DAMAGE SEGREGATION AT FISSIONING MAY INCREASE GROWTH RATES: A SUPERPROCESS MODEL

STEVEN N. EVANS AND DAVID STEINSALTZ

ABSTRACT. A fissioning organism may purge unrepairable damage by bequeathing it preferentially to one of its daughters. Using the mathematical formalism of superprocesses, we propose a flexible class of analytically tractable models that allow quite general effects of damage on death rates and splitting rates and similarly general damage segregation mechanisms. We show that, in a suitable regime, the effects of randomness in damage segregation at fissioning are indistinguishable from those of randomness in the mechanism of damage accumulation during the organism's lifetime. Moreover, the optimal population growth is achieved for a particular finite, non-zero level of combined randomness from these two sources. In particular, when damage accumulates deterministically, optimal population growth is achieved by a moderately unequal division of damage between the daughters, while too little or too much division is sub-optimal. Connections are drawn both to recent experimental results on inheritance of damage in protozoans, and to theories of aging and resource division between siblings.

1. INTRODUCTION

One of the great challenges in biology is to understand the forces shaping age-related functional decline, termed *senescence*. Much current thinking on senescence (*cf.* [SG06]) interprets the aging process as an accumulation of organismal damage. The available damage repair mechanisms fall short, it is often argued, because of limitations imposed by natural selection, which may favor early reproduction, even at the cost of later decrepitude. One line of research aims to clarify these trade-offs by examining the non-aging exceptions that test the senescence rule. Of late, it has even been argued that negligible [Fin90] or even negative [VBD^{+}04] senescence may not be as theoretically implausible as some had supposed, and that it might not even be terribly rare [Gue04].

Fissioning protozoans have been generally viewed as a large class of exceptions to the senescence rule. Indeed, their immortality has been considered almost tautological by the principle enunciated by P. Medawar [Med57], that

individual birth is a fundamental prerequisite for aging. This principle has been sharpened by L. Partridge and N. Barton [PB93], who remark

> The critical requirement for the evolution of ageing is that there be a distinction between a parent individual and the smaller offspring for which it provides. If the organism breeds by dividing equally into identical offspring, then the distinction between parent and offspring disappears, the intensity of selection on survival and reproduction will remain constant and individual ageing is not expected to evolve.

Recent experiments [AGRN03, LJBJ02, ASJ03, SMPT05] have focused attention on the elusive quality of the "distinction" between parent and offspring. If aging is the accumulation of unrepaired damage, then "age" may go up or down. The metazoan reproduction that results in one or more young (pristine) offspring, entirely distinct from the old (damaged) parent, is an extreme form of rejuvenation. This may be seen as one end of a continuum of damage segregation mechanisms that include the biased retention of carbonylated proteins in the mother cell of budding yeast [AGRN03] and perhaps the use of aging poles inherited by one of the pair of *Escherichia coli* daughter cells as, in the words of C. Stephens [Ste05], cellular "garbage dumps". Even where there is no conspicuous morphological distinction between a mother and offspring, the individuals present at the end of a bout of reproduction may not be identical in age, when age is measured in accumulated damage. Whereas traditional theory has focused on the extreme case of an aging parent producing pristine offspring, it now becomes necessary to grapple with the natural-selection implications of strategies along the continuum of damage-sharing between the products of reproduction.

Our approach is a mathematical model of damage-accumulation during a cell's lifetime and damage-segregation at reproduction that quantifies (in an idealized context) the costs and benefits of unequal damage allocation to the daughter cells in a fissioning organism. The benefits arise from what G. Bell [Bel88] has termed "exogenous repair": pushing more of the damage into one daughter cell than into the other,

For a conceptually simple class of models of population growth that flexibly incorporate quite general structures of damage accumulation, repair and segregation, we analytically derive the conditions under which increasing inequality in damage inheritance will boost the long-term population growth rate. In particular, for organisms whose lifetime damage accumulation rate is deterministic and positive, some non-zero inequality will always be preferred. While most immediately relevant for protozoans, this principle and our model may have implications more generally for theories of intergenerational effects, such as transfers of resources and status.

One consequence of exogenous repair may seem surprising: If inherited damage significantly determines the population growth rate, and if damage is split unevenly among the offspring, there may be a positive benefit to

accelerating the turnover of generations. In simple branching population growth models, the stable population growth rate is determined solely by the net birth rate. In the model with damage, increasing birth and death rates equally may actually boost the population growth rate. This may be seen as the fission analogue of Hamilton's principle [Ham66], that the likelihood of future decline, and increasing mortality rates, places a selective premium on early reproduction. Of course, if the variance in damage accumulation is above the optimum, then this principle implies that reducing the inequality in inheritance, or decreasing birth and death rates equally, would be favored by natural selection.

2. Background

Popular reliability models of aging (such as [Kol81, GG01, Dou82] and additional references in section 3 of [SG06]) tend to ignore repair, while the class of growth-reproduction-repair models (such as [Kir77, AL95, Cic97, Man01, CL06] and further references in section 2 of [SG06]) tend to ignore the fundamental non-energetic constraints on repair. A living system will inevitably accumulate damage. Damage-repair mechanisms are available, but these can only slow the process, not prevent it. The repair mechanism of last resort is selective death. Any individual line will almost certainly go extinct, but the logic of exponential profusion means that there may still some lines surviving.[*] Following this logic one step further brings us to our central question: What benefit, if any, would accrue to a line of organisms that could not purge damage, but could selectively segregate it into one of its children?

This mechanism of selective segregation of damage was described by G. Bell [Bel88], who called it "exogenous repair". Bell's theoretical insight derived from his analysis of a class of experiments that were popular a century ago, but have since largely been forgotten. The general protocol allowed protozoans to grow for a time, until a small sample was plated to fresh medium, and this was repeated for many rounds. Effectively, this created an artificial selection of a few surviving lines, selected not for maximum fitness (as would be the case if the population were allowed to grow unmolested), but at random. In most settings, in the absence of sexual recombination, *population senescence* — slackening and eventual cessation of growth — was the rule.

One would like to follow the growth of individual cells, but this was inconceivable with the technology of the time. Only lately has such an undertaking become not only conceivable, but practicable. Recent work [SMPT05] has followed individual *E. coli* over many generations, following the fates of the "old pole" cell (the one that has inherited an end that

---

[*]While this argument is simplest for haploid fissioning organisms, the same logic could be applied to the germ line of higher organisms, as in [BP98]. Sexual recombination, in this picture, only facilitates the rapid diffusion of high-quality genetic material, and the bodies are rebuilt from good raw materials in each generation.

has not been regenerated) and the "new pole" cell. Whereas individual cells do not have a clearly defined age, it makes more sense to ascribe an age to a pole. Unpublished work from the same laboratory (described in October 2004 at a workshop held at the Max Planck Institute for Demographic Research in Rostock), as well as the work of [AGRN03, LJBJ02] on *Saccharomyces cerevisiae* goes even further, tracking the movement of damaged proteins or mitochondria through the generations, and showing that the growth of the population is maintained by a subpopulation of relatively pristine individuals. The demography of damage accumulation in the fissioning yeast *Schizosaccharomyces pombe* has recently been described in [MFD$^+$06]. These striking experiments have helped focus attention on the elusive nature of the asymmetries that underly microbial aging.

We propose a model to address the following question: Suppose the "costs" of accumulating damage are inevitable. What may be under evolutionary control is the equality of dividing this damage between the two daughters. Of course, perfectly equal splitting of damage is physically impossible, and one must always take care not to read an evolutionary cause into a phenomenon that is inevitable. At the same time, it is worth posing the question, whether there is an optimal level of asymmetry in the segregation of damage which is non-zero. If this is true in the models, it suggests possibilities for future experiments, to determine whether the asymmetry is being actively driven by the cell, or whether possibilities for reducing the asymmetry are being neglected.

In principle, this is a perfectly generic evolutionary phenomenon. It depends upon the "old-pole" experiments only to the extent that they reveal at least one mechanism producing such an asymmetry. Our model is intended to represent a large population of fissioning organisms, each of which has an individual "damage level", which determines its rate of growth and division, and its likelihood of dying. When a cell divides, its daughters divide the parent's damage unequally, with the inequality controlled by a tunable parameter. The evolution of this population is described formally by a mathematical object called a "superprocess".

An illustration of the underlying branching model is in Figure 1. In this example, each individual cell accumulates damage at a constant rate during its lifetime, so that the lifelines of cells are parallel sloping lines. The only way to reduce the damage load is to pass the damage on disproportionately to one of the daughters at a division. Note the following:

- Any fixed line of descent eventually dies.
- The population as a whole continues to grow.
- Death is more likely, and fissioning comes more slowly, for cells that are further right — that is, with more damage.
- The population eventually clusters at low levels of damage.

At this point, we should acknowledge [WPJK06], which appeared while the present paper was under review, and which puts forward an account
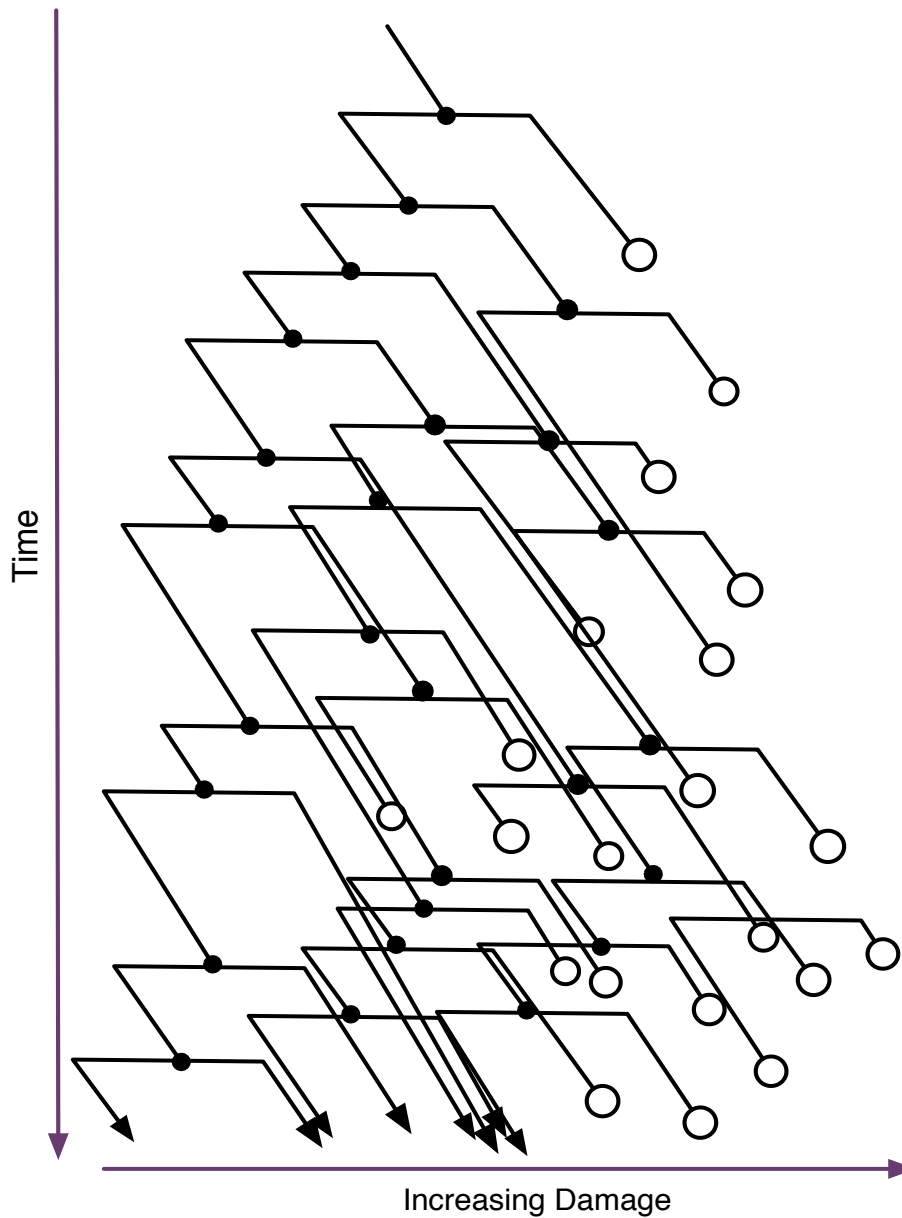
FIGURE 1. Illustration of the branching model. Sloping lines are lifelines of cells, moving downward in time and rightward in damage space. Filled circles represent fission events. Open circles represent deaths. Arrows represent cells that survive to the end of the experiment.

of the possible advantages of asymmetric damage division in many respects

quite similar, in others substantially different. The paper [WPJK06] complements the present paper in several important respects:

(1) The present paper presents an abstract model of damage segregation and its effects, whereas [WPJK06] is specifically a model of the "old-pole" effect.

(2) The present paper offers analytical solutions for models that incorporate a broad range of mechanisms for damage segregation and the effect of damage on death and splitting rates, and it provides general results about the effect of damage segregation on growth rates, whereas the specific parametric model of [WPJK06] is amenable to simulation and computational exploration of its particular parameter space.

(3) The present paper performs its analysis in an asymptotic regime, the relevance of which to the behavior of actual finite populations depends on scaling assumptions which are not required in [WPJK06]. (Roughly speaking, the scaling assumptions are analogous to those that are required for the validity of the diffusion approximations introduced by researchers such as Kimura into population genetics.)

(4) The present paper includes no explicit representation of cell growth.

The important lesson is that the same fundamental behavior is seen in two very different models, analyzed with very different methods. In each case, increasing the inequality in transmission of damage to the daughter cells is found to increase the population growth rate in some circumstances.

3. Description of the model

Our model for the growth of a population of fissioning organisms such as *E. coli* is an infinite population measure-valued diffusion limit of a sequence of finite population branching models. The formal description of this measure-valued process is contained in the Appendix. In the present section we confine ourselves to an intuitive description of the model.

3.1. **Diffusion.** The state of the process at any time t is a collection of cells, each of which has some level of damage. We represent the level of damage as a positive real number. Each cell develops independently of its fellows, performing four different behaviors: Damage creation, damage repair, death, and fissioning. Damage creation and repair sum to a net damage process, which we model as a diffusion. Diffusion processes, which are most commonly applied in population genetics as models for fluctuating proportions of alleles in a population (*cf.* [Ewe79]), may be thought of as continuous analogues of random walks. A real-valued diffusion is a general model of a random process that changes continuously in time and satisfies the Markov property: future behavior depends only on the current state, not on the more distant past. The diffusion model of damage accumulation in a cell is determined by two parameters: the diffusion rate $\sigma_{\mathrm{mot}}(x)$, giving the intensity of random fluctuation of the damage level as a function of the current damage

level x; and the drift $b(x)$, giving the trend in damage, whether increasing (positive) or decreasing (negative), as a function of current damage.

3.2. **Branching diffusions and measure-valued diffusions.** While cells move independently through damage space, they are also splitting in two and dying, at rates that depend on their current damage state. The obvious way to represent the state of this "branching diffusion" process at any given time is as a list of a changing number of cells, each labeled with its damage state. It turns out to be mathematically more convenient to invert this description and present all the damage states, each with a number (possibly zero) representing the number of cells in that state. Formally, such a description is called an *integer-valued measure* on the space of damage states (that is, on the positive real numbers). A stochastic process whose state at any given time is one of these measures is a *measure-valued (stochastic) process*.

We take this mathematical simplification one step further, at the expense of increasing the amount of hidden mathematical machinery. The discrete numbers of individuals in the population prevent us from applying the powerful mathematical tools of analysis. This is exactly analogous to the difficulties that arise in analyzing the long-term behavior of discrete branching models, or inheritance models such as the Wright-Fisher and Moran models [Ewe79]. The famous solution to that problem was W. Feller's [Fel51] diffusion approximation. By an essentially analogous method (see, for example, [Eth00] or [Per02]), rescaling the time and giving each cell "weight" $1/n$, while letting the population size and the birth and death rates grow like n, and now sending n to infinity, we obtain in the limit a stochastic process that has as its state space continuous distributions of "population" over the damage states. Such general distributions are called *measures* and may be identified in our setting with density functions on the positive real numbers. We stress that the limiting stochastic process is not deterministic and can be thought of as an inhomogeneous cloud of mass spread over the positive real numbers that evolves randomly and continuously in time. Such a stochastic process is called a *measure-valued diffusion* or *superprocess*. An accessible introduction to measure-valued process produced by this sort of scaling limit, including the original superprocess, called "super-Brownian motion," is [Sla02].

As described in [Saw76], branching diffusions [Mor62, CK70, Ewe69] and the related stepping-stone models [Kim53, KW64] were well established in the 1960s as models for the geographic dispersion, mutation, and selection of rare alleles. Important early applications of spatially structured branching models include [Kin77, SF81], which helped to elucidate the spatial population distributions that are likely to arise from from populations under local dispersion and local control. The utility of measure-valued stochastic processes in population biology was established by the celebrated limit version of allele frequency evolution in a sampling-replacement model due to

W. Fleming and M. Viot [FV79], which followed quickly upon the mathematical innovations of D. Dawson [Daw75]. In particular, studies such as [EG87, GT99] show how the measured-valued diffusion approach helps in taming the complexities of infinite sites models. Superprocesses have found broad application in the study of persistence and extinction properties of populations evolving in physical space (such as [You01, Eth04]) or in metaphorical spaces of genotypes (such as [DK99, WB02, DH83]). A thorough introduction to the subject, including extensive notes on its roots and applications in branching-diffusion and sampling-replacement models, is [Daw93a].

3.3. **The damage-state superprocess.** Formally, we posit a sequence of branching models, converging to our final superprocess model. If the scaling assumptions are reasonable, important characteristics of the branching models — in particular, the connection between the process parameters and the long-term growth rate — should be well approximated by the corresponding characteristics of the superprocess.

The nth model in the sequence begins with a possibly random number N_n of individuals. Individuals are located at points of the positive real line $\mathbb{R}^+$. The location of an individual is a measure of the individual's degree of cellular damage. We code the ensemble of locations at time $t \geq 0$ as a measure X_t^n on $\mathbb{R}^+$ by placing mass $1/n$ at each location, so that the initial disposition of masses X_0^n is a random measure with total mass N_n/n. During its life span the damage level fluctuates, as the organism accumulates and repairs damage. An individual's level of damage evolves as an independent diffusion on $\mathbb{R}^+$ with continuous spatially varying drift $b(x)$, continuous diffusion rate $\sigma_{\text{mot}}(x)$, and continuous killing rate (depending on n) $k^n(x)$. While our mathematical framework allows general behavior (mixtures of reflection and killing) at the boundary point 0, it seems sensible for applications to assume complete reflection. Other boundary behavior would imply a singular mortality mechanism at damage level 0.

An individual can split into two descendants, which happens at spatially varying rate $a^n(x)$. As in the standard Dawson-Watanabe superprocess construction [EK86, Daw93b, Eth00], we assume that birth and death rates grow with n but are nearly balanced, so that there is an asymptotically finite net birth rate

$$(1) \qquad \beta(x) := \lim_{n \to \infty} \big(a^n(x) - k^n(x)\big) < \infty$$

while the total rate at at which either death or splitting occurs satisfies

$$(2) \qquad \rho(x) := \lim_{n \to \infty} n^{-1}\left(a^n(x) + k^n(x)\right) < \infty.$$

In other words, an individual at location x attempts to split at a rate which is asymptotically $n\rho(x)$, and such an attempt is successful (resp. unsuccessful) with a probability that is asymptotically $\frac{1}{2}(1+\beta(x)/n)$ (resp. $\frac{1}{2}(1-\beta(x)/n)$). We assume that $\beta^* := \sup_x \beta(x) < \infty$ and $\beta_\infty := \lim_{x \to \infty} \beta(x)$ exists

(though it may be $-\infty$). Both of these conditions hold under the biologically reasonable assumption that β is non-increasing (that is, asymptotic net birth rate is non-increasing in the amount of damage).

The unbalanced transmission of damaged material leads to one important difference from the standard Dawson-Watanabe superprocess construction: When a split occurs the two descendants are not born at the same point as the parent. A parent at location x has descendants at locations $x - Y$ and $x + Y$, where Y is randomly chosen from a distribution π_x^n on $\mathbb{R}^+$. We suppose that

$$(3) \qquad \sigma_{\text{seg}}^2(x) := \lim_{n \to \infty} n \int_{-\infty}^{\infty} y^2 \, d\pi_x^n(y) < \infty$$

for some continuous function σ_{seg}^2. The quantity $\sigma_{\text{seg}}^2(x)$ is a measure of the amount of damage segregation that takes place when a parent with level of damage x splits.

We show in the Appendix that the process X^n converges to a limit process X, as $n \to \infty$, as long as the initial damage distributions X_0^n converge to some finite measure X_0. The limit is a Dawson-Watanabe superprocess whose underlying spatial motion is a diffusion with drift b (the same as the original motion) and diffusion rate σ, where

$$(4) \qquad \sigma^2(x) := \sigma_{\text{mot}}^2(x) + \sigma_{\text{seg}}^2(x)\rho(x)$$

Thus the asymptotic effect of segregation is equivalent to an increase in the diffusion rate, which may be thought of as the extent of random fluctuation in the the underlying motion of an individual cell through damage space. The same effect may be achieved by increasing simultaneously the fission and death rates, leaving fixed the net rate of birth. The quantity $\sigma_{\text{seg}}^2(x)$ measures a re-scaled per generation degree of damage segregation, and multiplication by the re-scaled splitting rate $\rho(x)$ produces a quantity $\sigma_{\text{seg}}^2(x)\rho(x)$ that measures a re-scaled per unit time rate of damage segregation.

4. Major results

Write Z_t for the asymptotic re-scaled population size at time t. That is, Z_t is the total mass of the measure X_t. We show that there is an *asymptotic population growth rate* $\underline{\lambda}$ in the sense that the asymptotic behavior of the expectation of Z_t satisfies

$$(5) \qquad \lim_{t \to \infty} t^{-1} \log \mathbb{E}[Z_t] = \underline{\lambda}.$$

Thus, $\mathbb{E}[Z_t]$ grows to first order like $e^{\underline{\lambda}t}$.

When the asymptotic growth rate $\underline{\lambda}$ is positive, this result may be significantly strengthened. Theorem 7.4 tells us then (under mild technical conditions) that:

- To first order, the total population size at time t, Z_t, grows like $e^{\underline{\lambda}t}$. More precisely, $Z_t/\mathbb{E}[Z_t]$ converges to a finite, non-zero, random limit as $t \to \infty$.

- The random distribution describing the relative proportions of dam-
  age states of cells at time t converges to a non-random distribution
  with density $c\phi$ as $t \to \infty$, where ϕ is the unique solution to the
  ordinary differential equation

$$\frac{1}{2}\left[\sigma^2(x)\phi(x)\right]'' - [b(x)\phi(x)]' + \beta(x)\phi(x) = \lambda\phi$$

$$\text{with } \frac{\sigma(0)^2}{2}\phi'(0) = 2b(0)\phi(0)$$

  and c is the normalization constant required to make $c\phi$ integrate 1.
  That is, for any $0 \le a < b < \infty$ the proportion of the population with
  damage states between a and b converges to $\int_a^b \phi(x)\,dx / \int_0^\infty \phi(x)\,dx$.

Suppose now that we identify (as is commonly done) fitness of a cell type
with the asymptotic growth rate $\underline{\lambda}$. It is not obvious, under arbitrary fixed
conditions of average damage accumulation and repair (b), splitting rate (ρ),
and net reproduction (β), what level of randomness in damage accumula-
tion and repair (σ_{mot}) and damage segregation (σ_{seg}) has the highest fitness.
Under the biologically reasonable assumption that the average damage ac-
cumulation rate is everywhere positive, though, it is generally true that
moderate degrees of randomness in both mechanisms lead to higher growth
rates than either very small or very large degrees of randomness. Theorem
7.5 (in section 7.3) tells us that, under fairly general conditions, if the dif-
fusion rate σ is reduced uniformly to 0, or increased uniformly to ∞, this
pushes the asymptotic growth rate down to $\beta_\infty = \lim_{z\to\infty} \beta(z)$.

Since the growth rate at any damage level is higher than β_∞, this result
tells us that the growth rate is minimized by sending σ uniformly either to 0
or to ∞. Too much or too little randomness in damage accumulation yields
lower growth rates; optimal growth must be found at intermediate levels of
diffusion.

Imagine now a situation in which the upward drift in damage has been
brought as low as possible by natural selection, optimizing repair processes
and tamping down damage generation. We see that there may still be some
latitude for natural selection to increase the lineage's growth rate, by tin-
kering with this randomness. Recall that σ is composed of two parts: the
randomness of damage accumulation during the lifecourse, and the inequal-
ity of damage transmission to the daughters. Without altering damage gen-
eration or repair, but only the equality of transmission to the offspring, the
cell type's long-term growth rate may be increased. In particular, if dam-
age accumulation rates are positive and deterministic — a fixed rate $b(x)$ of
damage accumulation per unit of time, when a cell has damage level x —
the growth rate will always be improved by unequal damage transmission.

5. AN EXAMPLE

Suppose that damage accumulates deterministically during the life of an
organism, at a rate proportional to the current level of damage. In the

absence of damage segregation, then, the damage at time t grows like e^{bt} (this corresponds to $b(x) = bx$ and $\sigma^2_{\text{mot}} = 0$). We suppose that the combined parameter $\sigma^2_{\text{seg}}\rho(x)$ describing the time rate of damage segregation for an organism that fissions at damage level x is $\tau^2 x^2$, where τ is a tunable non-negative parameter (hence, $\sigma(x) = \sqrt{\sigma^2_{\text{seg}}\rho(x)} = \tau x$). The generator for the spatial motion in the limit superprocess is thus

$$\frac{\tau^2}{2}x^2 f''(x) + bx f'(x).$$

This is the generator of the geometric Brownian motion $\exp(\tau B_t + (b - \frac{\tau^2}{2})t)$. We see immediately that adding enough noise can push the spatial motion toward regions with less damage. To make this fit formally into our theorems, we assume complete reflection at 1. (We have previously taken the range of damage states to be the positive real numbers $(0, \infty)$, whereas here we have taken the interval $(1, \infty)$. The choice of interval is irrelevant as far as the mathematics goes, and we could convert this choice to our previous choice by simply re-defining $b(x)$ and $\sigma(x)$).

Suppose that the bias of reproduction over dying in the superprocess is of the form $\beta(x) = \beta_0 - \beta_1 x$. The population growth rate will be the same as for the process $Y_t = B_t + (\frac{b}{\tau} - \frac{\tau}{2})t$, with reflection at 0, and killing at rate $\beta_0 - \beta_1 e^{\tau Y_t}$. The eigenvalue equation is

$$\frac{1}{2}f''(y) + \tilde{b}x f'(y) + (\beta_0 - \beta_1 e^{\tau y})f(y) = \lambda f(y),$$

where $\tilde{b} := \frac{b}{\tau} - \frac{\tau}{2}$, with boundary condition $f'(0) = 0$.

Using standard transformations as in section 6 of [SE05], or symbolic mathematics software such as *Maple*, we may compute a basis for the space of solutions to be the modified Bessel functions

$$I_\nu\left(\sqrt{8\beta_1/\tau^2}e^{\tau y/2}\right)e^{-\tilde{b}y} \text{ and } K_\nu\left(\sqrt{8\beta_1/\tau^2}e^{\tau y/2}\right)e^{-\tilde{b}y},$$

where

$$(6) \qquad \nu = \frac{2\sqrt{\tilde{b}^2 - 2(\beta_0 - \lambda)}}{\tau}.$$

By definition, $\underline{\lambda}$ is the infimum of those λ such that the solution f is non-negative. Since $f'(0) = 0$, it cannot be the case that $f(0) = 0$. Hence, the solution for $\underline{\lambda}$ has no zero, but the solution for every $\lambda < \underline{\lambda}$ does have a zero in $\mathbb{R}^+$. By continuity (as argued for the same problem in [SE05]), it follows that the solution for $\underline{\lambda}$ is a multiple of K_ν. The boundary condition translates to

$$(7) \qquad \frac{K'_\nu}{K_\nu}\left(\frac{\sqrt{8\beta_1}}{\tau}\right) = \frac{\tilde{b}}{\sqrt{2\kappa_1}}.$$
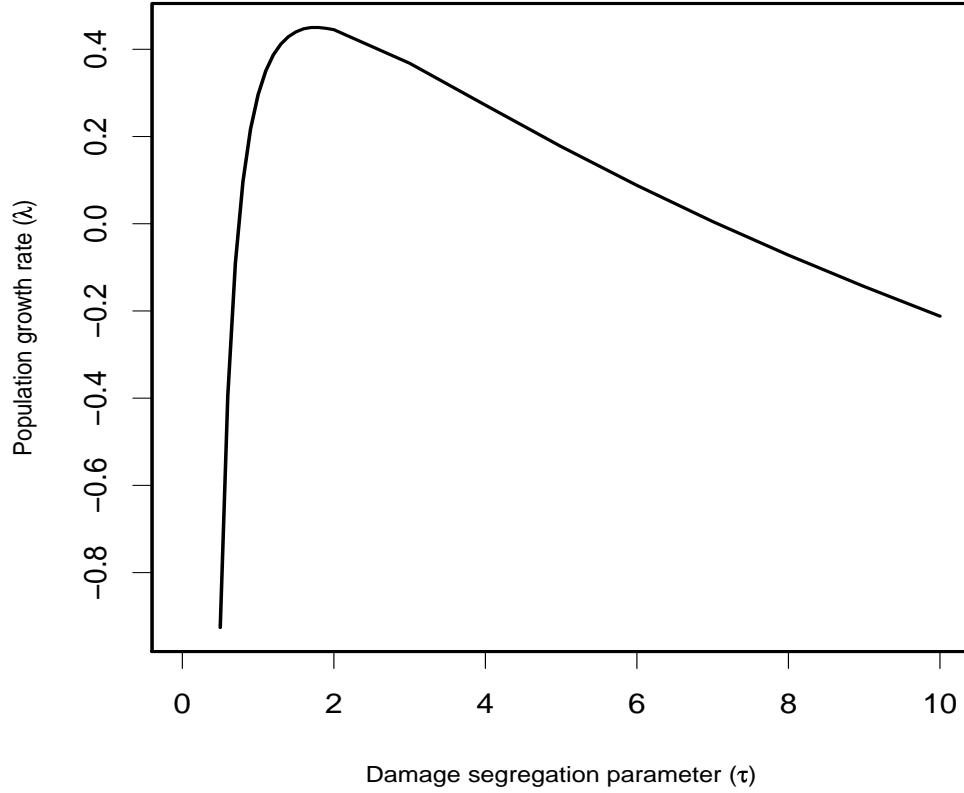
FIGURE 2. Asymptotic growth rates $\underline{\lambda}$ computed from (11) for populations whose deterministic rate of damage accumulation is equal to the current damage level, and whose relative excess of births over deaths is $1.9 - x/2$ at damage level x. Damage segregation is added at rate τx for births to parents at damage level x.

Find ν_0 real such that the last zero of $K_{i\nu_0}$ is at $\sqrt{8\beta_1}/\tau$, and represent the corresponding λ by

$$\lambda_0 = -\frac{\tau^2 \nu_0^2}{8} - \frac{\tilde{b}^2}{2} + \beta_0.$$

Then

$$\underline{\lambda} = \inf \left\{ \lambda \in (\lambda_0, \infty) : \frac{K'_\nu}{K_\nu} \left(\frac{\sqrt{8\beta_1}}{\tau} \right) = -\frac{\tilde{b}}{\sqrt{2\beta_1}} \right\}.$$
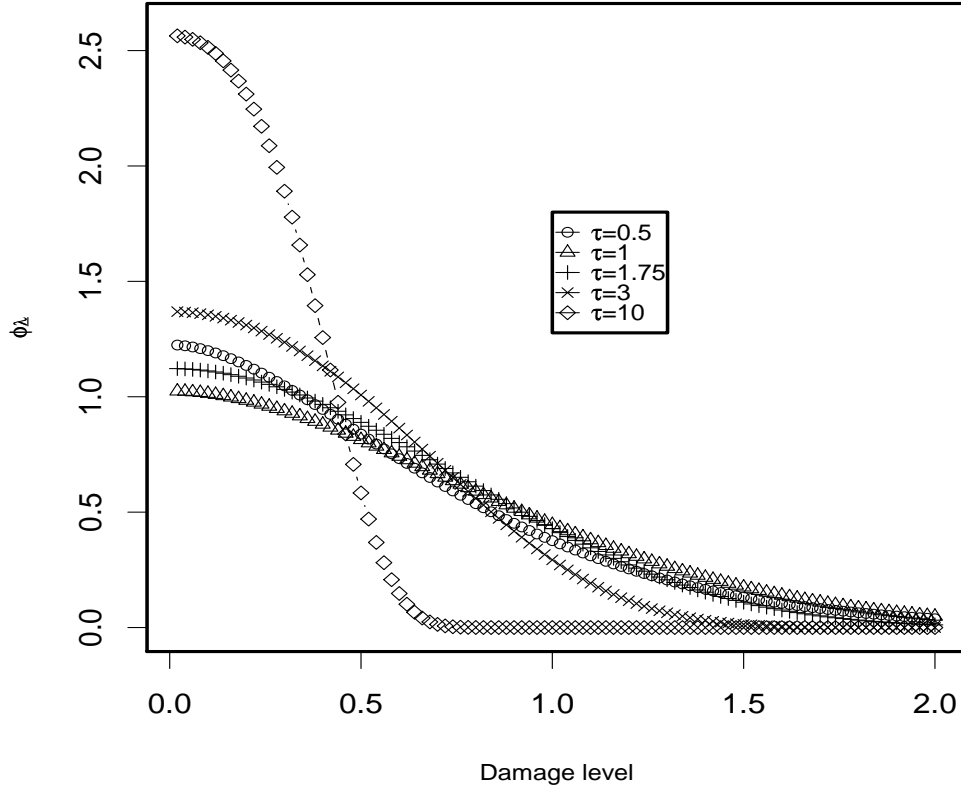
FIGURE 3. Asymptotic distribution of damage for the choice
of parameters $\beta_1 = \frac{1}{2}$, $b = 1$ and $\beta_0 = 1.9$, and various choices
of τ.

As an example, take $\beta_1 = \frac{1}{2}$, $b = 1$ and $\beta_0 = 1.9$. Using the mathematical
programming language *Maple* we compute the asymptotic growth rates given
in Figure 2. The maximum growth rate of occurs at $\tau = 1.75$. Figure 3 shows
the asymptotic distribution of damage for different values of τ. Note that
as τ increases, the asymptotic distribution becomes increasingly compressed
into the lower range of damages.

Remember that $\sigma = \sqrt{\sigma_{\text{mot}}^2 + \sigma_{\text{seg}}^2 \rho}$, where σ_{mot}^2 quantifies the random-
ness of fluctuations in the damage during the life of a cell; σ_{seg}^2 quantifies
the extent to which the damage is split unequally between the daughters
and ρ is the splitting rate. More unequal distribution of damage among the
daughter cells means that there will be effectively more randomness in the
rate of damage accumulation within a line.

We point out one implication for the evolution of generation time. Suppose that there is no mechanism available for altering the extent of damage segregation in each fission event. (Perhaps damage segregation is not actively determined, but is only a consequence of the inevitable one-way inheritance of an "old pole", or simple random fluctuation.) Suppose, though, that the organism can accelerate the generations. This has the effect of increasing σ, which may be enough to shift the asymptotic growth rate into the positive.

To be specific, suppose there is a population of 1000 bacteria, with deterministic damage accumulation at a rate x units per day when the cell has x units of damage. A cell with x units of damage has a hazard rate for reproduction in the next instant of $25.95 - x/4$, and a hazard rate for dying of $24.05 + x/4$. (Measuring time in days, this corresponds to a mean time between fission events of about 1 hour.) In the notation of our model, this means that $\rho(x) = 50/1000 = 0.05$ and $\beta(x) = 1.9 - x/2$. The minimum level of damage in a cell is 1 unit. At a fission event, if the mother has x units of damage, one daughter gets 90% of x and the other 110% of x. (Damage units must be thought of as proportional to the total volume of the cell. Thus, when a cell with x damage units divides, there is $2x$ damage to be divided up.) From equation (3), we compute that $\sigma_{\mathrm{seg}}(x) = 3.1x$. Since σ_{mot} was assumed to be 0, this means that $\sigma(x) = \sigma_{\mathrm{seg}}(x)\sqrt{.05} = 0.7x$. We see from Figure 2 that the asymptotic growth rate of the population will be -0.09, meaning that the population may be expected to decline over time.

Suppose now there were a mutant strain which had boosted its rate of reproduction to $40 - x/4$, but was penalized with a rate of dying $38.2 + x/4$. That is, fission rates were increased by 14.05 (about 35% at the minimum damage state), but the mortality rate was increased by a bit more, by 14.15. Everything else stays the same. We now have $\rho = 78.2/1000 = .0782$, meaning that $\sigma(x) = 0.87x$, and despite the mortality penalty we see that the population now has a positive asymptotic growth rate of 0.09. Instead of declining, this strain will tend to double in numbers about every 10 days.

6. Conclusions

We have introduced a mathematical model of population growth, for a population of haploid organisms that accumulate damage. This is a limit of branching processes, in which individuals accumulate damage, rising and falling at random, with an upward tendency. Under fairly general assumptions we have shown

- The population growth rate converges to a fixed rate, determined by the solutions to an ordinary differential equation (ODE);
- If the asymptotic growth rate is positive, the relative proportions of damage levels within the population converge to a fixed distribution, also given by the solution to an ODE;

- The effect of increasing damage segregation in the model (that is, causing one daughter cell to have higher damage than the parent after the split and one lower) is equivalent to increasing the randomness (diffusion) of the damage-accumulation process;
- Accelerating the turnover of generations — increasing birth and death rates equally, leaving the net birth rate unchanged — effectively increases damage segregation;
- In general, the optimum level of combined damage diffusion and damage segregation (as measured by the growth rate) is not 0, but is some finite non-zero level.

This is one possible mathematical analysis of exogenous repair. A strain of cells with deterministic damage accumulation will eventually run itself to extinction because of the increasing damage load. Perhaps surprisingly, the simple expedient of dividing the damage unequally between the offspring may be enough to rescue the line. In general, if the damage diffusion rate were sub-optimal, a mutant line could obtain a selective advantage by increasing the level of damage segregation. In fact, damage segregation could be a worthwhile investment even if it came at the cost of a slight overall increase in damage accumulation. Perhaps even more surprising, simply accelerating cell division and cell death equally, leaving the net birth rate unchanged, may be enough to shift a negative population growth rate into the positive range. Of course, there can also be too much damage segregation, and there is potential for improving growth rates by equalizing the inheritance between the daughter cells, if the variation in damage accumulation is excessive.

An abstract model such as presented in this paper is primarily a guide to thinking about experimental results, rather than a template for analyzing the data from any given experiment. This does not mean that this model cannot be experimentally tested. Some general predictions of the model are:

(1) Mechanisms for actively increasing damage segregation in reproduction should be common.
(2) While individual lines tend toward increasing damage, the overall distribution of damage in the population stabilizes.
(3) Damage segregation compensates for "too little" randomness in damage accumulation. Thus more unequal division of damage might be expected in organisms whose rate of damage accumulation is more deterministic.
(4) Manipulating the extent of damage segregation should affect the population growth rate. Under some circumstances, increasing segregation should increase the growth rate.
(5) One way of manipulating damage segregation is to manipulate the generation time. Increasing the fission rate and the death rate equally has the effect of increasing the segregation effect.

The first "prediction" is already fairly established. While asymmetric reproduction and exogenous repair were implicit in the century-old line of experiments recounted in [Bel88], the direct measure of asymmetry in protozoan reproduction has only recently become possible. Some of the organisms studied are

(1) *Caulobacter cresentus*: This bacterium grows from one end and then divides. The old end accumulates damage and senesces, while the new end experiences "rejuvenating reproduction" [ASJ03].

(2) *Escherichia coli*: While this bacterium seems to divide symmetrically, rejuvenation seems to happen preferentially in the middle, while the poles accumulate damage. [SMPT05] found declining vigor with increasing age of the inherited cellular poles.

(3) *Saccharomyces cerevisiae*: The aging of the mother cell in these budding yeast was established as long ago as [MJ59], and the functional asymmetry between mother and daughter was established by [HU77]. [LJBJ02] showed that the continuing lineage growth depends upon maintaining the asymmetry in damage state between mother (more damaged) and daughter (less damaged). An *atp2* mutant strain that failed to segregate active mitochondria preferentially to the daughter cell succumbed to clonal senescence. [AGRN03] found that carbonylated proteins are selectively retained by the mother cell, and that this requires an active SIR2 gene. (Higher activity of SIR2 also increases the longevity of the mother cell itself, which seems surprising on the face of it; but this is likely a consequence of epistatic effects, *cf.* [KMG99].)

(4) *Schizosaccharomyces pombe*: These fissioning yeast seem superficially to divide symmetrically. While there is no gross morphological distinction on the basis of which the two products of reproduction could be allocated to categories "parent" and "offspring," the fission, there is heritable asymmetry between the two fission products in size [BW99] and number of fission scars [CZB80]. The inheritance of damaged proteins was studied in [MFD$^+$06], but asymmetry of inheritance was not measured directly.

Yeast seem to be a promising class of organisms for studying the inheritance of damage. As remarked by Lai *et al.* [LJBJ02],

> The aging process of yeast cells best illustrates the cellular and generational asymmetry [....] The immortality of the yeast clone] depends upon the establishment of an age difference between a daughter cell and the mother cell that produces it. Although the daughter cell receives cellular components from the mother cell, it does not inherit the mother cells age and is always younger than the mother cell. This

age asymmetry implies that any substance or process respon-
sible for the aging of mother cells must be carefully isolated
from the daughter cells.

The biodemography of both *S. cerevisiae* and *S. pombe* is relatively well un-
derstood, and methods for tracking fission scars, carbonylated proteins and
inactive mitochondria are well developed. We have two species with quite
different types of damage segregation, and comparisons are likely to prove
illuminating. The identification of other clonal senescence mutants that act
on damage segregation, whether variant mutations to SIR2 or another gene,
would expand the toolkit for tuning damage segregation in *S. pombe*.

The recent study of carbonylation [MFD$^+$06] seems particularly amenable
to analysis in terms of exogenous repair and our model. This study examined
the distribution of damaged proteins in the whole population, finding that
the dividing cells were concentrated down near 0, while the non-dividing
(senescent) cells had a significantly higher level of damage. The main pa-
rameters in our model — the rate of damage accumulation in stationary
phase, the vital rates for cells with a given damage level, the type of damage
inheritance — could all be measured in principle. Indeed, the symmetry of
damage inheritance between the daughters was examined, but only to point
out that there is some sharing of damage, that the carbonylated proteins are
not all retained by one of the two daughters. Pushing this further, it would
be possible to measure the inequality of damage inheritance, both of car-
bonylated proteins and inactive mitochondria. Once these parameters had
been estimated, it would be possible to compare the damage distribution in
the paper with our theoretically predicted asymptotic distribution.

Comparing mutant strains with different damage segregation properties
would further refine the comparison. It would also be possible to perform
competition experiments: Broadly speaking, we would predict that as the
overall damage load increases — perhaps by exposure to paraquat or dis-
abling of antioxidants — this would shift the optimal level of damage segre-
gation. In some simple choices of parameters for the model this shift would
be toward more extreme damage segregation, the same effect that would be
predicted from decreasing the variability of damage accumulation. Thus,
we might expect that strains exposed to such toxic environments over some
time would evolve to show higher levels of damage segregation. If damage
segregation is not controlled by active mechanisms, this means that increas-
ing damage accumulation should select for a faster turnover of generations:
simultaneously higher rates of cell death and fissioning.

Perhaps no simple resolution should be expected. We are examining the
interaction of individual-level aging downward, with aging of parts of indi-
viduals, and simultaneously upward, toward population-level aging. In the
present model one might say that there is a partial individualization of senes-
cence. That is, while there is no identifiable individual who ages and dies,
leaving behind youthful descendants, damage segregation has transformed

the senescence problem plaguing the entire population into a problem of some individual cells.

There has been some controversy (see [Wol05], and the response [ST05]) about whether results such as those of [SMPT05] reflect genuine "aging." Perhaps more profitable is to see, in this growing family of experimental results, clues to the broader context of aging: Paradigmatic aging in our species and similar ones is one of a class of mechanisms which function to redistribute damage within a population. Most metazoans, perhaps inevitably, have converged on the extreme strategy of keeping essentially all the damage (even generating much more damage in the process), and produce pristine offspring. In protozoans, there seem to be a broader range of mechanisms, and degrees of damage differentiation in the end-products of reproduction.

Is this relativization of senescence of any relevance for metazoans, then? It is, for at least two separate reasons. The first is that the propagation of the germ line is in many senses comparable to the propagation of a line of protozoans. As eloquently commented by Lai *et al.* [LJBJ02], "Some of the key questions in aging concern the differences between germline and soma. Any mechanism invoked to explain the aging of the soma must also be able to accommodate the immortality of the germline. At the level of the organism, the issue is the renewal that occurs at each generation, providing the progeny a fresh start with the potential for a full life span." This principle may also be significant for the regulation of replicative senescence in somatic stem cells or other somatic cells. The recent discovery of non-random segregation in mouse mitotic chromosome replication [AK06] may be a hint in this direction.

The other reason is perhaps more profound, and certainly more speculative. Over the past several decades, mathematical theory has played a significant part in the evolving discussion of risk-management and bet-hedging in natural selection. J. Gillespie's seminal treatment [Gil74] notes that

> the variance in the numbers of offspring of a genotype has two components, the within-generation component resulting from different individuals of the same genotype having different numbers of offspring, and a between-generation component due to the effects of a changing environment.

The general conclusion has been that lower variance in essential demographic traits is selectively favored [FS90, Goo84], although this picture is complicated by varying environments, if the variance is associated with variable response to the environment [EH94]. Damage accumulation falls into a third class of variance: variable epigenetic inheritance of a resource shared between offspring.

Our model departs from the models of within-generation variation in which the varying phenotypes of siblings are independent, but is allied

with models of resource sharing within families. In the case of damage-accumulation the "resource" is the undamaged cell components, but this model might in principle be applied to the transmission of resources or status from parents to offspring. In contrast to the general selective advantage for reduced within-generation variability in the uncorrelated setting, the results of our analysis suggest that increased variability may be selectively favored when the phenotype is a shared resource.

This beneficial variance may have some relevance for the growing recognition that the evolution of longevity depends fundamentally on the nature of intergenerational transfers. All the work on this problem of which we are aware, particularly [Lee03, KR02, RK03, CL06] implicitly presumes that resources are divided equally according to need (though [HDS02] points out that the goal of equality may still produce systematic biases based on birth-order). The key paper of Trivers [Tri74] explicitly opposes a parental goal of equality against the offspring's interest in monopolizing resources. Models of offspring provisioning in this tradition, such as [PML89, RHP02], seem to assume a "diminishing returns" to investment, hence higher fitness for reduced spread in offspring quality, except when there is a threshold for survival that only one is likely to cross. Our model suggests that the cumulative effect of exponential growth can easily make unequal division of resources a winning strategy. This inequality may be purely random, and need not depend on sibling competition or some other strategy for identifying and rewarding the inherently superior offspring.

7. Mathematical methods

Define $(P_t)_{t \geq 0}$ to be the semigroup generated by

$$\mathcal{L}\phi := \frac{1}{2}\sigma^2\phi'' + b\phi' + \beta\phi$$

with boundary condition

$$(8) \qquad p_0 \frac{\sigma(0)^2}{2}\phi'(0) = (1 - p_0)\phi(0)$$

for some fixed $0 \leq p_0 \leq 1$. (This semigroup will not, in general, be sub-Markovian because β can take positive values). As we observe in Section 7.2, $\mathbb{E}[\langle \phi, X(t) \rangle] = \int_{\mathbb{R}^+} P_t\phi(x)\,d\nu(x)$ when X_0 is the deterministic measure ν, and so the behavior of $(X_t)_{t \geq 0}$ is governed by that of $(P_t)_{t \geq 0}$, at least at the level of expectations. The choice $p_0 = 1$ is most relevant for the description of fissioning organisms, because it corresponds to complete reflection at the state 0 representing no damage. Other choices of p_0 would imply the rather anomalous presence of an additional singular killing mechanism at 0. However, since the mathematical development is unchanged by the assumption of a general boundary condition, we do not specialize to complete reflection.

It turns out that the entire long-term behavior of $(X_t)_{t \geq 0}$ is rather simply connected to that of $(P_t)_{t \geq 0}$. Let $(P_t^*)_{t \geq 0}$ be the adjoint semigroup generated

by

$$\mathcal{L}^*\phi(x) := \frac{1}{2}\frac{d}{dx^2}\left[\sigma^2(x)\phi(x)\right] - \frac{d}{dx}\left[b(x)\phi(x)\right] + \beta(x)\phi(x).$$

with boundary condition

$$(9) \qquad p_0 \frac{\sigma(0)^2}{2}\left(\phi'(0) - 2b(0)\phi(0)\right) = (1-p_0)\phi(0).$$

For any λ, define ϕ_λ to be the unique solution to the initial value problem
(10)

$$\mathcal{L}^*\phi_\lambda = \lambda\phi_\lambda \quad \text{with } \phi_\lambda(0) = p_0 \text{ and } \frac{\sigma(0)^2}{2}\left(\phi'_\lambda(0) - 2b(0)\phi_\lambda(0)\right) = 1 - p_0.$$

Put

$$(11) \qquad \underline{\lambda} := \inf\left\{\lambda : \phi_\lambda(x) \text{ is non-negative for all } x\right\}.$$

We recall in Proposition 7.2 that, under suitable hypotheses, for a compactly supported finite measure ν

$$\lim_{t\to\infty} \frac{\langle P_{t+s}\mathbf{1}, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle} = e^{\underline{\lambda}s}$$

so that *a fortiori*

$$\lim_{t\to\infty} t^{-1}\log\langle P_t\mathbf{1}, \nu\rangle = \underline{\lambda},$$

and, moreover,

$$\lim_{t\to\infty} \frac{\langle P_t\varphi, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle} = \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}$$

for a bounded test function φ. We subsequently show in Theorem 7.4, again under suitable hypotheses, that if $\underline{\lambda} > 0$, then

$$\lim_{t\to\infty} \frac{\langle\varphi, X_t\rangle}{\langle P_t\mathbf{1}, \nu\rangle} = W\frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}$$

in probability, where W is a non-trivial random variable (that doesn't depend on φ). In particular, the asymptotic growth rate of the total mass $\langle\mathbf{1}, X_t\rangle$ is $\underline{\lambda}$ and

$$\lim_{t\to\infty} \frac{\langle\varphi, X_t\rangle}{\langle\mathbf{1}, X_t\rangle} = \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}$$

We show in Section 7.3 under quite general conditions (including the assumption that β is non-increasing so that $\beta_\infty = \inf_x \beta(x)$) that the presence of some randomness in either the damage and accumulation diffusion or the damage segregation mechanism is beneficial for the long-term growth of the population but too much randomness is counterproductive. That is, if b, β and ρ are held fixed, then $\underline{\lambda}$ converges to β_∞ as the diffusion rate function $\sigma = \sqrt{\sigma_{\text{mot}}^2 + \sigma_{\text{seg}}^2}$ goes to either 0 or ∞, whereas $\underline{\lambda} > \beta_\infty$ for finite σ.

7.1. **Results from** [SE05]. Essential to linking the long-term growth be-
haviour of the superprocess to the theory of quasistationary distributions is
the observation that $\mathcal{L} - \beta^*$ (recall that β^* is a constant, the upper bound
on β) is the generator of a killed diffusion semigroup $Q_t\phi = e^{-\beta^* t}P_t\phi$. Thus,
when we have a result stating that Q_t converges to a stationary distribution
with density a multiple of $\phi_{\underline{\lambda}}$, meaning that for any bounded test function
$\varphi : \mathbb{R}^+$, and any compactly supported finite measure ν,

$$\lim_{t\to\infty} \frac{\langle Q_t\varphi, \nu \rangle}{\langle Q_t\mathbf{1}, \nu \rangle} = \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz},$$

then the same holds for P_t.

For $t \geq 0$ and ν a compactly supported finite measure on $\mathbb{R}^+$, set

$$(12) \qquad\qquad \omega_t(\nu) := \frac{\langle P_t\mathbf{1}, \nu \rangle}{P_t\mathbf{1}(1)}.$$

When $\nu = \delta_x$, write $\omega_t(x)$. Note that

$$(13) \qquad\qquad \omega_t(\nu) = \int_0^\infty \omega_t(x)\,d\nu(x)$$

for any compactly supported finite measure ν. Define

$$(14) \qquad\qquad \omega_*(x, \nu) = \sup_{t\geq 0} \frac{\omega_t(x)}{\omega_t(\nu)}.$$

Assume the following condition: For all compactly supported finite mea-
sures ν on $\mathbb{R}^+$, and some $\epsilon > 0$

$$(GB2) \qquad \sup_{s\geq 0}\sup_{x\in\mathbb{R}^+} e^{-(2\underline{\lambda}-\epsilon)s}\int \omega_*(y, \nu)^2 P_s(x, dy) < \infty.$$

While (GB2) is an abstract condition, it is implied by a fairly concrete
condition on the diffusion parameters.

Lemma 7.1. *Condition (GB2) always holds if the net birth rate β is mono-
tone non-increasing, and there is complete reflection at 0.*

Proof. Changing β by a constant leaves ω_t, hence ω_* as well, unchanged.
Thus, we may assume that $\beta \leq 0$, so that P_t is the semigroup of a killed
diffusion.

Given $x < x'$, we may couple the diffusion X_t started at x with a diffusion
X'_t, with identical dynamics but started at x', so that $X_t \leq X'_t$ for all
t. By the monotonicity of β, this implies that $P_t\mathbf{1}(x) \geq P_t\mathbf{1}(x')$, since
$P_t\mathbf{1}(x) = \mathbb{P}_x\{\tau_\partial > t\}$. Consequently, ω_t is monotonically non-increasing,
and so is ω_*. In particular, for all y, $\omega_*(y, \nu) \leq \omega_*(0, \nu)$, which is finite, by
the results of section 2.5 of [SE05]. Then

$$\sup_{s\geq 0}\sup_{x\in K} e^{-(2\underline{\lambda}-\epsilon)s}\int \omega_*(y, \nu)^2 P_s(x, dy) \leq \omega_*(0, \nu)^2 < \infty.$$

$\square$

We will also need to assume the technical condition

(LP) $\mathcal{L}^*$ is in the limit-point case at ∞.

We define
$$\tilde{b}(z) := \frac{b \circ F^{-1}(x)}{\sigma \circ F^{-1}(x)} - \frac{1}{2}\sigma' \circ F^{-1}(x),$$

and $\tilde{\beta}(x) := \beta \circ F^{-1}(x)$, where $F(y) := \int_0^y du/\sigma(u)$ is the Liouville trans-form, the spatial transformation that converts the diffusion coefficient into a constant. Then Lemma 2.1 of [SE05] says that (LP) holds whenever

(LP') $\liminf\limits_{x \to \infty} x^{-2}(\tilde{b}(x)^2 + \tilde{b}'(x) + 2\tilde{\beta}(x)) > -\infty.$

Examples which do not satisfy this condition must have pathological fluctu-ations in b.

Define ψ_λ to be the unique solution to the initial value problem

(15) $\mathcal{L}\psi_\lambda = \lambda\psi_\lambda$ with $\psi_\lambda(0) = p_0$ and $\dfrac{\sigma(0)^2}{2}\psi_\lambda'(0) = 1 - p_0.$

We summarize relevant results from Lemma 2.2, Theorem 3.4 and Lemma 5.2 of [SE05].

Proposition 7.2. *Assume the conditions (GB) and (LP).*

(i) *The eigenvalue $\underline{\lambda}$ is finite.*

(ii) *The semigroup $(P_t)_{t \geq 0}$ has an asymptotic growth rate η. That is, for any compactly supported ν, and any positive s,*

(16) $$\lim_{t \to \infty} \frac{\langle P_{t+s}\mathbf{1}, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle} = e^{\eta s}.$$

(iii) *The following implications hold:*
$$\underline{\lambda} > \beta_\infty \Longrightarrow \eta = \underline{\lambda} > \beta_\infty$$
$$\underline{\lambda} = \beta_\infty \Longrightarrow \eta = \underline{\lambda} = \beta_\infty$$
$$\underline{\lambda} < \beta_\infty \Longrightarrow \eta = \underline{\lambda} \text{ or } \eta = \beta_\infty$$

(iv) *If $\eta = \underline{\lambda} \neq \beta_\infty$, then, for any compactly supported finite measure ν,*

(17) $$\lim_{t \to \infty} \omega_t(\nu) = \int \frac{\psi_\eta(x)}{\psi_\eta(1)}\, d\nu(x),$$

and, for any bounded test function φ,

(18) $$\lim_{t \to \infty} \frac{\langle P_t\varphi, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle} = \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}.$$

(v) *If β is non-constant and non-increasing and $p_0 = 1$ (that is, there is complete reflection at 0), then (18) holds if and only if $\underline{\lambda} > \beta_\infty$. In particular, (18) holds if $p_0 = 1$ and β is non-increasing and un-bounded below (so that $\beta_\infty = -\infty$).*

Proof. The only part that is not copied directly from [SE05] is (v). If $\underline{\lambda} > \beta_\infty$, then $\eta = \underline{\lambda} > \beta_\infty$ by (iii) and (18) holds by (iv). Suppose that (18) holds but $\underline{\lambda} \leq \beta_\infty$. Since there is no killing at 0 ($p_0 = 1$), by (8), the constant function is in the domain of $\mathcal{L}$. Thus, we may apply the Kolmogorov backward equation to see that by (16),

$$
\begin{aligned}
\eta &= \frac{d}{ds}\Big|_{s=0} \left(\lim_{t\to\infty} \frac{\langle P_{t+s}\mathbf{1}, \nu \rangle}{\langle P_t \mathbf{1}, \nu \rangle} \right) \\
&= \frac{d}{ds}\Big|_{s=0} \left(\lim_{t\to\infty} \frac{\langle P_t(P_s\mathbf{1}), \nu \rangle}{\langle P_t \mathbf{1}, \nu \rangle} \right) \text{ by (18)} \\
&= \frac{d}{ds}\Big|_{s=0} \left(\frac{\int_0^\infty P_s\mathbf{1}(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz} \right) \\
&= \frac{\int_0^\infty \mathcal{L}\mathbf{1}(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz} \\
&= \frac{\int_0^\infty \beta(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}.
\end{aligned}
$$

Hence $\eta > \beta_\infty$ because β is non-constant and $\phi_{\underline{\lambda}}(z)$ is non-negative for all z and strictly positive for z close to 0. (In fact, $\phi_{\underline{\lambda}}$ is strictly positive for all z). However, this contradicts (iii). $\qquad\square$

A simple consequence of Proposition 7.2 is the following.

Corollary 7.3. *For any compactly supported finite measure ν and any $\epsilon > 0$, there are positive constants $0 < c_{\epsilon,\nu} \leq C_{\epsilon,\nu} < \infty$ such that if $0 \leq t' \leq t'' < \infty$, then*

$$
\text{(19)} \qquad c_{\epsilon,\nu}e^{(\eta-\epsilon)(t''-t')} \leq \frac{\langle P_{t''}\mathbf{1}, \nu \rangle}{\langle P_{t'}\mathbf{1}, \nu \rangle} \leq C_{\epsilon,\nu}e^{(\eta+\epsilon)(t''-t')}.
$$

Proof. By replacing P_t by $e^{-\beta^* t}P_t$, we may suppose that $(P_t)_{t\geq 0}$ is the semi-group of a killed diffusion, so that $\langle P_t\mathbf{1}, \nu \rangle$ is non-increasing in t.

There is some integer N such that if $N \leq n$ is an integer, then

$$
e^{\eta-\epsilon} \leq \frac{\langle P_{n+1}\mathbf{1}, \nu \rangle}{\langle P_n\mathbf{1}, \nu \rangle} \leq e^{\eta+\epsilon}.
$$

If $N \leq n' \leq n''$ are integers, then, since

$$
\frac{\langle P_{n''}\mathbf{1}, \nu \rangle}{\langle P_{n'}\mathbf{1}, \nu \rangle} = \prod_{n=n'}^{n''-1} \frac{\langle P_{n+1}\mathbf{1}, \nu \rangle}{\langle P_n\mathbf{1}, \nu \rangle},
$$

it follows that

$$
e^{(\eta-\epsilon)(n''-n')} \leq \frac{\langle P_{n''}\mathbf{1}, \nu \rangle}{\langle P_{n'}\mathbf{1}, \nu \rangle} \leq e^{(\eta+\epsilon)(n''-n')}.
$$

Note that if n', n'' are arbitrary non-negative integers, then

$$
\frac{\langle P_{n''}\mathbf{1}, \nu \rangle}{\langle P_{n'}\mathbf{1}, \nu \rangle} = \frac{\langle P_{n''}\mathbf{1}, \nu \rangle}{\langle P_{n''\vee N}\mathbf{1}, \nu \rangle} \frac{\langle P_{n'\vee N}\mathbf{1}, \nu \rangle}{\langle P_{n'}\mathbf{1}, \nu \rangle} \frac{\langle P_{n''\vee N}\mathbf{1}, \nu \rangle}{\langle P_{n'\vee N}\mathbf{1}, \nu \rangle}.
$$

On the one hand,

$$\min_{m',m''\leq N} \frac{\langle P_{m''}\mathbf{1},\nu\rangle}{\langle P_N\mathbf{1},\nu\rangle}\frac{\langle P_N\mathbf{1},\nu\rangle}{\langle P_{m'}\mathbf{1},\nu\rangle} \leq \frac{\langle P_{n''}\mathbf{1},\nu\rangle}{\langle P_{n''\vee N}\mathbf{1},\nu\rangle}\frac{\langle P_{n'\vee N}\mathbf{1},\nu\rangle}{\langle P_{n'}\mathbf{1},\nu\rangle} \leq \max_{m',m''\leq N} \frac{\langle P_{m''}\mathbf{1},\nu\rangle}{\langle P_N\mathbf{1},\nu\rangle}\frac{\langle P_N\mathbf{1},\nu\rangle}{\langle P_{m'}\mathbf{1},\nu\rangle}.$$

On the other hand,

$$e^{-N|\eta-\epsilon|}e^{(\eta-\epsilon)(n''-n')} \leq \frac{\langle P_{n''\vee N}\mathbf{1},\nu\rangle}{\langle P_{n'\vee N}\mathbf{1},\nu\rangle} \leq e^{N|\eta+\epsilon|}e^{(\eta+\epsilon)(n''-n')}.$$

Thus the claimed inequality holds with suitable constants for t', t'' restricted to the non-negative integers.

For arbitrary $t' \leq t''$ with $\lceil t'\rceil \leq \lfloor t''\rfloor$ we have

$$c_{\epsilon,\nu}e^{-2|\eta-\epsilon|}e^{(\eta-\epsilon)(t''-t')} \leq c_{\epsilon,\nu}e^{(\eta-\epsilon)(\lceil t''\rceil-\lfloor t'\rfloor)}$$
$$\leq \frac{\langle P_{\lceil t''\rceil}\mathbf{1},\nu\rangle}{\langle P_{\lfloor t'\rfloor}\mathbf{1},\nu\rangle} \leq \frac{\langle P_{t''}\mathbf{1},\nu\rangle}{\langle P_{t'}\mathbf{1},\nu\rangle} \leq \frac{\langle P_{\lfloor t''\rfloor}\mathbf{1},\nu\rangle}{\langle P_{\lceil t'\rceil}\mathbf{1},\nu\rangle}$$
$$\leq C_{\epsilon,\nu}e^{(\eta+\epsilon)(\lfloor t''\rfloor-\lceil t'\rceil)} \leq e^{2|\eta+\epsilon|}C_{\epsilon,\nu}e^{2|\eta+\epsilon|}e^{(\eta+\epsilon)(t''-t')}.$$

and the result holds for such t', t'' by suitably adjusting the constants.

If $t' \leq t''$ but $\lceil t'\rceil > \lfloor t''\rfloor$ (so that $t'' - t' \leq 1$), then the observation

$$\left(\frac{\langle P_{\lceil t'\rceil}\mathbf{1},\nu\rangle}{\langle P_{\lfloor t''\rfloor}\mathbf{1},\nu\rangle}\right)^{-1} \leq \frac{\langle P_{t''}\mathbf{1},\nu\rangle}{\langle P_{t'}\mathbf{1},\nu\rangle} \leq \left(\frac{\langle P_{\lfloor t'\rfloor}\mathbf{1},\nu\rangle}{\langle P_{\lceil t''\rceil}\mathbf{1},\nu\rangle}\right)^{-1}$$

shows that a further adjustment of the constants suffices to complete the proof. □

7.2. **Scaling limit.** The asymptotic behavior of Dawson-Watanabe super-processes has been undertaken by Engländer and Turaev [ET02], who applied general spectral theory to demonstrate, under certain formal conditions, the convergence in distribution of the rescaled measure $e^{-\lambda_c t}X_t$, where λ_c is the generalized principal eigenvalue. Convergence in distribution was improved to convergence in probability by Engländer and Winter [EW05]. We take a different route to proving a similar scaling limit, which has two advantages.

(1) Our proof is more direct, and the conditions, when they hold, straightforward to check.
(2) Our proof holds in some cases when the results of [ET02] do not apply. In particular, the scaling need not be exactly exponential.

On the other hand, our approach is more restrictive, in being applicable only to processes on $\mathbb{R}^+$.

Our proof depends on Dynkin's formulae [Dyn91] for the moments of a Dawson-Watanabe superprocess. For any bounded measurable $\varphi, \varphi' : \mathbb{R}^+ \to$

$[-1,1]$, any starting distribution ν, and any $0 \le t \le t'$,

$$\mathbb{E}_\nu\left[\langle \varphi, X_t \rangle\right] = \langle P_t \varphi, \nu \rangle,$$

(20)
$$\mathbb{E}_\nu\left[\langle \varphi, X_t \rangle \langle \varphi', X_{t'} \rangle\right] = \langle P_t \varphi, \nu \rangle \langle P_{t'} \varphi', \nu \rangle$$
$$+ \left\langle \int_0^t P_s \left[\rho \cdot P_{t-s}\varphi \cdot P_{t'-s}\varphi'\right] ds, \nu \right\rangle.$$

Note by Proposition 7.2 that in the following result the assumptions $\eta = \underline{\lambda} > 0$ and (18) are implied by the assumptions $\eta = \underline{\lambda} > 0$ and $\underline{\lambda} \ne \beta_\infty$.

Theorem 7.4. *Suppose that the conditions (LP) and (GB2) of Section 7.1 hold. Suppose further that $\eta = \underline{\lambda} > 0$ and (18) holds. Then the rescaled random measure $\widetilde{X}_t := \langle P_t \mathbf{1}, \nu \rangle^{-1} X_t$ converges in L^2 to a random multiple of the deterministic finite measure which has density $\phi_{\underline{\lambda}}$ with respect to Lebesgue measure. That is,*

(21)
$$W := \lim_{t \to \infty} \langle \mathbf{1}, \widetilde{X}_t \rangle$$

exists in L^2, and if φ is any bounded test function,

(22)
$$\lim_{t \to \infty} \mathbb{E}_\nu\left[\left\{ \langle \varphi, \widetilde{X}_t \rangle - W \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)\,dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)\,dz} \right\}^2\right] = 0.$$

The long-term growth rate of the total mass of X_t is $\lim_{t \to \infty} t^{-1}\log\langle \mathbf{1}, X_t \rangle = \underline{\lambda}$.

Proof. From Proposition 7.2, we know that

$$\lim_{t \to \infty} \mathbb{E}_\nu[\langle \varphi, \widetilde{X}_t \rangle] = \frac{\langle P_t \varphi, \nu \rangle}{\langle P_t \mathbf{1}, \nu \rangle} = \frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}.$$

Also,

$$\langle P_t \mathbf{1}, \nu \rangle^{-1} \langle P_{t'} \mathbf{1}, \nu \rangle^{-1} \int_0^t P_s\left[\rho \cdot P_{t-s}\varphi \cdot P_{t'-s}\varphi'\right](x)ds$$
$$= \int_0^\infty \int \mathbf{1}_{s \le t} \frac{\langle P_{t-s}\mathbf{1}, \nu \rangle}{\langle P_t \mathbf{1}, \nu \rangle} \frac{\langle P_{t'-s}\mathbf{1}, \nu \rangle}{\langle P_{t'}\mathbf{1}, \nu \rangle}$$
$$\times \rho(y)\frac{\omega_{t-s}(y)}{\omega_{t-s}(\nu)}\frac{\omega_{t'-s}(y)}{\omega_{t'-s}(\nu)}\frac{P_{t-s}\varphi(y)}{P_{t-s}\mathbf{1}(y)}\frac{P_{t'-s}\varphi'(y)}{P_{t'-s}\mathbf{1}(y)}P_s(x, dy)ds.$$

For fixed y the integrand converges as $t, t' \to \infty$ to

$$\rho(y)\left(\frac{\psi_{\underline{\lambda}}(y)}{\langle \psi_{\underline{\lambda}}, \nu \rangle}\right)^2\left(\frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz}\right)^2 e^{-2\underline{\lambda}s}.$$

By (19), for any $t \le t'$ the integrand is bounded for any positive ϵ by

$$\rho^* \frac{1}{c_{\epsilon,\nu}} e^{-2s(\underline{\lambda}-\epsilon)}\left(\sup_\tau \frac{\omega_\tau(y)}{\omega_\tau(\nu)}\right)^2 \le \rho^* \frac{1}{c_{\epsilon,\nu}} e^{-2s(\underline{\lambda}-\epsilon)}\omega_*(y, \nu)^2,$$

where $\rho^* := \sup_x \rho(x)$. Condition (GB2) implies that this upper bound has finite integral for ϵ sufficiently small. This allows us to apply the Dominated Convergence Theorem to conclude that

$$
\begin{aligned}
(23) \quad & \lim_{t' \geq t \to \infty} \langle P_t \mathbf{1}, \nu \rangle^{-1} \langle P_{t'}, \mathbf{1}, \nu \rangle^{-1} \left\langle \int_0^t P_s \left[\rho \cdot P_{t-s}\varphi \cdot P_{t'-s}\varphi' \right] ds, \nu \right\rangle \\
& = \left(\frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\langle \psi_{\underline{\lambda}}, \nu \rangle \int_0^\infty \phi_{\underline{\lambda}}(z)dz} \right)^2 \int_0^\infty e^{-2\underline{\lambda}s} \langle P_s(\rho\psi_{\underline{\lambda}})^2, \nu \rangle ds.
\end{aligned}
$$

That is, for any $\epsilon > 0$, there is T such that for all $t' \geq t \geq T$

$$
\left| \langle P_t \mathbf{1}, \nu \rangle^{-1} \langle P_{t'}, \mathbf{1}, \nu \rangle^{-1} \left\langle \int_0^t P_s \left[\rho \cdot P_{t-s}\varphi \cdot P_{t'-s}\varphi' \right] ds, \nu \right\rangle - M(\nu, \varphi) \right| < \epsilon,
$$

where $M(\nu, \varphi)$ is the right-hand side of (23).

By (20), we may find T_ϵ such that for all $t' \geq t \geq T_\epsilon$,

$$
\begin{aligned}
& \left| \mathbb{E}_\nu[\langle \varphi, \widetilde{X}_t \rangle \langle \varphi', \widetilde{X}_{t'} \rangle] \right. \\
& \left. - K \left(\frac{\int_0^\infty \varphi(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz} \right) \left(\frac{\int_0^\infty \varphi'(z)\phi_{\underline{\lambda}}(z)dz}{\int_0^\infty \phi_{\underline{\lambda}}(z)dz} \right) \right| < \epsilon,
\end{aligned}
$$

where

$$
K := 1 + \langle \psi_{\underline{\lambda}}, \nu \rangle^{-2} \int_0^\infty e^{-2\underline{\lambda}s} \langle P_s(\rho\psi_{\underline{\lambda}})^2, \nu \rangle ds.
$$

Then, for $t' \geq t \geq T_\epsilon$,

$$
\begin{aligned}
& \mathbb{E}_\nu \left[\left(\langle \varphi, \widetilde{X}_t \rangle - \langle \varphi, \widetilde{X}_{t'} \rangle \right)^2 \right] \\
& = \mathbb{E}_\nu[\langle \varphi, \widetilde{X}_t \rangle^2] + \mathbb{E}_\nu[\langle \varphi, \widetilde{X}_{t'} \rangle^2] - 2\mathbb{E}_\nu[\langle \varphi, \widetilde{X}_t \rangle \langle \varphi, \widetilde{X}_{t'} \rangle] \\
& < 4\epsilon.
\end{aligned}
$$

Thus $\langle \varphi, \widetilde{X}_t \rangle$ is a Cauchy sequence in L^2 and converges to a limit. In particular, there is a random finite measure $\tilde{X}_\infty$ such that $\tilde{X}_t \to \tilde{X}_\infty$ in probability in the topology of weak convergence of finite measure on $\mathbb{R}^+$.

It remains only to show that the limit is a multiple of the finite measure with density $\phi_{\underline{\lambda}}$. For any bounded test function φ, let

$$
A_t := \langle \varphi, \widetilde{X}_t \rangle - \langle \mathbf{1}, \widetilde{X}_t \rangle \langle \varphi, \phi_{\underline{\lambda}} \rangle.
$$

By (20),

$$\mathbb{E}[A_t^2] = \left(\frac{\langle P_t\varphi, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle}\right)^2 + \left\langle \int_0^t P_s\left[\rho \cdot \left(\frac{P_{t-s}\varphi}{\langle P_t\mathbf{1}, \nu\rangle}\right)^2\right] ds, \nu\right\rangle$$

$$+ \langle\varphi, \phi_{\underline{\lambda}}\rangle^2 + \langle\varphi, \phi_{\underline{\lambda}}\rangle^2 \left\langle \int_0^t P_s\left[\rho \cdot \left(\frac{P_{t-s}\mathbf{1}}{\langle P_t\mathbf{1}, \nu\rangle}\right)^2\right] ds, \nu\right\rangle$$

$$- 2\langle\varphi, \phi_{\underline{\lambda}}\rangle\frac{\langle P_t\varphi, \nu\rangle}{\langle P_t\mathbf{1}, \nu\rangle}$$

$$- 2\langle\varphi, \phi_{\underline{\lambda}}\rangle\left\langle \int_0^t P_s\left[\rho \cdot \frac{P_{t-s}\mathbf{1}}{\langle P_t\mathbf{1}, \nu\rangle}\frac{P_{t-s}\varphi}{\langle P_t\mathbf{1}, \nu\rangle}\right] ds, \nu\right\rangle,$$

which converges to 0 as $t \to \infty$. $\qquad\square$

7.3. Optimal growth conditions.

Theorem 7.5. *Suppose b is a fixed drift function, β is a fixed non-increasing, non-constant net reproduction function, and (σ_m) is a sequence of diffusion functions. Write $(P_t^{(m)})_{t\geq 0}$ for the semigroup associated with σ_m, b, and β, assuming complete reflection at 0. Assume that (18) holds for each m. Denote the corresponding asymptotic growth rate by $\underline{\lambda}_m > \beta_\infty$.*

Suppose that either of the following two conditions hold.

(a)

$$\inf_m \inf_{x\in\mathbb{R}^+} \frac{b(x)}{\sigma_m(x)} - \sigma'_m(x) =: \gamma > -\infty$$

and

$$\lim_{m\to\infty} \inf_{x\in\mathbb{R}^+} \sigma_m(x) = \infty,$$

(b)

$$\inf_{x\in\mathbb{R}^+} b(x) =: b_* > 0$$

and

$$\lim_{m\to\infty} \sup_{x\in\mathbb{R}^+} \sigma_m(x) = 0.$$

Then $\lim_{m\to\infty} \underline{\lambda}_m = \beta_\infty$.

Proof. The condition and the conclusion remain true if β is changed by a constant, so we may assume, without loss of generality, that β is non-positive. This means that $P_t^{(m)}$ is the semigroup of a killed diffusion $\hat{Y}^{(m)}$. Let $\tau_\partial^{(m)}$ be the killing time of $\hat{Y}^{(m)}$. Write $Y^{(m)}$ for the diffusion without killing that corresponds to $\hat{Y}^{(m)}$. Assume that $\beta_\infty > -\infty$. The proofs for $\beta_\infty = -\infty$ are similar and are left to the reader. Since $\underline{\lambda}_m > \beta_\infty$ always holds, it suffices in both cases to establish that $\liminf_{m\to\infty} \underline{\lambda}_m \leq \beta_\infty$.

Consider first the case of condition (a). It follows from the assumption that 0 is a regular boundary point that the Liouville transformation

$F_m(x) := \int_0^x du/\sigma_m(u)$ is finite for all $x \in \mathbb{R}^+$. The transformed diffusion $\hat{V}^{(m)} := F_m \circ \hat{Y}^{(m)}$ has diffusion function the constant 1, drift function

$$(24) \qquad \frac{b \circ F_m^{-1}}{\sigma \circ F_m^{-1}} - \frac{1}{2}\sigma' \circ F_m^{-1},$$

and killing rate function $-\beta \circ F_m^{-1}$. The asymptotic growth rate for $\hat{V}^{(m)}$ is also $\underline{\lambda}_m$. Write $V^{(m)} := F_m \circ Y^{(m)}$ for the diffusion without killing that corresponds to $\hat{V}^{(m)}$.

Since $\lim_{m \to \infty} \inf_{x \in \mathbb{R}^+} \sigma_m(x) = \infty$, it follows that $\lim_{m \to \infty} F_m^{-1}(x) = \infty$ for all $x > 0$. Hence, given $\epsilon > 0$ there exists M such that for $m \geq M$,

$$\beta \circ F_m^{-1}(x) \leq \beta_\epsilon(x),$$

where

$$\beta_\epsilon(x) := \begin{cases} 0, & 0 \leq x < \epsilon, \\ (\beta_\infty + \epsilon)\frac{(x-\epsilon)}{\epsilon}, & \epsilon \leq x < 2\epsilon, \\ \beta_\infty + \epsilon, & x \geq 2\epsilon. \end{cases}$$

Write W for Brownian motion with drift γ and complete reflection at 0. By the comparison theorem for one-dimensional diffusions and the assumption that β is non-increasing,

$$\mathbb{E}\left[\exp\left(\int_0^t \beta \circ F_m^{-1}(V_s^{(m)})\,ds\right)\right] \leq \mathbb{E}\left[\exp\left(\int_0^t \beta \circ F_m^{-1}(W_s)\,ds\right)\right]$$
$$\leq \mathbb{E}\left[\exp\left(\int_0^t \beta_\epsilon(W_s)\,ds\right)\right]$$

if $V^{(m)}$ and W have the same initial distribution. Thus $\underline{\lambda}_m \leq \tilde{\underline{\lambda}}_\epsilon$, where

$$\tilde{\underline{\lambda}}_\epsilon := \inf\{\lambda : \tilde{\phi}_{\lambda,\epsilon}(x) \text{ is non-negative for all } x\}$$

for $\tilde{\phi}_{\lambda,\epsilon}$ the unique solution to the initial value problem

$$(25) \quad \frac{1}{2}\tilde{\phi}''_{\lambda,\epsilon} - \gamma\tilde{\phi}_{\lambda,\epsilon} + \beta_\epsilon\tilde{\phi}_{\lambda,\epsilon} = \lambda\tilde{\phi}_{\lambda,\epsilon} \quad \text{with } \tilde{\phi}_{\lambda,\epsilon}(0) = 1 \text{ and } \tilde{\phi}'_\lambda(0) = \gamma.$$

Solutions of the equation

$$\frac{1}{2}f''(x) - \gamma f'(x) - rf(x) = \lambda f(x)$$

for some constant r are linear combinations of the two functions

$$\exp\left(\left(\gamma - \sqrt{\gamma^2 + 2(\lambda + r)}\right)x\right)$$

and

$$\exp\left(\left(\gamma + \sqrt{\gamma^2 + 2(\lambda + r)}\right)x\right).$$

Solutions of the equation

$$\frac{1}{2}f''(x) - \gamma f'(x) + (p - qx)f(x) = \lambda f(x)$$

for some constants p and q are linear combinations of the two functions

$$e^{\gamma x}\mathrm{Ai}\left(\frac{\gamma^2 + 2(\lambda - p + qx)}{2^{2/3}q^{2/3}}\right)$$

and

$$e^{\gamma x}\mathrm{Bi}\left(\frac{\gamma^2 + 2(\lambda - p + qx)}{2^{2/3}q^{2/3}}\right),$$

where Ai and Bi are the Airy functions (see Section 10.4 of [AS65]). It follows that for fixed λ the first and second derivatives of $\tilde{\phi}_{\lambda,\epsilon}$ are bounded on $[0, \epsilon]$ and of orders at most $\epsilon^{-1/3}$ and $\epsilon^{-2/3}$, respectively, on $[\epsilon, 2\epsilon]$. Thus

$$(26) \qquad \lim_{\epsilon\downarrow 0}\sup_{0\le x\le 2\epsilon}|\tilde{\phi}_{\lambda,\epsilon}(x) - 1| = 0 \text{ and } \lim_{\epsilon\downarrow 0}\sup_{0\le x\le 2\epsilon}|\tilde{\phi}'_{\lambda,\epsilon}(x) - \gamma| = 0.$$

Consider the initial value problem

$$\frac{1}{2}\breve{\phi}''_{\lambda,c,g} - \gamma\breve{\phi}''_{\lambda,c,g} + \beta_\infty\breve{\phi}_{\lambda,c,g} = \lambda\breve{\phi}_{\lambda,c,g} \quad \text{with } \breve{\phi}_{\lambda,c,g}(0) = c \text{ and } \breve{\phi}'_{\lambda,c,g}(0) = g.$$

Now

$$\inf\{\lambda : \breve{\phi}_{\lambda,1,\gamma}(x) \text{ is non-negative for all } x\}$$

is simply the negative of the asymptotic killing rate of reflected Brownian motion with drift γ killed at constant rate $-\beta_\infty$, namely β_∞ (this also follows from explicit computation). If $\lambda > \beta_\infty$, then an explicit computation of the solution shows that $\breve{\phi}_{\lambda,c,g}$ is non-negative for c sufficiently close to 1 and g sufficiently close to γ.

Choose any $\lambda > \beta_\infty$. On $(2\epsilon, \infty)$, the eigenfunction $\phi_{\lambda,\epsilon}$ coincides one of the functions $\breve{\phi}_{\lambda,c,g}$. From (26) we know that by choosing ϵ sufficiently small, we can make c as close as we like to 1 and g as close as we like to γ; hence, $\phi_{\lambda,\epsilon}$ is non-negative on $(2\epsilon, \infty)$. The initial values of (25) show that it is also non-negative on $[0, 2\epsilon]$ for ϵ sufficiently small. Thus $\liminf_{\epsilon\downarrow 0}\tilde{\underline{\lambda}}_\epsilon \le \lambda$; since λ was chosen arbitrary $\le \beta_\infty$, it follows $\liminf_{\epsilon\downarrow 0}\tilde{\underline{\lambda}}_\epsilon \le \beta_\infty$. Combining this with (11), we see that and the proof for condition (a) is complete.

Now we consider the case of condition (b). Set

$$\Sigma_m^2 = \sup_{x\in\mathbb{R}^+}\sigma_m^2(x)$$

and

$$Z_t^{(m)} = Y_t^{(m)} - Y_0^{(m)} - \int_0^t b(Y_s^{(m)})ds - \ell_t^0(Y^{(m)}),$$

where $\ell^0(Y^{(m)})$ is the local time at 0 of $Y^{(m)}$. Then $Z_t^{(m)}$ is a martingale with quadratic variation process bounded by $\Sigma_m^2 t$. Put

$$Z_t^{(m)*} := \sup_{0\le s\le t}|Z_s^{(m)}|.$$

Because a continuous martingale is a time-change of Brownian motion, there is a universal constant C such that

$$\mathbb{P}\{Z_t^{(m)*} \ge \epsilon\} \le C\exp(-\epsilon^2/2\Sigma_m^2 t).$$

For any $\delta > 0$,

$$
\begin{aligned}
\mathbb{P}\{\tau_\partial^{(m)} > t\} &= \mathbb{E}\left[\exp\left(\int_0^t \beta(Y_s^{(m)})\,ds\right)\right] \\
&\leq \mathbb{E}\left[\exp\left(\int_{\delta t}^t \beta(b_* s - b_* t\delta/2)\,ds\right)\right] + \mathbb{P}\{Z_t^{(m)*} > b_* t\delta\} \\
&\leq \exp\left((1-\delta)t \sup_{x \geq b_* t\delta/2} \beta(x)\right) + \mathbb{P}\{Z_t^{(m)*} > b_* t\delta/2\} \\
&\leq \exp((1-\delta)\,\beta(b_* t\delta/2)\,t) + C\exp(-t(b_*\delta)^2/8\Sigma_m^2).
\end{aligned}
$$

(Recall we have assumed that β is non-increasing.) Since $\lim_{m\to\infty} \Sigma_m^2 = 0$ and $\lim_{x\to\infty} \beta(x) = \beta_\infty$, we may find T such that

$$
\mathbb{P}\{\tau_\partial^{(m)} > t\} \leq \exp((1-2\delta)\beta_\infty t)
$$

for all $t \geq T$ and all m sufficiently large. It follows that $\underline{\lambda}_m \leq (1-2\delta)\beta_\infty$ for m sufficiently large. Thus $\liminf_{m\to\infty} \underline{\lambda}_m \leq \beta_\infty$, as required. □

Appendix: Convergence of the branching processes

We show in this section that the sequence of measure-valued processes (X^n) converges to a Dawson-Watanabe superprocess X under suitable conditions. We first recall the definition of the limit X as the solution of a martingale problem.

For simplicity, we deal with the biologically most relevant case where there is no killing at 0 in the damage and accumulation diffusion; that is, $p_0 = 1$ in the boundary condition (8), so that the domain $\mathcal{D}(\mathcal{L})$ of the operator $\mathcal{L}$ consists of twice differential functions ϕ that vanish at infinity, satisfy (8) for $p_0 = 1$, and are such that $\mathcal{L}\phi$ is continuous and vanishes at infinity. Similar arguments handle the other cases.

Suppose that the asymptotic rescaled branching rate ρ is bounded and continuous. Recall that the asymptotic net birth rate β is continuous and bounded above. Let $\mathcal{M}$ denote the space of finite measures on $\mathbb{R}^+$ equipped with the weak topology. For each $\nu \in \mathcal{M}$ there is a unique-in-law, cádlág, $\mathcal{M}$-valued process X such that $X_0 = \nu$ and for every non-negative $\phi \in \mathcal{D}(\mathcal{L})$

$$
\exp(-\langle \phi, X_t \rangle) - \exp(-\langle \phi, \nu \rangle) - \int_0^t \exp(-\langle \phi, X_s \rangle)\langle -\mathcal{L}\phi + \frac{1}{2}\rho\phi^2, X_s \rangle\,ds
$$

is a martingale. Moreover, X is a Markov process with continuous paths.

Our convergence proof follows the proof of convergence of branching Markov processes to a Dawson-Watanabe superprocess, as found in Chapter 1 of [Eth00] or in Chapter 9 of [EK86]. Because we only wish to indicate why a superprocess is a reasonable approximate model for a large population of fissioning organisms, we don't strive for maximal generality but instead impose assumptions that enable us to carry out the proof with a minimal amount of technical detail.

Let $(\Pi_t)_{t\geq 0}$ be the Markovian semigroup generated by

$$\mathcal{G}\phi := \frac{1}{2}\sigma_{\mathrm{mot}}^2\phi'' + b\phi'$$

with boundary condition (8) for $p_0 = 1$. That is, the generator of $(\Pi_t)_{t\geq 0}$ is the operator $\mathcal{G}$ acting on the domain $\mathcal{D}(\mathcal{G})$ consisting of twice differential functions ϕ that vanish at infinity, satisfy (8) for $p_0 = 1$ with σ^2 replaced by σ_{mot}^2, and are such that $\mathcal{G}\phi$ is continuous and vanishes at infinity. Thus $(\Pi_t)_{t\geq 0}$ is the Feller semigroup of the particle motion for the measure-valued processes X^n.

Let E denote the state space formed by taking the one-point compactification of $\mathbb{R}^+$. The semigroup $(\Pi_t)_{t\geq 0}$ can be extend to functions on E in a standard manner. The point at infinity is a trap that is never reached by particles starting elsewhere in E. The domain of the extended semigroup is the span of $\mathcal{D}(\mathcal{G})$ and the constants (which we will also call $\mathcal{D}(\mathcal{G})$) and the generator is extended by taking $\mathcal{G}\mathbf{1} = 0$. We also extend the measure-valued processes X^n – the point at infinity never collects any mass if no mass starts there.

Set $\beta^n(x) := a^n(x) - k^n(x)$ and $\rho^n(x) := n^{-1}(a^n(x) + k^n(x))$. Suppose that β^n and ρ^n are bounded and continuous. Given a bounded continuous function $g : \mathbb{R}^+ \to \mathbb{R}$, put $\mathcal{J}_+^n g(x) := \int g(x + y)\, d\pi_x^n(y)$ and $\mathcal{J}_-^n g(x) := \int g(x - y)\, d\pi_x^n(y)$

We have for $f \in \mathcal{D}(\mathcal{G})$ with $\inf_x f(x) > 0$ that

$$\exp(\langle n\log f, X_t^n\rangle) - \exp(\langle n\log f, X_0^n\rangle)$$

$$- \int_0^t \exp(\langle n\log f, X_s^n\rangle)$$

$$\times \left\langle \frac{n}{f}\left\{\mathcal{G}f + n\rho^n\left[\frac{a^n}{n\rho^n}\cdot\mathcal{J}_+^n f\cdot\mathcal{J}_-^n f + \frac{k^n}{n\rho^n} - f\right]\right\}, X_s^n\right\rangle ds$$

is a càdlàg martingale (cf. the discussion at the beginning of Section 9.4 of [EK86]).

If X_0^n is a non-random measure $\nu \in \mathcal{M}$, then essentially the same argument as in the proof of Lemma 9.4.1 of [EK86] shows that

$$(27) \qquad \mathbb{E}_\nu\left[\langle\mathbf{1}, X_t^n\rangle\right] \leq \langle\mathbf{1}, \nu\rangle \exp\left(t \sup_x \rho^n(x)\beta^n(x)\right)$$

and

$$(28) \qquad \mathbb{P}\left\{\sup_t \langle\mathbf{1}, X_t^n\rangle \exp\left(-t\sup_x \rho^n(x)\beta^n(x)\right) > z\right\} \leq \frac{\langle\mathbf{1}, \nu\rangle}{z}$$

(the result in [EK86] has the analogue of $\sup_x |\rho^n(x)\beta^n(x)|$ in place of $\sup_x \rho^n(x)\beta^n(x)$, but an examination of the proof shows that it carries through with this constant).

In order to motivate our next set of assumptions, imagine just for the moment that the jump distribution π_x^n is the distribution of a random variable

$n^{-1/2}Y_x$ where Y_x has moments of all orders. For ϕ sufficiently well-behaved and $f_n := 1 - n^{-1}\phi$, a Taylor expansion shows that

(29)
$$\frac{n}{f_n(x)}\left\{ \mathcal{G}f_n(x) + n\rho^n(x)\left[\frac{a^n(x)}{n\rho^n(x)} \cdot \mathcal{J}^n_+ f_n(x) \cdot \mathcal{J}^n_- f_n(x) + \frac{k^n(x)}{n\rho^n(x)} - f_n(x) \right] \right\}$$

is of the form

$$-\left\{ \frac{1}{2}\sigma^2_{\text{mot}}(x)\phi''(x) + b(x)\phi'(x) + \beta^n(x)\phi(x) \right.$$
$$\left. + \frac{a^n(x)}{a^n(x) + k^n(x)}n\left(\int y^2\, d\pi^n_x(y) \right)\phi''(x) - \frac{\rho^n(x)a^n(x)}{a^n(x) + k^n(x)}\phi^2(x) \right\}$$

plus lower order terms, and this converges pointwise to

$$-\left\{ \frac{1}{2}\sigma^2(x)\phi''(x) + b(x)\phi'(x) + \beta(x)\phi(x) - \frac{1}{2}\rho(x)\phi^2(x) \right\}$$

under the assumptions (1), (2), and (3).

With this informal observation in mind, assume that $\mathcal{D}(\mathcal{L}) \subseteq \mathcal{D}(\mathcal{G})$ and that if $f_n := 1 - n^{-1}\phi$ with $\phi \in \mathcal{D}(\mathcal{L})$ and $\inf_x \phi(x) > 0$, then the function in (29) converges uniformly to $-\mathcal{L}\phi + \frac{1}{2}\rho\phi^2$.

Under this assumption, we can follow the proof of Theorem 9.4.3 in [EK86] (using (28) to verify the compact containment condition in the same manner that the similar bound (9.4.14) is used in [EK86]) to establish that if X^n_0 converges in distribution as a random measure on E, then the process X^n converges in distribution as a càdlàg E-valued process to X.

References

[AGRN03] Hugo Aguilaniu, Lena Gustafsson, Michel Rigoulet, and Thomas Nyström. Asymmetric inheritance of oxidatively damaged proteins during cytokinesis. *Science*, 299(5613):1751–3, 14 March 2003.

[AK06]   Athanasios Armakolas and Amar J.S. Klar. Cell type regulates selective segregation of mouse chromosome 7 DNA strands in mitosis. *Science*, 311:1146–1149, 2006.

[AL95]   Peter A. Abrams and Donald Ludwig. Optimality theory, Gompertz' law, and the disposable soma theory of senescence. *Evolution*, 49(6):1055–66, December 1995.

[AS65]   Milton Abramowitz and Irene Stegun. *Handbook of mathematical functions, with formulas, graphs, and mathematical tables.* Dover, New York, 1965.

[ASJ03]   Martin Ackermann, Stephen C. Stearns, and Urs Jenal. Senescence in a bacterium with asymmetric division. *Science*, 300:1920, June 20 2003.

[Bel88]   Graham Bell. *Sex and death in protozoa : The history of an obsession.* Cambridge University Press, Cambridge, 1988.

[BP98]   Carl T. Bergstrom and Jonathan Pritchard. Germline bottlenecks and the evolutionary maintenance of mitochondrial genomes. *Genetics*, 149:2135–46, August 1998.

[BW99]   M. G Barker. and R. M. Walmsley. Replicative ageing in the fission yeast *schizosaccharomyces pombe. Yeast*, 15:1511–18, 1999.

[Cic97]   Mariusz Cichón. Evolution of longevity through optimal resource allocation. *Proceedings of the Royal Society of London, Series B: Biological Sciences*, 264:1383–8, 1997.

[CK70]   J. F. Crow and M. Kimura. *An Introduction to Population Genetics Theory*. Harper and Row, New York, 1970.

[CL06]   Cyrus Y. Chu and Ronald D. Lee. The co-evolution of intergenerational transfers and longevity: an optimal life history approach. *Theoretical Population Biology*, 69(2):193–2001, March 2006.

[CZB80]   G. B. Calleja, M. Zuker, and B. Analyses of fission scars as permanent records of cell division in *schizosaccharomyces pombe*. *Journal of Theoretical Biology*, 84:523–44, 1980.

[Daw75]   D. A. Dawson. Stochastic evolution equations and related measure processes. *Journal of Multivariate Analysis*, 5:1–52, 1975.

[Daw93a] Donald A. Dawson. Measure-valued Markov processes. In *École d'Été de Probabilités de Saint-Flour XXI—1991*, volume 1541 of *Lecture Notes in Mathematics*, pages 1–260. SV, Berlin, 1993.

[Daw93b] Donald A. Dawson. Measure-valued Markov processes. In *École d'Été de Probabilités de Saint-Flour XXI—1991*, volume 1541 of *Lecture Notes in Math.*, pages 1–260. Springer, Berlin, 1993.

[DH83]   Donald A. Dawson and Kenneth J. Hochberg. Qualitative behavior of a selectively neutral allelic model. *Theoretical Population Biology*, 23(1):1–18, February 1983.

[DK99]   Peter Donnelly and Thomas G. Kurtz. Genealogical processes for Fleming-Viot models with selection and recombination. *Ann. Appl. Probab.*, 9(4):1091–1148, 1999.

[Dou82]   Stanislav Doubal. Theory of reliability, biological systems and aging. *Mechanisms of Ageing and Development*, 18:339–53, 1982.

[Dyn91]   E. B. Dynkin. Branching particle systems and superprocesses. *The Annals of Probability*, 19(3):1157–94, 1991.

[EG87]   S. N. Ethier and R. C. Griffiths. The infinitely-many-sites model as a measure-valued diffusion. *Annals of Probability*, 15(2):515–45, 1987.

[EH94]   Stephen Ellner and Nelson G. Hairston, Jr. Role of overlapping generations in maintaining genetic variation in a fluctuating environment. *The American Naturalist*, 143(3):403–17, March 1994.

[EK86]   Stewart Ethier and Thomas Kurtz. *Markov Processes: Characterization and Convergence*. John Wiley & Sons, 1986.

[ET02]   János Engländer and Dmitry Turaev. A scaling limit for a class of diffusions. *The Annals of Probability*, 30(2):683–722, 2002.

[Eth00]   Alison M. Etheridge. *An introduction to superprocesses*, volume 20 of *University Lecture Series*. American Mathematical Society, Providence, RI, 2000.

[Eth04]   Alison M. Etheridge. Survival and extinction in a locally regulated population. *Annals of Applied Probability*, 14(1):188–214, 2004.

[EW05]   J. Engländer and A. Winter. Law of large numbers for a class of superdiffusions. *Annales de l'Institut Henri Poincaré. Probabilités et Statistiques*, 42(2):171–85, 2005.

[Ewe69]   Warren J. Ewens. *Population genetics*. Methuen, London, 1969.

[Ewe79]   Warren J. Ewens. *Mathematical Population Genetics*. Springer-Verlag, New York, Heidelberg, Berlin, 1979.

[Fel51]   William Feller. Diffusion processes in genetics. In Jerzy Neyman, editor, *Proceedings of the Second Berkeley Symposium in Mathematical Statistics and Probability*, pages 227–46, Berkeley, 1951. University of California Press.

[Fin90]   Caleb Finch. *Longevity, Senescence, and the Genome*. University of Chicago Press, Chicago, 1990.

[FS90]   Steven A. Frank and Montgomery Slatkin. Evolution in a variable environment. *The American Naturalist*, 136(2):244–60, August 1990.

[FV79]   Wendell Fleming and Michel Viot. Some measure-valued markov processes in population genetics theory. *Indiana University Mathematics Journal*, 28:817–43, 1979.

[GG01]   Leonid A. Gavrilov and Natalia S. Gavrilova. The reliability theory of aging and longevity. *Journal of Theoretical Biology*, 213:527–45, 2001.

[Gil74]   John H. Gillespie. Natural selection for within-generation variance in offspring number. *Genetics*, 76:601–6, March 1974.

[Goo84]   Daniel Goodman. Risk spreading as an adaptive strategy in iteroparous life histories. *Theoretical Population Biology*, 25:1–20, 1984.

[GT99]   R. C. Griffiths and Simon Tavaré. The ages of mutations in gene trees. *Annals of Applied Probability*, 9(3):567–90, 1999.

[Gue04]   John C. Guerin. Emerging area of aging research: Long-lived animals with "negligible senescence". *Proceedings of the New York Academy of Sciences*, 1019:518–20, 2004.

[Ham66]   W. D. Hamilton. The moulding of senescence by natural selection. *J. Theor. Bio.*, 12:12–45, 1966.

[HDS02]   Ralph Hertwig, Jennifer Nerissa Davis, and Frank J. Sulloway. Parental investment: How an equity motive can produce inequality. *Psychological Bulletin*, 128(5):728–45, 2002.

[HU77]   Leland H. Hartwell and Michael W. Unger. Unequal division in *Saccharomyces cerevisiae* and its implications for the control of cell division. *Journal of Cell Biology*, 75:422–35, 1977.

[Kim53]   Motoo Kimura. "stepping stone" model of population. *Annual Report of the National Institute of Genetics, Japan*, 3:62–63, 1953.

[Kin77]   J. F. C. Kingman. On the properties of bilinear models for the balance between genetic mutation and selection. *Mathematical Proceedings of the Cambridge Philosophical Society*, 81:443–53, 1977.

[Kir77]   Thomas B. L. Kirkwood. Evolution of ageing. *Nature*, 270(5635):301–4, November 24 1977.

[KMG99]   Matt Kaeberlein, Mitch McVey, and Leonard Guarente. The *SIR2/3/4* complex and *SIR2* alone promote longevity in *Saccharomyces cerevisiae* by two different mechanisms. *Genes & Development*, 13:2570–80, 1999.

[Kol81]   V. K. Koltover. Reliability of enzymatic protection of cells from superoxide radicals and aging. *Doklady Akademii Nauk SSSR*, 156:3–5, 1981.

[KR02]   Hillard S. Kaplan and Arthur J. Robson. The emergence of humans: The coevolution of intelligence and longevity with intergenerational transfers. *Proceedings of the National Academy of Sciences, USA*, 99(15):10221–6, 2002.

[KW64]   Motoo Kimura and George H. Weiss. The stepping stone model of population structure and the decrease of genetic correlation with distance. *Genetics*, 49:561–76, April 1964.

[Lee03]   Ron Lee. Rethinking the evolutionary theory of aging: Transfers, not births, shape senescence in social species. *Proceedings of the National Academy of Sciences, USA*, 2003.

[LJBJ02]   Chi-Yung Lai, Ewa Jaruga, Corina Borghouts, and S. Michal Jazwinski. A mutation in the *ATP2* gene abrogates the age asymmetry between mother and daughter cells of the yeast *Saccharomyces cerevisiae*. *Genetics*, 162:73–87, September 2002.

[Man01]   Marc Mangel. Complex adaptive systems, aging and longevity. *J. Theor. Bio.*, 213:559–71, 2001.

[Med57]   Peter Medawar. An unsolved problem in biology. In *The Uniqueness of the Individual*, pages 1–27. Basic Books, 1957.

[MFD⁺06]   Nadege Minois, Magdalena Frajnt, Martin Dölling, Francesco Lagona, Matthias Schmid, Helmut Küchenhoff, Jutta Gampe, and James W. Vaupel.

Symmetrically dividing cells of the fission yeast *schizosaccharomyces pombe* do age. *Biogerontology*, 7:261–7, 2006.

[MJ59]   Robert K. Mortimer and John R. Johnston. Life span of individual yeast cells. *Nature*, 183:1751–2, June 20 1959.

[Mor62]   Patrick A. P. Moran. *The statistical processes of evolutionary theory*. Clarendon Press, Oxford, 1962.

[PB93]   L. Partridge and N. H. Barton. Optimality, mutation and the evolution of ageing. *Nature*, 362:305–11, 25 March 1993.

[Per02]   Edwin Perkins. Dawson-Watanabe superprocesses and measure-valued diffusions. In *Lectures on probability theory and statistics (Saint-Flour, 1999)*, volume 1781 of *Lecture Notes in Math.*, pages 125–324. Springer, Berlin, 2002.

[PML89]   Geoffrey A. Parker, Douglas W. Mock, and Timothy C. Lamey. How selfish should stronger sibs be? *The American Naturalist*, 133(6):846–68, June 1989.

[RHP02]   Nick J. Royle, Ian R. Hartley, and Geoff A. Parker. Begging for control: when are offspring solicitation behaviours honest? *Trends in Ecology & Evolution*, 17(9):434–40, September 2002.

[RK03]   Arthur J. Robson and Hillard S. Kaplan. The evolution of human life expectancy and intelligence in hunter-gatherer economies. *The American Economic Review*, 93(1):150–69, March 2003.

[Saw76]   Stanley Sawyer. Branching diffusion processes in population genetics. *Advances in Applied Probability*, 8(4):659–689, 1976.

[SE05]   David Steinsaltz and Steven N. Evans. Quasistationary distributions for one-dimensional diffusions with general killing. Accepted for publication in *Trans. Amer. Math. Soc.*, 2005.

[SF81]   Stanley Sawyer and Joseph Felsenstein. A continuous migration model with stable demography. *Journal of Mathematical Biology*, 11(2):193–205, February 1981.

[SG06]   David Steinsaltz and Lloyd Goldwasser. Aging and total quality management: Extending the reliability metaphor for longevity. *Evolutionary Ecological Research*, 8(8):1445–59, December 2006.

[Sla02]   Gordon Slade. Scaling limits and super-Brownian motion. *Notices of the American Mathematical Society*, 49(9):1056–67, 2002.

[SMPT05]   Eric Stewart, Richard Madden, Gregory Paul, and François Taddei. Aging and death in an organism that reproduces by morphologically symmetric division. *Public Library of Science (Biology)*, 3(2), 2005.

[ST05]   Eric Stewart and François Taddei. Aging in *esherichia coli*: signals in the noise. *BioEssays*, 27(9):983, 2005.

[Ste05]   Craig Stephens. Senescence: Even bacteria get old. *Current Biology*, 15(8):R308–R310, April 26 2005.

[Tri74]   Robert L. Trivers. Parent-offspring conflict. *American Zoologist*, 14(1):249–64, 1974.

[VBD$^+$04] James W. Vaupel, Annette Baudisch, Martin Dölling, Deborah A. Roach, and Jutta Gampe. The case for negative senescence. *Theoretical Population Biology*, 65(4):339–51, 2004.

[WB02]   G. F. Webb and M. J. Blaser. Dynamics of bacterial phenotype selection in a colonized host. *Proceedings of the National Academy of Sciences*, 99(5):3135–40, February 26 2002.

[Wol05]   Conrad L. Woldringh. Is *escherichia coli* getting old? *BioEssays*, 27(8):770–4, 2005.

[WPJK06]   Milind Watve, Sweta Parab, Prajakta Jogdand, and Sarita Keni. Aging may be a conditional strategic choice and not an inevitable outcome for bacteria. *Proceedings of the National Academy of Sciences*, 103(40):14831–5, October 3 2006.

[You01]	W. R. Young. Brownian bugs and superprocesses. In Peter Müller and Diane Henderson, editors, *Proceedings of the 12th 'Aha Huliko'a Hawaiian Winter Workshop*, pages 123–9, 2001.

STEVEN N. EVANS, DEPARTMENT OF STATISTICS #3860, 367 EVANS HALL, UNIVERSITY OF CALIFORNIA, BERKELEY, CA 94720-3860, USA
E-mail address: evans@stat.berkeley.edu

DAVID STEINSALTZ, DEPARTMENT OF MATHEMATICS AND STATISTICS, QUEEN'S UNIVERSITY, KINGSTON, ON K7L 3N6, CANADA
E-mail address: steinsaltz@mast.queensu.ca