Programmed death is favored by natural selection in spatial systems

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Standard evolutionary theories of aging and mortality, implicitly based on mean-field assumptions, hold that programmed mortality is untenable, as it opposes direct individual benefit. We show that in spatial models with local reproduction, programmed deaths instead robustly result in long-term benefit to a lineage, by reducing local environmental resource depletion via spatiotemporal patterns causing feedback over many generations. Results are robust to model variations, implying that direct selection for shorter lifespan may be quite widespread in nature.

Lifespans of different organisms in nature can vary over orders of magnitude, even among closely related species \cite{1-4}. Why should otherwise self-repairing organisms eventually die without external causes, and what sets a species’ characteristic lifespan? Standard evolutionary theory explains intrinsic mortality in the context of senescence as the result of two main effects, attendant on the decreasing strength of selection with increasing age: (1) mutations with late-appearing detrimental effects are not strongly selected against \cite{mutation acc}; (2) genes that increase early-life reproductive success but contribute to later-life failures can be selected for \cite{antag pleiotropy and disposable soma}. These effects are typically held to account for all senescent phenomena, and it is widely accepted in evolutionary theory and mainstream medicine that aging is a non-adaptive by-product of the diminishing strength of age-specific selection, and not an adaptation for the explicit control of lifespan for its own sake \cite{8, 9}—indeed that lifespan limitations cannot be directly adaptive. However, phenomena such as plasticity of lifespans in response to genetic modification \cite{10-13} and selective breeding \cite{14, 15}, apparent programmed death \cite{16}, and anomalous patterns of longevity \cite{17} and senescence \cite{3, 18}, which are difficult to reconcile with accepted frameworks \cite{7}, suggest that the classic theories may be incomplete.

We demonstrate here a mechanism for adaptive limitation of lifespan, using a spatial evolutionary model. The key to identifying this mechanism is the proper treatment of spatial symmetry breaking, a condition which violates mean-field assumptions commonly used in mathematical evolutionary biology. We find that spatial heterogeneity of limiting resources and self-organizing population structures result in robust selection for lifespan limitation. In our model, intrinsic mortality leaves resources for descendants, which are more likely to be found in the same local region, increasing long-term strain success. The mechanism is fundamentally different from those underlying standard evolutionary theories. In contrast to the classic mechanisms, which are based on selection directly on the reproductive success of individual organisms, our mechanism predicts the evolution of traits that may become advantageous only for descendants after many generations. There is no compensating reproductive benefit to the individual of the shortened lifespan, as there would have to be in a mean-field model.

Simulations allow the identification of effects of symmetry breaking in spatial evolutionary dynamics including the short-term advantages but long-term disadvantages of overly exploitative variants \cite{19, 20}. “Selfish” variants that outcompete their neighbors, at the expense of depleting their local environment, have an advantage on short spatial and temporal scales. However, on longer scales, their descendants are left in impoverished environments and can be outcompeted by others in richer areas. This mechanism cannot occur in analytic models that rely on mean-field approximation and that examine the evolution of mutations affecting lifespan in homogenous populations. This clarifies why traditional theory discounts direct selection for shorter lifespan, while we find it dominates a wide range of spatial model conditions.

We consider an explicit spatial model of an interacting pair of organism types, in which one population relies on the second for survival, to the latter’s detriment. Such spatial consumer-resource (e.g., predator-prey, pathogen-host, herbivore-plant) models have previously shed light on the evolutionary origins of phenomena such as reproductive restraint \cite{20}, sexual reproduction \cite{21}, limitations to pathogen virulence \cite{20, 22}, and social altruism \cite{19}; here we apply them to the evolution of lifespan limits and intrinsic mortality.

The model uses a 2D stochastic cellular automaton to consider a population of abstract organisms (“consumers”) with limited but self-renewing resources (e.g., prey or hosts). Sites represent empty space \((E)\), available resources \((R)\), or a consumer together with resources \((C)\); a consumer cannot occupy a site in the absence of resources. Resources alone can reproduce into neighboring empty sites, with probability \(g\) per time step per such
site; similarly, consumers can reproduce into neighboring resource-only sites, with probability $p$ per time step per site. Additionally, consumers can exhaust resources in their site, leaving an empty site, with probability $v$ per time step and $c$ per reproduction; or they can die due to intrinsic mortality, leaving a resource-only site, with probability $q$ per time step. A consumer’s mean intrinsic lifespan is $L = 1/q$. Subscripts on $p$ and $q$ (i.e., $p_1, q_1$) may be used to indicate that $p$ and $q$ vary by consumer. If more than one consumer “tries” to reproduce into a given resource-only site in the same time step, one is chosen as the parent, with equal probability for each. Thus, at each time step, an empty site has probability

$$P_{E \rightarrow R} = 1 - (1 - g)^{N_R}$$

of transitioning to a resource-only site, where $N_R$ is the number of resource-only sites in the empty site’s four-cell neighborhood; a resource-only site has probability

$$P_{R \rightarrow C} = 1 - \prod_i (1 - p_i)$$

of transitioning to a consumer site, where $N_C$ is the number of consumers among its four neighbors and the values $p_i$ are the corresponding consumer reproduction probabilities; and a consumer site has probability $P_{C \rightarrow E} = v + kc$ of transitioning to an empty site, where $k$ is the number of offspring the consumer produces in this time step, and probability $P_{C \rightarrow R} = q_i$ of transitioning to a resource-only site. Boundary conditions are periodic. Lattice updates are synchronous.

Consider a competition between two strains $C_1 \rightarrow \{p_1, q_1\}$ and $C_2 \rightarrow \{p_2, q_2\}$ in a mean-field analysis [25]. The fraction of sites in each of the four possible states $\{C_1, C_2, R, E\}$ at each time step can be expressed as a recurrence relation:

$$n_{C_1}(t+1) = n_{C_1}(t)(1 + n_R(t)\gamma p_1 - (v + q_1)/(1 - c))$$
$$n_{C_2}(t+1) = n_{C_2}(t)(1 + n_R(t)\gamma p_2 - (v + q_2)/(1 - c))$$
$$n_R(t+1) = n_R(t)(1 + n_E(t)\gamma g - \gamma(n_{C_1}(t)p_1 + n_{C_2}(t)p_2) + n_{C_1}(t)q_1 + n_{C_2}(t)q_2$$
$$n_E(t+1) = n_E(t)(1 - n_R(t)\gamma g$$
$$+ n_{C_1}(t)(v + q_1 c)/(1 - c)$$
$$+ n_{C_2}(t)(v + q_2 c)/(1 - c)$$

where $\gamma = 4$ is the number of neighbors. By inspection these equations state that higher reproduction probability $p$ and lower intrinsic mortality probability $q$ are always favored. If

$$\frac{v + q_1}{p_1} < \frac{v + q_2}{p_2}$$

then $C_1$ drives $C_2$ to extinction [25]. Lower $q$ values will take over the entire consumer population (Figure 1A–C, dashed lines). This is the prediction of traditional theories of lifespan as well as simple intuition: a longer life means more opportunity to reproduce.

Critically, this mean-field prediction does not correctly describe the behavior of the spatial model, as revealed by numerical simulations. We performed three types of simulations, “competition,” “ascendance” and “invasion,” to

FIG. 1. Longer lifespan can give short-term advantage and long-term disadvantage in spatial models, in contrast to predictions based on mean-field approximation. (A–C) Plots show, for invaders with lifespan $L$ introduced into a steady-state population with equilibrium lifespan $L = L_0$, reproductive success (average number of consumers of the introduced type present) as a function of time. (Dashed) Mean-field calculations give the incorrect prediction that longer lifespan is always favored. (Solid) Numerical results from the spatial model show that longer lifespan can be favored for periods of hundreds or thousands of time steps but outcompeted in the long term. The time scale of the true dynamics is also much slower than that of the mean-field prediction [23]. Parameter values are (A) $g = 0.13, v = 0.2, L_0 = 2.7$, (B) $g = 0.17, v = 0.1, L_0 = 7.6$, (C) $g = 0.2, v = 0.005, L_0 = 170$, with resource growth $g$, consumption $v$, and reproduction cost $c = 0$. Error bars show the standard error of the mean among ten independent runs, each recording the mean for a set of 40,000 invasions. (D–E) Longer-lived consumers deplete their local environment compared to shorter-lived ones. (D) Effective contact rate $\rho' = \sum_{j \in \text{neighbours in state } R}(1/N_C(j))$ [25], averaged over all invaders, as a function of time since introduction. The local environment changes from a value characteristic of the invaded population to a value characteristic of the invader within a few dozen time steps. (Data for high $q$ are more variable since the invaders are quickly out-competed and so fewer samples are available.) (E) Expected lifetime reproduction $\rho' p/(v + q)$. (Solid) Numerical results, based on the empirical $\rho'$ (as in (D), averaged over time steps 51–100) where the invader has transformed its local environment, show a disadvantage for invaders with lifespan longer or shorter than the equilibrium value of 0.215. (Dashed) Mean-field calculations for invasion of an infinite population, with no local effect on environment, incorrectly predict an advantage for invaders with longer lifespan. Parameter values are $g = v = 0.1, c = 0, p = 0.9991$. 


investigate the evolution of lifespan control. All tests show that, counter to the mean field analysis, the evolutionarily optimal value of \( q \) in the simulated spatial model is nonzero.

“Competition” directly tests the dynamics of two competing strains. We introduce one consumer of the first type into a population of the second, and track the number of each over time. Longer-lived (smaller \( q \)) strains can have a temporary advantage that may last for hundreds of generations, but eventually they are outcompeted by the shorter-lived types (Figure 1A–C, solid lines). The mean-field approximation fails because local resource availability quickly becomes characteristic of the local strain rather than of the population as a whole; longer-lived types have resource-impoverished environments (Figure 1D–E).

“Ascendance” studies (Figure 2) explore the evolution of lifespan in a consumer population undergoing mutation. We make the intrinsic death probability per time step \( q \) as well as the reproduction probability \( p \) heritable and independently subject to mutation. With probability \( \mu_q \) (\( \mu_p \)), a consumer offspring has a value of \( q \) (\( p \)) differing from that of the parent by \( \pm \epsilon_q \) (\( \pm \epsilon_p \)); mutants with \( q \) (\( p \)) outside the range \([0, 1 - v] \) \([0, 1] \) are set to the corresponding boundary value. Numerical simulations (Figure 2A) show that after initialization [26], a transient is followed by a dynamic state with consistent mean values of \( q \) and \( p \), with only small fluctuations in these average measures (Figure 2B), that persists as long as simulations are run in large enough lattices. Reported results use square lattices, with edge size equal to the smallest multiple of 250 for which a steady-state population with given \( g \) and \( v \) persists in all trials [25]: larger sizes do not affect the quantitative results. Results reported here use \( \mu_q = \mu_p = 0.1275, c = 0 \), and \( g \) and \( v \) as specified. To ensure that the bounds on \( q \) and \( p \) do not cause artifacts in their evolved steady-state values due to finite-size mutations, mutation sizes \( \epsilon_q \) and \( \epsilon_p \) were progressively reduced: after \( 10^5 \) time steps at \( \epsilon_q = \epsilon_p = 0.005 \) to achieve initial steady state, they were halved every \( 10^4 \) steps for an additional \( 10^5 \) steps, followed by \( 5 \times 10^4 \) steps with \( \epsilon_q \) and \( \epsilon_p \) fixed [25]. The results showed that self-limited lifespan was consistently favored, for all parameter values tested (Figure 2D).

“Invasion” studies (Figure 3; animation in the Supplementary Material) explore the question of evolutionary origin and stability of the trait of intrinsic mortality: If a rare mutation could confer or remove the capacity for lifespan control, would that mutant have an advantage or a disadvantage in its later spread through the population? These studies take a steady-state lattice configuration, randomly choose one consumer to convert to the invading type, and follow its lineage until fixation (extinction of either invaders or invaded), tracking the probability of successful invasion in \( 10^5 \) such trials (\( 5 \times 10^5 \) trials in cases where no successful invasions were observed). “Mortals”

**FIG. 2.** (Color online) Ascendance studies favor intrinsic mortality in numerical simulations with a spatial model. (A) Snapshots showing different spatial distributions of resources (yellow) and immortal (left, magenta) or mortal (right, cyan) consumers (50 × 50 subsets of 250 × 250 lattices). (B) History of evolving consumer intrinsic mortality \( q \) in one example trial (\( g = v = 0.1, c = 0, \mu_p = \mu_q = 0.01 \)). Mean-field analysis (red, dashed; arrow) predicts mean \( q \) quickly goes to 0. Numerical simulations (blue, solid; population mean/maximum/minimum) show long-term stability of finite \( q \) and elimination of low-\( q \) strains from the population. (C,D) Steady-state average values of (C) consumer reproduction probability \( p \) and (D) intrinsic lifespan \( L = 1/q \), for different values of parameters \( g \) and \( v \) and for (C,D) mortal (solid) and (C) immortal (dashed) populations. (E) Steady-state evolved \( q \) in mortal populations (\( g = v = 0.05, c = 0 \)) for increasing neighborhood size \( \gamma \). For \( \gamma \geq 36 \), consumers with \( q = 0 \) are no longer eliminated from the population. (F) Steady-state evolved \( q \) for the mortal populations of (D) approximately falls on a single curve (line is a power-law fit: \( q = 0.245(g/v)^{-0.07} \)) when plotted as a function of “consumption ratio” \( g/v \), for all \( g \) and \( v \) tested. All error bars show the standard error of the mean from ten independent trials.
because this result contrasts with the predictions of traditional theories, it is important to identify which model details are those relevant to limited lifespan being favored. We therefore explored a large number of variants [24, 25] related to different real-world considerations in order to evaluate how that key result depends on model assumptions. In addition to robustness to changes in the values of parameters \((g, v, c, \mu_{(p,q)}, \epsilon_{(p,q)})\) in the base model as described above, changes to the model that continue to result in lifespan control include: (1) explicit deterministic lifespan (i.e., programmed mortality/rapid senescence) or (2) increasing mortality with age (i.e., gradual senescence), rather than constant probability of death with time; (3) various forms of local consumer rearrangement and migration; (4) longer-range (but still limited) dispersal of consumers or resources during reproduction; (5) gradual, deterministic depletion of continuous-valued resources, rather than binary-valued resources stochastically depleted; (6) ability of consumers to adjust their “rate of living”, lowering consumption, reproduction, and intrinsic mortality in response to low-resource conditions; (7) spontaneous resource generation, not requiring nearby resources to seed growth; (8) consumer offspring supplanting existing neighbors, so that occupation of a site does not preclude reproduction there; (9) limited reproduction of exploited resources; and (10) sexual reproduction by consumers. The robustness of the finding that self-limited lifespan is favored across model variations provides evidence for its applicability to a variety of biological systems.

Intrinsic mortality is not favored for long-range spatial mixing or if resources are unlimited. Figure 2E shows that increasing consumer dispersal range for a fixed-size lattice results in increasing lifespans. Figure 2F shows the evolved lifespan diverges with the “consumption ratio” \(g/v\), a measure of the rate of resource replenishment. Note that in typical real-world systems, mixing and resources are both limited.

These results provide theoretical support for the idea that direct lifespan control, and programmed mortality and senescence as ways of achieving it, are consistent with natural selection. In contrast, it is widely reported that theory is incompatible with the evolution of explicit lifespan control [7–9, 25]. This perspective has guided and constrained the interpretation of empirical findings. Our results suggest that classic mechanisms relevant to the evolution of lifespan are incomplete. Direct selection for intrinsic mortality and senescence—not just selection for an individual benefit with senescence as a deleterious side effect—can be used to help understand empirical phenomena [24], particularly for cases that have posed problems for traditional theory [7] but are straightforward to explain with direct selection.

The idea that shorter lifespans can be and are selected for directly goes back to at least 1870 [1]. It was later rejected based on theoretical arguments that evolution of such a trait opposed to individual self-interest, like other altruistic behaviors, must require group selection, whose applicability should be accepted only as a last resort [6]. The theories developed consistently describe spatially averaged systems in mean-field analyses [24, 25] and well-mixed experimental populations [27]. However, the real world possesses spatial extent, and spatial systems routinely demonstrate altruistic behaviors [19, 20, 28, 29] which are not evolutionarily stable in mean-field models [24, 25] or well-mixed laboratory populations [29]. Previous models, some spatial, have demonstrated that selection for self-limited lifespan is not a theoretical impossibility, under assumptions such as continual introduction of highly advantageous mutations [30], pre-existing senescence in the form of decreasing fecundity [31] or decreasing competitive fitness [32] with increasing age, or explicit group selection among nearly-isolated subpopu-
The robustness of our result that self-limited lifespan is favored, under many variations of model details and parameter values, suggests that genetically programmed senescence may indeed be a quite general phenomenon, with strong implications for human medicine. If aging is programmed, rather than a collection of secondary breakdowns or genetic tradeoffs, then effective health and life extensions through dietary, pharmacological, or genetic interventions [34, 35] are likely to be possible, with potential for significant impact (e.g., altering two genes extends nematode lifespan fivefold [11]). That the fundamental understanding of evolution can play a critical role in guiding health research should motivate a wider reevaluation of the evidence in relation to the theoretical frameworks.

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[25] See Supplemental Material at [URL] for details of all model variations explored, animations showing model behavior, analytic mean-field approximation calculations, and additional discussion.
[26] Each lattice site is initially empty with probability 0.55, resource-only with probability 0.4, and consumer with probability 0.05, with \( p \) and \( q \) in the latter case randomly chosen from a uniform distribution between 0 and 1. Steady-state results are not sensitive to these values, except for extreme cases (e.g., initializing the lattice with no consumers will necessarily result in an atypical steady state without consumers).