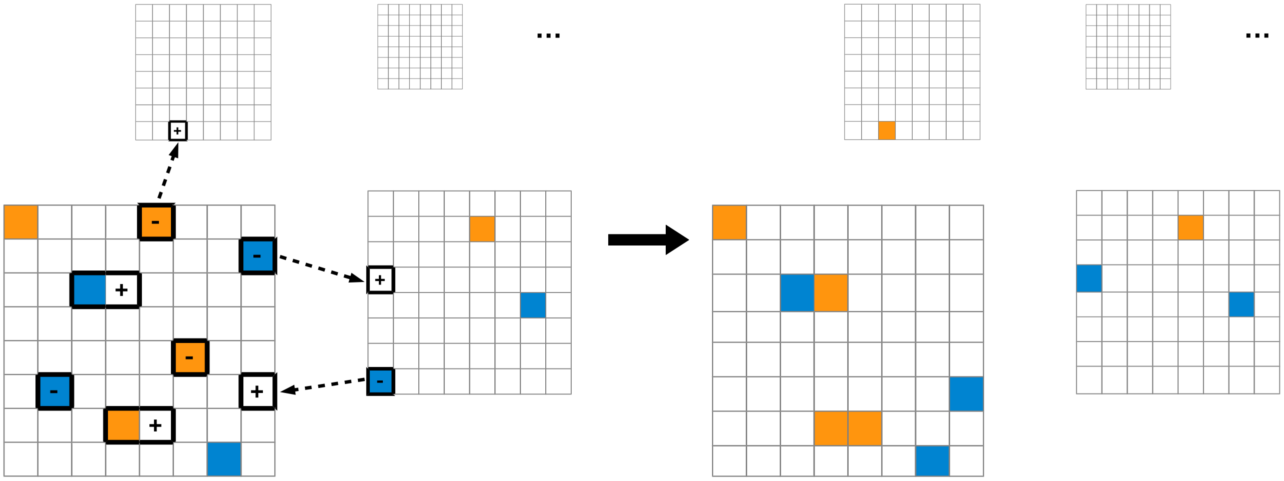

FIG. 1. Schematic illustration of the birth, death, and dispersal processes. Each patch is represented by a grid and has a finite capacity represented by the number of cells in the grid; an empty cell represents a vacant site, and a colored cell represents an individual, whose phenotype is indicated by its color. The cells highlighted by thick borders are being updated: A cell with a "+" sign means an individual appears, either being born to another individual (sharing a thick border) or having immigrated from another patch (dashed arrow); a cell with a "−" sign means an individual disappears, either due to death (isolated thick border) or emigration (dashed arrow). Individuals can move freely within a patch or disperse to any other patch.

local populations. More importantly, we find that a bet-hedging strategy that generates coexisting subpopulations of fast-growing and better-surviving phenotypes may help a species achieve the maximum abundance in the long term. The emergence of the optimal bet-hedging strategy is solely a consequence of demographic fluctuations. This contrasts with the results of previous studies that considered bet hedging as a strategy for maximizing long-term growth in varying environments.

Our model is illustrated in Fig. 1. We consider a biological species whose individuals may give birth to a new individual, die, or disperse to another patch. For simplicity, we assume that the patches are equally well connected and have the same carrying capacity K. Individuals may express different phenotypes, characterized by different pairs of birth and death rates; dispersal happens passively with a predetermined dispersal rate [22]. For simplicity, consider two phenotypes, A and B, which satisfy $r_A > r_B$ and $q_A > q_B$; hence, phenotype A is fast growing and phenotype B is better surviving. To allow for bet-hedging strategies, we assume that each individual randomly expresses one of the phenotypes with probability $\pi_A = \rho$ and $\pi_B = 1 - \rho$, respectively ($0 \le \rho \le 1$), regardless of its parent's phenotype [23]; the phenotype does not change over the lifetime.

A typical time course of the total population size is shown in Fig. 2 (inset). The simulation starts with one patch filled with individuals, whose phenotypes are randomly chosen. After an initial phase with relatively large demographic fluctuations, the total population size and the number of occupied patches start to grow at a steady rate. When many patches are available, the species will asymptotically expand at this rate and simultaneously colonize more and more patches. We use this "asymptotic expansion rate" W to measure the evolutionary success of the species.

The value of W, calculated using *Methods* below (see also [24]), depends on the phenotype distribution ρ. Let ρ^* be the value of ρ that maximizes W. If $\rho^* = 1$ or 0, then a pure strategy with a single phenotype A or B is

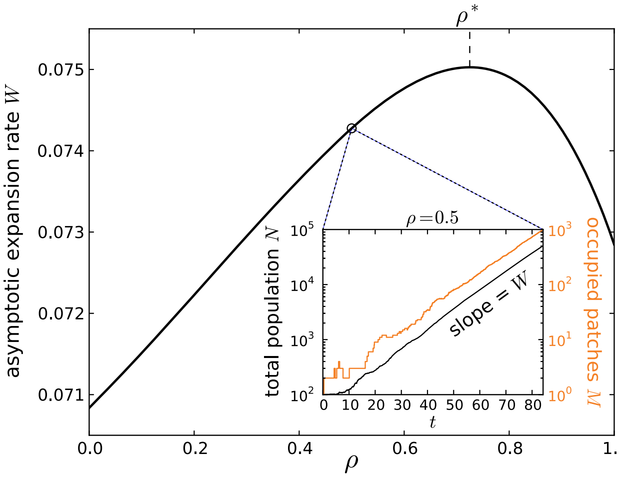

FIG. 2. Asymptotic expansion rate W as a function of phenotype distribution ρ. The birth, death, and dispersal rates are $\beta_A = 2$, $\delta_A = 1$, $\beta_B = 0.5$, $\delta_B = 0.1$, and $\mu = 0.002$, and the carrying capacity is $K = 100$. Inset: Time course of the total population size N and the number of occupied patches M, simulated using the Gillespie algorithm. The slope of the curves determines the value of W for a given ρ.

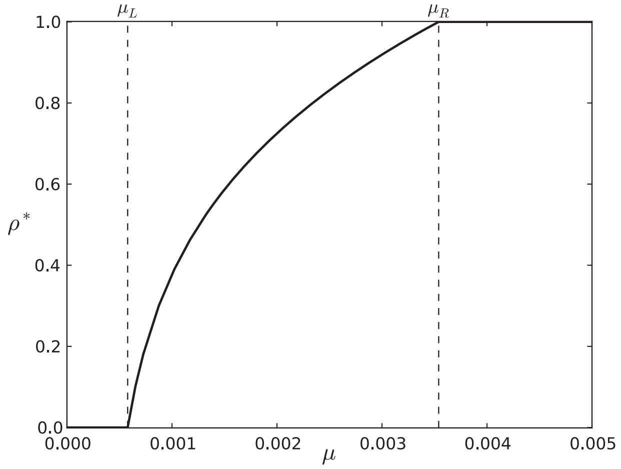

FIG. 3. Optimal phenotype distribution ρ^* as a function of dispersal rate μ, where one phenotype has a faster growth rate and the other has a lower extinction risk. The birth and death rates of each phenotype are $\beta_A = 2$, $\delta_A = 1$, $\beta_B = 0.5$, and $\delta_B = 0.1$; the carrying capacity of each patch is $K = 100$. For dispersal rates between μ_L and μ_R, a mixed strategy offers the maximum asymptotic expansion rate for the species.

evolutionarily most successful. However, if the maximum W is reached at an intermediate value $0 < \rho^* < 1$, as in Fig. 2, then a mixed (bet-hedging) strategy, by which a population constantly diversifies into subpopulations of both phenotypes, is more successful in the long term.

Those strategies are shown in Fig. 3, where ρ^* is plotted as a function of the dispersal rate μ. We find $\rho^* = 0$ for μ below a threshold value, μ_L, and $\rho^* = 1$ above another threshold, μ_R. In these two regimes, a pure strategy of having a single phenotype is thus favored. The fact that each regime favors a different phenotype demonstrates the trade-off between growth and survival. More interestingly, for values of μ between μ_L and μ_R, we find a new regime where $0 < \rho^* < 1$. In this case, a bet-hedging strategy that produces mixed populations consisting of both phenotypes is evolutionarily favorable. Such a favorable bet-hedging strategy arises only because of intrinsic uncertainties in demographic fluctuations.

So far, we have assumed a constant environment for all patches, in contrast to previous studies of bet hedging that assume a large population in a varying environment [25]. In the latter case, bet hedging results from a trade-off between phenotypes that are favorable for different environmental conditions, whereas in our case the trade-off between growth and survival is solely due to demographic fluctuations. These two scenarios can be unified in our model by introducing environmental variations that occur independently for different patches.

For simplicity, assume that there are two possible environmental conditions, X and Y, where X is the "normal" environment considered above and Y is a "hostile" environment such that the fast-growing phenotype A in environment X becomes unfavorable in Y, while the better-surviving phenotype B is unaffected. A good example is bacterial populations that produce both normal cells which thrive in growth media but die under antibiotic treatment and persister cells which are slow growing but tolerant to antibiotics [26]. Thus, the birth and death rates of the two phenotypes satisfy $\beta_A^{(X)} > \beta_A^{(Y)} = 0$, $\delta_A^{(Y)} \gg \delta_A^{(X)}$, $\beta_B^{(Y)} = \beta_B^{(X)}$, and $\delta_B^{(Y)} = \delta_B^{(X)}$. Each patch switches randomly between the two environmental conditions, with switching rates α_X ($Y \to X$) and α_Y ($X \to Y$). Hence, the stationary distribution of the environment is $p_X = \alpha_X/(\alpha_X + \alpha_Y) \equiv \epsilon$ and $p_Y = 1 - \epsilon$. We assume that the carrying capacity K and the dispersal rate μ do not depend on the local environment.

To see the effect of local environmental variations, we vary the environment distribution ϵ while keeping $\alpha \equiv \alpha_X + \alpha_Y$ fixed. The optimal phenotype distribution ρ^* that maximizes W now depends on both μ and ϵ. This can be characterized by a "phase diagram" shown in Fig. 4 [27]. Again, there are three regimes corresponding to pure strategies $\rho^* = 0$ or 1 and a mixed strategy $0 < \rho^* < 1$. The top edge ($\epsilon = 1$) corresponds to the case where the environment is X at all times, the same as in Fig. 3, with a $0 < \rho^* < 1$ phase in between the threshold values μ_L and μ_R. This mixed phase extends to smaller values of ϵ, until reaching a point (μ_T, ϵ_T), where it disappears and is replaced by a sharp boundary between the pure phases $\rho^* = 0$ and 1.

The topology of the phase diagram can be largely inferred from the behavior of ρ^* near the edges of the

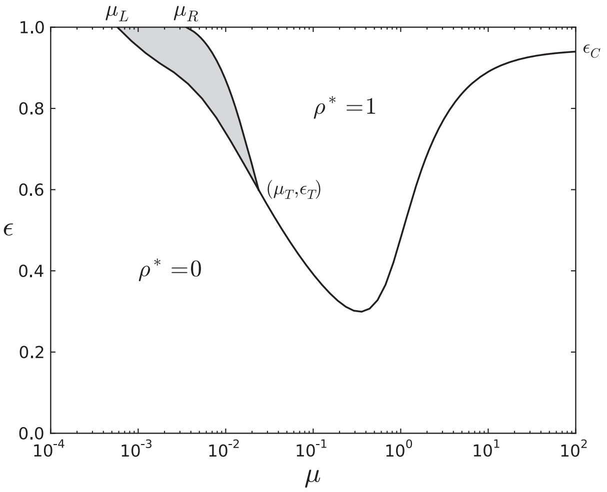

FIG. 4. Optimal phenotype distribution ρ^* for different values of the dispersal rate μ and the environment distribution ϵ. The shaded region marks a $0 < \rho^* < 1$ phase in which a mixed strategy offers the maximum asymptotic expansion rate. The birth and death rates are $\beta_A^{(X)} = 2$, $\delta_A^{(X)} = 1$, $\beta_A^{(Y)} = 0$, $\delta_A^{(Y)} = 10$, $\beta_B^{(X)} = \beta_B^{(Y)} = 0.5$, and $\delta_B^{(X)} = \delta_B^{(Y)} = 0.1$. Each patch has carrying capacity $K = 100$ and environment switching rates $\alpha = 0.1$.

diagram, i.e., in the limits $\epsilon \to 0$ or 1 and $\mu \to 0$ or ∞, which can be found analytically [24]. Intuitively, near the bottom edge ($\epsilon \to 0$), $\rho^* = 0$, since phenotype A is unfit for a constantly hostile environment Y. On the far left ($\mu < \mu_L$), $\rho^* = 0$ for all ϵ, because phenotype A is disadvantageous even if the environment is always favorable ($\epsilon = 1$). On the far right ($\mu \gg \mu_R$), there is a threshold value ϵ_C, above which $\rho^* = 1$ and below which $\rho^* = 0$ [24]. By smoothly interpolating the phases of ρ^* from the edges to the middle of the diagram, we recover the shape of Fig. 4.

The phase diagram shows that different bet-hedging strategies against demographic and environmental variations are special cases of a general adaptation strategy against both types of uncertainties. The shape of the diagram changes depending on the phenotypes and the environments [28]. In extreme cases, bet hedging could arise mainly because of demographic fluctuations, such as when phenotype A is fast growing and phenotype B is better surviving in both environments X and Y [Fig. S3(a)]. Alternatively, bet hedging may be optimal mainly due to environmental variations, such as when phenotype A is both fast growing and better surviving in environment X, whereas phenotype B is fast growing and better surviving in Y [Fig. S3(b)].

Our results indicate the generality of bet hedging as a means of coping with various types of uncertainties encountered by biological populations. In reality, organisms live in much more complex environments and interact with many other species—their habitats may be spatially structured, and their dispersal may be affected by ecological conditions [15–19]. Nevertheless, our simple model, which shows that organisms can bet hedge even against purely stochastic demographic fluctuations, clearly suggests a broader perspective for understanding the advantage of bet-hedging behavior widely observed in nature.

The trade-off between growth and survival exists in many situations and is not particular to the simple dispersal process considered in our model. The idea that bet hedging can be effective against stochastic fluctuations due to small numbers is applicable to other fields, such as financial investment and information processing.

Methods.—Here we briefly describe methods for calculating the asymptotic expansion rate W and the optimal phenotype distribution ρ^* for the basic model with a constant environment; technical details and generalization to locally fluctuating environments are given in Ref. [24].

For a given dispersal rate μ, W is calculated by considering the following "patch dynamics" [24]. Let a patch be labeled by the type P_{nl} if it has n individuals, l of which have phenotype A and $n-l$ phenotype B, satisfying $0 \le n \le K$ and $0 \le l \le n$. Let m_{nl} be the number of such patches; then the number of occupied patches is $M = \sum_{n,l} m_{nl}$, and the total population size is $N = \sum_{n,l} n m_{nl}$. The birth, death, and dispersal processes can be described in terms of the patches as

$$P_{n,l} \xrightarrow{\rho\beta_{nl}} P_{n+1,l+1}, \tag{1}$$

$$P_{n,l} \xrightarrow{(1-\rho)\beta_{nl}} P_{n+1,l}, \tag{2}$$

$$P_{n,l} \xrightarrow{\gamma_{nl}} P_{n-1,l-1}, \tag{3}$$

$$P_{n,l} \xrightarrow{\delta_{nl}} P_{n-1,l}, \tag{4}$$

$$P_{n,l} \xrightarrow{\mu_l} P_{n-1,l-1} + P_{1,1}, \tag{5}$$

$$P_{n,l} \xrightarrow{\mu_{n-l}} P_{n-1,l} + P_{1,0}, \tag{6}$$

where the rate constants are $\beta_{nl} = [\beta_A l + \beta_B(n-l)](1-n/K)$, $\gamma_{nl} = \delta_A l(1-n/K)$, $\delta_{nl} = \delta_B(n-l)(1-n/K)$, and $\mu_n = \mu n$. For (5) and (6), we have assumed that there is a large supply of available patches, so that a dispersed individual would always end up in an empty patch. The deterministic dynamics of the patch numbers is given by

$$\begin{aligned}\dot{m}_{n,l} = {} & \rho\beta_{n-1,l-1}m_{n-1,l-1} + (1-\rho)\beta_{n-1,l}m_{n-1,l} \\ & + (\gamma_{n+1,l+1} + \mu_{l+1})m_{n+1,l+1} + (\delta_{n+1,l} + \mu_{n-l+1})m_{n+1,l} \\ & - (\beta_{n,l} + \gamma_{n,l} + \delta_{n,l} + \mu_n)m_{n,l} \\ & + \delta_{n,1}\sum_{n'=1}^{K}\sum_{l'=0}^{n'}(\delta_{l,1}\mu_{l'} + \delta_{l,0}\mu_{n'-l'})m_{n',l'}.\end{aligned} \tag{7}$$

This equation can be cast in a matrix form (with composite indices): $\dot{m}_{nl} = \sum_{n'l'} H_{nl,n'l'} m_{n'l'}$. The largest real eigenvalue of the matrix $\boldsymbol{H}$ yields W, which can then be numerically maximized over ρ to find ρ^* [27].

Approximate expressions of W can be obtained in the limit where the dispersal rate μ is large or small [24]. For $\mu \gg \beta_a$ and δ_a, where $a = A$ or B, we find $W \approx r_m$, where $r_m(\rho)$ is the growth rate of a mixed population with phenotype distribution ρ. Intuitively, when the dispersal rate is high, individuals move freely between the patches, so the whole species behaves as one large population, and hence W is given by r_m. Now, $r_m(\rho)$ increases with ρ, since the higher the percentage of phenotype A is, the faster the population grows. Therefore, in this regime, maximizing W yields $\rho^* = 1$, which means the fast-growing phenotype A is favored.

On the other hand, for $\mu \ll \beta_a/K$ and δ_a/K, we find $W \approx \mu K(1 - q_m)$, where $q_m(\rho)$ is the probability that a mixed population founded by one individual goes extinct before reaching the carrying capacity [24]. Intuitively, when the dispersal rate is low, the occupied patches are mostly full; hence, the overall rate of dispersal to new patches is proportional to μK; among those colonization attempts, only a fraction escapes local extinction, hence the factor $(1 - q_m)$. But $q_m(\rho)$ increases with ρ, because the larger the proportion of phenotype B, the lower the extinction risk. Hence, in this regime, W is maximized by $\rho^* = 0$, favoring the better-surviving phenotype B.

The value of ρ^* increases continuously from 0 to 1 as μ varies between two thresholds μ_L and μ_R. The values of μ_L and μ_R depend on the parameters (β_a, δ_a). For a wide range of parameters that satisfy $r_A > r_B$ and $q_A > q_B$, the $0 < \rho^* < 1$ regime exists [27], where a bet-hedging strategy is most favorable.

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[22] For models that also consider the dispersal rate as part of a phenotype, see, e.g., [18].

[23] See Supplemental Material Sec. V at http://link.aps.org/supplemental/10.1103/PhysRevLett.119.108103 for a generalization of the model where the distribution of individual phenotypes may depend on the parental phenotype.

[24] See Supplemental Material Sec. II A at http://link.aps.org/supplemental/10.1103/PhysRevLett.119.108103 for details of deriving the patch dynamics and calculating the asymptotic expansion rate W (similar methods are used in treating structured metapopulation models [13,14]); Sec. II B generalizes the method to the case of mixed populations; Sec. II C considers the case of patchy and fluctuating environments.

[25] But see [6,7] for models that include two local populations and migration between them. See also [8] for range expansion in a multipatch environment with nonuniform growth conditions.

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[27] See Supplemental Material Sec. III at http://link.aps.org/supplemental/10.1103/PhysRevLett.119.108103 for numerical calculations of the optimal phenotype distribution ρ^*.

[28] See Supplemental Material Sec. IV at http://link.aps.org/supplemental/10.1103/PhysRevLett.119.108103 for more examples of the possible phase diagrams.