Stochastic failure accumulation as a foundation for exponential mortality and selective disappearance

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Abstract

Most organisms become increasingly likely to die as they grow older, a phenomenon known as demographic senescence. Despite this statement saying nothing about the particular shape of a mortality curve, the Gompertz–Makeham law remains remarkably accurate in a broad range of species. We develop a general mathematical framework in which individuals are modelled as comprising a fixed number of interacting intra-organismal sub-systems, each characterised by stochastic failure and repair rates, such that the number of failed sub-systems follows a birth–death process. In many organisms, 'failure begets failure' because sub-systems are typically interdependent. We use diffusion approximations to demonstrate that this interdependence generically produces Gompertz-Makeham mortality curves. Since individuals who die can no longer age, observed cohorts become increasingly composed of 'lucky' individuals that avoided death by (stochastically) taking paths in failure space associated with lower mortality despite no intrinsic differences in their quality. Selective disappearance of 'unlucky' individuals generates deviations from Gompertz-Makeham predictions at advanced ages, producing a late-life mortality plateau. We show that while these deviations must always exist, they may often be too small to detect, either because the failure accumulation process is stereotyped or because detection requires unreasonably large cohort sizes. Our work establishes Gompertz-Makeham curves arising from stochastic failure accumulation as a null expectation in organisms with many interdependent sub-systems.

Keywords: Gompertz-Makeham; senescence; reliability theory; frailty; demography; selective disappearance

Introduction

Senescence, or ageing, is defined as a persistent increase in mortality or decrease in fecundity from the time since the birth of an organism (Shefferson et al., 2017). Explaining the prevalence of senescence across the tree of life is a classic problem in evolutionary biology (Medawar, 1952), and a variety of theories have been put forth to attack the problem (Williams, 1957; Hamilton, 1966; Kirkwood, 1977). Classic evolutionary theories of senescence crucially rely on either age-specific mutations to fecundity and survival (Williams, 1957; Hamilton, 1966) or strong trade-offs between the maintenance of somatic function and germline integrity (Kirkwood, 1977). However, these theories often do not concern themselves with the mechanistic, physiological basis for observed senescence patterns in any particular organism, and, furthermore, typically do not make predictions about lifespans or the shapes of realised mortality curves (Lehtonen, 2020).

An alternative, more mechanistic approach to understanding senescence is via the accumulation of damage, or 'failures', of various physiological processes required for organismal function (Gavrilov and Gavrilova, 1991; Bega and Hadany, 2026). In this view, an organism is a complex system consisting of many interdependent biological processes, each with some intrinsic risk of failure due to the vagaries of life. Senescence is then thought to arise via a catastrophic propagation of failures between interdependent sub-systems (Gavrilov and Gavrilova, 1991; Boonekamp et al., 2015). While classic studies arrange intra-organismal subsystems either 'in series', 'in parallel', or as a combination of parallel blocks connected in series (Gavrilov and Gavrilova, 2001; Laird and Sherratt, 2009, 2010; Boonekamp et al., 2015), more complicated dependency structures in terms of networks are also possible (Rosen, 1958; Vural et al., 2014; Sun et al., 2020; Nielsen et al., 2024). However, while these models typically dedicate considerable effort towards deriving and studying the dynamics of intra-individual failure accumulation, less attention has been paid to studying the consequences of inter-individual stochasticity when accumulating failures impact mortality.

Here, we need to distinguish between inter-individual stochasticity in the trajectories of failure

accumulation and heterogeneity in a fixed quality, typically called 'frailty', that sets each individual on its unique trajectory towards increased mortality. Frailty models focus specifically on the role of inter-individual heterogeneity in affecting observed mortality curves (Balan and Putter, 2020), but they typically do so by assigning individuals to classes, each of whose ageing clock ticks at different speeds. Observed population-level mortality curves in this setting are fundamentally due to *selective disappearance*, where the more frail individuals are more likely to die early and thus not contribute to the late-life part of the mortality curve (Vaupel and Missov, 2014; Balan and Putter, 2020). Importantly, while frailty models include stochasticity in the sense of assigning individuals into different classes according to some distribution (Vaupel et al., 1979; Vaupel and Missov, 2014), they typically do not deal with the subsequent stochastic accumulation of damage/failures through the course of the life of an organism; a lucky individual at birth cannot deteriorate faster than expected if it is unlucky later (or vice versa).

There is a notable exception to the assumption of fixed frailty through life: the 'state space random walk' model introduced by Woodbury and Manton (1977) and refined by Yashin et al. (1985). In the Woodbury-Manton model, individuals are characterised by their position in an abstract physiological 'state space', and this position determines their mortality rate. Individuals are modelled as executing a (possibly biased) random walk in the state space through the course of their lives, with individuals additionally being stochastically removed from the population based on their mortality (Woodbury and Manton, 1977, 1983; Yashin et al., 1985). Cast in frailty language, this amounts to a stochastic walk through frailty space. Despite being nearly as old as some classic theories in the senescence literature (Kirkwood, 1977), the Woodbury-Manton model remains relatively undercited and underused. Its usage appears largely restricted to statistical inference and estimation in human cohorts (Manton and Woodbury, 1983; Woodbury and Manton, 1983; Manton and Woodbury, 1985; Yashin et al., 1985; Mulder, 1993), and the broader implications remain unexplored.

The Woodbury-Manton model also makes some rather restrictive assumptions: that the future physiological state of an individual depends linearly on the current state, and that the mortality

risk is a quadratic function of the physiological state (equations 4 and 5 in Woodbury and Manton, 1977; also see section IV(E) in Yashin et al., 1985). These functional forms are not systematically derived from underlying intraorganismal biological processes, but used for convenience, as such functions are amenable to statistical estimation (Woodbury and Manton, 1983; Yashin et al., 1985; Mulder, 1993; Manton and Yashin, 1997). Though Yashin et al. (1985) also derive some general equations for their extension of the Woodbury-Manton model without assuming these specific functional forms, the terms that appear in Yashin et al.'s (1985) equations are totally abstract, being written down in full generality with little underlying biological motivation. As a result, the terms in their equations cannot be unambiguously assigned biological meaning.

We take the above state of affairs as a starting point, as it appears desirable to establish stochastic, mechanistically grounded damage/failure accumulation processes as a foundation for ageing (Meyer et al., 2025). Here, the reliability theory perspective (Gavrilov and Gavrilova, 2001) suggests that different forms of failure accumulation, and different connections between failures and mortality dynamics, may be appropriate for different organisms (Gavrilov and Gavrilova, 2001) based on the organisation of intra-organismal subsystems (Bernard et al., 2020). We present a flexible modelling framework in which both stochastic failure accumulation dynamics at the organismal level and observed mortality patterns at the population level are systematically derived from intra-organismal first principles.

We integrate the failure accumulation perspective with stochastic selective disappearance that occurs due to population heterogeneity in individual risk of death. Specifically, we first derive results for a simple model where individuals are assigned mortalities that are a function of accumulating failures, but we explicitly exclude selective disappearance as the mortalities do not translate into actual deaths. Much like the titular figure in the ancient Greek myth of Tithonus (Graves, 2017, chapter 40), individuals in our first model can become arbitrarily damaged by accumulating failures, which permits an ever increasing mortality risk, but they are not allowed to actually die (note that Williams (1999) also used the Tithonus myth in a similar allegorical sense to criticise focusing on the age of death as opposed to studying the preceding period where an

organism is alive but physiologically declining). Our 'Tithonus model' has a benefit (immortality permits us to measure any individual's accumulated failures at any age), but comes with the obvious cost of having to accept a contradiction of deriving mortality predictions for a cohort without death actually removing any individual. However, this model is not without value, as the treatment of mortality rate as an abstract summary of the individual's state allows separating the effects of mortality risk arising from failure accumulation from those of selective disappearance, which are the focus of our second, contradiction-free model.

For our main model (called 'main model with selective disappearance'), we remove the contradictory assumption of the Tithonus model by incorporating mortality as an individual-level stochastic rate, thus connecting failures to a true mortality hazard that removes dead individuals. This approach follows the spirit of Woodbury and Manton (1977) and Yashin et al. (1985), in which both failure accumulation and mortality occur simultaneously at the individual-level, and population-level dynamics are derived from stochastic first principles accounting for selective disappearance. However, we improve on their past work by grounding their 'state space' process in a mechanistic framework (namely reliability theoretic failure accumulation) and avoiding their arguably most restrictive assumptions about the functional forms of physiological state change and mortality hazards.

Throughout, we are interested in whether failure accumulation can generate mortalities that increase exponentially with age, *i.e.* following the Gompertz (1825) pattern, possibly with an additional Makeham (1860) component modelling constant extrinsic mortality. Using the Tithonus model, we find the exponential increase to hold if we assume that "failure begets failure" — *i.e.* the rate at which sub-systems fail increases with the proportion of those that have already failed — and more failures translate into increased mortality in a biologically realistic manner where individuals cannot remain alive when all their sub-systems have failed. This result, however, relies on the contradictory assumption set of the Tithonus model. Intuition suggests that the effect of the contradiction is an overestimation of mortality, especially at older ages, since very damaged individuals are assumed to be available to die when in reality they have been weeded out by

selective disappearance at an earlier age (Weitz and Fraser, 2001; Vaupel and Missov, 2014).

We confirm the overestimation by deriving mortality under selective disappearance from first principles (our main model), which leads us to our second question: why does Gompertz describe so many populations so well when a perfect match appears to require a model that contains an inherent contradiction? Given that selective disappearance always affects average measurements in our contradiction-free framework, we study when its effects should remain small, rendering them difficult to detect in data. Whenever this is the case, the Tithonus model remains a relevant approximation and we can still typically expect observed survivorship curves resemble those predicted by Gompertz-Makeham mortalities. In short, if the failure accumulation or mortality processes are themselves stereotyped between individuals, then 'luck' plays a smaller role and there is less 'opportunity' for selective disappearance simply because the cohort remains relatively homogeneous at all ages. If there is large stochastic heterogeneity in the failure accumulation or mortality processes, then selective disappearance could cause deviations from Gompertz-Makeham mortality patterns. However, these deviations would nevertheless be difficult to detect in data if the overall expected survivorship is low (*i.e.* the 'lucky' individuals need to be incredibly lucky). Our results establish that Gompertz-Makeham mortality curves should be expected as a baseline in species in which individuals comprise many interdependent sub-systems, failure begets failure, and death is guaranteed once all sub-systems have failed (but may also occur earlier).

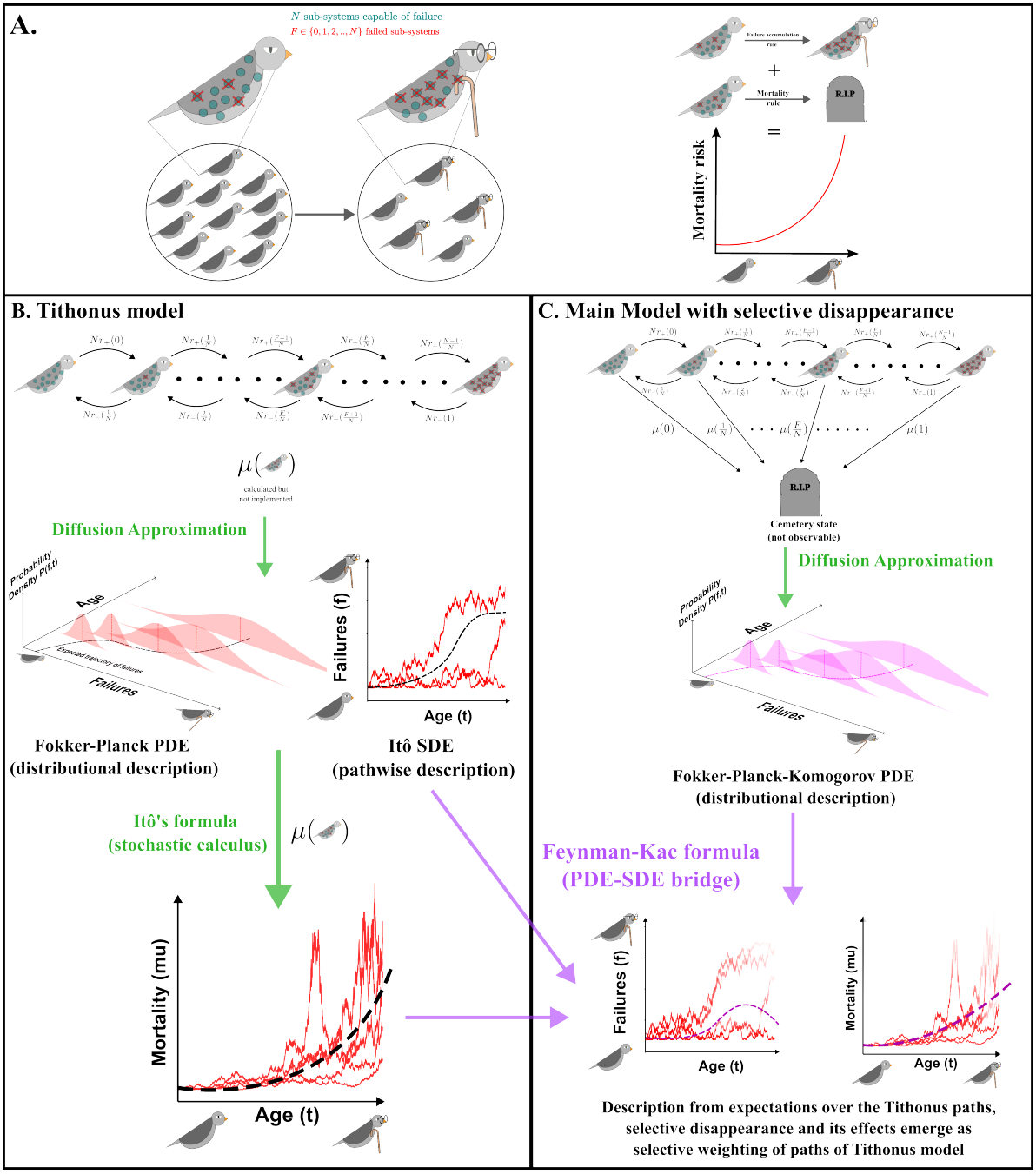

Figure 1: An outline of the general approach of this paper. **(A)** We model a large population of independent, non-interacting organisms. Senescence at the individual level occurs as intra-organismal sub-systems fail and impact each other's failure rate. Our goal is to understand how failure accumulation and mortality together predict mortality curves, which in this framework are an emergent pattern. **(B)** The Tithonus model focuses on the failure dynamics alone, allowing to investigate relationships between age, failures and mortality. An individual in which $f = \frac{F}{N}$ sub-systems have failed has a failure rate $Nr_+(f)$ and a repair rate $Nr_-(f)$. We calculate mortality according to some mapping between failures and mortality, but no individuals actually die. Here, a direct 'pathwise' description of that follows focal individuals through the course of their life is possible. **(C)** In the main model, mortality is incorporated along with failure and repair as a stochastic transition rate at the individual level; the original state space is augmented with an additional, unobserved 'cemetery' state for dead organisms. An individual in which $f = \frac{F}{N}$ sub-systems have failed has a failure rate $Nr_+(f)$, a repair rate $Nr_-(f)$, and a mortality rate $\mu(f)$. For the main model, the pathwise description is in terms of paths of the Tithonus model.

The Tithonus model: Modelling failure accumulation and mortality separately

According to ancient Greek mythology, Tithonus was a mortal lover of Eos, Goddess of the Dawn. After much pleading from Eos, Zeus granted Tithonus immortality so he could be with Eos forever. However, Eos asked that Tithonus be immortal, neglecting to also request he remain eternally youthful or healthy. As the years passed, Tithonus thus withered away, becoming progressively more weak, frail, wrinkled, and shrunken; yet, no matter how feeble and decrepit he became, Tithonus could not die (Graves, 2017, chapter 40). In this section, we assume all our organisms are like Tithonus and intentionally do not worry about the contradictions involved in deriving mortality rates while also assuming immortality. The intention is to separate failure accumulation and resultant mortality risk cleanly and examine them separately to understand when to expect Gompertz-Makeham curves.

We consider a population of independent, identical, non-interacting organisms in which each individual has N intra-organismal sub-systems in total, is born with $F_0 \geq 0$ failed sub-systems, and in which sub-systems stochastically fail due to wear-and-tear or stochastic damage accumulation throughout its lifetime. If an individual has F failed sub-systems, we assume that an additional sub-system fails at rate $R_+(F)$, whereas a failed sub-system is repaired at rate $R_-(F)$. The number of failures as a function of age is thus described as a continuous time birth-death process with transition rates

$$F \to F+1 \text{ at rate } R_+(F),$$

$$F \to F-1 \text{ at rate } R_-(F)$$

For simplicity, we will assume throughout that it is difficult to keep organisms pristine (failure-free), or, alternatively, that repair processes are imperfect (Gorbunova et al., 2007), by asserting that $R_+(F) - R_-(F) > 0$ for every F. In other words, we assume that the number of failed sub-systems

is always more likely to increase than decrease. We sketch some consequences of relaxing this assumption in our Discussion.

We further assume that that the failure rates depend on the *proportion* of failed sub-systems, and that the total number N only rescales this dependence (technically, this is achieved by assuming $R_{\pm}(F) = Nr_{\pm}(F/N)$, where $r_{\pm}$ are $\mathcal{O}(1)$ functions). We will thus track the proportion of failed sub-systems $f := F/N$ rather than the total number of failed sub-systems F. For conciseness, in discussing failure dynamics we use the term 'failures' for f, the proportion of failed sub-systems out of N. In terms of f, the transitions are

$$f \to f + \frac{1}{N} \text{ at rate } Nr_+(f),$$
$$f \to f - \frac{1}{N} \text{ at rate } Nr_-(f)$$

Since $r(f) := r_+(f) - r_-(f) > 0$ is the expected rate of failure accumulation in an individual with f failures, we call $f \mapsto r(f)$ the *failure accumulation rule* of the model. The quantity $\tau(f) := r_+(f) + r_-(f)$ quantifies the total rate at which an individual with f failures experiences a change in failures. Following work in other areas of population biology, we will call τ the *turnover rate* (Bhat, 2025; Bhat and Guttal, 2025; Komarova and Wodarz, 2025; Kuosmanen et al., 2025).

Failure dynamics in the Tithonus model

We are interested in tracking $P(f, t|f_0, 0)$, the probability that an individual that starts life (at age 0) with f_0 failures has f failures at age t. For brevity, we will henceforth suppress the initial condition and write $P(f, t)$. Note that all individuals will reach every age t (immortality). We use a system size expansion ('diffusion approximation' in population biology literature) to show (Supplementary section S1) that if N is not too small, $P(f, t)$ is very well approximated by the equation

$$\frac{\partial P(f,t)}{\partial t} = -\frac{\partial}{\partial f}\left\{r(f)P(f,t)\right\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{\tau(f)P(f,t)\right\}. \quad (1)$$

Eq. 1 is a partial differential equation called a Kolmogorov forward equation or a Fokker-Planck equation, and describes how a probability distribution $P(f,t)$ changes over state (f) and time (t). An alternative, equivalent description (Gardiner, 2009, section 4.3.5) of the failure dynamics described by Eq. 1 is as the solution to a stochastic differential equation (SDE)

$$d\mathfrak{f}_t = r(\mathfrak{f}_t)dt + \frac{1}{\sqrt{N}}\sqrt{\tau(\mathfrak{f}_t)}dW_t, \tag{2}$$

where W_t is a standard Brownian motion, or Wiener process. We provide a brief introduction to stochastic differential equations in Box 1.

Eq. 2 implies that during the infinitesimally short timespan in which an individual goes from age t to age $t+dt$, the accumulation of failures $d\mathfrak{f}_t := \mathfrak{f}_{t+dt} - \mathfrak{f}_t$ is a Normally distributed random variable with expectation value and variance given by

$$\mathbb{E}[d\mathfrak{f}_t] = r(\mathfrak{f}_t)dt \tag{3a}$$

$$\mathbb{V}[d\mathfrak{f}_t] = \frac{\tau(\mathfrak{f}_t)}{N}dt. \tag{3b}$$

Thus, the expected change in the number of failures is controlled by the failure accumulation rule r and the variance in the number of failures is controlled by the turnover rate τ. Furthermore, the variance decreases as N, the total number of sub-systems, increases.

Upon taking $N \to \infty$ in Eq. 2, the stochastic aspects of the system disappear and Eq. 2 becomes the ordinary differential equation

$$\frac{df}{dt} = r(f). \tag{4}$$

We have switched notation from $\mathfrak{f}_t$ to $f(t)$ to remind the reader that the former is a stochastic process, whereas the latter is a deterministic function.

Box 1: Stochastic differential equations for the uninitiated

A stochastic differential equation (SDE) for a continuous time stochastic process X_t takes the form

$$dX_t = F(t, X_t)dt + G(t, X_t)dW_t, \tag{i}$$

for two functions F and G. The quantity W_t is a stochastic process called a standard Brownian motion or Wiener process. The Wiener process can be thought of as a continuous time, continuous state Markov process such that whenever we advance time by a very small (infinitesimal) amount, $t \to t + dt$, the increment $dW_t \coloneqq W_{t+dt} - W_t$ of the Wiener process is Normally distributed with mean 0 and variance dt. Similarly writing $dX_t \coloneqq X_{t+dt} - X_t$, we can informally view dX_t as a random variable representing the change in X over an infinitesimal time dt. The SDE Eq. i thus states that the change in the value of the stochastic process X over an infinitesimal time interval dt follows a Normal distribution with mean value $\mathbb{E}[dX_t]$ and variance $\mathbb{V}[dX_t]$ given by

$$\mathbb{E}[dX_t] = F(t, X_t)dt,$$
$$\mathbb{V}[dX_t] = G^2(t, X_t)dt.$$

The functions F and G^2 are called the infinitesimal mean and infinitesimal variance of X_t respectively (Øksendal, 1998), since they thus describe the mean and varianace of the change in X_t over an infinitesimal time interval dt. Solutions to SDEs such as Eq. i are called *Itô diffusions* after Kiyosi Itô, one of the first to mathematically formalise and study such processes (Itô, 1951; Øksendal, 1998).

What should a good failure accumulation rule look like?

What kind of properties would we want our $r(f)$ to have to reflect biologically reasonable behaviours? For one, since only sub-systems which have not yet failed are capable of failure, no more failures should be possible when all sub-systems have failed (*i.e.* we should have $r(1) = 0$). By our earlier assumption that repair is imperfect and failures tend to increase on average, the failure rate must always be positive when there are at least some functioning sub-systems (*i.e.* $r(f) > 0 \; \forall \; f \in [0, 1)$, and, in particular, $r(0) > 0$). Furthermore, since the failure rate depends

only on the proportion (but not on the identity) of failed sub-systems, we should be able to define a per-capita failure rate for each functioning sub-system. Since the fraction of functioning sub-systems is $1 - f$, a sensible general choice for the $r(f)$ is of the form

$$r(f) = (1 - f)\rho(f), \tag{5}$$

where $\rho(f) > 0$ is a function returning the per-capita failure rate of each functioning sub-system when a proportion f of the systems have failed. During the initial part of the failure accumulation process (*i.e.* when $f - f_0$ is small), we can Taylor expand ρ about f_0 in Eq. 5 to write

$$\rho(f) = \rho_0 + (f(t) - f_0) \left.\frac{\partial \rho}{\partial f}\right|_{f=f_0} + \cdots \tag{6}$$

where we have used the shorthand $\rho_0 = \rho(f_0)$ for the per-capita failure rate at birth (when f_0 systems have failed). Discarding higher order terms, we can define $k_\rho := \left.\frac{\partial \rho}{\partial f}\right|_{f=f_0}$ and $\phi_\rho := \rho_0 - k_\rho f_0$ and substitute Eq. 6 into Eq. 4 to arrive at

$$\frac{df}{dt} = r(f) \approx (1 - f)\left(\phi_\rho + k_\rho f\right). \tag{7}$$

Henceforth, we assume the equality in Eq. 7 holds exactly. However, we retain the ρ in the sub-scripts to remind the reader that ϕ_ρ and k_ρ are both quantities defined *for a given per-capita failure rate function* $\rho(f)$.

Since we required $r(0) > 0$, Eq. 7 implies $\phi_\rho > 0$. We now wish to mathematically capture the notion that organisms are integrated entities and different sub-systems thus typically dependent on each other for functioning. If sub-systems are indeed inter-dependent, the probability that an additional sub-system of the organism fails should increase as the number of failures increases. Such an increase could reflect organismal function as a whole declining as the number of failures increases, causing increased failure rate via 'vicious cycles' of dysfunction (Belikov, 2019). Alternatively, some sub-systems may directly depend on the well-being of others for their

functioning (Tian et al., 2023). Whatever the underlying cause may be, such 'failure begets failure' dynamics are mathematically captured by demanding that the per-capita failure rate ρ in Eq. 5 is an increasing function of the proportion of failures f, and thus

$$\frac{\partial \rho}{\partial f} > 0. \tag{8}$$

Since Eq. 8 is postulated as true at every point of the function $\rho(f)$, it must also be true at birth, when $f = f_0$. We thus conclude that $k_\rho := \frac{\partial \rho}{\partial f}\big|_{f=f_0}$ in Eq. 7 is also strictly positive.

Once it is established that ϕ_ρ and k_ρ are both non-negative, the functional form Eq. 7 admits a biologically appealing interpretation: The parameter ϕ_ρ acts as a constant baseline failure rate of each sub-system, and k_ρ modulates the additional (linear) increase in per-capita failure rate due to functional interdependencies between sub-systems ('failure begets failure'). Thus, ϕ_ρ is a measure of the resilience of each individual sub-system and could be affected by external parameters such as hazardous environments, whereas k_ρ is a measure of the integratedness of the organism as a whole: In a completely modular organism in which every sub-system is independent of every other, we would have $k_\rho \approx 0$, whereas in a completely integrated organism in which every sub-system affected the functioning of every other sub-system, k_ρ would be high.

Eq. 7 resembles the logistic equation (if $\phi_\rho = 0$, it is exactly the logistic equation) and can be solved exactly using the method of partial fractions. Supplied with the initial condition $f(0) = f_0$, the solution to Eq. 7 is given by

$$f(t) = \frac{\alpha e^{\beta t}}{\beta + \alpha\left(e^{\beta t} - 1\right)} - A(t), \tag{9}$$

where we have defined the aggregate terms

$$\alpha := \phi_\rho + k_\rho f_0 > 0,$$

$$\beta := \phi_\rho + k_\rho > \alpha,$$

$$A(t) := \frac{\phi_\rho(1 - f_0)}{\beta + \alpha\left(e^{\beta t} - 1\right)}.$$

Eq. 9 describes a sigmoidal curve. In demographic literature, a mortality curve that resembles the RHS of Eq. 9 is said to be described by the 'Perks curve' (Perks, 1932; Gavrilov and Gavrilova, 2001, Section 2.4), but note that f describes failures, not mortality, and assuming a linear relationship between them may lead to unrealistic behaviour (see below). When $k_\rho > \phi_\rho$, the trajectory described by Eq. 9 initially rises exponentially until the critical time t^* when a fraction

$$f^* := f(t^*) = \frac{1}{2}\left[1 - \frac{\phi_\rho}{k_\rho}\right] \tag{10}$$

of the subsystems in the organism have failed. After this point, $f(t)$ begins to decelerate, eventually ($t \to \infty$) plateauing at $f(\infty) = 1$. The intuitive reason for this finding is that when most subsystems have already failed, fewer are left to fail; put even more simply, failures, when expressed as a proportion, cannot exceed 1. The critical fraction f^* is larger if the baseline failure rate ϕ_ρ is small and the accumulation rate k_ρ is high — in other words, the plateau point is higher when most failures are due to accumulation/interdependency structure rather than stochastic intrinsic failures of sub-systems. If instead $k_\rho \leq \phi_\rho$, the failure accumulation curve is only the decelerating part of the sigmoidal curve. Since we are interested in organisms with many interdependencies where failure accumulation is mostly due to the fact that systems depend on each other for functioning, we henceforth restrict ourselves to the case $k_\rho > \phi_\rho$.

Mortality dynamics in the Tithonus model

To connect failures to mortality (while recalling that the Tithonus model ignores the effect that mortality causes selective disappearance), we assume that an organism with f failures has a mortality rate $\mu(f)$. We will call the map $f \mapsto \mu(f)$ the 'mortality rule' of the model. Using the chain rule from calculus, we see that if failures follow Eq. 4, then mortality $\mu(f(t))$ follows the ODE

$$\frac{d\mu}{dt} = \mu'(f)r(f) \tag{11}$$

where $\mu'(f) := \frac{d\mu(x)}{dx}\Big|_{x=f}$ is the first derivative of the mortality map μ, evaluated at the point f.

What should a good mortality rule look like?

What would we expect a mapping $f \mapsto \mu(f)$ to look like? For one, we must have $\mu(f) \geq 0$, since μ is describing a rate. Further, we want individuals with more failures to have a greater mortality than those with fewer failures *ceteris paribus*, and the mortality rule must hence satisfy, for every f,

$$\mu'(f) > 0.$$

We may also want mortality to have an age and failure-independent component due to extrinsic causes such as predation and chance events.

We will first discuss the consequences of assuming a linear relationship between failures f and mortality. As we shall see, this is not a particularly realistic choice, but it serves to make the point that even without selective disappearance (which does not occur in the Tithonus model), actuarial senescence may deviate from a Gompertz-Makeham shape, such that old ages instead move towards a mortality plateau. The simple linear function (Gavrilov and Gavrilova, 1991, section 6.4; Nielsen et al., 2024, Eq. 5) takes the form

$$\mu(f,t) = \mu_e + \chi f, \tag{12}$$

where $\mu_e > 0$ and $\chi > 0$ are constants. In addition to linearity, Eq. 12 includes a constant age-independent component of mortality μ_e. In this case, the dynamics of mortality are simply a shifted version of the dynamics of failures: specifically, if failures follow Eq. 9, the predicted mortality hazard is also logistic. In this case, the model predicts that mortality hazard first rises exponentially (fitting a Gompertzian shape), but shows an increasing deviation from exponential increase as individuals move towards a state where all subsystems have failed. Thus, even without selective disappearance (which is ignored here), actuarial senescence will ultimately deviate from a Gompertzian shape, and mortality instead plateaus at $\mu_e + \chi$ because f can be at most 1.

However, biologically, an organism should not remain alive when all of its sub-systems have failed. Another desirable property of a mortality rule is thus to assert that $\lim_{f \to 1^-} \mu(f) = \infty$ so that the mortality hazard is infinitely high, corresponding to instantaneous death, at the point $f = 1$ (in other words, total failure implies death). The linear mortality rule Eq. 12 does *not* satisfy this property. The simplest mortality rule that satisfies all the previously mentioned properties and additionally has an infinitely high mortality hazard at $f = 1$ is the function

$$\mu(f(t)) = \mu_e + \chi \frac{f(t)}{1 - f(t)} \tag{13}$$

Once again, the first term on the RHS of Eq. 13 captures extrinsic mortality, while the second captures mortality due to failed sub-systems. We henceforth call Eq. 13 a 'geometric mortality rule', since it can be rewritten as an infinite geometric series

$$\mu((f(t)) = \mu_e + \chi \frac{f(t)}{1 - f(t)} = \mu_e + \chi \left(f(t) + f^2(t) + f^3(t) + f^4(t) + f^5(t) + \cdots \right).$$

Substituting Eq. 9 into Eq. 13 yields, after some algebra,

$$\mu(t) = \underbrace{\left[\mu_e - \frac{\chi \phi_\rho}{k_\rho - \phi_\rho} \right]}_{\text{'Makeham' part}} + \underbrace{\chi \left(\frac{\phi_\rho + k_\rho f_0}{(k_\rho - \phi_\rho)(1 - f_0)} \right) e^{(\phi_\rho + k_\rho)t}}_{\text{'Gompertz' part}} \tag{14}$$

Remarkably, logistic failure accumulation (Eq. 7 or Eq. 9) together with the geometric mortality rule (Eq. 13) leads to (exact) Gompertz-Makeham mortality curves! Since we argued that general models of failure accumulation should look like Eq. 5, and further showed that such an equation will always look like Eq. 7 whenever the Taylor expansion is fairly accurate, we expect mortality curves to generically look like a Gompertz-Makeham curve during the initial part of the failure accumulation process or if $\rho(f)$ does not have significant higher-order non-linearities.

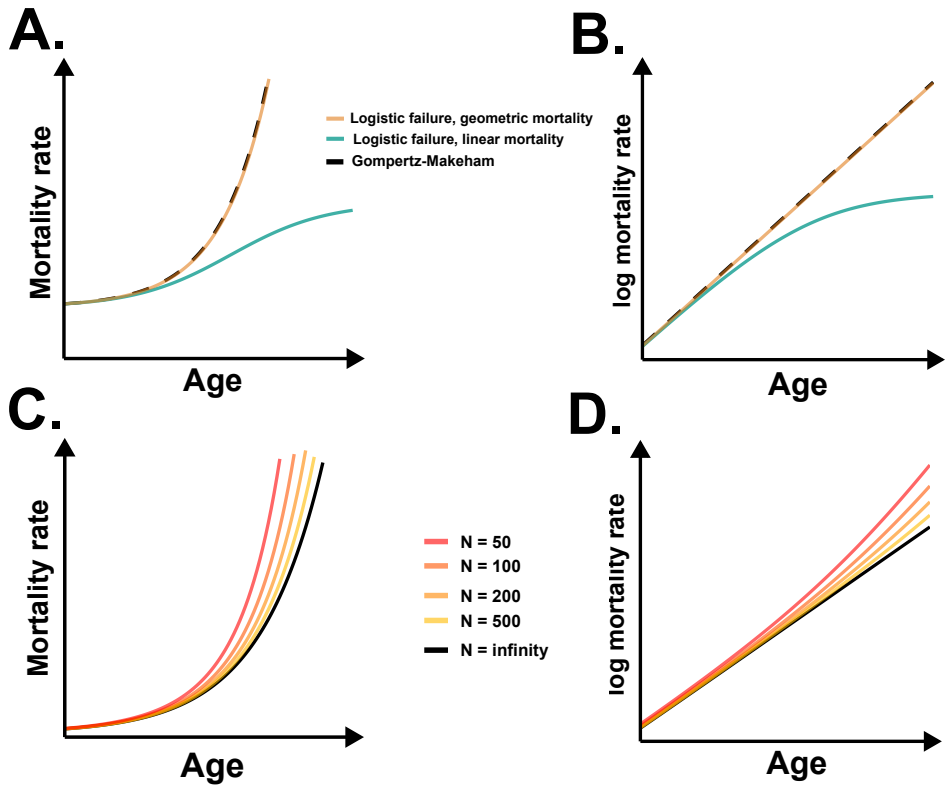

Figure 2: The predictions from the Tithonus model. In all plots, we use $r_+(f) = (1-f)(2\phi_\rho + k_\rho f)$ and $r_-(f) = (1-f)\phi_\rho$, so that the failure accumulation rule is $r(f) = (1-f)(\phi_\rho + k_\rho f)$, *i.e.* the logistic rule Eq. 7. Panels **(A)** and **(B)** illustrate the $N \to \infty$ predictions in comparison to a Gompertz-Makeham curve. If the mortality rule is linear (Eq. 12), the predicted mortality curve deviates from Gompertz-Makeham later in life, leading to a plateau. If we instead use the geometric mortality rule Eq. 13, the predicted mortality curve is exactly Gompertz-Makeham. Panels **(C)** and **(D)** illustrate the expected behaviour of the Tithonus model with the geometric mortality rule for finite N, from Eq. 16. The mortality curve for finite N is uniformly higher than the $N \to \infty$ curve. Axis ticks are deliberately left blank to underscore that quantitative values of ages and mortality hazards are arbitrary, because we are focused on the shape rather than the scale of the predicted mortality curve. Parameter values: **(A,B)** $\phi_\rho = 10^{-3}, k_\rho = 0.1, \mu_e = 0.01, \chi = 1, f_0 = 0.001$; **(C,D)** $\phi_\rho = 10^{-3}, k_\rho = 0.1, \mu_e = 0.01, \chi = 0.2, f_0 = 0.01$.

Connecting failures to mortality in the Tithonus model

If $N < \infty$, then $\mathfrak{f}_t$, the proportion of failures at age t, is a stochastic process governed by Eq. 2 rather than a deterministic process. Biologically, this is because $r_\pm$ are stochastic rates and there is thus (stochastic) heterogeneity in the failures f accumulated by age t. In other words, the failures accumulated at a fixed age t are described by a probability density function rather than a single value. We may naively try to connect the mortality $\mu(\mathfrak{f}_t)$ associated with having $\mathfrak{f}_t$ failures at age t by simply applying the mortality rule to the failure dynamics (we use 'naive' here in the sense of intentionally ignoring the contradiction that high-failure individuals, that are likely to have died already, are assumed still present at any t). Since $\mathfrak{f}_t$ is now a stochastic process, we cannot use the chain rule from calculus directly, but must instead use Itô's formula from stochastic calculus (Box 2 presents an introduction to stochastic calculus).

Itô's formula tells us the mortality rate at age t in this case obeys the stochastic differential equation

$$d\mu(\mathfrak{f}_t) = \left[r(\mathfrak{f}_t)\mu'(\mathfrak{f}_t) + \frac{\tau(\mathfrak{f}_t)}{2N}\mu''(f_t) \right] dt + \frac{1}{\sqrt{N}}\sqrt{\tau(\mathfrak{f}_t)}\mu'(\mathfrak{f}_t)dW_t \tag{15}$$

where W_t is the same Wiener process that appears in Eq. 2. The quantities

$$\mu'(f) := \left.\frac{d\mu(x)}{dx}\right|_{x=f} \quad \text{and}$$

$$\mu''(f) := \left.\frac{d^2\mu(x)}{dx^2}\right|_{x=f}$$

are the first two derivatives of the mortality rule evaluated at the current number of failures. Heuristically, $\mu'(f)$ tells us whether mortality is (locally) increasing or decreasing with f, and $\mu''(f)$ tells us whether this dependence is (locally) accelerating or decelerating.

Taking expectations on both sides of Eq. 15 now gives us

$$\mathbb{E}\left[\frac{d\mu(\mathfrak{f}_t)}{dt}\right] = r(f)\mu'(f) + \frac{\tau(f)}{2N}\mu''(f). \tag{16}$$

Eq. 16 is systematically different from the infinite sub-system prediction (Eq. 11) when the mortality rule is non-linear and the number of sub-systems N is finite.

Box 2: Itô's formula for non-linear transformations of SDEs

Imagine a deterministic quantity $x(t)$ satisfying the ordinary differential equation $\frac{dx}{dt} = f(x) + g(x)$ for two functions f and g. Given any function h, we can calculate how the quantity $h(x(t))$ changes over time using the chain rule of differentiation from calculus. The chain rule tells us that

$$\frac{dh}{dt} = \frac{dh}{dx}\frac{dx}{dt} = h'(x)f(x) + h'(x)g(x).$$

In standard 'SDE notation' (introduced in Box 1), we can rewrite this relation as

$$dx = f(x)dt + g(x)dt \quad \Rightarrow \quad dh(x) = h'(x)f(x)dt + h'(x)g(x)dt \tag{ii}$$

We may thus guess that the behaviour of $h(X_t)$, where X_t is an Itô diffusion that solves the SDE

$$dX_t = F(X_t)dt + G(X_t)dW_t,$$

follows the same principle, with gdt simply being replaced by GdW_t on the RHS of Eq. ii. Counter-intuitively, this idea fails due to the rapid stochastic fluctuations of the Itô diffusion X_t. The correct description of $h(X_t)$ is instead given by *Itô's formula* (Itô, 1951)

$$dh(X_t) = h'(X_t)F(X_t)dt + h'(X_t)G(X_t)dW_t + \frac{h''(X_t)}{2}G^2(X_t)dt.$$

There is now an extra $h''(X_t)G^2(X_t)/2$ term that does not exist in the deterministic setting! Furthermore, since this term is multiplied by dt rather than dW_t, the additional term changes the expectation value of $h(X_t)$ (see Box 1). An intuitive visual interpretation of this extra term in the context of eco-evolutionary dynamics appears in Box 3 of Bhat and Guttal (2025). Since Itô's formula is a stochastic version of the chain rule from ordinary calculus, the resulting theory of the rate of change of transformations of (Itô) diffusions is called (Itô) *stochastic calculus* (Øksendal, 1998).

If the mortality rule is accelerating in the proportion of failed sub-systems ($\mu''(f) > 0$), then, for any age, the mortality curve predicted by Eq. 16 is always higher than the curve predicted by Eq. 11 (Fig 2C-D). On the other hand, if the mortality rule is decelerating ($\mu''(f) < 0$), the mortality curve predicted by Eq. 16 is always lower than the curve predicted by Eq. 11 (but it is not clear whether we would ever biologically expect to find such decelerating mortality rules).

The main model with selective disappearance

The simplicity of the Tithonus model comes at a cost of assigning mortality rates in a post-hoc way to every possible individual state (number of failures), without taking into account that individuals who die can no longer age. Thus, it may not be possible to reach some states (failure values) while remaining alive, or the probability of doing so may be low. To better understand whether and how sinful this simplification is, we now present a model that fully takes account of mortality's power to remove individuals from the set of observables, at the appropriately stochastic and individual-level rate. This allows us to study how the mortality process itself feeds back, via the disappearance of some individuals, into predicting the mortality curve that we expect to observe at the population level.

We now model the failure dynamics $\{\widetilde{f}_t\}_{t\geq 0}$ as a birth-death process with killing (Karlin and Taylor, 1981, p. 161) on $\{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\} \cup \{\mathcal{C}\}$ with transition rates

$$f \to f + \frac{1}{N} \text{ at rate } Nr_+(f) \tag{17a}$$

$$f \to f - \frac{1}{N} \text{ at rate } Nr_-(f) \tag{17b}$$

$$f \to \mathcal{C} \text{ at rate } \mu(f) \tag{17c}$$

Here, $\mathcal{C}$ is a 'cemetery state' (a term borrowed from human demography) used to denote the death of the individual (Karlin and Taylor, 1981, p. 161). The Markov process defined by Eq. 17 unfolds in continuous time, and can be simulated exactly using the Gillespie algorithm (Kokko, 2024).

We once again track the probability that an individual who begins with $f_0 = F_0/N$ failures at age 0 will have a proportion f failed systems at age t. We will denote the probability density of this process by $\widetilde{P}(f,t)$ to distinguish it from the probability that appears in Eq. 1. An argument identical to that used to derive Eq. 1 (Supplementary section S1) shows that $\widetilde{P}(f,t)$ obeys (Woodbury and Manton, 1977; Yashin et al., 1985)

$$\frac{\partial \widetilde{P}(f,t)}{\partial t} = -\frac{\partial}{\partial f}\left\{r(f)\widetilde{P}(f,t)\right\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{\tau(f)\widetilde{P}(f,t)\right\} - \mu(f)\widetilde{P}(f,t) \tag{18}$$

Eq. 18 is a generalisation of a Fokker-Planck/diffusion equation that allows for the loss of individuals from the cohort due to (stochastic) mortality (Woodbury and Manton, 1977; Yashin et al., 1985). Continuous state stochastic processes whose probability densities are described by equations of the form Eq. 18 are called *killed diffusions* or *diffusions with killing* (Karlin and Tavaré, 1982; Steinsaltz and Evans, 2006; we also characterise the process in terms of its infinitesimal generator in supplementary section S2.1). While a neat result, Eq. 18 comes with an important limitation that we need to overcome: it is not correct to interpret $\widetilde{P}(f,t)$, when read for a specific value t, as the probability distribution of failures of an age-t individual. This is because the density of individuals as a whole declines over time (due to death) and approaches zero; a probability density function must sum up to 1, however. We will thus need to condition on the individual being alive.

The remaining task is thus to focus on the subset of individuals still alive. Technically, this means deriving the probability distribution function conditional on the individual having reached age t, in other words, asserting that the time of death $T_{\text{mort}} > t$. Yashin et al., 1985 (their Eq. 7 and their Appendix A) have proved that the conditional probability density $\widehat{P}(f,t) := \widetilde{P}(f,t|f_0, t < T_{\text{mort}})$ of this processs obeys the partial differential equation

$$\frac{\partial \widehat{P}(f,t)}{\partial t} = -\frac{\partial}{\partial f}\left\{r(f)\widehat{P}(f,t)\right\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{\tau(f)\widehat{P}(f,t)\right\} - \left[\mu(f) - \overline{\mu}(t)\right]\widehat{P}(f,t) \tag{19}$$

where

$$\overline{\mu}(t) \coloneqq \mathbb{E}\left[\mu(f,t) \mid f_0, t < T_{\text{mort}}\right] = \int_0^1 \mu(x,t)\widehat{P}(x,t)dx \tag{20}$$

is the expected force of mortality conditioned on remaining alive.

Eq. 19 describes $\widehat{P}(f,t)$, the probability (density) of a live individual having f failures at age t. However, while Eq. 19 describes how a probability distribution function as a whole changes over age, it would be much more intuitive if we could instead come up with a 'pathwise' description that lets us follow an individual through the course of its life and ask how its number of failures and mortality risk are expected to change in terms of means and variances (see Fig 1 for a visual representation of the two different descriptions). For the Tithonus model, we were able to derive such a description, namely a stochastic differential equation (Eq. 2, see Box 1 for why this is a pathwise description), using the fact that a process whose probability density is given by a Fokker-Planck equation always corresponds to the solution of an SDE (Gardiner, 2009, section 4.3.5). No such direct correspondence with an SDE exists for equations such as Eq. 18 and Eq. 19 because individuals may enter the cemetery state (*i.e.* die) at any time, at which point the 'path' of the individual through failure space disappears, instantaneously jumping to the cemetery state. To overcome this difficulty, we derive a path-wise description in terms of the Tithonus model using a fundamental theorem from the heart of stochastic analysis called the Feynman-Kac formula (Feynman, 1948; Kac, 1949; Øksendal, 1998, section 8.2).

The Feynman-Kac formula reveals the emergence of selective disappearance

Suppose an individual is born with f_0 failures at birth, and then accumulates failures and experiences mortality risk according to our main model with selective disappearance defined by Eq. 19. Let us denote this stochastic process by $\widehat{f}_t$. Let $M : [0,1] \to \mathbb{R}$ be a function that takes in a number of failures f and outputs a real number. $M(f)$ should be thought of as a measurement

made on an individual that bears f failures. For instance, choosing $M(\cdot) := \cdot$ measures the number of failures, and choosing $M(\cdot) := \mu(\cdot)$ measures the mortality associated with having a given number of failures subject to the mortality rule μ. One could also imagine M calculating reproductive output, nesting ability, or any other quantity, as long as M only depends on the failures f that the organism possesses and does not otherwise depend on chronological age (the technical phrase is that the measurement M is 'time homogeneous').

We are interested in $\mathbb{E}[M(\widehat{f}_t)|\widehat{f}_0 = f_0]$, the value of the measurement performed on the typical individual following our main model Eq. 19 and initiated with $\widehat{f}_0 = f_0$. Notice that Eq. 19 is conditioned on the individual being alive, and so the expectations and so on are genuine probabilities. In supplementary sections S2-S3, we use a version of the Feynman-Kac formula (Øksendal, 1998, theorem 8.2.1(b)) to show that $\widehat{M}(f_0, t) := \mathbb{E}[M(\widehat{f}_t)|\widehat{f}_0 = f_0]$ can be written as

$$\widehat{M}(f_0,t) = \frac{\mathbb{E}\left[M(\mathfrak{f}_t)\, e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]}{\mathbb{E}\left[e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]} =: \frac{\widetilde{M}(f_0,t)}{\overline{S}(t)}\,, \tag{21}$$

where $\mathfrak{f}_t$ is the stochastic process defined by Eq. 2 from the Tithonus model, and the conditional expectation is over paths of the Tithonus model $\{\mathfrak{f}_t\}_{t\geq 0}$ starting from f_0 at 0. We describe one intuitive way to think about the meaning of an expectation over the paths taken by a stochastic process in Box 3. We have defined the composite terms $\widetilde{M}$ for the numerator and $\overline{S}$ for the denominator for convenience, so we may discuss them both in turn.

We begin with the numerator,

$$\widetilde{M}(f_0,t) := \mathbb{E}\left[M(\mathfrak{f}_t)\, e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right], \tag{22}$$

Since $\mu(f)$ is the instantaneous mortality risk when an individual has f failures, $\int_0^t \mu(f_s)ds$ is the cumulative mortality risk associated with the entire path $\{f_s\}_{s\in[0,t]}$. The quantity $\exp(-\int_0^t \mu(f_s)ds)$, typically called the survivorship, thus measures the probability of survival up to age t, starting

at age t, when failure accumulation follows the path $\{f_s\}_{s\in[0,t]}$. In words, the RHS of Eq. 22 is thus 'summing up' all the possible values of the measurement M performed on a hypothetical individual following the Tithonus model Eq. 2, while weighting each possible measurement by the survivorship along the particular path the process took to arrive at its final value.

Box 3: Expectations over the paths taken by an Itô diffusion

Consider a continuous time stochastic process $\{X_t\}_{t\geq 0}$ that takes values in $[a,b] \subseteq \mathbb{R}\cup\{-\infty,\infty\}$ and solves the SDE $dX_t = F(X_t)dt + G(X_t)dW_t$. Let $H(X_T)$ be a function that depends on the entire path or 'history' of $\{X_t\}_{t\geq 0}$ up to the time $T > 0$. For instance, the survivorship function $\exp(-\int_0^T \mu(X_s)ds)$ is one such function. One way of understanding the meaning of the conditional expectation $\mathbb{E}[H(X_T) \mid X_0 = x]$ is to partition $[0,T]$ into n discrete time intervals, each of width $(\Delta t)_n := T/n$. For each $k \in \{0,1,\ldots,n\}$, let $t_k := kT/n$ denote the k^{th} timepoint in the partition. Note that $t_0 = 0$ and $t_n = T$. The conditional expectation of $H(X_T)$ over the paths of the Itô diffusion X_t can be written as (Karatzas and Shreve, 1998, Theorem 2.4.20 with Theorem 3.5.1)

$$\mathbb{E}[H(X_T) \mid X_0 = x] = \lim_{n\to\infty} \underbrace{\int_a^b \int_a^b \cdots \int_a^b \int_a^b}_{n \text{ times}} H(x_{t_n}) \left(\prod_{k=1}^{n} p_n(x_{t_k}|x_{t_{k-1}})\right) dx_{t_1} dx_{t_2} \cdots dx_{t_{n-1}} dx_{t_n} \quad \text{(iii)}$$

where we set $x_{t_0} = x$ to enforce the conditioning on the initial value, and each

$$p_n(x_{t_k}|x_{t_{k-1}}) := \frac{1}{\sqrt{2\pi G^2(x_{t_{k-1}})(\Delta t)_n}} \exp\left(-\frac{1}{2}\frac{[x_{t_k} - x_{t_{k-1}} - F(x_{t_{k-1}})(\Delta t)_n]^2}{G^2(x_{t_{k-1}})(\Delta t)_n}\right)$$

can be interpreted as the density function for the process $\{X_t\}_{t\geq 0}$ to take value x_{t_k} at time t_k given that its value at an earlier time t_{k-1} was $x_{t_{k-1}}$. The product $\prod_{k=1}^n p_n(x_{t_k}|x_{t_{k-1}})$ is thus just a joint density function for $(x_{t_1}, x_{t_2}, \cdots, x_{t_{n-1}}, x_{t_n})$, a vector that becomes a continuous path as $n \to \infty$, *i.e.* as $(\Delta t)_n \to 0$. The fact that $p_n(\cdot\,|x_{t_{k-1}})$ is the density function of a Normal distribution with mean $x_{t_{k-1}} + F(x_{t_{k-1}})(\Delta t)_n$ and variance $G^2(x_{t_{k-1}})(\Delta t)_n$ should make sense upon revisiting the meaning of the SDE $dX_t = F(X_t)dt + G(X_t)dW_t$ (Box 1). The limiting object on the RHS of Eq. iii can also be recast into a single, more abstract integral called an 'integral with respect to the Wiener measure' (Kac, 1949) in mathematics and a 'Euclidean path integral' (Feynman, 1948) in physics.

We now move to the denominator. We show in supplementary section S3 that

$$\overline{S}(t) := \mathbb{E}\left[e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right] = e^{-\int_0^t \overline{\mu}(s)ds}, \tag{23}$$

where $\overline{\mu}$ is given by Eq. 20. Thus, $\overline{S}(t)$ intuitively calculates the survivorship corresponding to the "average force of mortality" $\overline{\mu}$ conditioned on individuals not dying. We also show in the supplementary (Eq. S28) that $\overline{S}(t)$ quantifies the expected number of individuals who reach age t if we do not condition on remaining alive (*i.e.* if individuals are continually lost to the cemetery state as in Eq. 18). More precisely, if a population initially has K individuals of age 0, each individual following our main model Eq. 17, then a proportion $K\overline{S}(t)$ of them are expected to reach age t alive. Motivated by this, we henceforth call $\overline{S}(t)$ the "expected survivorship" in the population.

To summarise, the numerator of the RHS of Eq. 21 is the expected value of $M(\mathfrak{f}_t)$ if individuals followed the Tithonus model, with the contribution of each path $\{\mathfrak{f}_s\}_{s\in[0,t]}$ additionally being weighted by the probability that an individual following our main model does not disappear if it follows that path. The denominator is the expected survivorship across all possible paths. In both, the expectations over paths are in terms of realisations of the Tithonus model, which admits a direct pathwise description in terms of SDEs. The relation 21 clarifies the precise way in which selective disappearance affects measurements — those paths in failure space which are more likely to be associated with death/mortality are systematically less likely to contribute to the measurement $\widehat{M}(f_0, t)$ because these 'unlucky' individuals (also see Snyder et al., 2021) are more likely to die before reaching age t.

Since the Tithonus model can be written as the solution to an SDE, it is both easier to handle analytically and much more efficient (in both time and memory) to simulate numerically using standard SDE-based tools than the exact stochastic process Eq. 17, since the latter requires using the Gillespie algorithm (Kokko, 2024). Thus, our work provides efficient numerical methods to calculate the expected effects of selective disappearance on measurements, as long as the failure

accumulation rule, mortality rule, and the connection between the measurement and failures are known.

Setting $M(\cdot) = \cdot$, we find that $\widehat{E}(f_0, t) := \mathbb{E}[\widehat{f_t} | \widehat{f_0} = f_0]$, the expected number of failures accrued by an individual of age t following Eq. 19, is given by

$$\widehat{E}(f_0, t) = \frac{1}{\overline{S}(t)} \mathbb{E}\left[\mathfrak{f}_t \, e^{-\int_0^t \mu(\mathfrak{f}_s) ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]. \tag{24}$$

Similarly, setting $M(\cdot) = \mu(\cdot)$, we obtain the expressions for the expected mortality at age t conditioned on remaining alive as

$$\widehat{\mu}(f_0, t) = \frac{1}{\overline{S}(t)} \mathbb{E}\left[\mu(\mathfrak{f}_t) \, e^{-\int_0^t \mu(\mathfrak{f}_s) ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right] \tag{25}$$

where $\mu(\mathfrak{f}_t)$ solves the SDE Eq. 15. Eq. 25 says that we should weight the mortality $\mu(f)$ associated with having f failures by the probability of reaching the state f without dying (normalised by the average survivorship in the population). In figure 3, we illustrate that the analytical predictions from the Feynman-Kac prediction generally agree with direct individual-based simulation of the exact stochastic process 17 using the Gillespie algorithm (Kokko, 2024), and both differ significantly from the predictions when disappearance is ignored. The discrepancy between the Tithonus model and our main model is more pronounced at later ages, but since survivorship also declines with age (background gradient in Fig 3), not many individuals necessarily survive up to the point where the deviation becomes noticeable. Fig 3 exemplifies this by illustrating the age (vertical dotted lines) at which only 10% of the initial cohort is alive, and the deviation from Gompertz remains mild for the majority of individuals. Moreover, the survivorship plummets catastrophically past this point (notice that the gradient is on a logarithmic scale).

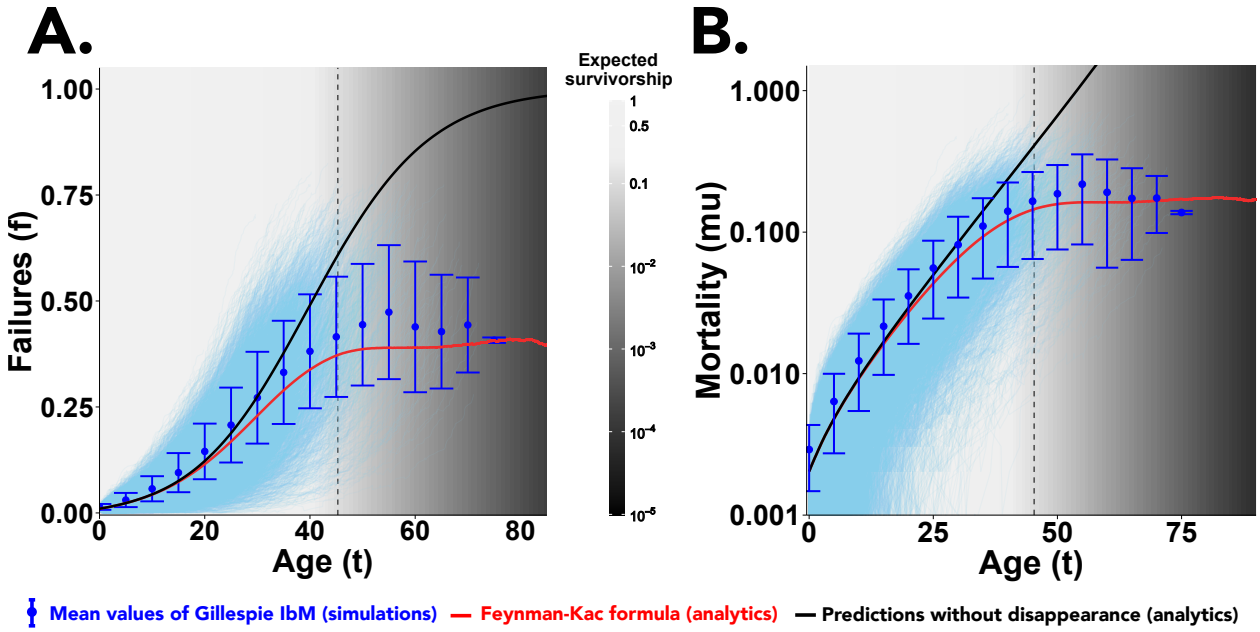

Figure 3: (A) Failure and **(B)** mortality accumulation curves predicted under the logistic failure accumulation rule Eq. 9 with the geometric mortality rule Eq. 13. Light blue trajectories are from 9500 Gillespie simulations of the exact stochastic process 17, and dark blue points (with error bars) are the mean values among these trajectories. Error bars are standard deviations. Black curve is the expected trajectory of the Tithonus model (Eq. 2 and Eq. 15), calculated by numerically simulating 20,000 realisations of the SDEs using the Euler-Maruyama method. Red curve is the Feynman-Kac formula (Eq. 24 for failures, Eq. 25 for mortality), with expectations calculated using the numerical simulations of the Tithonus SDEs. Shade of the background represents expected survivorship from Eq. 23. Dotted vertical line indicates the point when $\bar{S}(t) = 0.1$. We use $r_+(f) = (1-f)(2\phi_\rho + k_\rho f)$ and $r_-(f) = (1-f)\phi_\rho$, so that the failure accumulation rule is $r(f) = (1-f)(\phi_\rho + k_\rho f)$ and the turnover is $\tau(f) = (1-f)(3\phi_\rho + k_\rho f)$. The means of the Gillespie simulations are generally higher than the Feynman-Kac prediction because rare, extremely 'lucky' individuals with few failures and exceptional lifespans are (by definition) unlikely to be present in any finite size sample of realisations of a stochastic simulation. Parameter values: $\phi_\rho = 10^{-3}, k_\rho = 0.1, \mu_e = 10^{-5}, \chi = 0.2, N = 200, f_0 = 0.01$.

How much of a difference can selective disappearance make?

Since we have shown that selective disappearance can alter the observed values of measurements (Fig 3) from what would have been observed if there were no disappearance, a natural question is just how strong one can expect this effect to be. For instance, in humans, mortality beyond approximately 30 years of age fits the Gompertz curve well (see Figure 1 in Pichler and

Uhlig, 2023 for a recent example in Germany), with no obvious deviation at oldest ages, and the existence of mortality plateaus in general for humans is debated (see Discussion). In equations, we ask for the value of $\delta_M(f_0, t) := \mathbb{E}[M(\mathfrak{f}_t) \mid \mathfrak{f}_0 = f_0] - \mathbb{E}[M(\widehat{f}_t) \mid \widehat{f}_0 = f_0]$, the expected difference between the measurement M if there were no disappearance, and the corresponding value when disappearance is present (the latter measurement being conditioned on the observed individual remaining alive). Using Eq. 21 in the definition of $\delta_M(f_0, t)$ reveals that δ_M, the expected deviation of the measurement M from the Tithonus model dynamics, admits the representation

$$\delta_M(f_0, t) = -\frac{1}{\overline{S}(t)} \operatorname{Cov}\left[M(\mathfrak{f}_t) \ , \ e^{-\int_0^t \mu(\mathfrak{f}_s) ds} \ \middle| \ \mathfrak{f}_0 = f_0 \right] \tag{26}$$

where $\operatorname{Cov}[X_t, Y_t | X_0 = x_0] := \mathbb{E}[X_t Y_t | X_0 = x_0] - \mathbb{E}[X_t | X_0 = x_0]\mathbb{E}[Y_t | X_0 = x_0]$ is the conditional covariance process at time t between two stochastic processes $\{X_t\}_{t \geq 0}$ and $\{Y_t\}_{t \geq 0}$. Eq. 26 says that we expect selective disappearance to alter measurements significantly ($|\delta_M|$ is large) if the measurement M is correlated with survivorship. If larger numerical values of M are associated with lower survivorship, then the covariance is negative and δ_M is positive (the expected value of the measurement with disappearance is lower than if there were no disappearance), whereas if larger numerical values of M are associated with lower survivorship, then the covariance is positive and δ_M is negative (the expected value of the measurement with disappearance is higher than if there were no disappearance). The magnitude of the difference, $|\delta_M|$, is proportional to the magnitude of covariance between the measurement and survivorship. In Supplementary section S4, we show that the absolute value of δ_M can be bounded above by

$$|\delta_M(f_0, t)| \leq \sigma_M(f_0, t) \sqrt{\frac{1 - \overline{S}(t)}{\overline{S}(t)}}, \tag{27}$$

where $\sigma_M(f_0, t) := \sqrt{\operatorname{Cov}[M(\mathfrak{f}_t), M(\mathfrak{f}_t) | \mathfrak{f}_0 = 0]}$ is the standard deviation process for the measurement $M(\mathfrak{f}_t)$. The quantity $\sigma_M(f_0, t)$ can be thought of as measuring the heterogeneity in the failure accumulation process $\{\mathfrak{f}_t\}_{t \geq 0}$ at age t. The term within the square root can be interpreted as an

odds ratio, the denominator being the expected survivorship from Eq. 23, and the numerator being its complement.

As an application of Ineq. 27, we illustrate how mortality curves are affected by selective disappearance. Let us assume that the turnover $\tau(f)$ is bounded, *i.e.* that there is some finite number $\tau_{\max}$ such that $\tau(f) \leq \tau_{\max}\ \forall\ f \in [0,1]$ (this is a natural assumption for us because we expect the rates $r_{\pm}(f)$ to be bounded, since only so many things can happen within an organism per unit time). Let us further assume that $\mu'(f)$, the rate of change of mortality as a function of failures, is also bounded, *i.e.* there is a finite constant $\mu'_{\max}$ such that $\mu'(f) \leq \mu'_{\max}\ \forall\ f \in [0,1]$. In words, this latter assumption is saying that the mortality hazard μ never changes infinitely quickly. Using the SDE Eq. 15 corresponding to mortality in the Tithonus model, we show in supplementary section S4 that $\delta_\mu(f_0, t)$, the expected difference at age t between the mortality curve with disappearance and the curve when there is no disappearance, obeys

$$|\delta_\mu(f_0,t)| \leq \mu'_{\max} \sqrt{\frac{\tau_{\max}}{N}\left(\frac{1-\overline{S}(t)}{\overline{S}(t)}\right)\ t}\quad . \tag{28}$$

Thus, the maximum possible effects of selective disappearance are controlled by (a) $\mu'_{\max}$, how quickly mortality can change as failures change (slower means the effects of disappearance are less visible), (b) t, the age at which the measurement is made (the effects of selective disappearance are less visible at smaller ages), (c) N, the total number of sub-systems that can fail (larger means the effects of disappearance are less visible), and (d) $\overline{S}(t)$, the overall expected survivorship at age t (greater survivorship means the effects of disappearance are less visible).

The geometric mortality rule Eq. 13 that we advocated for earlier does *not* have a bounded derivative, since our model predicts infinitely high mortality risk when $f = 1$. Nevertheless, since $0 \leq f(t) \leq 1$, we can approximate Eq. 13 arbitrarily well by a finite geometric series,

$$\mu((f(t)) = \mu_e + \chi\frac{f(t)}{1-f(t)} \approx \mu_e + \chi\left(f(t) + f^2(t) + f^3(t) + f^4(t) + \cdots + f^{\alpha-1}(t) + f^{\alpha}(t)\right). \tag{29}$$

Here, $\alpha > 1$ can be any positive integer, chosen according to a desired degree of precision. Higher values of α provide strictly better approximations, and the equality is exact if we consider infinitely many terms. Letting α be any fixed, finite number, we show (supplementary section S4) that $\delta_\mu(f_0, t)$, the expected difference at age t between the mortality curve with disappearance and the curve when there is no disappearance, is bounded above by

$$|\delta_\mu(f_0, t)| \leq \chi \frac{\alpha\,(\alpha+1)}{2} \sqrt{\frac{\tau_{\max}}{N}\left(\frac{e^{\mu_e t} - \overline{S}_{\text{fail}}(t)}{\overline{S}_{\text{fail}}(t)}\right) t} \quad , \tag{30}$$

where $\overline{S}_{\text{fail}}(t)$ measures the expected survivorship when deaths due to extrinsic factors are excluded. In other words, we have partitioned the overall expected survivorship $\overline{S}(t)$ from Eq. 23 as $\overline{S}(t) = e^{-\mu_e t}\,\overline{S}_{\text{fail}}(t)$. Ineq. 30 tells us that

1. Deviations caused by selective disappearance are less important at smaller ages, but can become more important at later ages. This simply reflects the fact that the role of heterogeneity and 'luck' in affecting distributions via disappearance is more important as the cohort ages.

2. Selective disappearance becomes less powerful at causing deviations from Gompertz as the total number of sub-systems N grows larger. One way to phrase the effect is that a large N means that each individual's path to each death is rather unique: the identity of the subsystem that fails first is then likely to differ between individuals, as does the identity of the 'final straw', and all else in between. We predict that the uniqueness of the causal route to each death weakens the signature of selective disappearance in any longevity dataset. An imaginary organism with $N = \infty$ would not show it at all, while an organism with only meagre complexity (a small number of subsystems) shows the best prospects for selective disappearance playing a strong role in their observed life histories.

3. Selective disappearance becomes less important as $\tau_{\max}$ becomes smaller. Recalling from Eq. 3 that $\tau(f)$ controls the variance in the failure accumulation process over small timescales, this means that selective disappearance becomes less important as the failure accumulation

process itself becomes more stereotyped/canalised.

4. For a fixed value of μ_e, the role of extrinsic mortality in causing deviations due to selective disappearance is more important at later ages. Conversely, for a fixed age, selective disappearance becomes less important as the extrinsic mortality μ_e decreases. Though this may seem puzzling at first glance because extrinsic mortality traditionally masks patterns of senescence, it becomes more clear once we remember that we are calculating conditional probabilities. Intuitively, extrinsic mortality uniformly controls the probability of survival up to a certain age, independent of failures. Since we are conditioning on individuals remaining alive up to age t, this conditioning increasingly focuses on those 'lucky' individuals who avoided death as (a) extrinsic mortality increases, and (b) later ages are considered. In other words, though extrinsic mortality does not itself cause 'selective' disappearance in the sense of favouring some states over others, its effects are nevertheless to cause deviations from curves predicted without disappearance because extrinsic mortality is selecting for pure dumb luck. However, this is only true when failures do still have an impact on mortality (note the χ outside the square root) because extrinsic mortality can only amplify existing differences.

5. Selective disappearance becomes less visible as $\overline{S}_{\text{fail}}(t)$, the expected survivorship when deaths due to extrinsic causes are ignored, increases. The same logic also explains the multiplicative factor of χ outside the square root: if failures have a smaller impact on mortality aver all (χ is smaller), selective disappearance is less visible; if all mortality is extrinsic and failures do not impact mortality at all ($\chi = 0$), selective disappearance cannot cause any deviations of mortality curves from the predictions of the Tithonus model.

Thus, in many cases, selective disappearance may not impact observed datasets in a strong manner. In these cases, we predict, from our criteria for failure and mortality rules above, that the resultant mortality curves should generically follow the Gompertz-Makeham shape (see Eq. 14 and fig 2). Eq. 26 also shows that deviations from Gompertz-Makeham will always reduce

the mortality rate — moving towards a plateau-like shape —- because the covariance between mortality and survivorship is always negative (and thus δ_μ is always positive). Further, the $\sqrt{t}$ on the right hand side of Ineq. 30 indicates that δ_μ is constrained to be smaller at smaller ages. Thus, deviations of observed mortality curves from Gompertzian dynamics are always a reduction in mortality later in life (red curves and blue points in Fig 3). Theorem 3.4 in Steinsaltz and Evans (2006), together with Steinsaltz and Evans (2004), proves that the mortality curve arising from Eq. 19 (or, equivalently, Eq. 25) is also guaranteed to plateau in a strict sense, *i.e.* remain strictly constant with age, if we consider sufficiently advanced ages (in fact their results concern a broader class of stochastic processes).

The bound we have derived (Ineq. 30) is about the maximum value that δ_μ, the expected difference in mortality between the typical individual following the Tithonus model and a corresponding individual following our contradition-free main model, is mathematically allowed to take at age t. It can thus be thought of as an estimate of the 'opportunity' or 'potential' for selective disappearance to be important. Importantly, the bound is calculated *after* conditioning on finding living individuals of that particular age. Consequently, it automatically assumes that such an individual will indeed be found. Since survivorship also strongly declines with age (colour gradient in Fig 3), the value of δ_μ could be large and nevertheless be difficult to detect in data if the expected survivorship becomes very low before δ_μ becomes appreciably large. One way to visualise when deviations are difficult to detect due to low expected survivorship is to calculate $\overline{S}(t)$ at the time when the relative deviation $\delta_\mu(f_0, t)/\mathbb{E}[\mu(\mathfrak{f}_t)|\mathfrak{f}_0 = f_0] \in [0, 1)$ first exceeds a fixed 'detection threshold' θ. Setting θ to a low number should be interpreted to mean that the empirical data admits sufficient statistical power to detect small deviations from Gompertz-Makeham dynamics, whereas setting θ higher means that we need a larger difference in the relative mortality rate predictions $\delta_\mu/\mathbb{E}[\mu(\mathfrak{f}_t)|\mathfrak{f}_0 = f_0]$ before we have confidence that the curve being followed is indeed not Gompertz-Makeham and exhibits a detectable plateau.

In Fig 4, we use the exact expression Eq. 26 to plot the expected survivorship $\overline{S}$ at the age when $\delta_\mu/\mathbb{E}[\mu(\mathfrak{f}_t)|\mathfrak{f}_0 = f_0]$ first exceeds various threshold values θ. As the total number of sub-

systems N increases, the survivorship at the point where a fixed threshold θ is exceeded quickly becomes extremely small. Unlike the upper bound Ineq. 30, the expected survivorship (obviously) decreases as extrinsic mortality is increased, causing deviations from Gompertz-Makeham to be less detectable (compare Fig 4A vs Fig 4B), despite the deviations being less constrained by Ineq. 30. Loss of expected survivorship is thus an additional way in which observed mortality curves in data can resemble the trajectory of the Tithonus model (and hence often be Gompertz-Makeham curves).

Undetectability of deviations due to loss of expected survivorship is fundamentally a function of limits on measurement precision and statistical power. Blue hues in 4 indicate that only very few individuals are still alive when deviations of a specific size become visible. Yet, in principle, if one could start with sufficiently many sufficiently (and possibly unrealistically) large cohorts, patterns in data could be detected up to arbitrarily advanced ages (with arbitrarily low survivorship). In contrast, the upper bound Ineq. 27 is a mathematical constraint on the maximum possible value of δ_μ, and is hence conservative (*i.e.* the realised deviation could be well below this bound) but unaffected by considerations of sample size or statistical power. Put differently, the expected survivorship $\overline{S}(t)$ (Eq. 23, colour in Fig 4) tells us the probability of finding a living individual of age t in our main model, while the bound Ineq. 27 tells us how different the typical individual that has reached age t (without having died) in our main model is from the typical Tithonus individual of the same age.

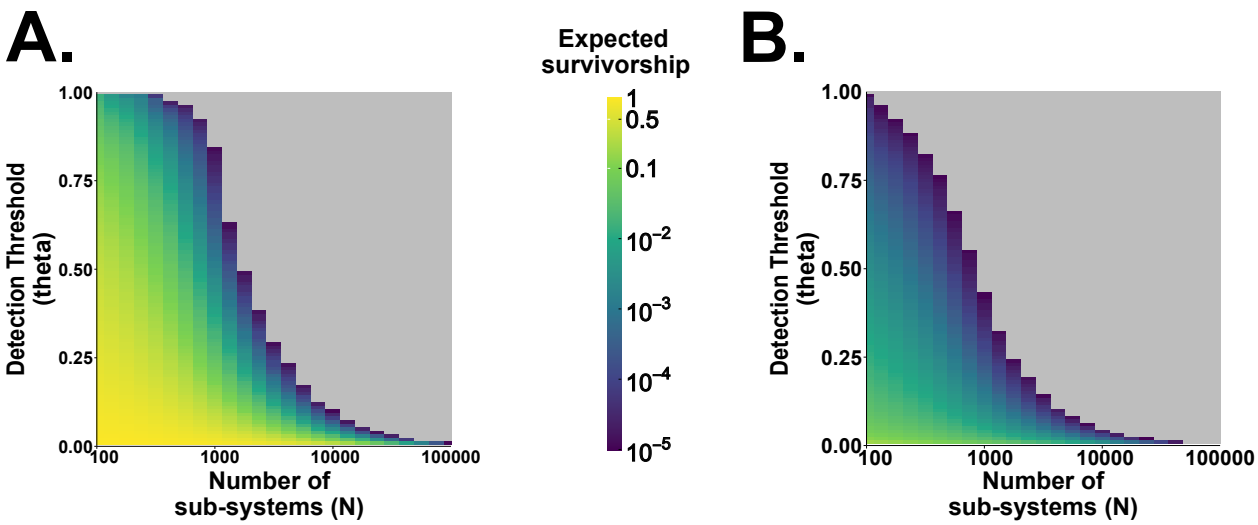

Figure 4: The mean survivorship at the point when the deviation between our main model and the Tithonus model first exceeds a fixed detectability threshold θ. X-axis is the number of sub-systems N, and colour is the expected survivorship $\overline{S}(t)$ from Eq. 23 at the age t when the relative deviation $\delta_\mu(f_0,t)/\mathbb{E}[\mu(\mathfrak{f}_t)|\mathfrak{f}_0 = f_0]$ first exceeds the corresponding point on the Y-axis (θ). Grey colour indicates that either the expected survivorship dropped below 10^{-5} or the detectability threshold θ was never reached by $t = 500$. Results are plotted for both **(A) Low extrinsic mortality**, $\mu_e = 10^{-5}$, and **(B) High extrinsic mortality**, $\mu_e = 0.1$. Relative deviation $\delta_\mu/\mathbb{E}[\mu(\mathfrak{f}_t)|\mathfrak{f}_0 = f_0]$ and expected survivorship $\overline{S}$ are both calculated using the Feynman-Kac representations by numerically simulating 20,000 realisations of the Tithonus SDEs using the Euler-Maruyama method for each value of N. We use $r_+(f) = (1-f)(2\phi_\rho + k_\rho f)$ and $r_-(f) = (1-f)\phi_\rho$, so that the failure accumulation rule is $r(f) = (1-f)(\phi_\rho + k_\rho f)$ and the turnover is $\tau(f) = (1-f)(3\phi_\rho + k_\rho f)$. Fixed parameter values across both panels: $\phi_\rho = 10^{-3}, k_\rho = 0.1, \chi = 0.2, f_0 = 0.01$.

Discussion

In this paper, we provide a mathematical framework that formally captures the idea that senescence arises from stochastic failures of, or damage to, intra-organismal sub-systems important for physiological function. The first of our two models is simple but inherently contradictory (the 'Tithonus model' where organisms can age, and this impacts mortality rates, but deaths are not actually implemented), while the main model strives towards more realism by removing the contradiction. The 'Tithonus model' has the benefit of creating simple predictions for failure accumulation and mortality curves when the goal is not to incorporate selective disappearance, which justifies presenting it while alerting the reader to its inherent contradiction.

To put our findings in a historical context, it is intriguing to note that George Williams, one of the grand old men of senescence theory, was quite pessimistic about both reliability theoretic thinking and Gompertz-Makeham curves later in his life (Williams, 1999), even referring to the same Tithonus myth we use here (though he used the metaphor to encourage study of ageing more broadly, not just in terms of lifespan shortening). His view was that the 'organisms as failing machines' analogy could not handle repair or replacement of failed systems, that Gompertz-Makeham mortality is often postulated only through statistical fitting (*i.e.* without mechanistic understanding), and that Gompertz-Makeham mortality cannot persist when populations are heterogeneous. Our work addresses all these criticisms. Firstly, we have incorporated repair rates in our model, only assuming that repair cannot perfectly balance failures forever, not least because repair mechanisms themselves can fail (Gorbunova et al., 2007). Secondly, we have derived exponential mortality curves as a generic consequence of two mechanistically grounded observations: (i) organisms are integrated systems with many interdependencies and thus failure begets failure, and (ii) an organism can never remain alive when all its sub-systems have failed (though it may also die earlier). Thirdly, we have demonstrated that while (stochastic) heterogeneity does cause deviations from Gompertz-Makeham curves (also see Weitz and Fraser, 2001), these deviations may often be so small as to be undetectable in data.

In addressing the last of Williams' (1999) criticisms by showing that deviations of our main model from Gompertz-Makeham mortality can often be very small, our work touches on an important, if somewhat overlooked, theoretical conundrum relevant to humans and related unitary organisms: if selective disappearance is inevitable and always lowers late life mortality (thus causing a plateau), why do so many organisms exhibit an excellent fit of the Gompertzian model to data? After all, the very existence of late-life plateaus in human mortality data is contentious (Barbi et al., 2018; Feehan, 2018; Newman, 2018; Gavrilov and Gavrilova, 2019), though evidence is stronger in some other organisms (Carey et al., 1992; Curtsinger et al., 1992; Chen et al., 2013), showing that plateaus do sometimes exist in the real world. Our model predicts that a late-life deceleration and eventual plateau should always "exist" in the sense of quantitatively affecting

683 measurements whenever the failure accumulation and mortality processes are stochastic, even
684 if the population is homogeneous for 'quality' (the deviation Eq. 26 is exactly zero only if N is
685 exactly infinite or the measurement does not covary with survivorship). However, the deviation
686 from Gompertz-Makeham curves may be undetectable in many biologically relevant cases, either
687 because the deviation itself is constrained to be small (Ineq. 27, Ineq. 30) or because expected
688 survivorship becomes very small before the deviation can become large (Fig 4).

689 An interesting finding from our model is that deviations remain small when the causal route
690 to each intrinsic death is relatively unique, *i.e.* different deaths due to sub-system failure have a
691 relatively unique path among all potential sequences of subsystem failures experienced before
692 mortality finally strikes. This is relatable for anyone studying human causes of death, which
693 — despite attempts to bin them into broad-brush categories such as 'cardiovascular issues' and
694 'cancer' — are extremely diverse. For humans in particular, therefore, our modelling framework
695 suggests that deviations from Gompertz-Makeham curves should generally be negligible. Empiri-
696 cally, finding a strong deviation from Gompertz-Makeham mortality at a parameter combination
697 for which our framework predicts a small deviation would decisively falsify the form of models
698 we propose here.

699 Ours is not the only post-Williams work that investigates mortality curves arising from first
700 principles (Gavrilov and Gavrilova, 2001; Laird and Sherratt, 2010; Webster, 2019; Ledberg,
701 2020). Rather than focus on particular ways in which intra-organismal processes depend on
702 each other (Gavrilov and Gavrilova, 2001; Laird and Sherratt, 2010; Webster, 2019), we have
703 chosen to coarse-grain the description of failure accumulation by assuming the rates $r_{\pm}$ exist and
704 depend only on the proportion of failed sub-systems, but not otherwise specifying a particular
705 interdependency structure ('series', 'parallel', 'scale-free', etc.). We have instead postulated some
706 general principles that biologically reasonable failure accumulation and mortality rules should
707 obey, thereby biologically grounding the more abstract state space models (Woodbury and Manton,
708 1977; Yashin et al., 1985) while also extending them mathematically and conceptually. We provide
709 a more detailed exposition of the relation of our work to Woodbury and Manton (1977) and Yashin

et al. (1985) in supplementary section S6.

The simplest failure accumulation rule ('logistic', Eq. 7) and mortality rule ('geometric', Eq. 13) that satisfy our proposed principles predict (exact) Gompertz-Makeham mortality curves in our Tithonus model. Beyond that, a large class of failure accumulation rules (characterised by Eq. 5) are also approximated by the logistic failure rule in the initial part of the failure accumulation process (*i.e.* when the Taylor expansion in Eq. 7 remains accurate). Thus, the details of the interdependencies between sub-systems are not important for the prediction that mortality curves should be approximately exponential during the initial part of failure accumulation process, as long as one can reasonably talk about a 'per-capita failure rate' $\rho(f)$ of a sub-system such that the total failure accumulation rate obeys Eq. 5.

In this sense, our results are aligned with Ledberg (2020), who showed that a broad class of models of stochastic damage accumulation predict (approximately) exponential mortality curves. His work uses quite a different mathematical approach (queuing theory), assuming mortality is proportional to the probability that the number of failed sub-systems 'queuing to be repaired' exceeds some fixed threshold, while we assume mortality is a continuous function of the proportion of failed sub-systems. The fact that two very different approaches predict similar outcomes further strengthens the view that the prediction of exponential mortality curves is robust to the gory mechanistic details of the failure/damage process.

Since the predictions that we have made so far rely on our Tithonus model in which organisms do not die, it appears unclear how seriously the awkward Tithonus assumption impacts the results. Our much more realistic main model corrects this assumption and yields analytic formulae that represent the expected value of failure-dependent measurements performed on senescing individuals that are additionally mortal, allowing a contrast with the same measurements performed on individuals following the simpler Tithonus model (Eq. 21). When measurements made on individuals following the main model do not differ greatly from the measurements made on those following the Tithonus model, the main model also predicts Gompertz-Makeham mortality curves as a null expectation. A corollary is that in those species where the deviation from the Tithonus

model is small, one can apply the simple Tithonus model by effectively ignoring any effects of mortality and selective disappearance on observed measurements.

This result may not initially seem very useful because empirical work on selective disappearance has largely focused on reproductive rather than actuarial senescence (Bouwhuis et al., 2009; Hayward et al., 2013; Hämäläinen et al., 2014). However, though we have chosen to focus on mortality here to explicate the main ideas and establish a connection to the wide-spread applicability of Gompertz-Makeham curves, our results on selective disappearance are much more general. , Our framework could just as well be used to study selective disappearance in reproductive traits — the 'measurement' function in equations such as Eq. 26 could measure anything, including reproductive output, as long as the quantity only depends on chronological age through the number of failures acquired by that age.

Since our model is agnostic about the type of organism it considers, it is also worth discussing whether our work has anything to say about more interesting organisms than humans and related unitary lifeforms. Finch (1994) has hypothesised that modular and non-unitary organisms should tend to exhibit a lower rate of senescence than unitary ones *ceteris paribus* due to the potential for continual replacement of damaged modules. Thus, the hypothesis predicts that modular organisms such as colonial ascidians, corals, and some vascular plants should age more slowly than unitary organisms such as nematodes, humans, and flies – an idea that has found some tentative empirical support (Finch, 2009; Bernard et al., 2020). In our model, the rate of ageing in our Gompertz-Makeham curve Eq. 14 depends crucially on k_ρ, the rate of increase of the per-capita failure rate ρ as the proportion of already failed sub-systems increases. Since k_ρ can be interpreted as a measure of the 'integratedness of the organism', with a lower k_ρ indicating that the failure of one sub-system does not have a strong effect on the failure rate of other sub-systems, our work lends theoretical support to Finch's hypothesis. We also illustrate this explicitly in supplementary section S5, where we formulate a model inspired by Nielsen et al. (2024) in which intra-organismal sub-systems are nodes (vertices) connected in a network (graph). We show that in this model, the 'rate' of the resultant Gompertz-Makeham curve is controlled by the average

number of sub-systems that a sub-system depends on (the average degree of the graph).

Our work predicts that descriptions of failure accumulation are stochastic, depending on both the failure accumulation rule $r(f)$ and the turnover rate $\tau(f)$ (Eq. 2, Eq. 18, Eq. 19), given that organisms have finitely many sub-systems capable of failure ($N < \infty$). Since models with distinct damage and repair rates $r_{\pm}(f)$ can predict the same failure accumulation patterns and mortality curves in the $N \to \infty$ limit but exhibit systematically different expected failure accumulation patterns (Fig 2C) and mortality curves (Fig 2D) due to stochasticity (recalling that $\tau(f)$ tells us about the variance), our work illustrates how stochasticity can cause systematic, directional patterns (Boettiger, 2018) rather than simply 'blurring out' deterministic predictions. More generally, many of the processes mechanistically involved in senescence and age-related dysfunction have a strong stochastic component (López-Otín et al., 2023; Meyer et al., 2025). Our work demonstrates how such stochasticity can be incorporated into mechanistic models of senescence from the ground up using birth-death processes and diffusion approximations.

The observation that stochasticity generates dynamic variation between initially identical individuals has also been made in a different life-history theory context unrelated to senescence, see Tuljapurkar et al.'s (2009) 'dynamic heterogeneity' and Snyder et al.'s (2021) 'state trajectory luck'. The idea that stochasticity can lead to late life mortality plateaus also appears in Weitz and Fraser (2001), whose model is similar to ours but less realistic in some key assumptions (see supplementary section S6). Our work thus adds strength to the extension of the well-known effect that late-life mortality plateaus can arise when there is unobserved heterogeneity in the population (with some individuals being more frail or having lower 'quality' than others, Vaupel and Missov, 2014). In our model, every individual begins with the same parameter values and initial condition f_0. Inter-individual differences emerge because the failure accumulation and mortality processes are stochastic, generating variation in the state (number of failures) of organisms that have the same chronological age. Selective disappearance and late-life mortality plateaus arise by acting on this variation, even in the absence of any intrinsic differences in 'quality', since individuals who (stochastically) accumulate less damage are less likely to die

and thus progressively more overrepresented at later ages. Our work hence underscores how selective disappearance is am unavoidable consequence of the observation that stochastic variation accumulates over age (López-Otín et al., 2023; Meyer and Schumacher, 2024; the $\sqrt{t}$ in Eq. 28).

Extensions and future directions

Though we have highlighted throughout how the precise interdependency structure of sub-systems is unlikely to qualitatively affect mortality curves, assessing more quantitative aspects requires deeper structure. One way to do this is to assume the interdependence of sub-systems is encoded in a graph or network (Vural et al., 2014; Sun et al., 2020). We sketch a brief outline of how such an approach interacts with our framework in supplementary section S5, where we use a model inspired by Nielsen et al. (2024) to derive a mean field failure rule for organisms whose sub-systems are organised in a class of extremely symmetric graphs; supplementary section S6 thereafter offers a detailed discussion of the differences between Nielsen et al.'s (2024) model and ours. Several physiological systems also have asymmetric or directional dependencies in function, and many failure cascades are 'multi-stage' and only occur if failures happen in a particular order (Armitage and Doll, 1954; Webster, 2019); extending the failure accumulation dynamics of our model to account for this possibility may prove fruitful, and the analytical results of Webster (2019) are a promising starting point.

The particular models we present in this paper preclude the possibility of negligible or negative senescence (Vaupel et al., 2004; Finch, 2009; Baudisch, 2012) at the outset by assuming that $r_+(f) > r_-(f)$ for every f (*i.e.* the failure rate is always greater than the repair rate). While our general modelling framework of failure accumulation as (directed) diffusion with killing does not require this assumption, the end result predicting exponential mortality curves as a baseline expectation likely does. If there is some intermediate value $f^* \in (0,1)$ for which $r_+(f^*) = r_-(f^*)$, more complex mortality patterns could be possible since the deterministic failure dynamics Eq. 4 will then admit an internal equilibrium where failure is exactly balanced by repair.

Furthermore, though every individual must eventually end up in a higher failure state and thus

experience increased mortality with age when there is stochasticity ($N < \infty$) by the infinite monkey theorem (or, more seriously, the Borel-Cantelli lemma, Chung and Erdös (1952)), the probability of this event could be very small and the first passage time to these high failure states could be extremely large (Woodcock and Falletta, 2024). Non-positive senescence is hence a distinct possibility for biologically relevant timescales and cohort sizes when the failure dynamics admit internal equilibria. Biologically, however, since repair mechanisms may themselves fail (Gorbunova et al., 2007), it is unclear how realistic it is to expect a stable internal equilibrium where failures are balanced by repair forever. Future studies should examine when (and whether) we should biologically expect $r_{\pm}(f)$ to allow stable internal equilibria in the failure dynamics and study what this means for the resultant mortality curves.

Though we have focused on exponential mortality and selective disappearance, our framework can also be used to study other phenomena in senescence theory through (conceptually) straightforward extensions that relax some of the simplifying assumptions we have made in this paper. For instance, while we have assumed that all organisms within the cohort are initially identical to underscore that fixed frailty classes are not required for selective disappearance, our framework can easily be extended to model populations with a mixture of fixed frailty classes (differences in parameter values of f_0, k_ρ, χ, etc.) using mixture distribution theory (Finkelstein and Esaulova, 2006). Since it is known that fixed frailty classes cause average mortality to be 'pulled down' towards less frail classes with age (Finkelstein and Esaulova, 2006; Vaupel and Missov, 2014), we may conjecture that adding some mixture of fixed frailty classes to our stochastic model could produce Siler-like curves (Siler, 1979). Whether this conjecture can be proven, and how different the frailty classes would need to be for a strong Siler pattern to be visible, remains open.

Many important aspects of senescence cannot be understood without incorporating trade-offs between very different organismal functions such as survival, fecundity, and growth (Vaupel et al., 2004; Baudisch, 2012; Maklakov and Chapman, 2019; Cohen et al., 2020; Avila and Lehmann, 2023; Chmilar et al., 2024). The recipe for incorporating trade-offs into our modelling framework to study these aspects is clear, since we only need to make f multi-dimensional (vector-valued),

with components representing sub-systems responsible for distinct organismal functions such as fecundity and survival. Trade-offs can then be included in a conceptually straightforward manner using (stochastic) optimal control theory (Avila et al., 2021; Avila and Lehmann, 2023).

Taking eco-evolutionary aspects seriously also presents concrete, biologically useful ways in which our model could be extended to gain a more holistic understanding of senescence. On the ecological front, while we have included extrinsic mortality in a basic sense in our equations, a thorough understanding of the long-term effects of extrinsic mortality on the evolution of senescence patterns would require us to reckon with density-dependence (de Vries et al., 2023). On the evolutionary side, Bega and Hadany (2026) recently studied how failure accumulation models interact with Hamilton's (1966) selection shadow and its evolutionary consequences. Though Bega and Hadany (2026) present a conceptual starting point to studying how parameters like our k_ρ and ϕ_ρ evolve and affect the evolution of lifespan, a key assumption they make about independence of Gompertz parameters is violated (Strehler and Mildvan, 1960) except in very special cases (see supplementary section S6).

Laird and Sherratt (2009) have introduced an evolutionary model in which organisms with multiple fully redundant sub-systems (systems 'in parallel') are allowed to evolve the number of redundant sub-systems, and shown that one should expect a decelerating selection for increased redundancy in such organisms. Laird and Sherratt, 2010 have since extended these results to networks in which systems are arranged in a 'cascade' (*i.e.* when failure percolates directionally) but the population evolves in discrete time. In our language, these studies hold the failure and mortality rule constant but allow the total number of sub-systems (N in our model) to evolve, and find that it reaches some finite value at selection-mutation-drift balance. Our framework, used in tandem with the techniques introduced by Laird and Sherratt (2009, 2010) and Bega and Hadany (2026), could allow for a reasonably general, unified understanding of how selective disappearance, interdependencies between sub-systems, and mortality due to failure accumulation together determine the ultimate evolutionary patterns of senescence.

Lastly, it has not escaped our notice that Eqs. 18-19 bear a striking resemblance to equations

arising in the multi-level selection literature (Kimura, 1984, Eq. 2.5; Fontanari and Serva, 2014, Eq. 11; Luo, 2014, Eq. 1; Cooney et al., 2023, Eq. 5). The fascinating conceptual connections between senescence and multi-level selection suggested by this similarity will be made precise using two-level Moran processes in forthcoming work.

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Author Contributions

Ananda Shikhara Bhat: Conceptualisation, Methodology, Formal Analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualisation; **Hanna Kokko:** Conceptualisation, Validation, Writing - Review & Editing, Supervision.

Data and Code Availability

All code and generated data used to generate the figures within this manuscript are available at https://github.com/Kokkonut-case/Bhat_Kokko_ageing_failures.

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Supplementary Information for Bhat and Kokko: Selective disappearance from first principles in mechanistic models of demographic senescence via failure accumulation

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S1 Deriving the Fokker-Planck-Kolmogorov equations

We present the derivation here for the main model with disappearance. The derivation for the Tithonus model is obtained by setting $\mu \equiv 0$ in all calculations in this section.

S1.1 Definition and master equation

In the main text, we formulated a continuous time stochastic process for failure accumulation with stochastic mortality. This process took values in $\{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\} \cup \{\mathcal{C}\}$, where $\mathcal{C} \notin \{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\}$ is a 'cemetery state'. The process is defined by the transitions

$$\begin{aligned} f &\to f + \frac{1}{N} \text{ at rate } Nr_+(f) \\ f &\to f - \frac{1}{N} \text{ at rate } Nr_-(f) \\ f &\to \mathcal{C} \text{ at rate } \mu(f) \end{aligned} \tag{S1}$$

where $r_\pm$ are $\mathcal{O}(1)$ functions. We are interested in computing $P(f,t)$, the probability that an individual of age t has f failures, given that individuals are born with f_0 failures at age 0.

To do this, we imagine tracking a large cohort of independent individuals from birth. In a large ensemble of individuals of age t, a proportion $P(f,t)$ of them will have a fraction f failures (by definition of probability). We can now simply measure the 'inflow' and 'outflow' of individuals from each state (Figure S1). Individuals with $f + \frac{1}{N}$ failures flow into the state f by repairing a failed sub-system. Repair occurs at rate $Nr_-(f + \frac{1}{N})$ and a fraction $P(f + \frac{1}{N}, t)$ of the cohort consists of such individuals. Similarly, individuals with $f - \frac{1}{N}$ failures flow into the state f by accumulating another failure. Failure is at rate $Nr_+(f - \frac{1}{N})$ and a fraction $P(f + \frac{1}{N}, t)$ of the cohort consists of such individuals. Thus, the rate of 'inflow' to the state f is given by

$$R_{\text{in}}(f,t) = \underbrace{Nr_+\left(f - \frac{1}{N}\right)}_{\substack{\text{Failure rate} \\ f-\frac{1}{N} \to f}} \underbrace{P(f - \frac{1}{N}, t)}_{\substack{\text{Proportion of cohort} \\ \text{with } f-\frac{1}{N} \text{ failures}}} + \underbrace{Nr_-\left(f + \frac{1}{N}\right)}_{\substack{\text{Repair rate} \\ f+\frac{1}{N} \to f}} \underbrace{P(f + \frac{1}{N}, t)}_{\substack{\text{Proportion of cohort} \\ \text{with } f+\frac{1}{N} \text{ failures}}} . \tag{S2}$$

Similarly, an individual with f failures may move into a different state by either accumulating another failure, repairing an existing failure, or dying. Thus, the rate of 'outflow' from the state f is

$$R_{\text{out}}(f,t) = \underbrace{Nr_+(f)}_{\substack{\text{Failure rate} \\ f \to f+\frac{1}{N}}} \underbrace{P(f,t)}_{\substack{\text{Proportion of} \\ \text{cohort with } f \text{ failures}}} + \underbrace{Nr_-(f)}_{\substack{\text{Repair rate} \\ f \to f-\frac{1}{N}}} \underbrace{P(f,t)}_{\substack{\text{Proportion of} \\ \text{cohort with } f \text{ failures}}} + \underbrace{\mu(f)}_{\substack{\text{Mortality rate} \\ f \to \mathcal{C}}} \underbrace{P(f,t)}_{\substack{\text{Proportion of} \\ \text{cohort with } f \text{ failures}}} \tag{S3}$$

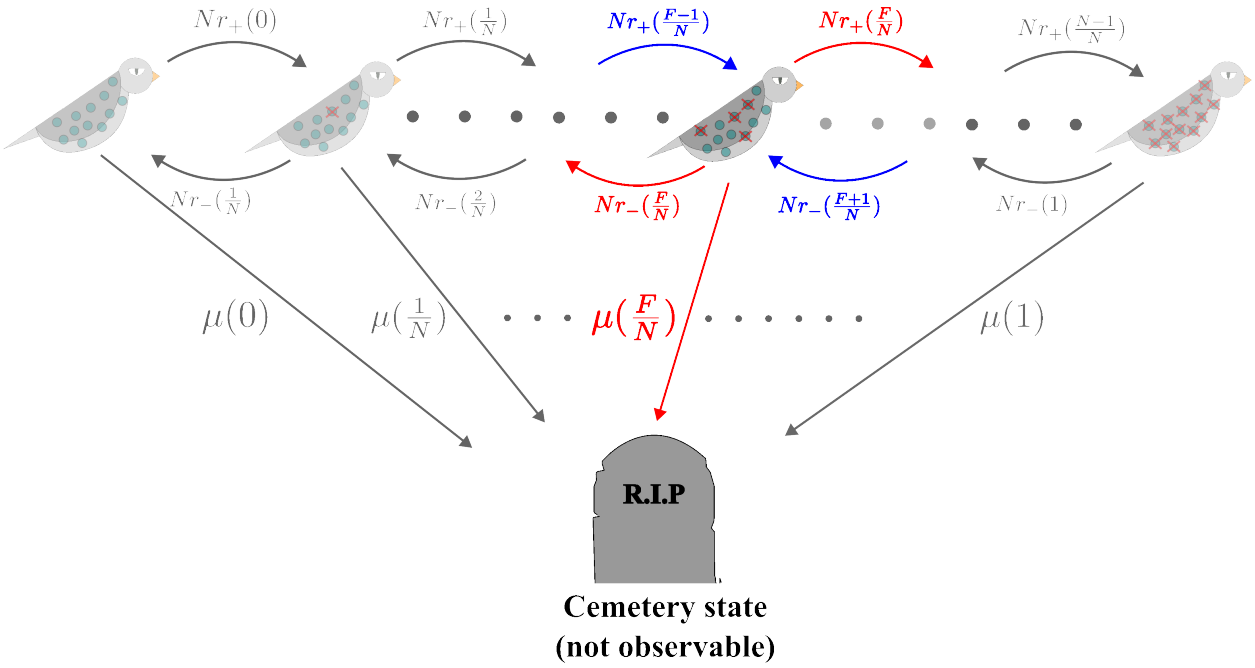

Figure S1: Schematic description of the possible transitions of our process. For a given state f, the blue arrows depict the rate of 'inflow' to the state, whereas the red arrows depict the rate of 'outflow'.

The rate of change of $P(f,t)$ is given by the rate of inflow minus the rate of outflow. Thus, we have

$$\frac{\partial P}{\partial t}(f,t) = R_{\text{in}}(f,t) - R_{\text{out}}(f,t) \tag{S4}$$

For convenience, let us define two 'step operators' $\mathcal{S}^{\pm}$, which act on any functions of failures by

either adding or removing a failure, *i.e*

$$\mathcal{S}^{\pm}G(f,t) = G(f \pm \frac{1}{N}, t)$$

Substituting Eq. S2 and Eq. S3 into the RHS of (S4) and using the step operators, we obtain the compact expression

$$\frac{\partial P}{\partial t}(f,t) = N\left[(\mathcal{S}^{-}-1)r_{+}(f)P(f,t) + (\mathcal{S}^{+}-1)r_{-}(f)P(f,t)\right] - \mu(f)P(f,t) \tag{S5}$$

Equation S5 is called a 'master equation' or 'Chapman-Kolmogorov equation' and completely describes our system exactly. To obtain the expressions presented in the main text, we now carry out a diffusion approximation.

S1.2 The diffusion approximation

Since the stochastic process defined by Eq. S1 takes values in $\{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\} \cup \{\mathcal{C}\}$ and jumps in units of $\frac{1}{N}$, the transitions of f within the space of failures $\{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\}$ begins to 'look continuous' as N grows very large. We thus Taylor expand[1] the action of the step operators $\mathcal{S}^{\pm}$ to find

$$\begin{aligned} \mathcal{S}^{\pm}G(f,t) &= G(f,t) \pm \frac{1}{N}\frac{\partial G}{\partial f} + \frac{1}{2N^2}\frac{\partial^2 G}{\partial f^2} + \mathcal{O}(N^{-3}) \\ \Rightarrow (\mathcal{S}^{\pm}-1)G(f,t) &= \pm\frac{1}{N}\frac{\partial G}{\partial f} + \frac{1}{2N^2}\frac{\partial^2 G}{\partial f^2} + \mathcal{O}(N^{-3}) \end{aligned}$$

and thus

$$N(\mathcal{S}^{\pm}-1)r_{\mp}(f,t)P(f,t) = \pm\frac{\partial}{\partial f}\{r_{\mp}(f)P(f,t)\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\{r_{\mp}(f)P(f,t)\} + \mathcal{O}(N^{-2}) \tag{S6}$$

[1] A more rigorous statement of this approximation appears in Ethier and Kurtz, 1986, Chapter 11. The description is mathematically involved but quite standard (the technical phrase is 'convergence of infinitesimal generators'), and we thus neglect mathematical precision here in favour of accessibility.

We now perform the diffusion approximation, which consists of neglecting terms of $\mathcal{O}(N^{-2})$. Biologically, neglecting the higher order terms amounts to saying that f_t, viewed as a random variable, is entirely characterised by its first two moments, and thus can be thought of as a Gaussian approximation (Black and McKane, 2012). Substituting Eq. S6 into Eq. S5 now yields, after some lines of algebra,

$$\boxed{\frac{\partial P}{\partial t}(f,t) = -\frac{\partial}{\partial f}\{(r_+(f) - r_-(f))P(f,t)\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\{(r_+(f) + r_-(f))P(f,t)\} - \mu(f)P(f,t)} \tag{S7}$$

Letting $r(f) := r_+(f) - r_-(f)$ and $\tau(f) := r_+(f) + r_-(f)$ in Eq. S7 yields Eq. 1 in the main text if $\mu \equiv 0$ and Eq. 18 in the main text if $\mu > 0$. The derivation of the equation for the conditional probability density Eq. 19 starting from Eq. S7 is more involved and appears in Yashin et al., 1985 (their Appendix A), so we do not repeat it here.

S2 The Feynman-Kac representation of the killed diffusion

In this section, we elaborate on how one arrives at the Feynman-Kac representations presented in the main text. To do this, we first need an alternate characterisation of the stochastic processes we study in terms of their *infinitesimal generators* (Øksendal, 1998, definition 7.3.1; Karatzas and Shreve, 1998, section 5.1). Given a time homogeneous Markov process X_t that lives in a domain $D \subseteq \mathbb{R}$, the *infinitesimal generator* of X_t is defined as the (unique) operator $\mathcal{G}$ satisfying

$$\mathcal{G}\psi(x) = \lim_{\Delta t \downarrow 0} \frac{\mathbb{E}\left[\psi(X_{t+\Delta t})|X_t = x\right] - \psi(x)}{\Delta t} \tag{S8}$$

for every 'nice'[2] function $\psi : D \to \mathbb{R}$. We require these generators because the Feynman-Kac formula is stated in terms of generators. Rather than asserting the form of the generator of a killed diffusion, we will derive the infinitesimal generator of our stochastic process starting from

[2] see Ethier and Kurtz, 1986 chapter 4 or Øksendal, 1998 section 7.3 for precise definitions of 'nice'. In this work, we will assume all required regularity conditions are satisfied whenever such generic functions appear.

Eq. S7, thus demonstrating that the process we obtain after our diffusion approximation (system size expansion) is indeed a bona fide killed diffusion.

S2.1 Deriving the infinitesimal generator of the killed diffusion

We aim to find the generator of the stochastic process defined by Eq. S7. Let $\Omega := [0,1] \cup \{\mathcal{C}\}$ be the state space of our stochastic process. Note that $P(f,t)$ vanishes at the cemetery state (by definition). We begin by multiplying both sides of Eq. S7 by an arbitrary smooth function ψ with compact support[3] in Ω and integrating over Ω:

$$\int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \int_\Omega \psi(f)\left(-\frac{\partial}{\partial f}\{r(f)P(f,t)\}\right)df + \frac{1}{2N}\int_\Omega \psi(f)\frac{\partial^2}{\partial f^2}\{\tau(f)P(f,t)\}df - \int_\Omega \psi(f)\mu(f)P(f,t)df \tag{S9}$$

We now use integration by parts on the first two terms of the RHS and discard the boundary terms since ψ has compact support. Doing this once on the first term of the RHS and twice on the second term of the RHS yields

$$\int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \int_\Omega \psi'(f)r(f)P(f,t)df + \frac{1}{2N}\int_\Omega \psi''(f)\tau(f)P(f,t)df - \int_\Omega \psi(f)\mu(f)P(f,t)df \tag{S10}$$

$$\Rightarrow \int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \int_\Omega \left[\psi'(f)r(f) + \frac{1}{2N}\psi''(f)\tau(f) - \psi(f)\mu(f)\right]P(f,t)df. \tag{S11}$$

Now, by the definition of the derivative, the LHS of Eq. S11 is

$$\int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \int_\Omega \psi(f)\left[\lim_{\Delta t\downarrow 0}\frac{P(f,t+\Delta t)-P(f,t)}{\Delta t}\right]df \tag{S12}$$

$$= \lim_{\Delta t\downarrow 0}\frac{1}{\Delta t}\left(\int_\Omega \psi(f)P(f,t+\Delta t)df - \int_\Omega \psi(f)P(f,t)df\right). \tag{S13}$$

[3] *i.e.* it vanishes at the boundaries of Ω.

Interchanging the order of limits and integrals is permissible by the dominated convergence theorem. The integrals on the RHS of Eq. S13 are, by definition, expectation values. We have thus obtained

$$\int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \lim_{\Delta t\downarrow 0}\frac{1}{\Delta t}\left(\mathbb{E}[\psi(f_{t+\Delta t})] - \mathbb{E}[\psi(f_t)]\right) \tag{S14}$$

$$= \lim_{\Delta t\downarrow 0}\frac{1}{\Delta t}\left(\mathbb{E}\ [\ \mathbb{E}[\psi(f_{t+\Delta t})\mid f_t]\ ] - \mathbb{E}[\mathbb{E}[\ \psi(f_t)\mid f_t]\ ]\right) \tag{S15}$$

where we have used the tower property $\mathbb{E}[X] = \mathbb{E}[\ \mathbb{E}[X\mid Y]\ ]$ to obtain the last equality. Using the linearity of the expectation value and once again interchanging the order of limits and integrals (expectations) gives us

$$\int_\Omega \psi(f)\frac{\partial P}{\partial t}(f,t)df = \int_\Omega \left[\lim_{\Delta t\downarrow 0}\frac{\mathbb{E}[\psi(f_{t+\Delta t})\mid f_t] - \mathbb{E}[\psi(f_t)\mid f_t]}{\Delta t}\right]P(f,t)df \tag{S16}$$

Replacing the LHS of Eq. S11 with the RHS of Eq. S16 now results in

$$\int_\Omega \left[\lim_{\Delta t\downarrow 0}\frac{\mathbb{E}[\psi(f_{t+\Delta t})\mid f_t] - \mathbb{E}[\psi(f_t)\mid f_t]}{\Delta t}\right]P(f,t)df = \int_\Omega \left[\psi'(f)r(f) + \frac{1}{2N}\psi''(f)\tau(f) - \psi(f)\mu(f)\right]P(f,t)df \tag{S17}$$

Since Eq. S17 is true for *every* (smooth, compactly supported) function ψ, we conclude that the generator $\mathcal{L}$ of our process is given by

$$\mathcal{L}\psi = r(f)\frac{\partial\psi}{\partial f} + \frac{\tau(f)}{2N}\frac{\partial^2\psi}{\partial f^2} - \mu(f)\psi(f). \tag{S18}$$

Besides being useful for further calculations, Eq. S18 also verifies that the process we have obtained after the diffusion approximation is indeed a killed diffusion (compare our Eq. S18 with Eq. 2 in Steinsaltz and Evans, 2006).

S2.2 A Feynman-Kac representation for functions of the killed diffusion

The infinitesimal generator of a Markov process is particularly useful to us due to a result called *Kolmogorov's backward equation* (Øksendal, 1998, Theorem 8.1.1; Karlin and Taylor, 1981, Eq. 15.5.7). Let $\{X_t\}_t$ be a time homogeneous Markov process on a nice domain $D \subseteq \mathbb{R}$. Let $\mathcal{G}$ denote the generator of X, and consider a real function $g \in C^2(D)$. Let $u(x,t) \coloneqq \mathbb{E}[g(X_t)|X_0 = x]$ denote the expected value of $g(X)$ after time t given that the process $\{X_t\}_{t\geq 0}$ began at state x. Kolmogorov's backward equation (Øksendal, 1998, Theorem 8.1.1) says that $u(x,t)$ satisfies

$$\frac{\partial u(x,t)}{\partial t} = \mathcal{G}_x u(x,t). \tag{S19}$$

The notation $\mathcal{G}_x$ is to indicate that the generator $\mathcal{G}$ is acting on the map $x \mapsto u(x,t)$. Notice that while the LHS of Eq. S19 is about the state at time t (forward in time), the RHS of Eq. S19 is in terms of changes to the *initial condition* x (contrast with, say, Eq. S7, where derivatives are with respect to the future/current state).

For our killed diffusion, the generator is Eq. S18. Let $\widetilde{M}(f_0,t)$ denote the expected value of a measurement $M(\widetilde{f}_t)$ given an individual is born with f_0 failures at age 0 and follows the killed diffusion $\{\widetilde{f}_t\}_{t\geq 0}$ defined by Eq. S18. Here, we specify that we require[4] $M \in C^2([0,1])$. Kolmogorov's backward equation states that $\widetilde{M}(f_0,t)$ satisfies the initial value problem

$$\frac{\partial \widetilde{M}(f_0,t)}{\partial t} = r(f_0)\frac{\partial \widetilde{M}}{\partial f_0} + \frac{\tau(f_0)}{2N}\frac{\partial^2 \widetilde{M}}{\partial f_0^2} - \mu(f_0)\widetilde{M}. \tag{S20}$$

with the initial condition $\widetilde{M}(f_0,0) = M(f_0)$. The Feynman-Kac formula in the PDE to SDE direction (Øksendal, 1998, theorem 8.2.1, (b)) now states that since $\widetilde{M}(f_0,t)$ satisfies Eq. S20, it

[4] in words, M and its first two derivatives should be continuous in $[0,1]$.

must admit the representation

$$\boxed{\widetilde{M}(f_0,t) = \mathbb{E}\left[M(\mathfrak{f}_t) e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]} \tag{S21}$$

where $\{\mathfrak{f}_t\}_{t\geq 0}$ is the process described by the Tithonus model that solves the SDE Eq. 2. Eq. S21 is Eq. 22 in the main text. The conditional expectation in Eq. S21 is understood as an expectation over paths (*i.e.* on the space $\{\omega \in C([0,t],[0,1]) \mid \omega(0) = f_0\}$ equipped with the Wiener measure induced by the diffusion $\mathfrak{f}_t$).

S3 Feynman-Kac representation of the killed diffusion conditioned on survival

Yashin et al., 1985 have shown that if we know that the processs enters the cemetery state at time T_{mort}, the conditional density $\widehat{P}(f,t)$ of the process conditioned on not entering the cemetery state ($t < T_{\text{mort}}$) obeys the Fokker-Planck type PDE

$$\frac{\partial \widehat{P}(f,t)}{\partial t} = -\frac{\partial}{\partial f}\left\{ r(f)\widehat{P}(f,t) \right\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{ \tau(f)\widehat{P}(f,t) \right\} - \left[\mu(f) - \overline{\mu}(t) \right] \widehat{P}(f,t) \tag{S22}$$

where

$$\overline{\mu}(t) := \mathbb{E}\left[\mu(f,t) \mid f_0, t < T_{\text{mort}} \right] = \int_0^1 \mu(x,t)\widehat{P}(x,t)dx \tag{S23}$$

is the expected force of mortality conditioned on remaining alive. Feynman-Kac formulae cannot be used directly for the conditioned process defined by Eq. S22 because Eq. S23 introduces a non-linearity in the probability density $\widehat{P}(f,t)$. In this section, we use Eq. S21 to derive a representation instead.

From Eq. S21, we found that the survival function $\exp(-\int_0^t \mu(f_s)ds)$ provided the correct weighting to modify expectations from the Tithonus model to find expectations of the process

with disappearance. Since conditioning effectively modifies the mortality term $\mu(f) \to \mu(f) - \overline{\mu}(t)$ in the Fokker-Planck equations (compare Eq. S22 with Eq. S7), we may guess that the survival function for the conditioned process should also be modified as $\exp(-\int_0^t \mu(f_s)ds) \to \exp(-\int_0^t (\mu(f_s) - \overline{\mu}(s))ds)$. To this end, let[5] $\overline{S}(t) := \exp(-\int_0^t \overline{\mu}(s)ds)$, and consider $\overline{S}(t)\widehat{P}(f,t)$. Differentiating with respect to time yields

$$\frac{\partial}{\partial t}\{\overline{S}(t)\widehat{P}(f,t)\} = \overline{S}(t)\frac{\partial \widehat{P}(f,t)}{\partial t} + \widehat{P}(f,t)\frac{d\overline{S}(t)}{dt}. \tag{S24}$$

Now,

$$\frac{d\overline{S}(t)}{dt} = -\overline{S}(t)\overline{\mu}(t) \tag{S25}$$

and $\partial\widehat{P}/\partial t$ is given by Eq. S22. Substituting into Eq. S24, the $\overline{S}(t)\overline{\mu}(t)$ terms cancel (since $\overline{S}(t)\partial\widehat{P}/\partial t$ contains a $+\overline{S}(t)\overline{\mu}(t)$ term) and we find

$$\frac{\partial}{\partial t}\{\overline{S}(t)\widehat{P}(f,t)\} = \overline{S}(t)\frac{\partial}{\partial f}\left\{r(f)\widehat{P}(f,t)\right\} + \overline{S}(t)\frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{\tau(f)\widehat{P}(f,t)\right\} - \overline{S}(t)\mu(f)\widehat{P}(f,t). \tag{S26}$$

Since $\overline{S}$ is independent of f, it can be taken inside the partial derivatives on the RHS, resulting in

$$\frac{\partial}{\partial t}\{\overline{S}(t)\widehat{P}(f,t)\} = \frac{\partial}{\partial f}\left\{r(f)\{\overline{S}(t)\widehat{P}(f,t)\}\right\} + \frac{1}{2N}\frac{\partial^2}{\partial f^2}\left\{\tau(f)\{\overline{S}(t)\widehat{P}(f,t)\}\right\} - \mu(f)\{\overline{S}(t)\widehat{P}(f,t)\}. \tag{S27}$$

Comparing Eq. S27 with Eq. S7, we find that $\overline{S}(t)\widehat{P}(f,t)$ is precisely the probability density function of the *unconditioned process* with disappearance! Letting $\widetilde{P}(f,t)$ denote the density of the unconditioned process (for consistency with the main text), we have thus shown that

$$\overline{S}(t)\widehat{P}(f,t) = \widetilde{P}(f,t). \tag{S28}$$

Eq. S28 is a powerful result because it establishes a relation between the unconditioned and

[5]The reader may have noticed that in the supplement, this is the definition rather than the result Eq. 23 in the main text; we will derive that it is equivalent to the definition as the denominator of Eq. 21. We switch the order of definition and result here in the supplementary to make the intuition for deriving the result more transparent.

conditioned processes at the level of their density functions. It also establishes that $(1 - \overline{S}(t))$ quantifies the loss of density to the cemetery state in the unconditioned process. However, $\overline{S}$ still involves the conditioned density $\widehat{P}$ via the non-linear term Eq. 20. We seek a better representation of $\overline{S}$ in terms of the Tithonus model.

Begin by integrating both sides of Eq. S28 over all possible values of f. Since $\widehat{P}(f,t)$ is a probability density function for a process that is conservative in the failure space, it integrates to 1 (intuitively because we conditioned on not dying and so the individual must have some value of f; also provable directly from Eq. S22, see Yashin et al., 1985). This results in the expression

$$\overline{S}(t) = \int_0^1 \widetilde{P}(f,t)df = \mathbb{E}[1|\widetilde{f}_0 = f_0] \tag{S29}$$

where $\widetilde{f}_t$ is a stochastic process with generator Eq. S18 (*i.e.* following the unconditioned process with disappearance) and the expectation on the RHS is not equal to 1 because individuals are lost to the cemetery state (*i.e.* the process is non-conservative).

We now want to represent the RHS of Eq. S29 in terms of the process described by the Tithonus model. To do this, we notice that the RHS of Eq. S29 is a special case of $\widetilde{M}(f_0,t) := \mathbb{E}[M(\widetilde{f}_t)|\widetilde{f}_0 = 0]$ with the choice of measurement function $M(\cdot) = 1$. Thus, from Eq. S21 with $M \equiv 1$, we find

$$\overline{S}(t) = \mathbb{E}\left[e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right] \tag{S30}$$

where $\{\mathfrak{f}_t\}_t$, like in Eq. S21, solves the SDE Eq. 2.

To find $\widehat{M}(f_0,t) := \mathbb{E}[M(\widehat{f}_t) \mid \widehat{f} = f_0]$, the expected number of failures accrued by an individual conditioned on survival (*i.e.* following the conditioned process defined by Eq. S22), multiply both sides of Eq. S28 by $M(f)$ and then integrate over all possible values of f. This yields

$$\int_0^1 M(f)\widehat{P}(f,t|f_0,0)df = \frac{1}{\overline{S}(t)}\int_0^1 M(f)\widetilde{P}(f,t|f_0,0)df. \tag{S31}$$

But by definition, the integral on the LHS is $\widehat{M}(f_0,t)$ and the one on the RHS is $\widetilde{M}(f_0,t)$. Substi-

tuting Eq. S21 and Eq. S30 now finally yields

$$\widehat{M}(f_0,t) = \frac{\mathbb{E}\left[M(\mathfrak{f}_t) e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]}{\mathbb{E}\left[e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right]} \tag{S32}$$

The RHS of Eq. S32 is entirely in terms of the Tithonus SDE $\mathfrak{f}_t$ and is Eq. 21 in the main text.

S4 Bounding the expected deviation in a measurement due to selective disappearance

We begin by squaring both sides of Eq. 26, thus finding that the squared discrepancy is given by

$$\delta_M^2(f_0,t) = \frac{\left(\mathrm{Cov}\left[M(\mathfrak{f}_t) \;,\; e^{-\int_0^t \mu(\mathfrak{f}_s)ds} \;\middle|\; \mathfrak{f}_0 = f_0 \right] \right)^2}{(\overline{S}(t))^2}. \tag{S33}$$

For convenience, we henceforth denote conditional expectations, variances, and covariances by $\mathbb{E}_f$, Var_f, and Cov_f respectively. Let[6] $S(\mathfrak{f}_t) := \exp\left(-\int_0^t \mu(\mathfrak{f}_s)ds \right)$. The Cauchy-Schwartz inequality immediately lets us bound the numerator of the RHS of Eq. S33,

$$\left(\mathrm{Cov}_f\left[M(\mathfrak{f}_t)\,, S(\mathfrak{f}_t)\right]\right)^2 \leq \mathrm{Var}_f[M(\mathfrak{f}_t)]\mathrm{Var}_f[S(\mathfrak{f}_t)] \tag{S34}$$

leading to

$$\delta_M^2(f_0,t) \leq \frac{\mathrm{Var}_f[M(\mathfrak{f}_t)]\mathrm{Var}_f[S(\mathfrak{f}_t)]}{(\overline{S}(t))^2}. \tag{S35}$$

[6]This is a slight abuse of notation, since $S(\mathfrak{f}_t)$ depends on the entire path $\{\mathfrak{f}_s\}_{s\in[0,t]}$, and not just the final value $\mathfrak{f}_t$.

We now bound the second variance in the numerator of the RHS of Eq. S35. By definition,

$$\mathrm{Var}_f[S(\mathfrak{f}_t)] = \mathbb{E}_f[(S(\mathfrak{f}_t))^2] - (\mathbb{E}_f[S(\mathfrak{f}_t)])^2 \tag{S36}$$

$$\leq \mathbb{E}_f[S(\mathfrak{f}_t)] - (\mathbb{E}_f[S(\mathfrak{f}_t)])^2 \tag{S37}$$

$$= \mathbb{E}_f[S(\mathfrak{f}_t)]\left(1 - \mathbb{E}_f[S(\mathfrak{f}_t)]\right) \tag{S38}$$

where we have used the fact that $0 \leq S(\mathfrak{f}_t) \leq 1$ and thus $S^2 \leq S$ to go from Eq. S36 to Ineq. S37. Now notice that $\mathbb{E}_f[S(\mathfrak{f}_t)] = \overline{S}(t)$ from Eq. S30, and we hence have

$$\mathrm{Var}_f[S(\mathfrak{f}_t)] \leq \overline{S}(t)\left(1 - \overline{S}(t)\right) \tag{S39}$$

From Ineq. S39 and Ineq. S35, we can conclude that

$$\delta_M^2(f_0, t) \leq \mathrm{Var}_f[M(\mathfrak{f}_t)]\left(\frac{1-\overline{S}(t)}{\overline{S}(t)}\right), \tag{S40}$$

i.e.,

$$\boxed{|\delta_M(f_0,t)| \leq \sigma_M(f_0,t)\sqrt{\frac{1-\overline{S}(t)}{\overline{S}(t)}}} \tag{S41}$$

where $\sigma_M(f_0,t) \coloneqq \sqrt{\mathrm{Var}_f[M(\mathfrak{f}_t)]}$ is the standard deviation process of $\{M(\mathfrak{f}_t)\}_{t\geq 0}$. This is Ineq. 27 in the main text.

We will now further bound the standard deviation on the RHS of Eq. S41 for the special case $M(\cdot) = \mu(\cdot)$. In this case, we know that $\mu(\mathfrak{f}_t)$ solves the SDE Eq. 15, allowing us to write

$$\mu(\mathfrak{f}_t) = \mu(f_0) + \int_0^t A_\mu(f_s)ds + \int_0^t B_\mu(f_s)dW_s \tag{S42}$$

where $A_\mu(f_s) \coloneqq r(f_s)\mu'(f_s) + \frac{\tau(f_s)}{2N}\mu''(f_s)$ and $B_\mu(f_s) \coloneqq \sqrt{\tau(f_s)}\mu'(f_s)/\sqrt{N}$. The Itô isome-

try (Karatzas and Shreve, 1998, Chapter 2, Proposition 2.10) then gives us

$$\mathrm{Var}_f[\mu(f_t)] := \mathbb{E}_f[\mu^2(f_t)] - (\mathbb{E}_f[\mu(f_t)])^2 = \mathbb{E}_f\left[\int_0^t B_\mu^2(f_s)ds\right]. \tag{S43}$$

We now assume that both $\tau(f)$ and $\mu'(f)$ are bounded above. In other words, we assume that there are finite numbers $\tau_{\max}, \mu'_{\max}$ such that $\tau(f) \leq \tau_{\max}$ and $\mu'(f) \leq \mu_{\max}$. In this case, we have

$$\mathrm{Var}_f[\mu(f_t)] = \mathbb{E}_f\left[\int_0^t B_\mu^2(f_s)ds\right] \leq \left(\max_{f\in[0,1]} B_\mu^2(f_s)\right)\left(\int_0^t ds\right) = \left(\frac{\tau_{\max}}{N}\right)(\mu'_{\max})^2 t \tag{S44}$$

and can hence conclude that

$$\sigma_M(f_0, t) \leq \left(\sqrt{\frac{\tau_{\max}}{N}}\right)\mu'_{\max}\sqrt{t}. \tag{S45}$$

We can now plug Ineq. S45 into Ineq. S41 to arrive at

$$|\delta_\mu(f_0, t)| \leq \left(\sqrt{\left(\frac{\tau_{\max}}{N}\right)\left(\frac{1-\bar{S}(t)}{\bar{S}(t)}\right)}\right)\mu'_{\max}\sqrt{t}, \tag{S46}$$

which is Eq. 28 in the main text. As an aside, note that the same idea would carry through to bound $|\delta_M|$ for any $C^2([0,1])$ measurement function M thanks to Itô's formula (box 2) as long as the absolute value of the derivative of M is bounded above[7] by $M'_{\max}$. The only change will be that $\mu'_{\max}$ will be replaced by $M'_{\max}$ in Eq. S46. If we were interested in, say, fecundity, for example, the relevant bound would be the maximum rate at which fecundity changes as a function of failures (assuming that fecundity as a function of failures is a twice continuously differentiable function).

Introducing the assumption of a finite $\mu_{\max}$ for mortality may seem like a bit of a cop out since the particular mortality rule we advocate for in the main text, Eq. 13, does *not* have a bounded derivative. Happily for us, $0 \leq f \leq 1$, and we can thus use a geometric series expansion for

[7] This is the same as saying M is $M'_{\max}$-Lipschitz continuous. Using Feynman-Kac also requires M to be $C^2([0,1])$ (for Eq. S20).

$f/(1-f)$. In other words, our mortality rule can be rewritten as

$$\mu(f) = \mu_e + \chi\left(\frac{f}{1-f}\right) = \mu_e + \chi\left(f + f^2 + f^3 + f^4 + \ldots\right), \tag{S47}$$

which will be bounded for any finite truncation of the infinite sum. Truncating Eq. S47 at a finite degree $\alpha > 1$ results in the approximate mortality rule

$$\mu(f) = \mu_e + \chi\left(f + f^2 + f^3 + f^4 + \ldots + f^{\alpha-1} + f^{\alpha}\right). \tag{S48}$$

Higher values of α will provide strictly better approximations to the mortality rule Eq. 13 used in the main text, and the equality is exact if we let $\alpha \to \infty$. For finite α, we can calculate and bound the derivative of Eq. S48, since

$$\mu'(f) = \chi\frac{d}{df}\left(\sum_{p=1}^{\alpha} f^p\right) = \chi\sum_{p=1}^{\alpha} p f^{p-1} \leq \chi\sum_{p=1}^{\alpha} p = \chi\frac{\alpha\,(\alpha+1)}{2} =: \mu_{\max}. \tag{S49}$$

Plugging into Ineq. S46 now reveals that

$$|\delta_\mu(f_0, t)| \leq \left(\sqrt{\left(\frac{\tau_{\max}}{N}\right)\left(\frac{1-\overline{S}(t)}{\overline{S}(t)}\right)}\right)\chi\frac{\alpha\,(\alpha+1)}{2}\sqrt{t}. \tag{S50}$$

Finally, we will make the dependence on extrinsic mortality explicit. Notice that

$$\overline{S}(t) := \mathbb{E}\left[e^{-\int_0^t\left[\mu_e+\chi\left(\mathfrak{f}_s+(\mathfrak{f}_s)^2+\ldots+(\mathfrak{f}_s)^{\alpha}\right)\right]ds} \;\middle|\; \mathfrak{f}_0 = f_0\right] = e^{-\mu_e t}\underbrace{\mathbb{E}\left[\prod_{p=1}^{\alpha} e^{-\chi\left(\int_0^t(\mathfrak{f}_s)^p ds\right)} \;\middle|\; \mathfrak{f}_0 = f_0\right]}_{=:\,\overline{S}_{\text{fail}}(t)} \tag{S51}$$

where $\overline{S}_{\text{fail}}(t)$ quantifies the survivorship when ignoring all deaths due to extrinsic mortality (we can do this because we have constructed the mortality rule such that it is the sum of an extrinsic

and an intrinsic component). Substituting into Ineq. S50 now yields Ineq. 30 in the main text:

$$\boxed{|\delta_\mu(f_0,t)| \leq \left(\sqrt{\left(\frac{\tau_{\max}}{N}\right)\left(\frac{e^{\mu_e t} - \overline{S}_{\text{fail}}(t)}{\overline{S}_{\text{fail}}(t)}\right)}\right)\chi\frac{\alpha\,(\alpha+1)}{2}\sqrt{t}} \tag{S52}$$

S5 A mean field failure accumulation rule when sub-systems are vertices of a vertex-transitive graph

In this section, we sketch how a plausible failure accumulation rule can be derived for organisms in which the sub-systems are organised in an (extremely symmetric) graph/network. This model is inspired by Nielsen et al. (2024).

S5.1 Definition of the process

We conceptualize an organism as a simple undirected connected graph G on N vertices. Each vertex of G is a sub-system important for organismal function, and edges represent interdependencies between systems. We assume that the graph G is *vertex transitive*, meaning that the vertices of the graph are indistinguishable (Godsil and Royle, 2001, section 3.1; For an application of such graphs in evolutionary biology, see McAvoy and Hauert, 2015). Biologically, this assumption is a symmetry assumption where we are assuming that every sub-system is equally important and structurally indistinguishable from the other. Since every vertex transitive graph is regular (Godsil and Royle, 2001, Section 3.1), our assumption also implies that every sub-system (vertex) has the same number of dependencies (edges), a quantity we denote by n. While vertex transitivity is a strong assumption, it is not overly restrictive for a first pass, since the number of connected vertex-transitive graphs on N vertices grows very quickly with N. For instance, there are 34333611 connected vertex transitive graphs on $N = 47$ vertices (OEIS A006800).

Failure accumulation is modelled as a continuous-time stochastic process that consists of relabelling the vertices of G as failed/non-functional. In particular, if a vertex v is functional, we

assume it has a failure rate $\phi + In_v(t)$, where $\phi > 0$ is a constant intrinsic failure rate due to factors like physical damage and wear and tear and $n_v(t)$ is the number of neighbours of v that have failed at time t. Here, $I > 0$ is a parameter that controls how much a focal subsystem is affected by the failure of the subsystems on which it depends. The special case $I = 1$ corresponds to the case where failure depends on the number of failed neighbours. Let $\mathbb{P}(E)$ denote the probability of the event E occurring. For conciseness, let us use the shorthand $f(i;j)$ for the rate at which the i th vertex fails when it has j failed neighbours, i.e.

$$f(i;j) := \lim_{\Delta t \downarrow 0} \frac{\mathbb{P}(i \text{ fails} \mid \ i \text{ has } j \text{ failed neighbours})}{\Delta t}. \tag{S53}$$

Our model above specifies the particular rule $f(i;j) = \varphi + Ij$, but we change notation here because we will be summing over i and j. Letting F_t be the stochastic process tracking the number of failures by time (age) t, we are interested in computing the failure rate

$$R_+(F) := \lim_{\Delta t \downarrow 0} \frac{\mathbb{P}(F_{t+\Delta t} = F + 1 | F_t = F)}{\Delta t}$$

with the ultimate goal of relating it to the s defined in the main text. Repair rates can be computed exactly analogously and we thus do not repeat the calculations.

S5.2 Computing the failure rate

By definition, the number of failed systems F_t increases iff a functional system fails. Thus, the rate at which the number of failed sub-systems F_t increases is given by the rate at which at least one functional vertex fails. In equations, we express this as

$$\lim_{\Delta t \downarrow 0} \frac{\mathbb{P}(F_{t+\Delta t} = F + 1 | F_t = F)}{\Delta t} = \lim_{\Delta t \downarrow 0} \sum_{\substack{\text{functional} \\ \text{vertices}}} \frac{\mathbb{P}(i \text{ fails})}{\Delta t} \tag{S54}$$

where the sum is over the set of sub-systems that have not yet failed, and we have neglected the possibility of two vertices failing at the same time because this is an $\mathcal{O}((\Delta t)^2)$ event. Let Δ_i denote

the (in)-degree of vertex i (*i.e.* the number of systems that i depends on). We can rewrite the probability on the RHS of (S54) as

$$\mathbb{P}(i \text{ fails}) = \sum_{k=1}^{N-1} \mathbb{P}(i \text{ fails} \mid \Delta_i = k)\mathbb{P}(\Delta_i = k) \tag{S55}$$

$$= \sum_{k=1}^{N-1} \mathbb{P}(\Delta_i = k) \sum_{j=0}^{k} \mathbb{P}(i \text{ fails} \mid \ i \text{ has } j \text{ failed neighbours}, \Delta_i = k)\mathbb{P}(i \text{ has } j \text{ failed neighbours} | \Delta_i = k) \tag{S56}$$

$$= \sum_{k=1}^{N-1} \mathbb{P}(\Delta_i = k) \sum_{j=0}^{k} \mathbb{P}(i \text{ fails} \mid \ i \text{ has } j \text{ failed neighbours})\mathbb{P}(i \text{ has } j \text{ failed neighbours} | \Delta_i = k) \tag{S57}$$

Thus, we have

$$\lim_{\Delta t \downarrow 0} \frac{\mathbb{P}(i \text{ fails})}{\Delta t} = \sum_{k=1}^{N-1} \mathbb{P}(\Delta_i = k) \sum_{j=0}^{k} f(i;j)\mathbb{P}(i \text{ has } j \text{ failed neighbours} | \Delta_i = k) \tag{S58}$$

where we have used the definition of $f(i;j)$. We now observe that $\mathbb{P}(i \text{ has } j \text{ failed neighbours} | \Delta_i = k)$ is the probability that a vertex has j failed neighbours given that it has k neighbours. Assuming (in the mean-field) that the probability that a given randomly chosen vertex is a failed vertex is F/N (the fraction of failed vertices), $\mathbb{P}(i \text{ has } j \text{ failed neighbours} | \Delta_i = k)$ must follow a Binomial$(k, F/N)$ distribution. Thus, we can rewrite Eq. (S58) as

$$\lim_{\Delta t \downarrow 0} \frac{\mathbb{P}(i \text{ fails})}{\Delta t} = \sum_{k=1}^{N-1} \mathbb{P}(\Delta_i = k) \sum_{j=0}^{k} f(i;j) \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j}, \tag{S59}$$

which, upon substituting into Eq. (S54) yields the failure rate

$$R_+(F) = \sum_{i \text{ functional}} \sum_{k=1}^{N-1} \mathbb{P}(\Delta_i = k) \sum_{j=0}^{k} f(i;j) \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j}. \tag{S60}$$

If vertices are indistinguishable, *i.e.* the process on every vertex i is identical, Eq. (S60) further simplifies to

$$R_+(F) = (N - F(t)) \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) \sum_{j=0}^{k} f(j) \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j} \tag{S61}$$

We will now substitute the functional form $f(i;j) = \varphi + Ij$. Upon doing this, Eq. (S61) becomes

$$R_+(F) = (N - F(t)) \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) \sum_{j=0}^{k} (\varphi + Ij) \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j} \tag{S62}$$

$$= \varphi(N - F(t)) \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) \sum_{j=0}^{k} \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j}$$

$$+ (N - F(t))I \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) \sum_{j=0}^{k} j \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j} \tag{S63}$$

We now observe that both sums over j are expressions for moments of the binomial distribution. If X is a $\text{Bin}(n, p)$ random variable, we have

$$\mathbb{E}[X^0] = \sum_{j=0}^{n} \binom{n}{j} p^j (1-p)^{n-j} = 1 \tag{S64}$$

$$\mathbb{E}[X] = \sum_{j=0}^{n} j \binom{n}{j} p^j (1-p)^{n-j} = np \tag{S65}$$

In our case, we have $n = k$ and $p = F/N$. Using this observation in Eq. (S63), we obtain

$$R_+(F) = \varphi(N - F) \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) + \frac{I}{N}(N - F)F \sum_{k=1}^{N-1} k\mathbb{P}(\Delta = k) \tag{S66}$$

The two sums on the RHS of Eq. (S66) are now just moments of the degree distribution. The first sum simply equals 1, and the second is the average degree $\langle \Delta \rangle$. We are thus led to the failure rate

$$R_+(F) = (N - F)\left(\varphi + \frac{I\langle \Delta \rangle}{N} F\right) = N\left(1 - \frac{F}{N}\right)\left(\varphi + I\langle \Delta \rangle \frac{F}{N}\right) \tag{S67}$$

Defining $f = F/N$, we see that our graph-structured model corresponds to the rule $r_+(f) = (1 - f)(\varphi + I\langle \Delta \rangle f)$. Since the ability to repair failed sub-systems *decreases* with the proportion of failed sub-systems, the logic for deriving the repair rate $r_-(f)$ is exactly analogous, and will just have different constants φ_2 and I_2. Thus omitting the derivation for the repair rate $r_-(f)$, we can identify that our per-capita failure accumulation rate is $\rho(f) = \varphi_{\text{eff}} + I_{\text{eff}}\langle \Delta \rangle f$, leading us to conclude that $\phi_\rho = \varphi_{\text{eff}}$, $k_\rho = I_{\text{eff}}\langle \Delta \rangle$. Thus, interdependence k_ρ is a constant times the average

degree $\langle\Delta\rangle$, an explicit measure of the number of sub-systems the average sub-system depends on.

Remark

If the failure rate of a vertex depends on the *proportion* of failed neighbours rather than the number of failed neighbours, we would have

$$\mathbb{P}(i \text{ fails} \mid \ i \text{ has } j \text{ failed neighbours}, \Delta_i = k) = \varphi + \frac{j}{k}$$

in Eq. S56. Using this new relation, the last term on the RHS of Eq. S63 is instead

$$(N - F(t))I \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k) \sum_{j=0}^{k} \frac{j}{k} \binom{k}{j} \left(\frac{F}{N}\right)^j \left(1 - \frac{F}{N}\right)^{k-j}$$

and the last term on the RHS of Eq. S66 hence becomes

$$\frac{I}{N}(N - F(t))F(t) \sum_{k=1}^{N-1} \frac{k}{k} \mathbb{P}(\Delta = k) = \frac{I}{N}(N - F(t))F(t) \sum_{k=1}^{N-1} \mathbb{P}(\Delta = k).$$

Thus, the rate $R_+(F)$ in this case becomes

$$R_+(F) = N \left(1 - \frac{F}{N}\right) \left(\varphi + I\frac{F}{N}\right).$$

In other words, unlike in Eq. S67, the network structure (parametrised by the average degree $\langle\Delta\rangle = n$) does not affect the mean field dynamics if failure rate depends on the proportion of failed neighbours.

S6 Explicit relation of our work to some previous mathematical models

In this section, we provide some explicit connections between our paper and some previous models of demographic senescence.

Our Eq. 18 is fundamentally a resurrection, extension, and refinement of Woodbury and Manton's (1977) 'state space random walk' model and extensions thereof (Woodbury and Manton, 1977, 1983; Manton et al., 1988; Mulder, 1993), connecting it to mechanistic reliability-theoretic notions of senescence as damage/failure accumulation. Since Yashin et al., 1985 make the extension that is cleanest and most relevant to our work, we focus on connections with Yashin et al. (1985) here.

The exact correspondence between our work and that of Yashin et al., 1985 can be made by identifying their $a(t,y)$ with our $r(f)$ and their $b^2(t,y)$ with our $\tau(f)/N$. Unlike Yashin et al., 1985, however, we derive these coefficients and Eq. 18 more generally, from first principles starting from a birth-death process (Eq. 17). As such, we believe our derivation biologically grounds the coefficients that appear in Yashin et al. (1985) (their Eq. 5, our Eq. 18) in terms of failures of intra-organismal sub-systems. We also provide some guidelines for how these functions should look (Eq. 7) and show that using these guidelines result in logistic failure accumulation curves, at least in the initial part of the failure accumulation process.

Yashin et al. (1985) are also focused on statistical inference rather than relatively qualitative descriptions and clarifications of logic, and as a result, make some rather restrictive assumptions about functional forms. For instance, in our language, Yashin et al., 1985 assume that the mortality rule μ must be quadratic in the failures (their section IV.E.2), whereas we make no such assumption, and indeed argue that a more biologically realistic mortality rule is not a finite degree polynomial (our 'geometric' mortality rule Eq. 13). Our Feynman-Kac representations also describe how precisely the stochastic mortality μ affects the dynamics of failure accumulation. In supplementary section S3, we are also able to obtain a direct correspondence (Eq. S28) between the probability densities of the unconditioned and the conditioned processes (our Eq. 18 and Eq. 19; Yashin et al.'s (1985) Eq. 5 and Eq. 7). By extending Woodbury and Manton's (1977) and Yashin et al.'s (1985) model to more general mortality functions and connecting it to the damage/failure accumulation literature, we hope to bring attention to it and render it usable by a wider audience. The Feynman-Kac formulae also allow direct and efficient numerical predictions

of expected mortality or failure curves under a given level of mortality/disappearance in terms of the much simpler Tithonus model Eq. 2.

Nielsen et al. (2024) have proposed a model they call the 'multiple and inter-dependent component cause model', where individuals are comprised of a large number of interdependent sub-systems, each capable of failure, arranged as a complete graph, and shown that their model predicts approximately Gompertz-Makeham mortality curves. Nielsen et al.'s (2024) model is the same as our logistic failure accumulation rule when our baseline failure rate is zero ($\phi_\rho = 0$, compare their Eq. 3 with our Eq. 7; also see our supplementary section S5 for a derivation for a more general class of graphs). However, Nielsen et al. (2024) assume the linear mortality rule Eq. 12 and thus find late-life plateaus in mortality, whereas we advocate for a more realistic mortality rule (the 'geometric mortality rule' Eq. 13) on biological grounds. Nielsen et al. (2024) also work with our 'Tithonus model' rather than accounting for stochastic mortality and selective disappearance (their main stochastic equation, their Eq. 9, corresponds to our Eq. 1, and in particular, the additional mortality terms that appear in our Eq. 19 are absent; to see this, note that their Eq. 9 is the Master equation obtained by setting $\mu \equiv 0$ in Eq. S4 in supplementary section S1). In other words, their equations are not quite accurate unless deviations due to selective disappearance, as quantified by Eq. 26, are small enough to neglect.

On the evolutionary side, Bega and Hadany (2026) have recently studied how failure accumulation models interact with Hamilton's (1966) selection shadow and its evolutionary consequences. Bega and Hadany's (2026) starting point is an equation that is an alternative form of the ending point of our deterministic logistic failure accumulation with the geometric mortality rule. This can be made explicit by introducing a new variable $D(t) \coloneqq f(t)/(1-f(t))$ and re-expressing our Eq. 7 and Eq. 13 in terms of this new variable; doing so and setting $\phi_\rho = 0$ yields the first set of ODEs in the leftmost box of Figure 1 of Bega and Hadany (2026) up to a change in notation. Importantly, Bega and Hadany (2026) assume the parameters A and b of a Gompertz curve of the form $\mu(t) = Ae^{bt}$ can evolve independently. For the Gompertz-Makeham curve that we have systematically derived in terms of more fundamental failure accumulation related parameters

(Eq. 14), this *only* happens when either $\phi_\rho = 0$ or $k_\rho = 0$, *i.e.* when either the 'baseline failure rate' of every sub-system is exactly zero or sub-systems have no effect on each other's functioning. Since intra-organismal sub-systems are typically interdependent to at least some degree ($k_\rho > 0$) and have some risk of spontaneous failure due to stochastic wear-and-tear ($\phi_\rho > 0$), we generally expect the Gompertz parameters in Eq. 14 to be correlated. Strehler and Mildvan (1960) and Gavrilov and Gavrilova (1991, sections 6.4-6.7) have also presented more mechanistically explicit reliability-theoretic models in which the Gompertz parameters are correlated when derived systematically from more fundamental underlying processes. At least for mortality curves arising from mechanistic failure accumulation models such as in Gavrilov and Gavrilova (1991) and our work, Bega and Hadany's (2026) central assumption is hence a stringent one, and care is required in assessing when it is a reasonable assumption for any particular mechanistic model.

Weitz and Fraser (2001) have also put forth the idea that stochasticity followed by selective disappearance/mortality can cause late life plateaus without fixed differences in inter-individual quality. Though our models are somewhat similar, they differ in two crucial assumptions. Weitz and Fraser (2001) assume that failure accumulation ('loss of vitality' in their language) occurs at a constant rate (their Eq. 5; their constant ε plays the role of our function $r(f)$, compare with our Eq. 2). In contrast, in our work, we have argued that we should expect failure to beget failure, and the overall failure accumulation rate is thus non-constant (it is increasing). Weitz and Fraser (2001) also assume that an organism dies exactly when all its sub-systems have failed and no sooner (in their language, exactly when vitality hits 0), whereas we work with the more realistic assumption that organisms experience a continuous failure-dependent mortality risk.

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