E-Article

A Life-History Perspective on Short- and Long-Term Consequences of Compensatory Growth

Marc Mangel* **and Stephan B. Munch†**

1. Center for Stock Assessment Research, Department of Applied Mathematics and Statistics, University of California, Santa Cruz, California 95064;
2. Marine Sciences Research Center, Stony Brook University, Stony Brook, New York 11794

Submitted December 16, 2004; Accepted June 23, 2005; Electronically published October 4, 2005

Online enhancement: MATLAB code.

abstract: Compensatory or catch-up growth (CG) is widely observed following periods of resource deprivation. Because of this commonness, it is generally assumed that compensatory growth is adaptive, but most theory to date has explicitly ignored considerations of fitness. Following a period of deprivation, when resources become plentiful again, individuals may not respond at all and continue on a "normal" trajectory from a smaller size at age, may exhibit faster-than-normal growth immediately following the end of the period, or may adopt a growth strategy that involves faster-than-normal growth at some later time. Compensating individuals may also overtake control individuals who have been growing normally throughout. We hypothesize that the key to understanding CG is that growth leads to the accumulation of damage at the cellular level that is expressed (and thus must be modeled) at the level of the organism. We show that a life-history model incorporating the mortality consequences of both size and damage provides a framework for understanding compensatory growth. We use the theory to classify physiological and life-history characteristics for which CG is predicted to be the optimal response to deprivation.

Keywords: compensatory growth, catch-up growth, life-history theory, metabolic damage, dynamic programming, acquisition.

Compensatory growth or catch-up growth (CG) refers to the ability of an organism to grow at an accelerated rate following a period of food shortage or a decline in reproductive weight (Timiras and Valcana 1972; McCance and Widdowson 1974; Sibly and Calow 1986; Whitledge et al. 1998; Jobling and Johansen 1999). Catch-up growth has been observed for many years (Reed 1921) in plants, invertebrates, and vertebrates, both in the laboratory and in the wild (Albon et al. 1987) and both in juveniles and in adults. Catch-up growth occurs following conditions of undernutrition rather than malnutrition (Boersma and Wit 1997). In juvenile fish, for example, CG may occur after only a few days of complete food deprivation or a few weeks of relatively low food availability. Because most species evolved in environments in which food supplies fluctuate, we may expect that natural selection has acted on those feeding behaviors and allocation processes in ways that will allow successful responses to food shortage (Comfort 1963; Sohal and Weindruch 1996). The commonness of CG also shows us that organisms typically grow at rates that are submaximal, although, as noted 70 years ago (McCay 1933), they may be optimal. The reasons for this are manifold; see Mangel and Stamps (2001) for a recent review.

The connections between early growth, caloric restriction, CG, survival, and life span have been reviewed by Feuers et al. (1993), Weindruck and Sohal (1997), Mousseau and Fox (1998), Metcalfe and Monaghan (2001), Beckerman et al. (2002), Lummaa and Clutton-Brock (2002), Rollo (2002), Ali et al. (2003), Metcalfe and Monaghan (2003), and most recently by Bateson et al. (2004) in the context of developmental plasticity and human health and by Dandona et al. (2004), Finch and Crimmins (2004), and Gluckman and Hanson (2004) in the context of disease, inflammation, and human health. Even with this level of review, Ali et al. (2003) note that the evolutionary consequences of CG are largely unexplored.

The short-term trade-off between rapid growth and predation mortality is one of the classic questions in behavioral ecology (Mangel and Stamps 2001), but it is often difficult to verify (e.g., Gotthard 2000). Here we are interested in the long-term trade-offs, which are even more difficult to verify. However, Olson and Shine (2002), Ruel and Whitham (2002), and Munch and Conover (2003)

* E-mail: msmangel@ucsc.edu.

† E-mail: zasummen@aol.com.

Am. Nat. 2005. Vol. 166, pp. E155–E176.

recently showed that rapidly growing individuals (lizards, trees, and fish, respectively) experienced lower long-term survival than slower growing conspecifics. Arendt and Wilson (2000) showed that pumpkinseed sunfish *Lepomis gibbosus* that had grown rapidly delayed cranial ossification, with potential fitness effects through reduced feeding ability, swimming ability, and/or defense against predators. In general, one should expect trade-offs between rapid growth and other functions such as development, repair, maintenance, defense, reproduction, and behavior (Ricklefs et al. 1994; Arendt 1997; Pedersen 1997). Furthermore, experimental evidence indicates that these costs are often deferred (Morgan and Metcalfe 2000): several months after the period of CG, the fish that had experienced CG entered a prolonged phase of poorer relative performance. The proximate mechanism for this could be due to damage to the white muscle, such as that observed in Arctic charr *Salvelinus alpinus* that had undergone rapid growth (Christiansen et al. 1992). As a consequence of reduced long-term performance, CG is often associated with decreased life span.

In appendix A, we provide a brief review of the varieties of compensation. In summary, we now understand that CG depends on species (e.g., Hayward and Wang 2001; Zhu et al. 2001), social environment (MacLean and Metcalfe 2001; Metcalfe and Monaghan 2001), Julian day, temperature, and food availability, and physiological factors such as internal state and age (e.g., Nicieza 1997). There is no single "fixed" pattern of CG (Pitts 1986), but there may be general principles that allow us to deepen understanding and to predict the pattern, given the context. In order to understand patterns of growth and compensatory growth, one should ultimately embed a description of growth in a life-history model (Sibly et al. 1985; Perrin 1992; Perrin and Sibly 1993; Perrin et al. 1993; Tenhumberg et al. 2000) because growth rates at any given size and time are determined by the trade-off between whatever risks are engendered by growth and the future benefits of larger size. However, current models generally perform poorly when used to study CG (Whitledge et al. 1998; Lika and Nisbet 2000; Shertzer and Ellner 2002; Gurney et al. 2003).

Another classic subject in life-history theory is allocation trade-off, in which a fixed amount of resource must be allocated to various physiological functions. Here, we consider an acquisition trade-off in which an organism may acquire additional resources now but incur the cost of additional mortality through damage later in life. In the literature, what precisely is meant by compensatory growth is subject to terminological inexactitude. For instance, most studies of CG utilize a control treatment in which individuals grow on unlimited rations for the duration of the experiment. However, because growth strategies may depend on size, age, and the time remaining for growth, this control can only provide information about the size effects on growth. In circumstances where early-life growth at small size is typically less than the growth of younger individuals of the same size later in the season, studies employing only one control line may mistake normal but late-season growth for CG.

Compensation, Mortality, and Longevity

It is clear that compensatory growth sometimes is associated with increased rates of mortality and decreased longevity. What is not clear is the source of the association. This connects to the larger question of human health and the relationship between height and longevity (e.g., Waaler 1984; Samaras et al. 2003). For example, if increased height (linear dimension) has a negative effect on longevity, can that be explained and predicted? In the field of human health, this is known as the "fetal origins hypothesis": CG experienced early in life (e.g., before age 11) is tightly correlated with a variety of midlife (age > 50) diseases (e.g., Desai et al. 1995; Barker 1998; Lucas et al. 1999; Ozanne and Hales 1999; Barker 2002).

The general relationship between metabolism and life span is still unresolved (Sohal et al. 2000), although they appear to be regulated separately (Cowen 2001). The two major theories (Pearl's rate of living [Pearl 1928] and Brand's mitochondrial uncoupling [Brand 2000], both based on the notion of free radical production and damage) of how energy metabolism is predicted to correlate with longevity give rise to contrary notions. But the experimental results themselves are contradictory and confusing (Speakman et al. 2004; van Voorhies 2004). There is evidence for adaptive response in the sense that across species, the generation of reactive oxygen species (ROS) that cause damage is not simply related to oxygen consumption (Filho et al. 2000). A theory that illuminates these connections by linking physiology and life history may help resolve many of the difficulties.

Previous Models of CG

The apparent flexibility in compensatory growth and the taxonomic variability in the capacity for it have led many authors to suggest that CG may be adaptive. However, no study thus far has fully assessed the fitness consequences of CG. It is conceivable, for instance, that the observed reduction in life span accompanying CG is more than made up for by the increased fecundity that typically comes with increased size.

There are only a few existing theories of compensatory

growth, and most of these are silent on the question of the adaptive nature of CG. A number of models of growth physiology have attempted to predict compensatory growth (e.g., Broekhuizen et al. 1994; Whitledge et al. 1998; Gurney et al. 2003; van Leeuwen et al. 2003). However, in all of these models, allocations are fixed, and no measure of fitness is used. Novoseltsev et al. (2000) use a very simple physiological model to characterize oxidative damage in Mediterranean fruit flies *Ceratitis capitata* and the effects of anticipated oxidative damage on mortality trajectories. However, their theory lacks any measure of fitness. Yearsley et al. (2004) recently developed a theory that includes measures of fitness and that shows that growth compensation may be an adaptive strategy, depending on the duration of the period of deprivation. Their theory is a special case of the one developed here. On the other hand, there have been a number of studies that have attempted to characterize fitness-optimizing growth trajectories when mortality and fecundity are size dependent (e.g., Sibly et al. 1985; Abrams et al. 1996), but none has dealt explicitly with compensatory growth. As we show later, a fundamentally different characterization of mortality is required to predict compensatory growth.

Our Approach

Our goal in this article is to develop a sound theory for compensatory growth and developmental plasticity by positioning ourselves at the nexus of physiology and life history (Ricklefs and Wikelski 2002) and thus constructing norms of reaction for ecological developmental biology (Sultan 2000; Gilbert 2001; Sarkar and Fuller 2003; S. B. Munch and M. Mangel, unpublished manuscript). We begin by clearly defining what is meant by CG. We then turn to the theory by viewing this as a problem of life in silico (sensu Wilke et al. 2001; Wilke and Adami 2002; Kirkwood and Proctor 2003; Lander 2004). With this view, we develop a life-history model describing the salient features of the biology that might give rise to growth compensation and then explore the range of behaviors that may be generated by the model for different combinations of physiological and life-history parameters. This approach differs from classical sensitivity analysis in that we do not limit ourselves to examining the consequences of small perturbations around a fixed set of parameters but rather explore the model's behavior over a wide range of values.

We hypothesize that the key to understanding CG is understanding that growth leads to the accumulation of damage at the cellular level (Martin et al. 1996; Miquel 1998) expressed at the level of the organism (Kirkwood 2005), so we model at the level of the organism in order to develop a life-history framework. We show that a life-history model incorporating the mortality consequences of both size and damage provides a framework for understanding compensatory growth (and, as a bonus, the effects of calorie restriction on aging). Furthermore, in appendix B, we show that a model without damage cannot lead to the prediction of compensatory growth.

Dobzhansky (1962) introduced damage in connection with longevity (also see Gavrilov and Gavrilova 2002). Our approach is generally consistent with the free radical theory of aging (Harman 1956; Ames et al. 1993; Shigenaga et al. 1994; Beckman and Ames 1998; Ashok and Ali 1999). In the "Discussion," we consider the nature of damage more explicitly, but here we make the following observations (Halliwell and Gutteridge 1999, p. 790ff.): oxidative damage is a common link between all theories of aging, there is no marked fall of antioxidant defences with age (p. 796), but net oxidative damage, especially lipid peroxidation, does generally increase with age (p. 798), which means that repair is not 100% effective. After developing the theory, we conduct a large-scale simulation experiment to evaluate the range of possible model behavior and use this to classify physiological and life-history characteristics (cf. Lander 2004) for which CG is predicted to be the optimal.

Methods

To begin, we consider the range of responses to a period of deprivation (Pitts 1986; fig. 1; see also Ali et al. [2003] and Jobling et al. [1994], who use a similar framework). First, individuals may not respond at all and continue on a normal trajectory from a smaller size at age. Second, individuals may exhibit faster-than-normal growth immediately following the end of the deprivation period (short-term compensation). Third, individuals may adopt a growth strategy that involves faster-than-normal growth at some later time (long-term compensation). Finally, individuals may overtake control individuals who have been growing normally throughout (overshooting). The goal of our theory is to explicate when each case will occur and why.

In order to consider the fitness consequences of compensatory growth, we develop a life-history model describing growth in terms of the rates at which energy is acquired and lost through metabolism, both of which are flexibly governed by an individual's level of activity. We focus on a nonreproductive period in the life history during which survival depends on size $X(t)$, activity $a(t)$, and another state variable representing the accumulation of oxidative or cellular damage $D(t)$ (also see Chicon 1997; Chicon and Kozlowski 2000). The fitness associated with a particular growth strategy is determined by the probability of surviving through the focal interval and the residual reproductive value associated with the size and dam-

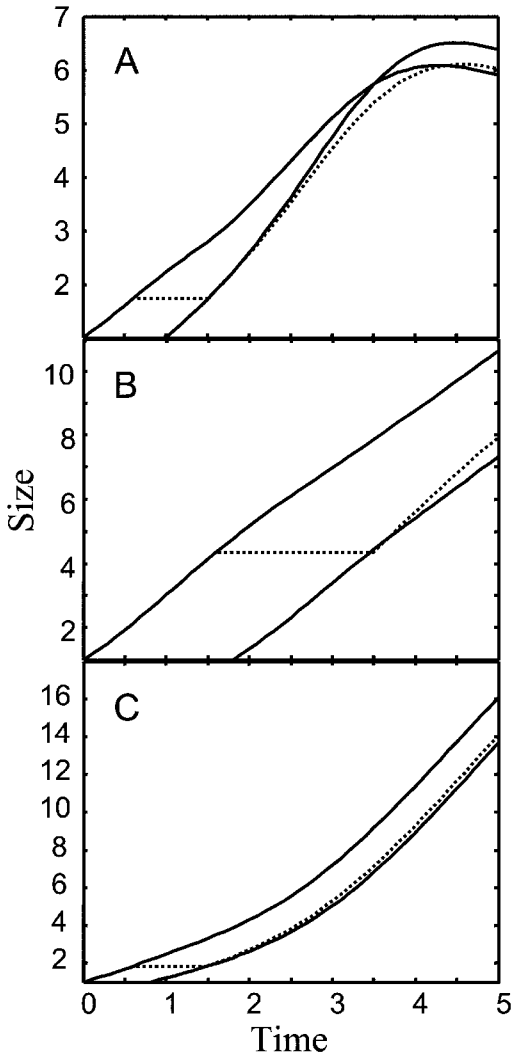

Figure 1: Three panels illustrate the different forms of compensatory growth generated by the model. In each of the panels, the solid lines represent growth trajectories of normally growing individuals. The line on the left represents the standard control, that is, individuals that began the experiment at the same size and age as the treatment individuals. The solid line on the right represents the size/time control, that is, normally growing individuals that are the same size as the treatment individuals at the end of the deprivation period. The dashed lines represent growth trajectories of individuals in an idealized compensatory growth experiment, with the flat portion of the dotted line indicating the deprivation interval. *A*, Overshooting. Note that the treatment trajectory is larger than the standard control at the end but grew more slowly than the size/time trajectory throughout. Parameters used to generate this figure were $\zeta = 4.5$, $\kappa = 0.2$, $\rho_D = 0$, $\nu = 0.1$, $\mu_a = 1$, $\mu_d = 0.328$, $\phi_1 = 9.655$, $\phi_2 = -5.863$, $\eta = 0.842$, $\beta = 1.684$, and $\rho_R = 0.106$. *B*, Short-term compensation. Note that the compensating trajectory grows more rapidly than either control compared at the same time and size. Parameters used to generate this figure were $\zeta = 4.25$, $\kappa = 0.1$, $\rho_D = 0.01$, $\nu = 1$, $\mu_a = 1$, $\mu_d = 0.017$, $\phi_1 = 4.759$, $\phi_2 = -2.931$, $\eta = 0.053$, $\beta = 7.158$, and $\rho_R = 0.705$. *C*, Long-term compensation. Note that although the compensating trajectory grows at the same rate as the size/time control immediately following the deprivation interval, subsequent growth is faster, and the treatment individual is larger than the size/age control trajectory by the end.

age attained by the end. Denoting the instantaneous mortality rate by $M(X, D, a)$ and reproductive value at the end of the growth period by $V(X, D)$, fitness at the end of the fixed growth interval T is

$$\Phi[X(T), D(T)] = V[X(T), D(T)] \times \exp\left\{-\int_0^T M[X(t), D(t), a(t)]dt\right\}. \quad (1)$$

Size, damage, and activity each vary through time, and our approach is to determine the activity level at each instant in time that maximizes fitness at T, given current size and damage. We then use the optimal activity schedule to conduct a virtual compensatory growth experiment. In this virtual CG experiment, individuals are subject to a period of deprivation during which only a maintenance ration is provided and are subsequently allowed to resume the optimal activity level for their present size and damage for the remainder of the growth interval. We use the results of our virtual CG experiments to determine which physiological and life-history parameters are associated with which type of CG, if any, that is predicted to occur following a period of deprivation and to determine how survival to the end of the growth interval is effected. A fully general analytical treatment of the conditions under which CG is predicted to evolve is tractable only when considering short-term compensation and then only under strongly limiting assumptions (app. B).

The Model

We modify the energy balance framework of West et al. (2001) and von Bertalanffy (1938) to allow for activity-mediated variation in growth and allocation of energy to the repair of damage. Specifically, we model growth as a function of size (X), damage (D), activity (a), and energy allocated to repair ($U(X, D)$) as

$$\frac{dX}{dt} = G_X(X, D, a) = C(a)X^{3/4} - R(a)X - U(X, D), \quad (2)$$

where $C(a)$ and $R(a)$ denote the influence of activity on anabolic and catabolic factors. Note that if repair (U) is

Table 1: Summary of variable and parameter definitions

Variable or parameter	Description	Minimum value	Maximum value	No. categories
X	Body size (mass)	1	80	
D	Accumulated damage	.1	30	
a	Activity (metabolic multiples)	0	7	
ζ	Maximum consumption rate	4	4.5	3
κ	Half-saturation of consumption	.1	.2	3
μ_a	Activity-dependent mortality	1	10	10
ρ_D	Damage reinforcement rate	0	.01	2
ρ_R	Energy to damage conversion	.001	1	20
μ_d	Damage-dependent mortality	.0001	.5	30
ν	Energetic efficiency of repair	.1	1	2
η	Maximum repair rate	0	1	20
β	Half-saturation for repair	0	8	20
ϕ_1	Value exponent for size	.001	10	30
ϕ_2	Value exponent for damage	.001	10	30

Note: For the state variables and control, the range indicates the set of achievable values within the optimization routine. For the parameters, the range indicates the support over which values were drawn at random.

set to 0 and $C(a)$ and $R(a)$ are held constant, we obtain the model of West et al. (2001). However, our model can quite naturally produce a much greater variety of growth trajectories than the West et al. model by allowing activity to vary through time. The 3/4-power scaling of anabolism and linear scaling for catabolism (i.e., costs are proportional to mass) represent the modal values from bioenergetics and contaminant accumulation studies (reviewed in Essington et al. 2001; also see Ursin 1967, 1979; Nagy et al. 1999) and are the values commonly used to model growth in many organisms.

We define the cost of activity as the multiples of the basal catabolism; thus,

$$R(a) = (1 + a). \tag{3}$$

In keeping with studies across a wide variety of species, we assume that maximum metabolic rate is six to seven times resting metabolism. Hence, there is a maximum value for activity (a_{sup}) that can be no more than ~6. We assume that no consumption occurs in the absence of activity and that consumption saturates with activity so that

$$C(a) = \frac{\zeta a}{a + \kappa}, \tag{4}$$

where ζ is the maximum rate of energy gain and κ is the activity level at which energy gain is half its maximum. For any size there is thus an activity level that maximizes the net rate of energy gain, found by elementary calculus.

We assume that damage occurs as a consequence of metabolism (e.g., through the generation of free radicals) and may be self-reinforcing (Beckman and Ames 1998; Jazwinski 2000). For example, damaged mitochondrial membranes may allow leakage of free radicals, which increases the probability of further membrane damage (e.g., Shigenaga et al. 1994; Kowald and Kirkwood 1996; Sastre et al. 2003; Fridovich 2004). Furthermore, damage is repaired (Promislow 1994; Ishii and Hartman 2004). We lump the various antioxidant (Sitte and von Zglinicki 2003) and repair (Seeberg 2003*a*, 2003*b*) enzymes together and model the rate of accumulation of damage as

$$\frac{dD}{dt} = G_D(X, D, a) = \rho_R[(1 + a)X - \nu U(X, D)] + \rho_D D, \tag{5}$$

where the ρ_R is a constant that converts energy to damage, ν is the energetic efficiency with which damage is repaired, and ρ_D is the rate at which damage is reinforced. These parameters are also allowed to vary (table 1).

We assume that repair occurs continuously at a rate determined by size and damage and is modeled as the amount of energy allocated to the reduction of damage (Gaver et al. 1997)

$$U(X, D) = \eta X \frac{D^2}{D^2 + \beta^2}, \tag{6}$$

where the maximum repair rate is η, and the half-saturation constant for repair is β. In this formulation, there will be relatively little repair when the damage is low.

Mortality has size-dependent and damage-dependent components. Although mortality that does not involve size

or damage is certainly possible, this additional mortality would be common to all growth strategies and thus would have no effect on the optimal growth strategy (although it might affect the evolution of senescence [Charlesworth 1994; Partridge and Mangel 1999], but that is the topic for a different article). In keeping with empirical evidence for the size dependence of mortality in a variety of species (Lorenzen 1996), we assume that mortality scales inversely with length and model the size dependence of mortality as a power function of mass with exponent $-1/3$. Under the assumption that size-dependent mortality arises through predation and that activity increases exposure to predators, the size-dependent mortality increases linearly in activity. For simplicity, damage-dependent mortality is proportional to damage. Thus the rate of mortality is

$$M(X, D, a) = (1 + \mu_a a)X^{-1/3} + \mu_d D, \tag{7}$$

where μ_a and μ_d are the activity-dependent and damage-dependent rates of mortality, respectively.

We assume that residual reproductive value increases with size and decreases with damage:

$$V(X, D) = X^{\phi_1}(1 + D)^{-\phi_2}, \tag{8}$$

where the exponents for size ϕ_1 and damage ϕ_2 are treated as parameters.

This 11-parameter model is already nondimensionalized to eliminate redundant parameters. Specifically, we have eliminated proportionality constants for metabolic losses and the size dependence of mortality. For the series of in silico experiments described below (sensu Lander 2004), we do not fix or estimate the 11 parameters that remain as one would do when fitting a model to data. Instead, we let these parameters range widely (table 1) and determine which parameter combinations promote the evolution of CG. However, we assume that the parameters are fixed prior to the interval that we model. Thus, for example, this model cannot be used to treat early programming of metabolism (Ozanne and Hales 2002) without extensions. We also understand that parameters may vary both between species and between individuals of the same species (e.g., Jobling and Koskela 1996; Wang et al. 1998). That is, we characterize the physiological constraints on the life history by the parameter vector $\vec{\mathbf{p}} = \{\zeta, \kappa, \nu, \rho_R, \rho_D, \beta, \eta, \mu_a, \mu_d, \phi_1, \phi_2\}$. Given these constraints, we compute fitness, defined by equation (1), by finding the optimal pattern of activity. We then ask whether this optimal pattern of activity generates compensatory growth.

In order to determine which parameter combinations promote the evolution of CG, we determine the optimal time and state-dependent pattern of activity for each set of parameters (which then determines the pattern of growth and survival). To do this, we define a function $F(x, d, t)$ by

$$\begin{aligned} F(x, d, t) &= \max_a [\Phi(X(T), D(T))|X(t) \\ &= x, D(t) \\ &= d], \end{aligned} \tag{9}$$

so that $F(x, d, t)$ is the maximum, taken over activity levels, of fitness at the end of the interval $[t, T]$. When $t = T$, from equation (1) we have $F(x, d, T) = V(x, d) = x^{\phi_1}(1 + d)^{-\phi_2}$, and for previous times, $F(x, d, t)$ satisfies an equation of dynamic programming (Mangel 1985; Mangel and Clark 1988; Abrams and Ludwig 1995; Houston and McNamara 1999; Clark and Mangel 2000):

$$\begin{aligned} F(x, d, t) = \max_a [&(1 - M(x, d, a)dt) \\ &\times F(x + dX, d + dD, t + dt)], \end{aligned} \tag{10}$$

and using equations (2) and (5), we conclude

$$\begin{aligned} F(x, d, t) = \max_a [&(1 - M(x, d, a)dt) \\ &\times F(x + G_X(x, d, a)dt, \\ &d + G_D(x, d, a)dt, t + dt)]. \end{aligned} \tag{11}$$

We solved equation (11) using interpolation (Mangel and Clark 1988; Clark and Mangel 2000). We explored Taylor expansion of equation (11), in which the differences on the right-hand side were replaced by appropriate partial derivatives (Mangel 1985). However, the latter approach—because it involves derivatives—was less stable and more susceptible to error. In appendix B, we describe how the optimization problem can be approached using the Pontryagin maximum principle. As with other equations of dynamic programming, equation (11) is solved backward in time, from $t = T - dt$ to $t = 0$. At each time and state, we generate the optimal level of activity $a^*(x, d, t)$.

Thus, given an initial size, the optimal increments of growth and damage can then be calculated by inserting the optimal activity into equations (2) and (5). By repeatedly looking up the optimal activity level given current size and damage, and incrementing both, optimal growth and damage trajectories are constructed. This procedure can also be used to construct the compensatory trajectories, except that the growth increments were set to 0 for the duration of the deprivation period. We set $T = 5$, and in general we used $dt = 0.05$, but setting $dt = 0.001$ did not change the results. We discretized size on a grid of 40 points between critical value $x_c = 1$ (sensu Mangel and

Clark 1988; Clark and Mangel 2000) and maximum value 80 and discretized damage on a grid of 30 points between 0.1 and 30. For each value of x, we determined the value of activity a_{max} that maximized the growth rate and then evaluated activity on a grid of 25 values between 0 and a_{max}, using a quadratic interpolation of the fitness function. We explored finer grids for mass, damage, and activity. Although this occasionally resulted in small quantitative differences in the forward simulated growth trajectories, there were no qualitative differences in predictions.

The Virtual CG Experiment

Our goal was to identify the parameter combinations that promote the evolution of CG by conducting a series of in silico CG experiments. For a given set of parameters, the virtual CG experiment consisted of seven treatment levels and multiple controls, defined by the onset and duration of the deprivation period (fig. 1). This experimental design was repeated for each parameter combination, allowing us to determine which parameter combinations and treatment levels most commonly led to CG.

We started the deprivation period after 10% or 30% of the growth interval $[0,T]$ had lapsed (hereafter "early" and "late" onset, respectively), and the deprivation period durations were 5%, 20%, 40%, or 60% of T. During the deprivation period, individuals were allowed only maintenance rations, so that $dx/dt = 0$. Thus, during the deprivation period, mass remained constant, but damage continued to accumulate (eqq. [1], [5]). We calculated growth trajectories for each combination of onset and duration except late onset/60% duration because the remaining interval (10%) was too short for reasonable growth to occur. For each trial, we calculated a "standard control" trajectory analogous to that used in typical CG experiments in which individuals are allowed to grow normally for the full duration of the growth interval. However, to fully control for effects of time, size, and age, we initiated additional controls from multiple time points throughout the growth interval. This experimental design allows comparison of treatment trajectories to both normally growing individuals of the same age and normally growing individuals of the same size while accounting for differences in growth due to the time remaining in the season.

We chose ranges for the 11 parameters in the model so that a reasonable amount of growth could be expected to occur in the interval $[0, T]$, and we searched this fairly large parameter space to determine those parameter combinations that were likely to promote different types of CG. An exhaustive search of this 11-dimensional parameter space would be impossible. Instead, we sampled parameters at random from the ranges for each parameter (table 1). To facilitate this sampling, the range of each parameter was divided into up to 30 distinct values (table 1), and each parameter was drawn independently from the resulting discrete uniform distribution. In this way, we generated 10,000 random parameter sets, and the CG experiment described above was repeated for each. Parameter sets from this range that produced implausible results (e.g., that the optimal growth trajectory was to never grow) were discarded, leaving approximately 3,000 viable parameter sets for analysis.

For each viable parameter set and for each treatment, we classify CG as overshooting, short-term compensation, or long-term compensation. Overshooting occurs when the compensating trajectory was larger at the end of the growth interval than the standard, age-matched control (fig. 1*A*). Short-term compensation is growth immediately subsequent to the deprivation period that exceeds growth of the age, size, and time controls (fig. 1*B*). Long-term compensation occurs when the compensating trajectory is larger than the size-matched control by the end of the growth interval (fig. 1*C*). Note that because each of these types of CG are defined with respect to different controls (overshooting vs. long-term CG) and different time intervals (short-term vs. long-term and overshooting), they do not necessarily co-occur, nor are they mutually exclusive.

We conducted these simulations in MATLAB (Mathworks, Natick, MA). The procedure was as follows. A random parameter set was drawn, and based on these parameters, the optimal activity schedule was determined using dynamic programming. Based on this activity schedule, growth trajectories for treatment and control groups were calculated, and treatment trajectories were tested for presence of each type of CG. This algorithm was repeated 10,000 times. The total run time for these virtual CG experiments was approximately 90 hours on a 2.8-GHz PC with 512 MB RAM.

Results

Growth Trajectories

Among the 3,000 viable parameter sets, CG occurred about 25% of the time (table 2). Within the three types of CG analyzed, the predicted commonness is long-term compensation > short-term compensation ~ short-term + long-term compensation > overshooting (table 2). Overshooting never co-occurred with either short- or long-term compensation in a given treatment, and across treatments only four of the 3,000 parameter sets exhibited both long-term compensation and overshooting, suggesting that very different physiologies are required.

Table 2: Absolute frequencies of different compensatory responses in the sampled parameter space

	Deprivation period							
	Early				Late			
Response	.05	.2	.4	.6	.05	.2	.4	Combined
No CG	.902	.871	.931	.972	.836	.882	.972	.754
OS	.018	.007	.000	.000	.000	.000	.000	.018
ST	.003	.032	.044	.025	.026	.056	.022	.085
LT	.077	.091	.025	.003	.138	.062	.006	.211
OS and ST	.000	.000	.000	.000	.000	.000	.000	.001
OS and LT	.000	.000	.000	.000	.000	.000	.000	.000
ST and LT	.003	.025	.019	.002	.016	.029	.005	.067
OS, ST, and LT	.000	.000	.000	.000	.000	.000	.000	.000

Note: For each treatment combination, multiple types of catch-up growth (CG) may occur; thus, the columns do not sum to 1. The "Combined" column indicates the fraction of parameter sets for which each type of CG was present in any treatment. Because different types of CG may occur independently for different treatments within the same parameter set, this column is not the sum of the preceding columns. OS = overshoot; ST = short term; LT = long term.

The occurrence of each type of CG depends on the onset or duration of the deprivation period (table 3). For example, short-term compensation is most likely to occur with a late onset deprivation interval of intermediate duration. Long-term compensation is more likely for late onset deprivation of short duration. In contrast, overshooting is most likely to occur under early onset deprivation of short duration.

Growth Parameters and Compensation

We analyzed the conditions required for each type of CG by comparing the average values of each parameter in cases where no CG occurred with the average parameter values associated with each type of CG. One way of thinking about this is that each set of parameters corresponds to an in silico individual (or species). We then compare the physiological and life-history parameters of individuals who exhibited CG with the population average of that parameter.

To begin, all types of CG are associated with above-average maximum consumption rates (fig. 2*A*), in accord with intuition. Below-average values of the half-saturation constant κ are associated with short- and long-term compensation, while overshooting requires above-average κ values (fig. 2*B*). This indicates that short- and long-term compensation are more likely when consumption is less sensitive to activity, that is, the activity dependence of consumption asymptotes rapidly, but that overshooting indicates a very different biology.

Catch-up growth of all types is generally associated with lower-than-average activity-dependent mortality (fig. 3*A*). However, the sensitivity of each type of CG to activity-dependent mortality is related to the duration of the deprivation period. Short-term compensation is most sensitive to activity-dependent mortality when the deprivation period is fairly short. In contrast, long-term compensation is most sensitive to activity-dependent mortality when the deprivation period is long.

Short-term compensation is influenced by the size dependence of residual reproductive value in a manner that depends on onset and duration (fig. 3*B*). High values of size-dependent reproductive value are associated with short-term compensation in early-onset, short-deprivation trials. This pattern is reversed in late-onset, long-duration trials where lower-than-average values of size dependence appear to promote short-term compensation. The relationship between long-term compensation and size-dependent reproductive value is much simpler: below-average values are common across all treatments, although the sensitivity increases with the deprivation period.

Table 3: Effects of deprivation period onset and duration on frequencies for each type of catch-up growth

	Onset		Duration		
	Early	Late	5%	20%	40%
OS	.025	.000	.019	.007	.000
ST	.081	.106	.029	.090	.067
LT	.195	.210	.217	.157	.031

Note: Numbers are the fraction of the ~3,000 viable parameter sets for which each type of catch-up growth was observed under the given onset or duration. OS = overshoot; ST = short term; LT = long term.

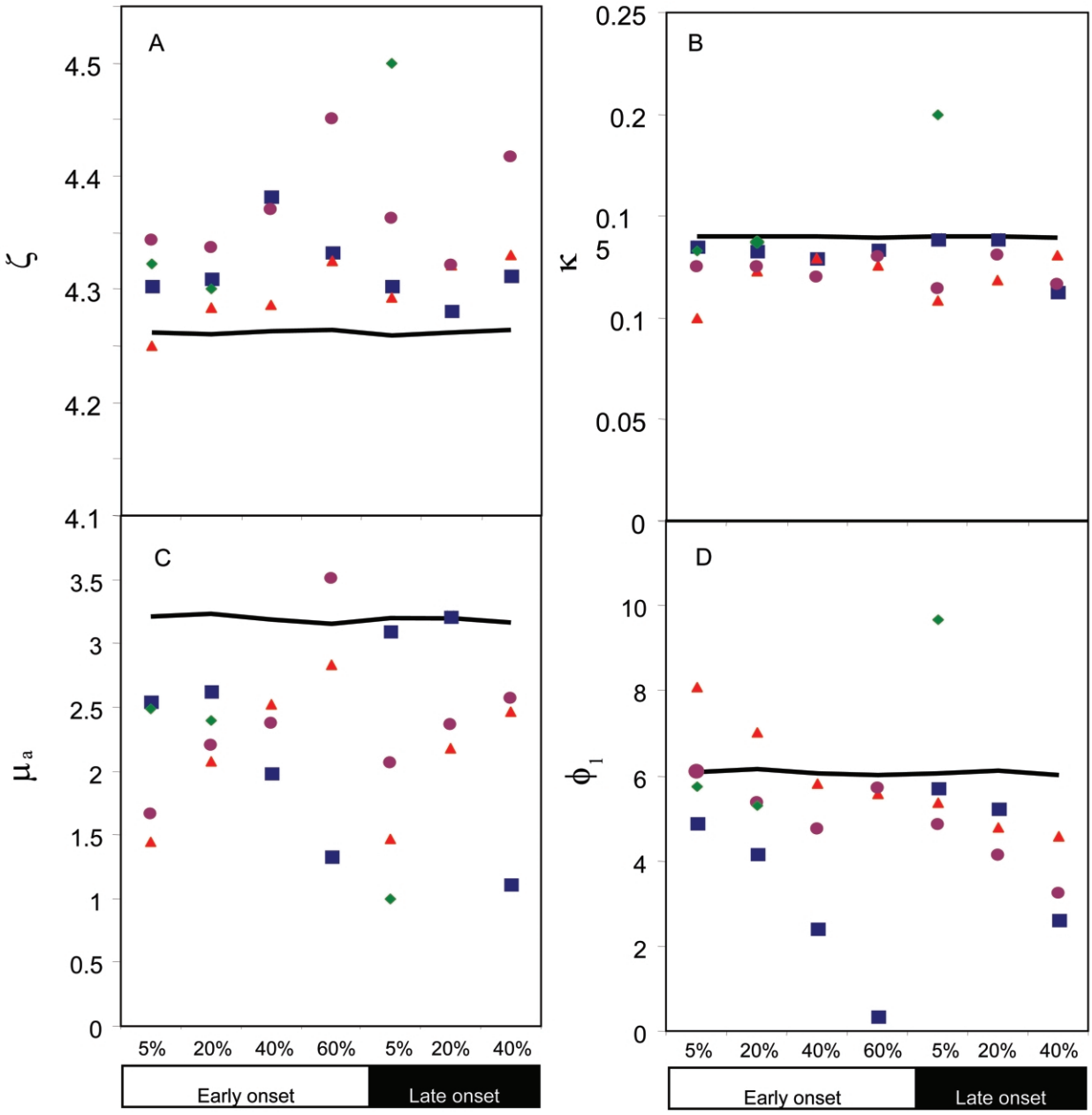

Figure 2: Average values of the parameters governing the growth dynamics for different categories of compensation. For each treatment level (*horizontal axis*), the black line gives the average value of the parameter in cases where no compensation occurred, while each point gives average parameter values in cases where compensation occurred. *Green diamonds* = overshooting, *red triangles* = short-term compensation, *blue squares* = long-term compensation, *purple circles* = co-occurrence of short- and long-term compensation. *A*, Maximum consumption rate. *B*, Half saturation for consumption. *C*, Activity-induced mortality. *D*, Size dependence of residual reproductive value.

Damage and Compensation

As shown in appendix B, it is not possible to generate compensatory growth with an optimality model in the absence of damage or some other additional state variable. Size-dependent mortality and growth alone are insufficient to explain compensatory growth. Thus, damage is a crucial element of our modeling framework. Consequently, as with the growth parameters discussed above, we examine how each type of CG depends on the damage parameters.

Damage-dependent mortality (fig. 4*A*) is lower in short-

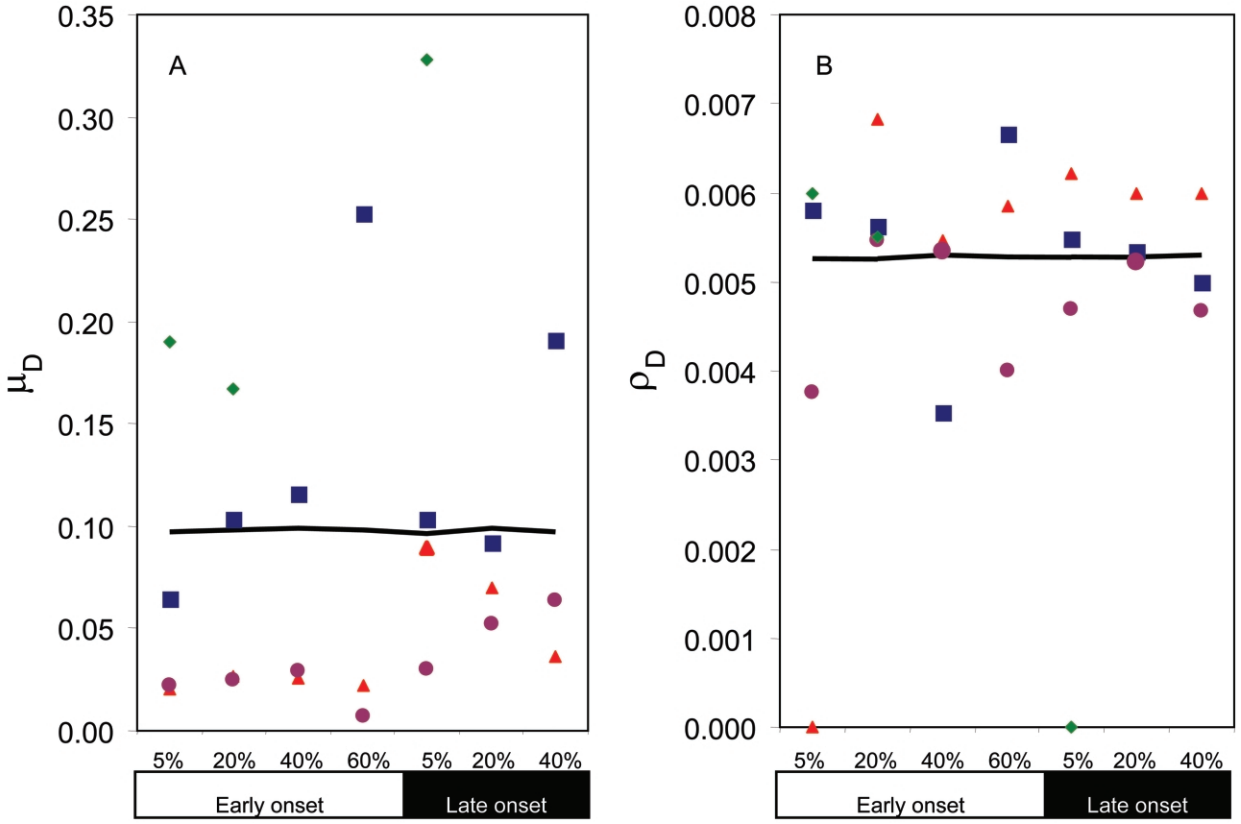

Figure 3: Average values of the parameters governing damage-dependent mortality and damage reinforcement. For each treatment level (horizontal axis), the black line gives the average value of the parameter in cases where no compensation occurred, while each colored point gives average parameter values in cases where compensation occurred. *Green diamonds* = overshooting, *red triangles* = short-term compensation, *blue squares* = long-term compensation, *purple circles* = co-occurrence of short- and long-term compensation. *A*, Damage-dependent mortality rate. *B*, Damage reinforcement rate.

term compensating cases and appears relatively insensitive to deprivation duration in the early onset trials. In late onset trials, however, short-term compensation is less sensitive to damage-dependent mortality overall, but this sensitivity increased with the duration of the deprivation period. Long-term compensation appears to be relatively insensitive to damage-dependent mortality except for the longest deprivation periods. In these cases, higher-than-average damage-dependent mortality appears to promote long-term compensation. Relatively high levels of damage reinforcement are associated with short-term compensation (fig. 4*B*), although damage reinforcement does not have a consistent effect on the other types of CG. Both short- and long-term compensation are promoted by high rates of damage accumulation. This is seen in the above-average values of the metabolism to damage conversion rate (ρ_R; fig. 5*A*) and to a lesser extent in the (typically) below-average values of repair efficiency (ν; fig. 5*B*).

Overshooting is strongly influenced by the capacity for repair (fig. 6). The maximum repair rate is substantially higher for parameter sets in which overshooting occurred compared with cases without CG. Moreover, the half-saturation constant β is substantially lower when overshooting occurred. Thus, overshooting is most likely when the repair rate is high at low levels of damage. The relationship between the capacity for repair and both short- and long-term compensation is ambiguous.

All types of CG are associated with above-average values for the damage dependence of residual reproductive value (fig. 7). Given our parameterization, this indicates that CG is most likely when residual reproductive value is extremely sensitive to low values of damage and relatively insensitive to greater levels. The exceedingly high value of ϕ_2 for overshooting in the late/5% treatment corresponds to a single parameter set, so its interpretation is unclear.

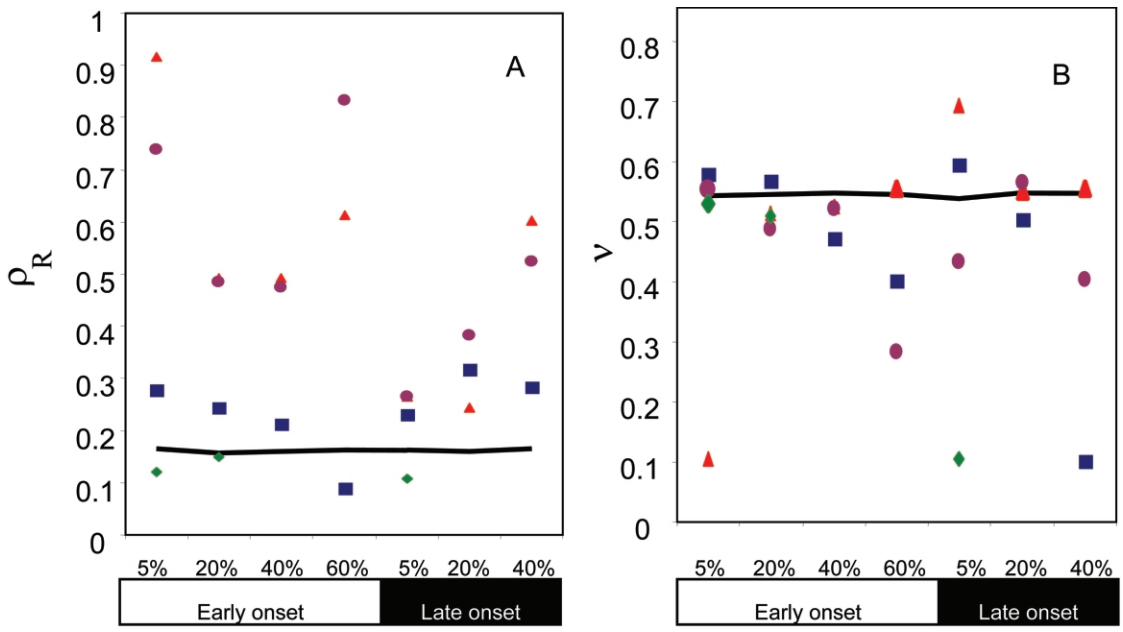

Figure 4: Average values of the parameters governing the conversion of energy to damage for different categories of compensation. For each treatment level (*horizontal axis*), the black line gives the average value of the parameter in cases where no compensation occurred, while each point gives average parameter values in cases where compensation occurred. *Green diamonds* = overshooting, *red triangles* = short-term compensation, *blue squares* = long-term compensation, *purple circles* = co-occurrence of short- and long-term compensation. *A*, Efficiency of conversion of catabolism to damage. *B*, Energetic efficiency of repair.

Mortality Trajectories

Wachter (2003) notes that evolutionary theories of aging generally fail to be able to predict mortality trajectories. However, as an emergent part of the computation, our theory of compensatory growth generates trajectories of mortality. Thus, we are able to predict the shape of mortality trajectories as a function of physiological and life-history parameters. We find that a variety of trajectories are possible under this modeling framework (also see Mangel and Bonsall 2004), ranging from Gompertz-like behavior through plateaus of mortality rate to declines of mortality rate. Theory for predicting mortality trajectories is an active area of research, and a more thorough exploration of the shape of mortality trajectories possible within this framework compensation will be the subject of a subsequent article.

Discussion

The General Situation

The overall picture that emerges from our analysis is fairly complex, as the review in appendix A suggests it would be. However, we are able to distill our results into a series of empirically verifiable predictions. To begin we have a number of null model predictions. First, in the absence of natural selection acting on the physiological parameters governing growth and the accumulation of damage, CG, while not rare, will not be a dominant physiological response. Second, within the three types of CG analyzed, the predicted commonness, without normalizing by terminal fitness, is long-term compensation > short-term compensation ~ short-term + long-term compensation > overshooting. Note that the first prediction stems from the observation that only 25% of the viable parameter sets resulted in some form of CG. However, in contrast to our simulation, natural selection is expected to result in nonuniform distributions of physiological parameters. Thus, natural selection may increase the frequency with which CG is observed in nature.

In addition, we have a series of strong predictions. These are summarized in table 4. Briefly, short-term compensation is predicted to occur when activity and damage incur low mortality penalties, but that damage is accrued fairly rapidly. Long-term compensation is less sensitive to the rate at which damage is accumulated, is more strongly affected by the maximum consumption rate, and is highly influenced by the residual reproductive value. Overshoot-

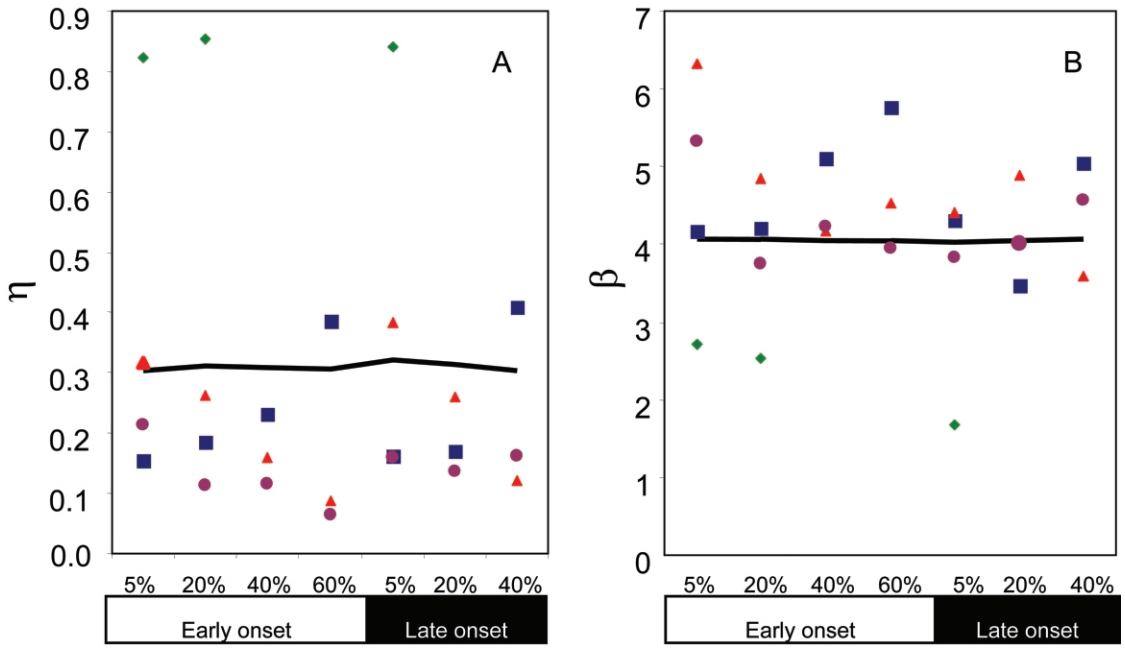

Figure 5: Average values of the parameters governing the allocation of energy to repair of damage for different categories of compensation. For each treatment level (*horizontal axis*), the black line gives the average value of the parameter in cases where no compensation occurred, while each colored point gives average parameter values in cases where compensation occurred. *Green diamonds* = overshooting, *red triangles* = short-term compensation, *blue squares* = long-term compensation, *purple circles* = co-occurrence of short- and long-term compensation. *A*, Maximum allocation to repair. *B*, Half saturation for repair.

ing is predicted primarily when repair is highest and reaches its maximum at low damage levels. Furthermore, for those parameters for which overshooting is predicted to occur, several of the control trajectories surpassed the standard control. Thus, overshooting should be thought of as a time-dependent growth strategy rather than compensatory growth per se. This result highlights the importance of having time-specific controls in empirical research into CG. With the results summarized in table 4 in mind, we predict that the capacity for CG will be strongly tied to the natural history of each species and may be reframed in terms of a comparative analysis. For instance, both short-term and long-term CG seem to require that consumption rates are relatively insensitive to activity levels while overshooting should be more likely for organisms whose intake rates depend strongly on activity. Thus, we should expect to find short-term and long-term CG more commonly among free-living organisms that forage fairly constantly and overshooting among relatively sedentary organisms such as sit-and-wait predators. Short-term CG is more likely in organisms that have low damage-induced mortality, while long-term CG is more likely in organisms that have high damage-induced mortality. Therefore, we hypothesize that organisms that have short life spans and relatively rapid senescence will be more likely to exhibit long-term CG and that relatively long-lived organisms will be more prone to exhibit short-term CG.

Our results are based on the assumption that growth rate is limited by the difference between energy acquisition and expenditure, but it is possible that the constraint may be the growth potential of tissues (Ricklefs et al. 1994; Arendt 2000; Ricklefs 2003). In addition, we have not separated mass and skeleton, although it is known that compensatory responses in each may differ (Hermanussen et al. 1996; Metcalfe et al. 2002). While such extensions of our approach are feasible, they are far from trivial. In addition, our treatment of repair, using a functional response, minimizes the adaptive deployment of repair enzymes (Novoseltsev et al. 2000; Zielinski and Pörtner 2000; Yanase et al. 2002), but we also leave this for a subsequent article.

The Nature of Damage

We have treated damage as a physical variable much like mass but have not specified it. This is often the first step in biological models, in which one does "not specify what

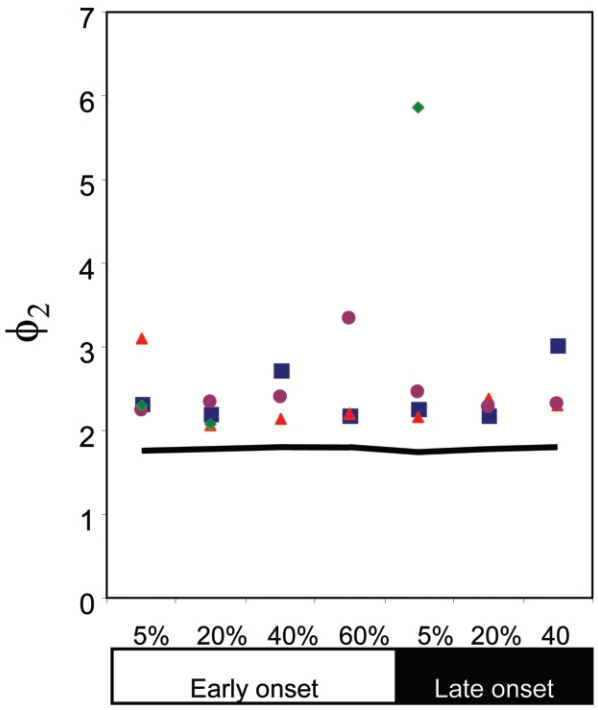

Figure 6: Average values of the parameters governing damage-dependent residual reproductive value for different categories of compensation. For each treatment level (*horizontal axis*), the black line gives the average value of the parameter in cases where no compensation occurred, while each gray point gives average parameter values in cases where compensation occurred. *Green diamonds* = overshooting, *red triangles* = short-term compensation, *blue squares* = long-term compensation, *purple circles* = co-occurrence of short- and long-term compensation.

the components of the model were made of, but only their formal relationships" (Maynard Smith 1986, p. 79). Later in the book, Maynard Smith (1986, p. 106) continues: "People who only believe in things when they know what they are made of will feel uneasy. My own view is that scientific theories usually start out by assuming the existence of entities that no one has ever seen or touched—genes, atoms, photons, viruses. If the theories are successful, someone will find a more direct way of showing that the hypothetical entities are actually there."

Existing evidence from a variety of sources tells us something about the characteristics of damage. Indeed, in some cases it might be very easy to identify damage. For example, Arendt et al. (2001) show that weakened scales are a cost of rapid growth in sunfish, so that the measure of damage is directly obtained from the scale strength of control and treatment individuals. Overwintering juvenile Atlantic salmon (*Salmo salar* L.) divide into resident and migrating fish; the former will spend at least another year in fresh water while the latter will move to the ocean the following spring. Individuals adopting the migrating strategy appear to maximize growth rate by minimizing the rate of protein turnover (Morgan et al. 2000), from which we may conclude that protein damage is more likely in migrating, faster-growing individuals than in resident, slower-growing ones.

There is mounting and generally agreed-on evidence that oxidative damage accumulates at mitochondria (Van Remmen and Richardson 2001; Driver et al. 2004; Hartman et al. 2004). There is also mounting evidence that DNA damage occurs as a consequence of oxidative damage (e.g., Minakami and Fridovich 1990; Chatgilialoglu and O'Neill 2001; Karanjawala and Lieber 2004; Lu et al. 2004),

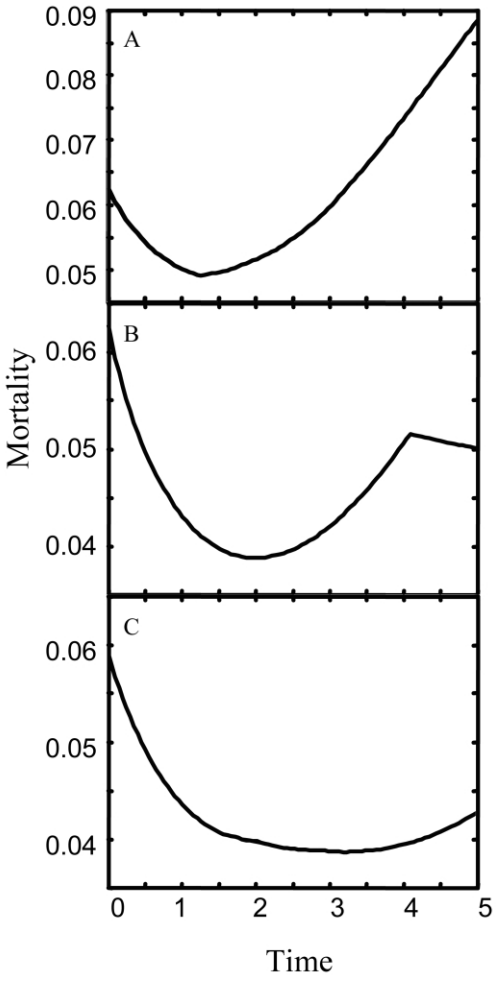

Figure 7: Mortality rates of optimal growth trajectories. Lines represent the time course of mortality rates experienced by the standard control, that is, individuals that have been growing optimally throughout the entire period. *A*, *B*, and *C* correspond to the overshooting, short-term compensation, and long-term compensation examples shown in figure 1.

Table 4: Predictions regarding the occurrence of catch-up growth (CG)

Form of CG	Factors making the form most likely
ST	Late onset, moderate duration; low sensitivity of consumption to activity; below-average damage-dependent mortality; above-average damage accumulation; above-average reinforcement; above-average values of size dependence for reproductive value
LT	Late onset, short duration; low sensitivity of consumption to activity; above-average damage-dependent mortality; above-average damage accumulation; below-average values of size dependence for reproductive value
OS	Early onset, short duration; high sensitivity of consumption to activity; above-average repair, particularly for low levels of damage

Note: The factors listed are those that discriminate among the three types of CG. Factors making all three more likely have been excluded. These are above-average maximum consumption, below-average activity-dependent mortality, and above-average values of damage dependence for reproductive value. OS = overshoot; ST = short term; LT = long term.

and the maintenance of genome integrity is increasingly recognized as a major factor in longevity and cell viability (Hasty et al. 2003). The in vivo level of peroxidation of lipids and protein carbonyls can be measured in a wide variety of organisms (Stadtman 1992; Rikans and Hornbrook 1997; Leeuwenburgh et al. 1998, 1999; Pollack and Leeuwenburgh 1999; Levine and Stadtman 2001; Partridge and Gems 2002; Spiteller 2001; Sukhotin et al. 2002; Lambert and Merry 2004) and in birds (which are relatively long-lived for their masses); these levels are lower than in mammals of comparable sizes. In some cases, the genetic/proteinomic basis of additional damage is understood too (Xin et al. 2003). Thus, directly measurable levels of lipid, protein, or DNA peroxidation is a measure of damage; drugs that will target this damage are under development (Gibson 2004).

What is less clear is how directly damage is connected to mortality rates and life span (Ozawa 1995; Agarwal and Sohal 1996; Finkel and Holbrook 2000; Block et al. 2002; Unterluggauer et al. 2003) even though there is a positive correlation between mammalian life span and cellular resistance to stress (Kapahi et al. 1999). Because antioxidants slow the shortening of telomeres (Serra et al. 2003), one possibility is that oxidative stress shortens telomeres (von Zglinicki 2002) and that telomere length is directly connected to the rate of mortality (e.g., Aviv et al. 2003; Cawthon et al. 2003; Wong and Collins 2003). Other possibilities are that oxidative damage increases the rate of apoptosis (Sastre et al. 2000; Pollack and Leeuwenburgh 2001), that oxidative damage affects cell cycle checkpoints (Serra et al. 2003), or that oxidative stress increases the development and progression of atherosclerosis or hypertension (von Zglinicki et al. 2000; Dobrian et al. 2001; Farrell 2003; Keaney et al. 2003; Morrow 2003).

Several alternative interpretations of damage independent of oxidative stress are possible as well. Dulloo et al. (2002) suggest that improper thermogenesis during CG may itself be a form of damage (and that this is why weight fluctuation early in life is a risk factor for chronic diseases later in life). Another alternative, suggested to us by Marcos A. Antezana (personal communication), is that transcription-associated mutations accumulate in highly expressed genes associated with growth. Trifunovic et al. (2004) recently reported premature aging in mice that expressed defective DNA polymerase, providing some direct evidence for the link. This source of damage could explain some of the classic comparative-biological trade-offs between fecundity or metabolic rate and longevity and suggests where to look for damage. There is already evidence concerning transcription and genomic instability (Aguilera 2002) and that Werner syndrome is associated with a deficient protein associated with optimizing DNA repair (Chen et al. 2003).

The Route to Linking Theory and Observation

During the period of deprivation, damage increases as a consequence of metabolism and reinforcement of damage while size remains constant. Thus, for compensatory growth to occur, the optimal strategy must be to grow faster when an individual has more damage than expected under normal growth for its size and age. Formally, if we can write that CG will occur if $a^*(X, D + \delta D, t) > a^*(X, D, t)$, where $a^*(X, D, t)$ is the optimal level of activity at time t when mass is X and damage is D.

This suggests a route to empirically evaluating our results; exposure to substances that will increase the rate of damage accumulation are predicted to affect growth in a manner similar to periods of deprivation. The difficulty is to apply the stress in such a way that the energetic cost of dealing with it is not excessive, but this is not impossible. The key will be to provide a pulse in damage after which predicted and observed growth trajectories can be compared and longevity measured (Sohal et al. 2000). Of course, measurement of damage itself would be an even better comparison. For example, Minakami and Fridovich (1990) show that paraquat inhibits growth without causing cell death in *E. coli* through increased production of O_2^-. In other words, the application of paraquat provided at a low level causes an increase in damage. Our theory allows

a prediction of the growth response to the increase in damage. In addition, one could use either very high levels of oxygen or hydrogen peroxide (Ogburn et al. 2001) or other stressors (Janssens et al. 2002) as means of inducing damage while simultaneously inhibiting repair, thus allowing another kind of treatment for comparison.

In addition to monitoring growth through changes in mass or linear variables, RNA : DNA ratios allow us to peek inside the organism as a more accurate indicator of feeding condition (Smith and Buckley 2003). Ultimately, however, molecular approaches will be required because identical phenotypic responses to oxidative stress may have very different genetic origins (Arking et al. 2000).

Acknowledgments

This work was partially supported by the Center for Stock Assessment Research, a partnership between the University of California, Santa Cruz, and the National Marine Fisheries Service Santa Cruz Laboratory, and by National Science Foundation grant DMS 03-10542. We thank two anonymous reviewers for comments that helped improve the manuscript.

APPENDIX A

On the Varieties of Growth Compensation

Organisms show a dazzling array of responses to deprivation. Ali et al. (2003) divide the responses to deprivation into no compensation, partial compensation, full compensation, and overcompensation, depending on the ultimate relationship between the control- and treatment-size trajectories. They review about 50 studies on a wide range of species, which show the entire possible range of responses. Furthermore, in some cases (e.g., rainbow trout and hybrid sunfish; Weatherley and Gill 1981; Dobson and Holmes 1984), individuals in the same study may show full compensation, partial compensation, and overcompensation (suggesting individual variation in parameters in eqq. [2], [5]). Nicieza (1997) showed that the timing and duration of the compensatory response of juvenile Atlantic salmon depended on the life-history pathway that the individual adopted (migration the following spring or resident in freshwater for another year) and the manipulation used to reduce growth (a reduction in water temperature or a reduction in food). Perch *Perca flavescens* did not show overcompensation under circumstances in which bluegill-sunfish crosses did (Hayward et al. 1997; Hayward and Wang 2001). Zhu et al. (2001) compared the compensatory responses of sympatric sticklebacks and minnows from a loch in Wales. Minnows were able to wholly compensate for 1 or 2 weeks of starvation while sticklebacks were not. Subsequently, Zhu et al. (2003) showed that two different protocols of deprivation (1 week food deprivation followed by 2 weeks maintenance rations vs. 1 week ad lib. food followed by 2 weeks deprivation) had no effect on the compensatory response, although the reason for this constancy of compensatory response is not clear. Ali and Wootton (2001) showed that three-spined sticklebacks *Gasterosteus aculeatus* recurrently deprived of food for 2, 4, or 6 days followed by 2 days ad lib. feeding almost fully compensated if the deprivation period was 2 days but not if it was 4 or 6 days, although the latter groups did achieve positive growth.

In juvenile barramundi *Lates calcarifer* (Bloch), CG can be induced by as little as 1 week of food deprivation (Tian and Qin 2003), but the magnitude and duration of compensation and body composition of individuals depended on the length of the deprivation period. Sogard and Olla (2002) compared the compensatory responses of juvenile walleye pollock *Theragra chalchgramma* and sablefish *Anoplopoma fimbria*, two sympatric north Pacific fish species. Following a 3-week starvation period, pollock compensated in length and overcompensated in mass. However, sablefish did not compensate in either length or mass following starvation periods of either 2 or 3 weeks. Sogard and Olla did not follow the long-term consequences of compensation but did measure critical swimming speeds (which may be viewed as a proxy for escape speed and thus an inverse proxy for mortality rate) at 4 and 9 weeks after refeeding for pollock and 4 weeks after refeeding for sablefish. The former showed no difference between treatment and control individuals in critical swimming speeds, but sablefish that had been deprived of food and had partially compensated had lower critical swimming speeds. This is not simply a matter of gut contents during refeeding because there was no significant difference in the gut contents of treatment and control individuals. Perch *Perca fluviatilis* on compensatory trajectories may omit spawning in a particular year (Holmgren 2003). Following a 3-week period of deprivation, roach *Rutilus rutilus* showed CG and associated behavioral responses through a diel pattern of temperature choice, migrating to cooler water in the dark. This behavior suggests an adaptive response to the trade-off between higher food density in warmer water and the reduced metabolic costs of cooler water. Jobling et al. (1994) alternated short periods of food deprivation with unlimited provision and found that Atlantic cod *Gadus morhua* fed on alternate weeks (1 : 1) ended up larger than those fed on 2 : 2 or 3 : 3 schedules.

The broad geographic distribution of Atlantic silversides *Menidia menidia* leads to a variety in the expression of compensatory growth within a single species and demonstrates that starvation is not necessary (maintenance ration is sufficient) to induce compensatory growth

(Schultz et al. 2002). Fish from northern (Nova Scotia) populations recovered from 10 days of limited rations by growing 12% faster in length and 46% faster in mass than control fish, but fish from southern populations (South Carolina) grew only 1.4% faster in length and 22% faster in mass than control fish. This pattern of greater capacity for CG in northern populations is predicted by our theory because northern populations have higher average rates of consumption compared to southern populations (Billerbeck et al. 2000).

In summary, compensatory responses can vary between species that are sympatric, within a species according to the developmental pathway, and between individuals apparently on the same developmental pathway. It is thus both the pattern of compensatory growth and its variation that we seek to understand.

Literature Cited Only in Appendix A

Ali, M., and R. J. Wootton. 2001. Capacity for growth compensation in juvenile three-spined sticklebacks experiencing cycles of food deprivation. Journal of Fish Biology 58:1531–1544.

Billerbeck, J. M., E. T. Schultz, and D. O. Conover. 2000. Adaptive variation in energy acquisition and allocation among latitudinal populations of the Atlantic silverside. Oecologia (Berlin) 122:210–219.

Dobson, S. H., and R. M. Holmes. 1984. Compensatory growth in the rainbow trout, *Salmo gairdneri* Richardson. Journal of Fish Biology 25:649–656.

Hayward, R. S., D. B. Noltie, and N. Wang. 1997. Use of compensatory growth to double hybrid sunfish growth rates. Transactions of the American Fisheries Society 126:316–322.

Holmgren, K. 2003. Omitted spawning in compensatory-growing perch. Journal of Fish Biology 62:918–927.

Schultz, E. T., T. E. Lankford, and D. O. Conover. 2002. The covariance of routine and compensatory juvenile growth rates over a seasonality gradient in a coastal fish. Oecologia (Berlin) 133:501–509.

Sogard, S. M., and B. L. Olla. 2002. Contrasts in the capacity and underlying mechanisms for compensatory growth in two pelagic marine fishes. Marine Ecology Progress Series 243:165–177.

Tian, X., and J. G. Qin. 2003. A single phase of food deprivation provoked compensatory growth in barramundi *Lates calcarifer*. Aquaculture 224:169–179.

Weatherley, A. H., and H. S. Gill. 1981. Recovery growth following periods of restricted rations and starvation in rainbow trout *Salmo gairdneri* Richardson. Journal of Fish Biology 18:195–207.

Zhu, X., L. Wu, Y. Cui, Y. Yang, and R. J. Wootton. 2003. Compensatory growth response in three-spined stickleback in relation to feed-deprivation protocols. Journal of Animal Ecology 62:195–205.

APPENDIX B

Conditions for Short-Term Compensation

Here we use optimal control theory (Stengel 1994) to determine the general conditions under which short-term compensation is predicted to occur. The analysis is much more convenient on a log scale, so we define

$$J = \ln [V(X_T, D_T)] - \int_0^T M(X_t, D_t, a_t)dt. \tag{B1a}$$

The general conditions for optimal growth (and short-term compensatory growth) may be derived using the Pontryagin maximum principle (PMP; Stengel 1994). Appending the dynamic constraints (eqq. [2], [5]) to our fitness functional (B1a), we have the augmented fitness functional

$$J_{\text{augmented}} = \ln V(X_T, D_T) + \lambda_X X_T + \lambda_D D_T - \int_{t_g}^T M(X_t, D_t, a_t)$$
$$+ \lambda_X G_X(X_t, D_t, a_t) + \lambda_D G_D(X_t, D_t, a_t) + \lambda'_X X_t + \lambda'_D D_t ds, \tag{B1b}$$

where λ_X and λ_D are adjoint variables representing the change in future fitness resulting from changes in X and D, respectively, and λ'_X and λ'_D are their time derivatives. The Hamiltonian (H) for this system is

$$H(X, D, a) = M(X, D, a) + \lambda_X G_X(X, D, a) + \lambda_D G_D(X, D, a). \tag{B2}$$

According to PMP, along the optimal trajectory the Hamiltonian must be minimized at each time step. This gives rise to the following three conditions for optimality:

$$\frac{\partial M}{\partial a} + \lambda_X \frac{\partial G_X}{\partial a} + \lambda_D \frac{\partial G_D}{\partial a} = 0, \tag{B3a}$$

$$\frac{\partial M}{\partial X} + \lambda_X \frac{\partial G_X}{\partial X} + \lambda_D \frac{\partial G_D}{\partial X} + \lambda'_X = 0, \tag{B3b}$$

$$\frac{\partial M}{\partial D} + \lambda_X \frac{\partial G_X}{\partial D} + \lambda_D \frac{\partial G_D}{\partial D} + \lambda'_D = 0. \tag{B3c}$$

These must hold throughout the focal interval and the transversality conditions that must hold at the end:

$$\frac{\partial \ln V(X_T, D_T)}{\partial X_T} + \lambda_X = 0, \tag{B4a}$$

$$\frac{\partial \ln V(X_T, D_T)}{\partial D_T} + \lambda_D = 0. \tag{B4b}$$

We deduce a number of results from equations (B3) and (B4).

First, if growth, mortality, and reproductive value are independent of damage, there is no possibility of short-term compensatory growth occurring in this model. Under these conditions, equations (B3) and (B4) reduce to

$$\frac{\partial M}{\partial a} + \lambda_X \frac{\partial G_X}{\partial a} = 0, \tag{B5a}$$

$$\frac{\partial M}{\partial X} + \lambda_X \frac{\partial G_X}{\partial X} + \lambda'_X = 0,$$

$$\lambda_D \frac{\partial G_D}{\partial D} + \lambda'_D = 0, \tag{B5b}$$

$$\frac{\partial \ln V(X_T)}{\partial X_T} + \lambda_X(T) = 0,$$

$$\lambda_D(T) = 0. \tag{B5c}$$

In this case, optimal size trajectories are determined solely by the individual's current size and the time remaining for growth. Therefore, optimal growth following a period of deprivation would be indistinguishable from an optimal trajectory taken by a younger individual that had grown normally to the same size. Thus CG is not possible.

Analysis of this model also reveals that if reproductive value depends on damage, then CG may be predicted to occur. However, we must consider in greater depth the conditions under which CG may evolve. First, recognize that a period of deprivation must result in an individual having more damage than expected for its size. This is a consequence of metabolism continuing even if growth is suppressed and there is no reinforcement of damage. Therefore, damage accumulates damage throughout the deprivation period. Consequently, for CG to evolve, fitness must be greater for an individual exhibiting faster growth when it finds itself with an excess of damage given its size and age. More formally, if we think of the optimal activity as a function of size, damage, and time, this condition indicates that $a^*(X, D + \delta D, t) > a^*(X, D, t)$ where δD is the excess damage accumulated during the period of deprivation. Recall that equation (B2) takes a minimum at a_{opt}. To ensure that $a^*(X, D + \delta D, t) > a^*(X, D, t)$, we must have $\partial H(X, D +$

$\delta D, a^*(X, D, t))/\partial a < 0$. Approximating H in a neighborhood of D, we arrive at the following condition for short-term CG:

$$\frac{\partial^2 H(X, D, a^*)}{\partial a \partial D} < 0. \tag{B7}$$

In this context, it is important to note that the adjoint variables correspond to particular trajectories emanating from specific terminal states and thus must be considered functions of X and D when evaluating (B7). Applying condition (B7) to (B2) we have

$$\frac{\partial^2 M}{\partial a \partial D} + \lambda_X \frac{\partial^2 G_X}{\partial a \partial D} + \lambda_D \frac{\partial^2 G_D}{\partial a \partial D} + \frac{\partial \lambda_X}{\partial D}\frac{\partial G_X}{\partial a} + \frac{\partial \lambda_D}{\partial D}\frac{\partial G_D}{\partial a} < 0. \tag{B8}$$

Assuming that mortality is linear and additive in damage and that all other model components are independent of damage, equation (B8) reduces to

$$\frac{\partial \lambda_X}{\partial D}\frac{\partial G_X}{\partial a} + \frac{\partial \lambda_D}{\partial D}\frac{\partial G_D}{\partial a} < 0. \tag{B9}$$

Because growth in size and damage must increase within the potentially optimal range of activity levels, the partial derivatives with respect to a are positive. (Generally speaking, our construction implies that $\partial G_X/\partial a < 0$ for $a > a_{max}(X)$. However, activity rates greater than this value will never be optimal, and we may reasonably restrict our attention to the range of activity values for which G_X is increasing with activity). Thus, for CG to occur, either one or both of $\partial \lambda_X/\partial D$ and $\partial \lambda_D/\partial D$ must be negative. While fairly cumbersome to evaluate directly, we may obtain some information about conditions required for short-term CG by noting that these partial derivatives must be of the same sign as $\partial \lambda_X/\partial D_T$ and $\partial \lambda_D/\partial D_T$. Consequently, we evaluate the signs of

$$\frac{\partial \lambda_X(T)}{\partial D_T} = -\frac{\partial^2 \ln V}{\partial X_T \partial D_T}, \tag{B10a}$$

$$\frac{\partial \lambda_D(T)}{\partial D_T} = -\frac{\partial^2 \ln V}{\partial D_T^2}. \tag{B10b}$$

Because we expect V to increase with size, the right hand side of equation (B10a) will be negative provided that increasing damage does not cause reductions in the marginal benefits of size.

Literature Cited Only in Appendix B

Stengel, R. 1994. Optimal control and estimation. Dover, New York.

APPENDIX C

MATLAB Code Used to Solve the Dynamic Programming Equation

The MATLAB code that we used to solve equation (11) can be found at MATLAB code. The code has not been peer-reviewed, and neither the journal nor the authors are able to provide support.

Literature Cited

Abrams, P. A., and D. Ludwig. 1995. Optimality theory, Gompertz' law, and the disposable theory of senescence. Evolution 49:1055–1066.

Abrams, P. A., O. Leimar, S. Nylin, and C. Wiklund. 1996. The effect of flexible growth rates on optimal sizes and development times in a seasonal environment. American Naturalist 147:381–395.

Agarwal, S., and R. S. Sohal. 1996. Relationship between susceptibility to protein oxidation, aging, and maximum life span potential of different species. Experimental Gerontology 31:387–392.

Aguilera, A. 2002. The connection between transcription and genomic instability. European Molecular Biology Organization Journal 21:195–201.

Albon, S. D., T. H. Clutton-Brock, and F. E. Guinness. 1987. Early development and population dynamics in red deer. II. Density-independent effects and cohort variation. Journal of Animal Ecology 56:69–81.

Ali, M., A. Nicieza, and R. J. Wootton. 2003. Compensatory growth in fishes: a response to growth depression. Fish and Fisheries 4: 147–190.

Ames, B. N., M. K. Shigenaga, and T. M. Hagen. 1993. Oxidants, antioxidants and the degenerative disease of aging. Proceedings of the National Academy of Sciences of the USA 90:7915–7922.

Arendt, J. D. 1997. Adaptive intrinsic growth rates: an integration across taxa. Quarterly Review of Biology 72:149–177.

———. 2000. Allocation of cells to proliferation vs. differentiation and its consequences for growth and development. Journal of Experimental Zoology 288:219–234.

Arendt, J. D., and D. S. Wilson. 2000. Population differences in the onset of cranial ossification in pumpkinseed (*Lepomis gibbosus*), a potential cost of rapid growth. Canadian Journal of Fisheries and Aquatic Sciences 57:351–356.

Arendt, J. D., D. S. Wilson, and E. Stark. 2001. Scale strength as a cost of rapid growth sunfish. Oikos 93:95–100.

Arking, R., V. Burde, K. Grave, R. Hari, E. Feldman, A. Zeevi, S. Soliman, et al. 2000. Identical longevity phenotypes are characterized by different patterns of gene expression and oxidative damage. Experimental Geronotology 35:353–373.

Ashok, B. T., and R. Ali. 1999. The aging paradox: free radical theory of aging. Experimental Geronotology 34:293–303.

Aviv, A., D. Levy, and M. Mangel. 2003. Growth, telomere dynamics and successful and unsuccessful human aging. Mechanisms of Ageing and Development 124:829–837.

Barker, D. J. P. 1998. Mothers, babies and health in later life. Churchill Livingstone, Edinburgh.

———. 2002. Fetal programming of coronary heart disease. Trends in Endocrinology and Metabolism 13:364–368.

Bateson, P., D. J. P. Barker, T. H. Clutton-Brock, D. Deb, B. D'Udine, R. A. Foley, P. Gluckman, et al. 2004. Developmental plasticity and human health. Nature 430:419–421.

Beckerman, A. P., T. G. Benton, E. Ranta, V. Kaitala, and P. Lundberg. 2002. Population dynamic consequences of delayed life-history effects. Trends in Ecology & Evolution 17:263–269.

Beckman, K. B., and B. N. Ames. 1998. The free radical theory of aging matures. Physiological Reviews 78:547–581.

Block, G., M. Dietrich, E. P. Norkus, J. D. Morrow, M. Hudes, B. Caan, and L. Packer. 2002. Factors associated with oxidative stress in human populations. American Journal of Epidemiology 156: 274–285.

Boersma, B., and J. M. Wit. 1997. Catch-up growth. Endocrine Reviews 18:646–661.

Brand, M. D. 2000. Uncoupling to survive? the role of mitochondrial inefficiency in ageing. Experimental Gerontology 35:811–820.

Broekhuizen, N., W. S. C. Gurney, A. Jones, and A. D. Bryant. 1994. Modelling compensatory growth. Functional Ecology 8:770–782.

Cawthon, R. M., K. R. Smith, E. O'Brien, A. Sivatchenko, and R. A. Kerber. 2003. Association between telomere length in blood and mortality in people aged 60 years or older. Lancet 361:393–395.

Charlesworth, B. 1994. Evolution in age-structured populations. Cambridge University Press, Cambridge.

Chatgilialoglu, C., and P. O'Neill. 2001. Free radicals associated with DNA damage. Experimental Gerontology 36:1459–1471.

Chen, L., S. Huang, L. Lee, A. Davalos, R. H. Schiestl, J. Campisi, and J. Oshima. 2003. WRN, the protein deficient in Werner syndrome, plays a critical structural role in optimizing DNA repair. Aging Cell 2:191–199.

Chicon, M. 1997. Evolution of longevity through optimal resource allocation. Proceedings of the Royal Society of London B 264:1383–1388.

Chicon, M., and J. Kozlowski. 2000. Ageing and typical survivorship curves result from optimal resource allocation. Evolutionary Ecology 2:857–870.

Christiansen, J. S., I. Martinez, M. Jobling, and A. B. Amin. 1992. Rapid somatic growth and muscle damage in salmonid fish. Basic and Applied Myology 2:235–239.

Clark, C. W., and M. Mangel. 2000. Dynamic state variable models in ecology: methods and applications. Oxford University Press, New York.

Comfort, A. 1963. The effect of delayed and resumed growth on the longevity of a fish (*Lebistes reticulatus*, Peters) in captivity. Gerontologia 8:150–155.

Cowen, T. 2001. A heady message for life span regulation. Trends in Genetics 17:109–113.

Dandona, P., A. Aljada, and A. Bandyopadhyay. 2004. Inflammation: the link between insulin resistance, obesity and diabetes. Trends in Immunology 25:4–7.

Desai, M., N. J. Crowther, S. E. Ozanne, A. Lucas, and C. N. Hales. 1995. Adult glucose and lipid metabolism may be programmed during fetal life. Biochemical Society Transactions 23:331–335.

Dobrian, A. D., M. J. Davies, S. D. Schriver, T. J. Lauteerio, and R. L. Prewitt. 2001. Oxidative stress in a rat model of obesity-induced hypertension. Hypertension 37:554–560.

Dobzhansky, T. 1962. Mankind evolving: the evolution of the human species. Yale University Press, New Haven.

Driver, C., A. Gerogiou, and G. Georgiou. 2004. The contribution by mitochondrially induced oxidative damage to aging in *Drosophila melanogaster*. Biogerontology 5:185–192.

Dulloo, A. G., J. Jacquet, and J.-P. Montani. 2002. Pathways from weight fluctuations to metabolic diseases: focus on maladaptive thermogenesis during catch-up fat. International Journal of Obesity 26(suppl.):46–57.

Essington, T. E., J. F. Kitchell, and C. J. Walters. 2001. The von Bertalanffy growth function, bioenergetics and the consumption rates of fish. Can J Fish Aquat Sci 58:2129–2138.

Farrell, A. P. 2003. Coronary arteriosclerosis in salmon: growing old or growing fast? Comparative Biochemistry and Physiology A 132: 723–735.

Feuers, R. J., R. Weindruch, and R. W. Hart. 1993. Caloric restriction, aging, and antioxidant enzymes. Mutation Research 295:191–200.

Filho, D. W., M. A. Torres, J. L. Marcon, C. G. Fraga, and A. Boveris. 2000. Comparative antioxidant defenses in vertebrates: emphasis on fish and mammals. Trends in Comparative Biochemistry and Physiology 7:33–45.

Finch, C. E., and E. M. Crimmins. 2004. Inflammatory exposure and historical changes in human life-spans. Science 305:1736–1739.

Finkel, T., and N. J. Holbrook. 2000. Oxidants, oxidative stress and the biology of ageing. Nature 408:239–247.

Fridovich, I. 2004. Mitochondria: are they the seat of senescence? Aging Cell 3:13–16.

Gaver, D. P., P. A. Jacobs, R. L.Carpenter, and J. G. Burkhart. 1997. A mathematical model for intracellular effects of toxins on DNA adduction and repair. Bulletin of Mathematical Biology 59:89–106.

Gavrilov, L. A., and N. S. Gavrilova. 2002. Evolutionary theories of aging and longevity. Scientific World Journal 2:339–356.

Gibson, B. W. 2004. Exploiting proteomics in the discovery of drugs that target mitochondrial oxidative damage. Science Aging Knowledge Environment 2004:pe12.

Gilbert, S. F. 2001. Ecological developmental biology: developmental biology meets the real world. Developmental Biology 233:1–12.

Gluckman, P. D., and M. A. Hanson. 2004. Living with the past: evolution, development and patterns of disease. Science 305:1733–1736.

Gotthard, K. 2000. Increased risk of predation as a cost of high growth

rate: an experimental test in a butterfly. Journal of Animal Ecology 69:896–902.

Gurney, W. S. C., W. Jones, A. R. Veitch, and R. Nisbet. 2003. Resource allocation, hyperphagia, and compensatory growth in juveniles. Ecology 84:2777–2787.

Halliwell, B., and J. M. C. Gutteridge. 1999. Free radicals in biology and medicine. Oxford University Press, Oxford.

Harman, D. 1956. Aging: a theory based on free radical and radiation chemistry. Journal of Gerontology 2:298–300.

Hartman, P., R. Ponder, H.-H. Lo, and N. Ishii. 2004. Mitochondrial oxidative stress can lead to nuclear hypermutability. Mechanisms of Ageing and Development 125:417–420.

Hasty, P., J. Campisi, J. Hoeijmakers, H. van Steeg, and J. Vijg. 2003. Aging and genome maintenance: lessons from the mouse. Science 299:1355–1359.

Hayward, R. S., and N. Wang. 2001. Failure to induce overcompensation of growth in maturing yellow perch. Journal of Fish Biology 59:126–140.

Hermanussen, M., M. d. L. A. R. de Lama, A. P. Romero, C. A. Ruiz, J. Burmeister, and J. A. F. Tresguerres. 1996. Differential catch-up in body weight and bone growth after short-term starvation in rats. Growth Regulation 6:230–237.

Houston, A. I., and J. M. McNamara. 1999. Models of adaptive behaviour. Cambridge University Press, Cambridge.

Ishii, N., and P. S. Hartman. 2000. Oxidative stress and aging in *Caenorhabditis elegans*. Results and Problems in Cell Differentiation 29:150–164.

Janssens, B. J., R. le Gall, and J.-F. Rees. 2002. Peroxide-triggered erythrocytes heamolysis as a model for the study of oxidative damage in marine fishes. Journal of Fish Biology 61:71–84.

Jazwinski, S. M. 2000. Metabolic control and ageing. Trends in Genetics 16:506–511.

Jobling, M., and S. J. S. Johansen. 1999. The lipostate, hyperphagia and catch-up growth. Aquaculture Research 30:473–478.

Jobling, M., and J. Koskela. 1996. Interindividual variations in feeding and growth in rainbow trout during restricted feeding and in a subsequent period of compensatory growth. Journal of Fish Biology 49:658–667.

Jobling, M., O. H. Meløy, J. dos Santos, and B. Christiansen. 1994. The compensatory growth response of the Atlantic cod: effects of nutritional history. Aquaculture International 2:75–90.

Kapahi, P., M. Boulton, and T. B. L. Kirkwood. 1999. Positive correlation between life span and cellular resistance to stress. Free Radical Biology & Medicine 26:495–500.

Karanjawala, Z. E., and M. R. Lieber. 2004. DNA damage and aging. Mechanisms of Ageing and Development 125:405–416.

Keaney, J. F., M. G. Larson, R. S. Vasan, P. W. F. Wilson, I. Lipinska, D. Corey, J. M. Massaro, P. Sutherland, J. A. Vita, and E. J. Benjamin. 2003. Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham study. Arteriosclerosis Thrombosis and Vascular Biology 23:434–439.

Kirkwood, T. B. L. 2005. Understanding the odd science of aging. Cell 120:437–447.

Kirkwood, T. B. L., and C. J. Proctor. 2003. Somatic mutations and ageing in silico. Mechanisms of Ageing and Development 124:85–92.

Kowald, A., and T. B. L. Kirkwood. 1996. A network theory of ageing: the interactions of defective mitochondria, aberrant proteins, free radicals and scavengers in the ageing process. Mutation Research 316:209–236.

Lambert, A. J., and B. J. Merry. 2004. Effect of caloric restriction on mitochondrial reactive oxygen species production and bioenergetics: reversal by insulin. American Journal of Physiology 286: R71–R79.

Lander, A. D. 2004. A calculus of purpose. Public Library of Science Biology 2:0712–0714.

Leeuwenburgh, C., P. A. Hansen, J. O. Holloszy, and J. W. Heinecke. 1998. Markers of protein oxidation by hydroxyl radical and reactive nitrogen species in tissues of aging rats. American Journal of Physiology 274:R453–R461.

———. 1999. Oxidized amino acids in the urine of aging rats: potential markers for assessing oxidative stress in vivo. American Journal of Physiology 276:R128–R135.

Levine, R. L., and E. R. Stadtman. 2001. Oxidative modification of proteins during aging. Experimental Gerontology 36:1495–1502.

Lika, K., and R. Nisbet. 2000. A dynamic energy budget model based on partitioning of net production. Journal of Mathematical Biology 41:361–386.

Lorenzen, K. 1996. The relationship between body weight and natural mortality in juvenile and adult fish: a comparison of natural ecosystems and aquaculture. Journal of Fish Biology 49:627–647.

Lu, T., Y. Pan, S.-Y. Kao, C. Li, I. Kohane, J. Chan, and B. A. Yanknere. 2004. Gene regulation and DNA damage in the ageing human brain. Nature 429:883–891.

Lucas, A., M. S. Fewtrell, and T. J. Cole. 1999. Fetal origins of adult disease: the hypothesis revisited. British Medical Journal 319:245–249.

Lummaa, V., and T. Clutton-Brock. 2002. Early development, survival and reproduction in humans. Trends in Ecology & Evolution. 17: 141–147.

MacLean, A., and N. B. Metcalfe. 2001. Social status, access to food, and compensatory growth in juvenile Atlantic salmon. Journal of Fish Biology 58:1331–1346.

Mangel, M. 1985. Decision and control in uncertain resource systems. Academic Press, New York.

Mangel, M., and M. Bonsall. 2004. The shape of things to come: using models with physiological structure to predict mortality trajectories. Theoretical Population Biology 65:353–359.

Mangel, M., and C. W. Clark. 1988. Dynamic modeling in behavioral ecology. Princeton University Press, Princeton, NJ.

Mangel, M., and J. Stamps. 2001. Trade-offs between growth and mortality and the maintenance of individual variation in growth. Evolutionary Ecology Research 3:583–593.

Martin, G. M., S. N. Austad, and T. E. Johnson. 1996. Genetic analysis of ageing: role of oxidative damage and environmental stresses. Nature Genetics 13:25–34.

Maynard Smith, J. 1986. The problems of biology. Oxford University Press, Oxford.

McCance, R. A., and E. M. Widdowson. 1974. The determinants of growth and form. Proceedings of the Royal Society of London B 185:1–17.

McCay, C. M. 1933. Is longevity compatible with optimum growth? Science 77:410–411.

Metcalfe, N., and P. Monaghan. 2001. Compensation for a bad start: grow now, pay later? Trends in Ecology & Evolution 16:254–260.

Metcalfe, N., and P. Monaghan. 2003. Growth versus lifespan: perspectives from evolutionary ecology. Experimental Gerontology 38: 935–940.

Metcalfe, N. B., C. D. Bull, and M. Mangel. 2002. Seasonal variation

in catch-up growth reveals state dependent somatic allocations in salmon. Evolutionary Ecology Research 4:1–11.

Minakami, H., and I. Fridovich. 1990. Relationship between growth of *Escherichia coli* and susceptibility to the lethal effect of paraquat. FASEB Journal 4:3239–3244.

Miquel, J. 1998. An update on the oxygen stress–mitochondrial mutation theory of aging: genetic and evolutionary implications. Experimental Gerontology 33:113–126.

Morgan, I. J., and N. B. Metcalfe. 2000. Deferred costs of compensatory growth after autumnal food shortage in juvenile salmon. Proceedings of the Royal Society of London B 268:1–7.

Morgan, I. J., I. D. McCarthy, and N. B. Metcalfe. 2000. Life-history strategies and protein metabolism in overwnterng juvenile Atlantic salmon: growth is enhanced in early migrants through lower protein turnover. Journal of Fish Biology 56:637–647.

Morrow, J. D. 2003. Is oxidant stress a connection between obesity and atherosclerosis? Arteriosclerosis Thrombosis and Vascular Biology 23:368–370.

Mousseau, T. A., and C. W. Fox. 1998. The adaptive significance of maternal effects. Trends in Ecology & Evolution 13:403–407.

Munch, S., and D. Conover. 2003. Rapid growth results in increased susceptibility to predation in *Menidia menidia*. Evolution 57:2119–2127.

Nagy, K. A., I. A. Girard, and T. K. Brown. 1999. Energetics of free-ranging mammals, reptiles, and birds. Annual Review of Nutrition 119:247–277.

Nicieza, A. G., and N. B. Metcalfe. 1997. Growth compensation in juvenile Atlantic salmon: responses to depressed temperature and food availability. Ecology 78:2385–2400.

Novoseltsev, V. N., J. R. Carey, P. Liedo, J. Novoseltseva, and A. I. Yashin. 2000. Anticipation of oxidative damages decelerates aging in virgin female medflies: hypothesis tested by statistical modeling. Experimental Gerontology 35:971–987.

Ogburn, C., E. K. Carlberg, M. A. Ottinger, D. J. Holmes, G. M. Martin, and S. N. Austad. 2001. Exceptional cellular resistance to oxidative damage in long-lived birds require active gene expression. Journal of Gerontology 56A:B468–B474.

Olson, M., and R. Shine. 2002. Growth to death in lizards. Evolution 56:1867–1870.

Ozanne, S. E., and C. N. Hales. 1999. The long-term consequences of intra-uterine protein malnutrition for glucose metabolism. Proceedings of the Nutrition Society 58:615–619.

———. 2002. Early programming of glucose-insulin metabolism. Trends in Endocrinology and Metabolism 13:368–373.

Ozawa, T. 1995. Mitochondrial DNA mutations associated with aging and degenerative diseases. Experimental Gerontology 30:269–290.

Partridge, L., and D. Gems. 2002. Mechanisms of ageing: public or private. Nature Reviews Genetics 3:165–175.

Partridge, L., and M. Mangel. 1999. Messages from mortality: the evolution of death rates in the old. Trends in Ecology & Evolution 14:438–442.

Pearl, R. 1928. The rate of living. Knopf, New York.

Pedersen, B. H. 1997. The cost of growth in young fish larvae: a review of new hypotheses. Aquaculture 155:259–269.

Perrin, N. 1992. Optimal resource allocation and the marginal value of organs. American Naturalist 139:1344–1369.

Perrin, N., and R. M. Sibly. 1993. Dynamic models of energy allocation and investment. Annual Review of Ecology and Systematics 24:379–410.

Perrin, N., R. M. Sibly, and N. K. Nichols. 1993. Optimal growth strategies when mortality and production rates are size-dependent. Evolutionary Ecology 7:576–592.

Pitts, G. C. 1986. Cellular aspects of growth and catch-up growth in the rat: a reevaluation. Growth 50:419–436.

Pollack, M., and C. Leeuwenburgh. 1999. Molecular mechanisms of oxidative stress in aging: free radicals, aging, antioxidants and disease. Pages 881–923 *in* C. K. Sen, L. Packer, and O. Hanninen, eds. Handbook of oxidants and antioxidants in exercise. Elsevier, Amsterdam.

———. 2001. Apoptosis and aging: role of the mitochondria. Journal of Gerontology 56A:B475–B482.

Promislow, D. E. L. 1994. DNA repair and the evolution of longevity: a critical analysis. Journal of Theoretical Biology 170:291–300.

Reed, H. S. 1921. The rate of growth following an initial period of suppression. American Naturalist 55:539–555.

Ricklefs, R. E. 2003. Is rate of ontogenetic growth constrained by resource supply or tissue growth potential? a comment on West et al.'s model. Functional Ecology 17:384–393.

Ricklefs, R. E., and M. Wikelski. 2002. The physiology/life history nexus. Trends in Ecology & Evolution 17:462–468.

Ricklefs, R. E., R. E. Shea, and I.-H. Choi. 1994. Inverse relationship between functional maturity and exponential growth rate of avian skeletal muscle: a constraint on evolutionary response. Evolution 48:1080–1088.

Rikans, L. E., and K. R. Hornbrook. 1997. Lipid peroxidation, antioxidant protection and aging. Biochimicia et Biophysica Acta 1362:116–127.

Rollo, D. 2002. Growth negatively impacts life span of mammals. Evolution and Development 4:55-61.

Ruel, J., and T. J. Whitham. 2002. Fast-growing juvenile pinyons suffer greater herbivory when mature. Ecology 83:2691–2699.

Samaras, T. T., H. Elrick, and L. H. Storms. 2003. Is height related to longevity? Life Sciences 72:1781–1802.

Sarkar, S., and T. Fuller. 2003. Generalized norms of reaction for ecological developmental biology. Evolution and Development 5: 106–115.

Sastre, J., F. V. Pallardo, and J. Vina. 2000. Mitochondrial oxidative stress plays a key role in aging and apoptosis. IUBMB Life 49:427–435.

———. 2003. The role of mitochondrial oxidative stress in aging. Free Radical Biology and Medicine 35:1–8.

Seeberg, E. 2003*a*. Oxidative damage to proteins. Pages 27–46 *in* T. von Zglinicki, ed. Aging at the molecular level. Kluwer, Dordrecht.

———. 2003*b*. Oxidative DNA damage and repair: implications for aging. Pages 11–26 *in* T. von Zglinicki, ed. Aging at the molecular level. Kluwer, Dordrecht.

Serra, V., T. von Zglinicki, M. Lorenz, and G. Saretzki. 2003. Extracellular superoxide dismutase is a major antioxidant in human fibroblasts and slows telomere shortening. Journal of Biological Chemistry 278:6824–6830.

Shertzer, K. W., and S. P. Ellner. 2002. State-dependent energy allocation in variable environments: life history evolution of a rotifer. Ecology 83:2181–2193.

Shigenaga, M. K., T. M. Hagen, and B. N. Ames. 1994. Oxidative damage and mitochondrial decay in aging. Proceedings of the National Academy of Sciences of the USA 91:10771–10778.

Silby, R. M., and P. Calow. 1986. Physiological ecology of animals: an evolutionary approach. Blackwell Scientific, Oxford.

Sibly, R., P. Calow, and N. K. Nichols. 1985. Are patterns of growth adaptive? Journal of Theoretical Biology 112:553–574.

Sitte, N., and T. von Zglinicki. 2003. Free radical production and antioxidant defense: a primer. Pages 1–10 *in* T. von Zglinicki, ed. Aging at the molecular level. Kluwer, Dordrecht.

Smith, T. R., and L. J. Buckley. 2003. RNA-DNA ratio in scales from juvenile cod provides a nonlethal measure of feeding condition. Transactions of the American Fisheries Society 132:9–17.

Sohal, R. S., and R. Weindruck. 1996. Oxidative stress, caloric restriction, and aging. Science 273:59–63.

Sohal, R. S., R. J. Mockett, and W. C. Orr. 2000. Current issues concerning the role of oxidative stress in aging: a perspective. Results and Problems in Cell Differentiation 29:46–66.

Speakman, J. R., D. A. Talbot, C. Selman, S. Snart, J. S. McLaren, P. Redman, E. Krol, D. M. Jackson, M. S. Johnson, and M. D. Brand. 2004. Uncoupled and surviving: individual mice with high metabolism have greater mitochondrial uncoupling and live longer. Aging Cell 3:87–95.

Spiteller, G. 2001. Lipid peroxidation in aging and age-dependent diseases. Experimental Gerontology 36:1425–1457.

Stadtman, E. R. 1992. Protein oxidation and aging. Science 257:1220–1224.

Sukhotin, A. A., D. Abele, and H.-O. Pörtner. 2002. Growth, metabolism and lipid peroxidation in *Mytilus edulis*: age and size effects. Marine Ecology Progress Series 226:223–234.

Sultan, S. E. 2000. Phenotypic plasticity for plant development, function and life history. Trends in Plant Science 5:537–542.

Tenhumberg, B., A. J. Tyre, and B. D. Roitberg. 2000. Stochastic variation in food availability influences weight and age at maturity. Journal of Theoretical Biology 202:257–272.

Timiras, P. S., and T. Valcana. 1972. Body growth. Pages 273–302 *in* Developmental physiology and aging. Macmillan, New York.

Trifunovic, A., A. Wredenberg, M. Falkenberg, J. N. Spelbrink, A. T. Rovlo, C. E. Bruder, M. Bohlooly-Y, et al. 2004. Premature ageing in mice expressing defective mitochondrial DNA polymerase. Nature 429:417–423.

Unterluggauer, H., B. Hampel, W. Zwerschke, and P. Jansen-Durr. 2003. Senescence-associated cell death of human endothelial cells: the role of oxidative stress. Experimental Gerontology 38:1149–1160.

Ursin, E. 1967. A mathematical model and some aspects of fish growth, respiration and mortality. Canadian Journal of Fisheries and Aquatic Sciences 24:2355–2453.

———. 1979. Principles of growth in fishes. Symposia of the Zoological Society of London 44:63–87.

van Leeuwen, I. M. M., F. D. L. Kelpin, and S. A. L. M. Kooijman. 2003. A mathematical model that accounts for the effects of caloric restriction on body weight and longevity. Biogerontology 3:373–381.

Van Remmen, H., and A. Richardson. 2001. Oxidative damage to mitochondria and aging. Experimental Gerontology 36:957–968.

van Voorhies, W. A. 2004. Live fast—live long? a commentary on a recent paper by Speakman et al. Aging Cell 3:327–330.

von Bertalanffy, L. 1938. A quantitative theory of organic growth (inquiries on growth laws II). Human Biology 10:181–213.

von Zglinicki, T. 2002. Oxidative stress shortens telomeres. Trends in Biochemical Sciences 27:339–344.

von Zglinicki, T., V. Serra, M. Lorenz, G. Saretzki, R. Lenzen-Grossimlighaus, R. Gessner, A. Risch, and E. Steinhagen-Thiessen. 2000. Short telomeres in patients with vascular dementia: an indicator of low antioxidative capacity and a possible risk factor? Laboratory Investigation 80:1739–1747.

Waaler, H. T. 1984. Height, weight and mortality: the Norwegian experience. Acta Medica Scandinavica Supplement 679:1–56.

Wachter, K. W. 2003. Hazard curves and life span prospects. Population and Development Review 29(suppl.):270–291.

Wang, N., R. S. Hayward, and D. B. Noltie. 1998. Variation in food consumption, growth, and growth efficiency among juvenile hybrid sunfish held individually. Aquaculture 167:43–52.

Weindruch, R., and R. S. Sohal. 1997. Caloric intake and aging. New England Journal of Medicine 337:986–994.

West, G. B., J. H. Brown, and B. J. Enquist. 2001. A general model for ontogenetic growth. Nature 413:628–631.

Whitledge, G. W., R. S. Hayward, D. B. Noltie, and N. Wang. 1998. Testing bioenergetics models under feeding regimes that elicit compensatory growth. Transactions of the American Fisheries Society 127:740–746.

Wilke, C. O., and C. Adami. 2002. The biology of digital organisms. Trends in Ecology & Evolution 17:528–532.

Wilke, C. O., J. L. Wang, C. Ofria, R. E. Lenski, and C. Adami. 2001. Evolution of digital organisms at high mutation rates leads to survival of the flattest. Nature 412:331–333.

Wong, J. M. Y., and K. Collins. 2003. Telomere maintenance and disease. Lancet 362:983–988.

Xin, M., J. Zhang, E. Block, and J. Patel. 2003. Senescence-enhanced oxidative stress is associated with deficiency of mitochondrial cytochrome *c* oxidase in vascular endothelial cells. Mechanisms of Ageing and Development 124:911–919.

Yanase, S., K. Yasuda, and N. Ishii. 2002. Adaptive responses to oxidative damage in three mutants of *Caenorhabditis elegans* (*age-1*, *mev-1* and *daf-16*) that affect life span. Mechanisms of Ageing and Development 123:1579–1587.

Yearsley, J. M., I. Kyriazakis, and I. J. Gordon. 2004. Delayed costs of growth and compensatory growth rates. Functional Ecology 18: 563–570.

Zhu, X., Y. Cui, M. Ali, and R. J. Wootton. 2001. Comparison of compensatory growth responses of juvenile three-spined stickleback and minnow following similar food deprivation protocols. Journal of Fish Biology 58:1149–1165.

Zielinski, S., and H.-O. Pörtner. 2000. Oxidative stress and antioxidative defense in cephalopods: a function of metabolic rate or age? Comparative Biochemistry and Physiology B 125:147–160.

Associate Editor: David N. Reznick
Editor: Michael C. Whitlock