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How Fitness Impacts and Tradeoff Costs Shape the Optimal Life History

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Abstract

Hamilton's formalization of the theory of the evolution of the life cycle assesses the force of selection acting on a mutation by implicitly differentiating Lotka's equation, to find the impact on r of perturbing a life history trait. He considers only direct effects and ignores costs and tradeoffs. Another approach finds the optimally shaped life cycle subject to assumed bio-engineering constraints, emphasizing physiological costs and tradeoffs. Genetic theories stress either the accumulation of deleterious mutations acting at different ages, or antagonistic pleiotropy, which occurs when a gene has a beneficial effect at one age but an adverse effect at another age. In other work, I recently added production, consumption, intergenerational transfers, and density dependence to the Hamilton theory.

Here, I discuss how these theories are interrelated. Consider two life history traits that affect reproductive fitness. Hold all other traits fixed, and vary these two in such a way that reproductive fitness is unchanged. The expressions derived by Hamilton describe the rate at which the two traits substitute for one another holding fitness constant. We can also think of the biological tradeoff costs in varying the two traits, based on the reduction in one trait incurred in order to increase the other trait. For an optimal life cycle, that is one which maximizes fitness, the rate at which the two traits substitute in fitness must equal the rate at which they tradeoff biologically. Thus Hamilton coefficients signal marginal tradeoff costs for an optimal life history. I further argue that, other things equal, high tradeoff costs will be associated with low mortality, and conversely. Thus traits with high Hamilton weights will also have highly favorable levels. In this way, the Hamilton approach may be joined with the optimal life cycle theory to identify one set of forces shaping the age pattern of mortality. But this result relies strongly on the "other things equal" condition, which is later shown to be questionable.

I develop a diagrammatic analysis of the two trait case. It shows how natural selection would move a species along the trait possibility frontier to the highest possible fitness or growth rate, at a point of tangency to a fitness isoquant. Then the frontier would shift in or out from the origin until it achieved tangency with the zero growth isoquant at the optimal equilibrium. An optimal life cycle, by virtue of tangency to a fitness isoquant, has a rate of physiological tradeoff between two traits that is exactly equal to the rate of fitness tradeoff, which in turn corresponds to the ratio of the Hamilton weights (for interior solutions).

This argument shows the close relationship between the Hamilton style perturbation analysis for life cycle traits, and the Kirkwood style optimization approach. It suggests that an optimal life cycle must be consistent with the results of the perturbation analysis, but also that the results of the perturbation analysis must be consistent with the

physiological tradeoffs. Neither can be said to determine the other. They are jointly determined by their interaction with one another.

The diagrammatic analysis reveals several situations in which the Hamilton weights would not correctly signal the level of the corresponding trait in an optimal life cycle. First, physiological constraints could lead to large differences in the slopes of trait possibility frontiers, which can dominate and reverse the effects of differences in Hamilton weights. Second, trait possibility frontiers could exhibit increasing returns over some range, which might be combined with diminishing returns over another range. In this case, the Hamilton weights could also be dominated by differences in the shapes of frontiers. Third, with increasing returns and other non-convexities, corner solutions could be optimal, in which case the equality of fitness tradeoffs and physiological tradeoffs need no longer hold.

This analysis has been developed in terms of Hamiltonian fitness and physiological tradeoffs. However, it should be equally applicable to Hamiltonian fitness and the resource constraints that are featured in the intergenerational tradeoffs theory. The next step is to apply these insights in that context.

1. Introduction

Why does mortality decline from birth until young adulthood in many species, and then begin a sustained rise? Why do organisms age, as signaled by rising mortality and declining strength and health? Why have organisms not evolved to invest enough in maintenance and repair to sustain their vigor indefinitely, barring accidents and predation? What is gained through intergenerational transfers? Why is fertility zero at early ages for many organisms, and why does it decline to zero at older ages in some organisms? These are some of the questions addressed by what biologists call life history theory, but which demographers might call the evolutionary theory of the life cycle.

Substantive Theories

There is a long tradition of work on this topic. Broadly speaking, there are two substantive theories. The first I will call the "fitness impact" theory, by which I mean theories that emphasize that the strength of natural selection acting on a mutation which alters the level of either fertility or mortality at some age can be assessed by calculating the pure fitness impact on the stable population growth rate of the perturbation. The second I will call the "optimal life cycle" theory, by which I mean theories, including the Disposable Soma theory, that emphasize the engineering tradeoffs in varying any life cycle trait, and that draw insights from investigating the features of a hypothetical optimal life cycle. The basic idea is that given the tradeoff costs of somatic maintenance and repair, it may be optimal to let the body deteriorate in order to invest more in reproductive effort – hence optimal senescence. In addition, I have suggested a theory that builds on the "fitness impact" approach by adding the effects of intergenerational transfers which represent a different and important kind of tradeoff cost. For simplicity, however, here I will consider only physiological tradeoff costs. A future paper will apply these insights to intergenerational transfers.

Genetic Mechanisms

In addition to these two substantive theories, there are two main genetic mechanisms through which evolution is believed to shape the life cycle. The first of these is mutation accumulation, according to which mutations occur continually, mostly with deleterious effects which are expressed at some particular age. Natural selection acts with different strength at different ages to remove them from the population, and at each age a mutation-selection balance is struck, with many or few bad genes depending on the strength of selection at that age. The second genetic mechanism is antagonistic pleiotropy, according to which a mutation may have a good effect at one age but a bad effect at another age. Depending on the relative strengths of selection at these two ages, it will be selected into or out of the population. If selection is weaker at older ages than at younger ones for some reason, then genes with unfavorable effects later in life will accumulate in the genome, leading to aging.

In this paper I consider the interrelations and synthesis of the substantive theories and genetic mechanisms.

2. Some Problems with the Theories

Fitness impact Analysis Ignores Tradeoffs

Hamilton's analysis is carried out by implicitly differentiating Lotka's equation for a stable population to find the effect of a perturbation in fertility or mortality at some particular age on the intrinsic rate of natural increase. When the effect of the perturbation is large, in either a positive or negative direction, then the force of natural selection on the mutation causing the perturbation will be strong. However, in taking the derivative, only single direct effects are considered. So first, it is assumed that a gene directly affects only one life history trait at a time, such as mortality at age 37. A mutation which reduces mortality at one particular age is assumed to have no direct effect on mortality at some other ages or on fertility, for example. Second, it is assumed that there are no indirect effects of a change in one life history trait on the others. For example, a mutation which raises fertility at some age can do so without consequences for the survival of offspring through increased competition among them for parental attention and resources, nor does the higher fertility come at the expense of survival or fertility later in life.

Hamilton himself was troubled by these assumptions. Regarding the implications of his theory for fertility, he said: "…it is not so plausible that a gene could simply add an element of fertility at a given age without affecting the rest of the schedule as it is that a gene might cause the elimination of a single element of mortality." (1966/1996:124). But one could raise similar concerns about mortality. While some mutations might be able to remove a single cause of mortality costlessly, it is also possible that increases in longevity might come about through postponing sexual maturity and thereby giving the organism longer to develop, or by lengthening telomeres, which might then cause higher cancer mortality at younger ages. Once we admit such possibilities, then Hamilton's perturbation analysis is no longer possible, because each derivative contains terms expressing unknown potential indirect effects on other rates. The overall effect on the intrinsic rate of increase cannot be determined. (I should note, however, that Hamilton did explicitly discuss indirect effects on all vital rates arising through density, if a beneficial mutation at one age permitted the population to grow.)

These difficulties undermine the Medawar, Williams, and Hamilton theory of aging based on fitness impacts which diminish as age increases. Because of this, they may also affect the genetic mechanism of mutation accumulation, because the process is supposedly driven by the diminishing force of selection at older ages that results from these diminishing fitness impacts.

Problems With Disposable Soma/Optimal Life Cycle Theory

The first problem is that mutation accumulation at older ages may prevent the evolved life cycle from converging on an optimal one. The weakening force of natural selection at older ages suggests that mutation accumulation at older ages precludes the evolution of an optimal life history. As Hamilton put it: "…our main thesis concerns the necessary failure of ideal adaptation, and the reason why this should tend to increase with age." (1966/1996:106). This problem is not addressed by those theories which use an hypothetical optimal life history to explain patterns in actual life histories.

A second problem is that concepts like tradeoffs and costs may be inappropriate for evolutionary theory, and in any event are not so simply linked to the actual mutations and selection through which an optimal life cycle would be shaped. The word "tradeoff" suggests a purpose or goal, to achieve which would entail a cost.

"Could you increase the water pressure?"
"Yes, but the pipes may burst."

"Could you double my fertility?"
"Yes, but that will require that you absorb much of your fat, muscle, digestive and immune systems, and die soon thereafter."

But evolution has no purpose. A Mutation typically has multiple effects. It might raise fertility and raise mortality, and we can think of one of these outcomes as favorable and one unfavorable. But suppose that fertility is raised at two ages. Which of these is the attained purpose, and which should we regard as a separate effect? Suppose there are a thousand different mutations that would increase fertility at age x, and each has multiple effects. Which of these is the tradeoff cost of raising fertility at age x?

3. The Hamilton analysis of "Fitness impacts"

Hamilton's analysis goes like this. Start with the standard stable population equation:

$$(1.1) \quad 1 = \int_0^{\omega} e^{-rx} l(x) m(x)\, dx$$

Now implicitly differentiate it with respect to a perturbation in the force of mortality at age a, call it $\delta_\mu(a)$, bearing in mind the relation between the force of mortality and *l(x)*. (There are well-known difficulties in differentiating an integral with respect to the value of a function in the integrand at a single value, but there are also well-known ways to get around this difficulty, and I will simply treat it as a legitimate operation for present purposes.) Solving for the effect on r, we find:

$$(1.2) \quad \frac{dr}{d\delta_\mu(a)} = \frac{F(a)}{A_m}$$

where A_m is the average age of childbearing in the stable population, and F(a) is the integral of $e^{-rx}l(x)m(x)$ above age a, which is the share of discounted life time net reproduction remaining above age a. This is the basic Hamilton result for mortality. The idea is that when there is a large effect of a perturbation on r, the mutation causing that perturbation will be strongly selected into or out of the population. At ages before the first positive value of m(x), F is constant at unity. Once reproduction starts, F begins to drop, reaching 0 when reproduction ceases. We infer that the force of selection declines with age, leading to increasing accumulation of deleterious mutations at older ages in mutation-selection balance.

A similar implicit differentiation of (1.1) with respect to a perturbation in fertility at age a, call it $\delta_m(a)$, yields its effect on reproductive fitness, r:

$$(1.3) \qquad \frac{dr}{d\delta_m(a)} = \frac{l(a)}{A_m}$$

I will return to these results later, using them as building blocks for a more general analysis. I will refer to the factors on the right hand side of equations (1.2) and (1.3) as the "Hamilton weights" or "fitness weights" for mortality and fertility, respectively, for age *a*.

Hamilton weights can be calculated from any given age schedules of fertility and mortality. Figure 1 plots Hamilton weights based on the vital rates of the Ache, a contemporary hunter-gatherer group in the Amazon Basin in Paraguay (Hill and Hurtado, 1996). The age pattern of weights for other human populations would look quite similar.

It is, perhaps, odd to build the analysis around a perturbation of an age specific vital rate, as is done above. I have already suggested some problems with this approach, mainly that it ignores tradeoff costs. We could simply extend the differentiation to take into account all possible cross derivatives, so that the perturbation in mortality at age 27, for example, might also have an indirect effect on mortality at age 73 and fertility at age 16. But what would this mean? It is not the perturbation in a rate at some age which has indirect effects. It is really the mutation that has many effects, including on mortality at ages 27 and 73, and fertility at 16, as well as many other effects, one would expect. For this reason, I will now consider mutations.

4. Mutations affecting multiple life history traits

When we think of the evolution of the life cycle, it is natural to think of mutations that have obvious and direct effects on life history traits, such as Huntington's disease which has a largely postreproductive onset. However, any mutation that is positively or negatively selected is selected because it affects life history traits in some way, since selection ultimately acts only through variations in fertility and mortality. Focusing only on those with an obvious link to these vital rates may misdirect our attention.

The mammalian skull evolved from a non-mammalian species over the course of one hundred million years through a series of small interlinked changes that reshaped and restructured the cranium, brain, jaw, dentition, ear and nose. Many or most of these changes must have altered fertility and survival, although some may have been neutral. The same can be said of the evolution of the pelvic structure of human females, which presumably had a complicated set of effects on foraging efficiency, fertility and mortality, at all ages (Ellison, 2001). For birds, consider a mutation that causes migratory behavior, perhaps reducing juvenile mortality while raising adult mortality due to the risks and costs of migration itself.

The effect of any mutation on the values of life history traits will also depend on the context in which it is expressed, including the following: a) the value of all life history traits of the organism; b) the preexisting genetic structure of the organism; c) the abundance of the species and of other species in the area; d) the physical environment. These multiple interactions mean that evolutionary trajectories will be path dependent

and will not converge on a single equilibrium. Despite this fundamental and inevitable indeterminacy, it may be possible to say something useful about the way that any particular evolved collection of life history traits should be interrelated. The Fitness impact theory is a good example of this. It provides no unconditional guidance as to what the age patterns of fertility or mortality should be. However, it makes strong statements about how an observed age schedule of fertility should be related to an observed age schedule of mortality. The Optimal Life Cycle theory, by contrast, appears to make strong and unconditional statements about the life history configuration toward which evolutions tends. Of course, optimization takes place in the context of a set of constraints, and by varying those constraints one could produce a broad range of optimal life cycles. But those constraints are themselves to a considerable degree the product of prior evolution.

In what follows, I will take a mutation as the unit of analysis. A mutation potentially has consequences for every age specific birth or death rate, consequences that can be expressed quite generally as derivatives of each life history trait with respect to the amount of this mutation. I assume for this conceptual purpose that the mutation can vary in size and effect, rather than being a single discrete occurrence of particular size. The effect on reproductive fitness, measured by r, will be the appropriate survival-weighted and discounted integral or sum of these effects at each age—each effect on a trait is multiplied by the corresponding Hamilton weight and then the products are summed. If this effect is large in absolute value, then the mutation will be strongly selected for or against, and conversely.

5. Mutations, Tradeoffs, Traits and Selection

Notation

$\delta_\mu(a) = d\mu(a)/d\kappa_i$ is the change in the force of mortality at age a due to mutation κ_i. This is analogous to the perturbation in age specific mortality that was the central object of analysis in Hamilton's study (I here suppress the subscript i in $\delta_{i,\mu}(a)$).

$\delta_m(a) = dm(a)/d\kappa_i$ is the change in fertility at age a due to mutation κ_i

$F(a) = \int_a^\omega e^{-rx} l(x) m(x) dx$ is cumulative net discounted fertility above age a. By construction, $0 \leq F(a) \leq 1.0$.

A_m is the average age of childbearing in the stable population.

Hamilton weights (the direct effect on the intrinsic growth rate of the perturbations $\delta_\mu(a)$ or $\delta_m(a)$, as discussed earlier). These are denoted H, with a subscript to indicate the particular perturbation, as below.

$H_\mu(a) = F(a)/A_m$ is the direct demographic impact on reproductive fitness of a perturbation in the force of mortality at age a, following Hamilton's analysis.

$H_m(a) = l(a)/A_m$ is the direct demographic impact on reproductive fitness of a perturbation in fertility at age a, following Hamilton's analysis.

mutation and selection

Generalizing the Hamilton result for the direct effect on reproductive fitness r of a single age specific perturbation, we can now express the effect on r of a mutation κ_i with an arbitrary range of effects on fertility and mortality, as:

$$(1.4) \qquad \frac{dr}{d\kappa_i} = \int_0^\omega \left\{ \delta_\mu(x) H_\mu(x) + \delta_m(x) H_m(x) \right\} dx$$

The mutation will be selected into or out of the population depending on the sign and size of $dr/d\kappa_i$.

The Scope of Possible Mutations

Below, we will be considering the collection of all possible mutations. One could, at this point, restrict the range of possible mutations in various specific ways. For example, one might want to exclude large changes of various sorts. Or one might want to incorporate phylogenic constraints on what is possible. One could also impose constraints on the degree of independent variation for the different traits as affected by a mutation. Perhaps the general shape of mortality by age is viewed as fixed for all mammals, and mutations can only stretch it out or shorten it, or perhaps rotate it a bit. Perhaps eye color is correlated with some other trait, and that could be imposed.

6. Mutation and the Optimal Life Cycle

Now consider the special case of an optimal life history. Since it is optimal by assumption, $dr/d\kappa_i \leq 0$ for every mutation κ_i, because otherwise, the initial life cycle could not have been optimal. If nature is sufficiently continuous, there will be at least one mutation for which the derivative is exactly 0, and possibly more than one. Pick one of these mutations. For this mutation, (1.4) becomes:

$$(1.5) \qquad 0 = \int_0^\omega \left\{ \delta_\mu(x) H_\mu(x) + \delta_m(x) H_m(x) \right\} dx$$

The "cost" of a variation in a given trait

This expression can be manipulated to give the tradeoff cost of varying a given reference trait through variations in the dose of mutation κ_i. For example, select $\mu(0\text{-}9)$, the average death rate between birth and age 10, to be the reference trait (note how arbitrary this is). To vary $\mu(0\text{-}9)$ through mutation κ_i we must incur the cost of the variations this mutation causes in all the other vital rates. Here the cost is multidimensional, with a different dimension for every trait. More conveniently, using (1.5) we can write:

$$(1.6)\quad -\frac{d\mu(0-9)}{d\kappa_i}H_\mu(0-9)=\int_{10}^{\omega}\{\delta_\mu(x)H_\mu(x)+\}dx+\int_0^{\omega}\delta_m(x)H_m(x)dx$$

If we divide through by $-H_\mu(0\text{-}9)$, we get the tradeoff cost expressed as a fitness-weighted average of the effects of κ_i on all the other traits:

$$(1.7)\quad -\frac{d\mu(0-9)}{d\kappa_i}=\frac{1}{H_\mu(0-9)}\left[\int_{10}^{\omega}\{\delta_\mu(x)H_\mu(x)+\}dx+\int_0^{\omega}\delta_m(x)H_m(x)dx\right]$$

Alternatively, we could express this as a fitness cost per unit change in $\mu(0\text{-}9)$ by dividing through all the other trait derivatives by $d\mu(0\text{-}9)/d\kappa_i$:

$$(1.8)\quad -H_\mu(0-9)=\frac{1}{\frac{d\mu(0-9)}{d\kappa_i}}\left[\int_{10}^{\omega}\{\delta_\mu(x)H_\mu(x)+\}dx+\int_0^{\omega}\delta_m(x)H_m(x)dx\right]$$

This expression is just a mathematical restatement of an assertion made verbally earlier. On an optimal life history, the Hamilton weight for a trait must be exactly equal to the tradeoff cost of varying that trait. Otherwise that trait would not have been set at the optimal level in the optimal life cycle. Note also that this must be the tradeoff cost for this trait for *any* mutation for which $dr/d\kappa=0$, so it is not mutation dependent.

The δ's on the right may be positive, negative or zero. They describe the tradeoffs, and their whole possibly complex pattern of variation across age is summarized by weighting them by their fitness impacts, and integrating. The tradeoff cost is given by their weighted sum. This may be thought of as the engineering cost of altering the reference life history trait. Although (1.8) tells us that every mutation must yield the same fitness tradeoff cost for varying the reference trait, this cost may be composed very differently for different mutations, with differing effects on traits, so long as the weighted sum of these effects is constant.

Costly Tradeoffs and Mortality Levels

The biological tradeoff cost for varying some age-specific trait is the marginal cost of achieving a unit variation in that trait, given its current level. Consider the case of mortality, for which Hamilton effectively assumed zero marginal cost of variation, that is, no tradeoff costs. Other things equal, we might expect that the lower is the level of mortality, the greater will be the marginal tradeoff cost of reducing it further. And the greater is the marginal tradeoff cost of reducing mortality, the lower we would expect the level of mortality to be. Later I will suggest that the "other things equal" condition is often not met, however.

Consider all the potential mutations that would reduce mortality $\mu(0\text{-}9)$ (or some other trait) at some specific age a, and then rank them according to the marginal cost of achieving a unit reduction in $\mu(0\text{-}9)$. We can imagine that each of these mutations could

reduce mortality by some amount, but then the possibility would be used up, and further decline could be achieved only through some other mutation. More expensive mutations that potentially could reduce μ(0-9) would not be incorporated in the genome of the optimal life cycle unless the effects of less expensive mutations had been exhausted first ("first" here refers to logical order, not chronological time). This argument implies that the marginal cost of reducing mortality through mutations would rise as the level of mortality fell, relative to some initial baseline level, call it G(0-9).

In Figure 2, the step function in the upper quadrant represents these ranked marginal costs, with the cheapest ones to the left, and increasingly costly (per unit change) mutations to the right. The vertical dashed line shows the actual optimal life history value for μ(0-9), or rather the amount of reduction from some baseline G(0-9) needed to reach this optimal level. In the process of getting to the dashed line, the cheaper mutations have been employed first. At the optimal level, the Hamilton weight for μ(0-9) should lie between the penultimate and the ultimate marginal cost shown, on either sides of the dashed vertical line which indicates the optimum. Discreteness prevents exact equality of the Hamilton weight and the marginal cost of reducing μ(0-9).

Suppose we make the strong assumption that the marginal cost of reducing mortality further, which for an optimal life cycle would be $H_\mu(a)$, is inversely proportional to the level already achieved: $H_\mu(a)=G/\mu(a)$, where G is a constant of proportionality. It follows that the force of mortality should be proportional to $1/H_\mu(a)$, or $\mu(a) = G/H_\mu(a) = GA_m/F(a)$. This is identical to the classic Hamilton result, with the assumption that the force of mortality is inversely proportional to the force of selection at each age. Conditional on "other things equal", this gives the Hamilton result in an optimal life cycle context.

But in truth, this is a highly unsatisfying analysis, and seems to be little more than a sophistic trick of some sort, arrived at by manipulating an accounting identity. Does it really mean anything? And what can be meant by baseline mortality G? Surely it is not constant across age. The simple diagrammatic exploration of the two trait case which follows should answer some of these questions, in the more satisfying context of the dynamic evolutionary processes through which the optimal life cycle might be attained. It will show that this symmetry of fitness impacts and physiological tradeoffs does have a deeper meaning and does provide useful insights. However, it will also show the limitations of this approach, and the circumstances in which the Hamilton weights do not indicate the relative values of life history traits. Finally, I will use it to argue that the mutation accumulation balance theory cannot explain senescence when there are tradeoffs between traits.

7. Diagrammatic Analysis of the Evolution of the Optimal Life Cycle for Two Traits

Let Y be a trait or composite trait chosen to be the reference trait and let Z be the composite of all the other values of age specific fertility and mortality. These traits can be thought of as combinations of elements of the Leslie matrix. For example, Y could be the TFR, and Z could be life expectancy at birth, as in the familiar contour map for the

demographic transition, although this choice would not be informative about age patterns. Alternatively, we could think of these as two more narrowly defined elements, such as fertility age 20-29 and survival from age 35 to 50, with all other life history traits assumed to be held constant in the background, and not shown. Or we could think of Y as being, say, juvenile survival or juvenile fertility, and Z as being the composite of all remaining life history traits.

The Trait Possibility Frontier and an Optimal Life Cycle

Figure 3 plots the trait possibility frontier, expressing the possibilities of trading off Y for Z, subject to physiological, resource, and genetic constraints, and given the general context. A indicates an initial point where trait Y has value Y_0, and Z has value Z_0. Where the slope of the curve is gentle, it means that a large variation in Z is required to compensate for a small variation in Y, so the marginal tradeoff cost of improvement in Y is very high. Conversely, where the slope of the curve is steep, it means that a small reduction in Z permits a large increase in Y, so the marginal cost of increasing Y at that point is cheap.

Some rate of population growth can be associated with point A, and we can draw the contour or fitness isoquant showing all other trait combinations that have the same growth rate. Every combination of traits will lie on some growth isoquants (fitness isoquants). When the isoquant is relatively flat, it means that a small reduction in Y must be offset by a large increase in Z in order to retain 0 growth. Where it is steep, it means the opposite. Natural selection will move the organism around the trait possibility frontier toward the highest attainable fitness, that is the highest attainable r, where a fitness isoquant will be tangent to the frontier. This is shown in Figure 4, with tangency at B. At this optimal point, the slopes of the fitness isoquant and the trait possibility frontier are equal. Note that the slope of this tangent line at the optimum depends on the shapes of both tradeoff curves, even though it can be expressed as the inverse ratio of the Hamilton weights of the two traits. If the fitness isoquant were steeper at B (meaning that Z has a more powerful effect on fitness than Y), then the optimal value of Y would be lower and of Z would be higher, and conversely. If the frontier were steeper (meaning the marginal cost of raising Y is low), the optimal value of Y would be higher and of Z lower.

The Optimal Equilibrium Life Cycle

At B the population is growing, so this optimal point is not a long run equilibrium. As the population grows, and density increases, the context changes in such a way that even with the same physiological structures, the frontier of attainable Y and Z will shrink in towards the origin. Only when a new tangency at a 0 growth isoquant has been reached will the system be in an optimum equilibrium, as shown in Figure 5. Here, as at B, the age pattern of life history traits like fertility and mortality will be determined jointly by physiological tradeoffs and fitness tradeoffs, which in equilibrium are exactly equal.

It is often argued that in addition to the variations in the force of selection that Hamilton pointed to as determinative of the age shape of mortality, other factors must be at work. For example, infants and juveniles have high mortality in part because they are small in size, and also because their organ systems are not fully developed. Older organisms tend

to have higher mortality due to the cumulative effects of wear and tear. To some degree, these intrinsic effects can be countered by the action of natural selection, which may lead to arrangements such as the donation of the mother's antibodies to her lactating infant, or investment in somatic maintenance and repair such as renewal of bones or proof reading DNA. But it would be less costly to reduce mortality at young and old ages were it not for these intrinsic physiological factors tending to raise mortality. In the diagram, such factors are reflected in the trait possibility frontier, where they condition the tradeoffs. If it takes more expenditure of resources to reduce mortality at age 60 than at age 20, other things equal, then the frontier will show that a small reduction in the favorable value of one trait will permit a large favorable increase in the other.

By contrast, if trait Y were survival above age 60, the fitness contours would be nearly horizontal, because Y has almost no effect at all on r, since it is largely post-reproductive (in the Hamilton theory). But the physiological tradeoff costs of improving Y would be quite low, because Y is moderately high, so the slope of the trait frontier would be steep.

Hamilton (1966) argued that the force of selection would be strongest in favor of traits with a high fitness impact or Hamilton weight, represented in Figure 5 by the steepness of the fitness contour. If that contour is steep, it indicates that selection would be strong in favor of mutations which would raise Y. But in general, the strength of selection will depend on the tradeoff costs as well. In the optimal case shown here, there is no force of selection to move away from C.

Research on nematodes over the past twenty years has shown that certain mutations with very favorable effects on longevity can be induced under laboratory conditions. However, all of these mutations also have tradeoff costs in terms of reproduction, and none has been observed in the wild – either because they do not occur or because they have been negatively selected when they do (Tom Johnson, lecture; proper citation to be provided). Figure 6 hypothetically illustrates this situation for several of the established mutations: age1, clk2 and the famous daf2 which has also been shown to affect longevity in mice. Also shown is a hypothetical mutation that causes trait values that fall inside the frontier, and therefore are inefficient. The others are efficient, but will not be chosen under normal conditions because of their small or negative effect on fitness.

Earlier, I argued that other things equal, a trait with a bigger Hamilton weight would also have a more favorable value. This is illustrated in Figure 7, where two scenarios are presented. In one, trait A has a large Hamilton weight relative to trait Z, and consequently has a more favorable value than does trait Z, since the optimal point in this case lies above the 45 degree line (not shown). In the other scenario, the trait possibility frontier is unchanged, but now trait A has a small Hamilton weight relative to trait Z, and the optimal point now has a less favorable value for A than for Z. This diagram recapitulates the result that a trait with a greater Hamilton weight will have a more favorable value – for example, age specific mortality will be lower. However, subsequent diagrams will show various ways in which this result need not hold.

Note that the result depends in part on the assumption that the frontier keeps the same shape while the Hamilton weight differs. It also depends on what that same shape is. As drawn, the frontier is convex, so that as the ratio of the two trait values rises (e.g. A increases relative to Z), the tradeoff along the frontier gets more and more costly (as A/Z rises, it takes a bigger reduction in Z to achieve a given increase in A) because dA/dZ declines. This reflects the same assumption of increasing marginal costs that was made earlier.

When Hamilton Weights Do Not Indicate Trait Values

Figure 8 depicts the case in which tradeoff costs differ while the Hamilton weights remain the same. When the tradeoff costs for trait A are low (the steeper frontier, closer to the origin) its optimal value is high. When the tradeoff cost is high (the gentler frontier, farther from the origin) the optimal value is low. These frontiers could represent mortality at younger and older ages, when the amount of cumulated unrepaired wear and tear differs, for example.

Figure 9 shows a different situation, where the frontier and fitness isoquants are not necessarily tangent because the optimum occurs at a corner. In the case shown, marginal costs decrease rather than increase as the ratio of the trait values increases. The diagram shows the trait possibility frontier for early life juvenile fertility for a mammal versus a composite of other traits. The idea is that there is a very large gain to having zero fertility early in life, permitting a complex structural development with a high payoff. Having any fertility at all, even a very little bit, would preclude this large payoff entirely. This leads to the increasing returns to reducing early life fertility instead of the diminishing returns shown in all the other diagrams so far. With increasing returns, a point of tangency, if one exists, might be a minimum rather than an optimum. As drawn, the optimal life history (combination of traits) involves zero fertility at a point where the frontier and the isofitness curve are not tangent. Small variations in the slope of the isofitness line would not alter this optimal point.

Figure 10 shows a frontier with initially increasing returns to reducing trait A, followed by diminishing returns. Now there is an interior optimum, but it occurs at a low value of A and a high value of Z, despite the fact that the Hamilton weight for A is greater than that for Z. The important paper on negative senescence by Vaupel et al (2004) may involve trait frontiers of this sort, with increasing returns followed by decreasing returns, I believe.

Mutation-Selection Balance

I have so far described the operation of evolution as if mutations were either selected for and immediately accepted, or selected against, and immediately discarded. I have also focused on mutations that lie on the trait possibility frontier (TPF) rather than deleterious mutations lying inside it. Once we consider that mutations constantly occur, that most are deleterious, and that selection may act slowly, the picture changes. Instead of arriving at the optimal equilibrium life history, a species will be located someplace toward the origin from the optimal equilibrium C of Figure 5, carrying a load of mutations, each having deleterious effects at some ages, along with either positive, negative or null effects at

other ages. The distance moved towards the origin will depend on how strongly the force of natural selection operates on each trait, which is measured by the Hamilton weights. It also depends on the rate at which mutations affecting each trait occur, and the degree to which they are deleterious. For simplicity, I will assume that the rate of occurrence and deleteriousness are the same for all traits.

This situation is illustrated in Figure 11. The optimal equilibrium is at C. Consider mutations that only reduce Z. The strength of selection against these is proportional to the horizontal distance between fitness isoquants and $1/H_Z$ and similarly for Y. The horizontal arrow indicates the size of the reduction in Z in mutation selection balance. A similar vertical arrow indicates the smaller reduction in Y in mutation selection balance, assuming there are other mutations which only reduce Y. The heads of the two arrows will lie on some negative growth isoquant, here designated $r=x<0$. The result is that the trait mix of the species is at D rather than C. The argument that follows would also apply if the rates of mutation affecting each trait differ, but D would be in a different position.

The original TPF is physiologically possible in principle, but mutation selection balance makes it unattainable in practice. It is replaced by the attainable TPF that is formed by shifting every point on the original TPF in toward the origin in exactly the same way that C was shifted to D. In Figure 12, arrows illustrate the way a number of points on the original frontier are shifted in, and the new TPF is drawn. Note that its shape has been altered by this pattern of shifts. Although I have assumed additive shifts, I think the argument would work equally with multiplicative shifts.

Point D cannot be an equilibrium because the associated growth rate is negative. As the population size and density decline, the trait possibility frontier expands outward. The neutral assumption is that it expands proportionately. In this case, the trait mix moves along the ray from the origin to point D, preserving the trait value ratio, as shown in Figure 13. This ray intersects the zero growth isoquant E, at which point population decline stops.

However, the trait mix at E is not efficient. Natural selection will move the life history to the right along the mutation-adjusted trait possibility frontier, toward higher growth rates. This motion, together with population growth and the consequent contraction of the frontier back toward the origin until tangency is reached, will bring the life history to a sustainable sub-optimal equilibrium at F, as shown in Figure 14.

Selection partially undoes the effects of mutation accumulation on the trait value ratios. It will not restore the optimal trait mix of C, nor will it restore overall efficiency, because selection cannot remove the mutations instantaneously. If mutation accumulation did not alter the shape of the TPF, then selection would completely offset the effects of mutation accumulation on the optimal trait mix. The new equilibrium would still be suboptimal, because it occurs at a lower density, and would be displaced by a strain which could equilibrate at a higher density with the same trait mix. However, mutation accumulation does alter the shape of the TPF in a way that changes the equilibrium (but sub-optimal)

trait mix in the direction indicated by the initial mutation accumulation impact at D or E. The compromise outcome is at F, at lower density and a different trait mix than at C.

8. Conclusion

There are real tradeoff costs to altering life history traits in a direction that would enhance fitness, other things equal. Without considering such costs, it would be impossible to understand why fertility is zero for the first fifteen years of life for human females, for example. But it is not straightforward to define what is meant by tradeoff costs, and it is even more difficult to characterize their size, age pattern, and so on. In this paper I have defined them in the context of a hypothetical optimal life cycle, and a hypothetical fitness-neutral mutation. Then the tradeoff cost of varying a trait equals the fitness-weighted sum of the mutation's effects on all other traits.

Given this notion of tradeoff costs, I argued that for a life cycle to be optimal, it is a necessary condition that the biological tradeoff cost for varying a trait must exactly equal the fitness tradeoff rate, as given by the Hamilton weight for the trait (for a trait that is not at a corner). Put differently, the slope of the trait possibility frontier must equal the slope of the iso-fitness (or growth isoquant) curve for any trait values in that life cycle.

I used a diagrammatic analysis to show how natural selection would move a species along the trait possibility frontier to the highest possible fitness or growth rate, at a point of tangency to a fitness isoquant. Then the frontier would shift in or out from the origin until it achieved tangency with the zero growth isoquant at the optimal equilibrium. An optimal life cycle, by virtue of tangency to a fitness isoquant, has a rate of physiological tradeoff between two traits that is exactly equal to the rate of fitness tradeoff, which in turn corresponds to the ratio of the Hamilton weights.

This argument shows the close relationship between the Hamilton style perturbation analysis for life cycle traits, and the Kirkwood style optimization approach. It suggests that an optimal life cycle must be consistent with the results of the perturbation analysis, but also that the results of the perturbation analysis must be consistent with the physiological tradeoffs. Neither can be said to determine the other. They are jointly determined by their interaction with one another.

Fitness is the objective function which natural selection or evolution tends to maximize, analogous to utility in a maximization problem in economics. Hamilton's perturbation analysis of traits and fitness amounts to an analysis of the objective function of a maximization problem, without considering the constraints on the maximization process. This would appear to be a doomed enterprise, at least for the beneficial mutations that Hamilton primarily had in mind.

According to the mutation accumulation balance approach, the accumulation of mutations with adverse effects, particularly those expressed at older ages, would prevent an optimum from being reached. At the same time, this mechanism would provide an alternative explanation of aging. My analysis suggests that mutation driven departures

from optimality will be partially offset by natural selection through trait substitution through. Their residual effect provides an additional influence on senescence.

To recapitulate the main points:

- Fitness tradeoffs and biological tradeoffs interact to shape the evolution of life histories.
- At an optimal life history, the Hamilton weight or fitness impact of a trait exactly corresponds to the tradeoff costs of altering it.
- If tradeoffs show diminishing returns, and are similar across traits and ages, then the Hamilton weights or fitness impacts may be positively related to the levels of the traits (measured in the favorable direction), giving the Hamilton result while incorporating tradeoffs.
- But contrary to the assumptions of similarity and diminishing returns, tradeoffs can vary greatly, leading to trait levels that could be quite inconsistent with the patterns suggested by the Hamilton weights.
- The bottom line is that we must consider both the Hamilton weights/fitness impacts and the physiological and resource tradeoffs to understand the evolution of life histories, and the levels and age profiles of the life history traits.
- Mutation accumulation balance with weakening force of selection at older ages does explain additional senescence beyond the optimal amount. However, this distorting effect is partially offset by natural selection.

This analysis has been developed in terms of Hamiltonian fitness and physiological tradeoffs. However, it should be equally applicable to Hamiltonian fitness and the resource constraints that are featured in the intergenerational tradeoffs theory. The next step is to apply these insights in that context.

References (Incomplete)

Charlesworth, Brian (1994) *Evolution in Age-Structured Populations* (Cambridge University Press).

Charlesworth, Brian (2000) "Fisher, Medawar, Hamilton and the Evolution of Aging" *Genetics* 156:927-931.

Cichon, M., Kozlowski, J. (2000) *Evol. Ecol. Res.* **2**, 857-870.

Cichon, M. (1997) *Proc. R. Soc. London Ser. B*, **264**, 1383-1388.

Hamilton, W. E. (1966) "The Molding of Senescence by Natural Selection" *Journal of Theoretical Biology* 12,12-45.

Hill, K., Hurtado, M.A. (1996) *Ache Life History* (Aldine de Gruyter, New York).

Kirkwood, T. B. L. & Austad, S. N. (2000) *Nature* **408**, 233-238.

Medawar, P.B. (1952) *An Unsolved Problem in Biology* H.K. Lewis, London.

Rose, Michael R. (1991) *Evolutionary Biology of Aging* (Oxford University Press).

Vaupel, James W., Annette Baudisch, Martin D¨olling, Deborah A. Roach, Jutta Gampe (in press) "The Case for Negative Senescence", working paper.

Williams, George C. (1957) "Pleiotropy, Natural Selection, and the Evolution of Senescence" *Evolution* 11, 398-411 (December).

Zera, Anthony and Lawrence Harshman (2001) "The Physiology fo Life History Trade-Offs in Animals" *Annu. Rev. Ecol. Syst*. 32:95-126.

Figure 1. The Hamilton weights are shown by age for fertility and for mortality. These are the implicit derivatives of the intrinsic rate of natural increase with respect to each trait. The calculations are based on the demography of the Ache (Hill and Hurtado, 1996).

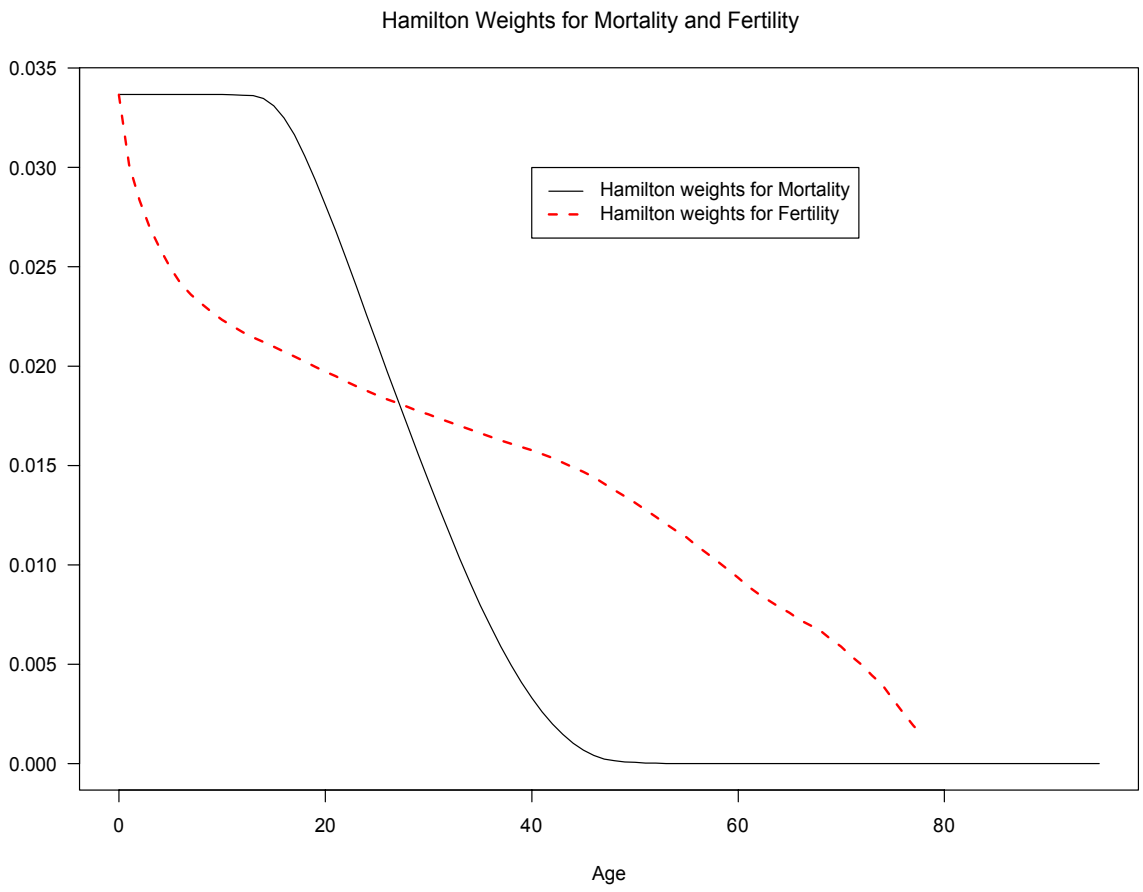
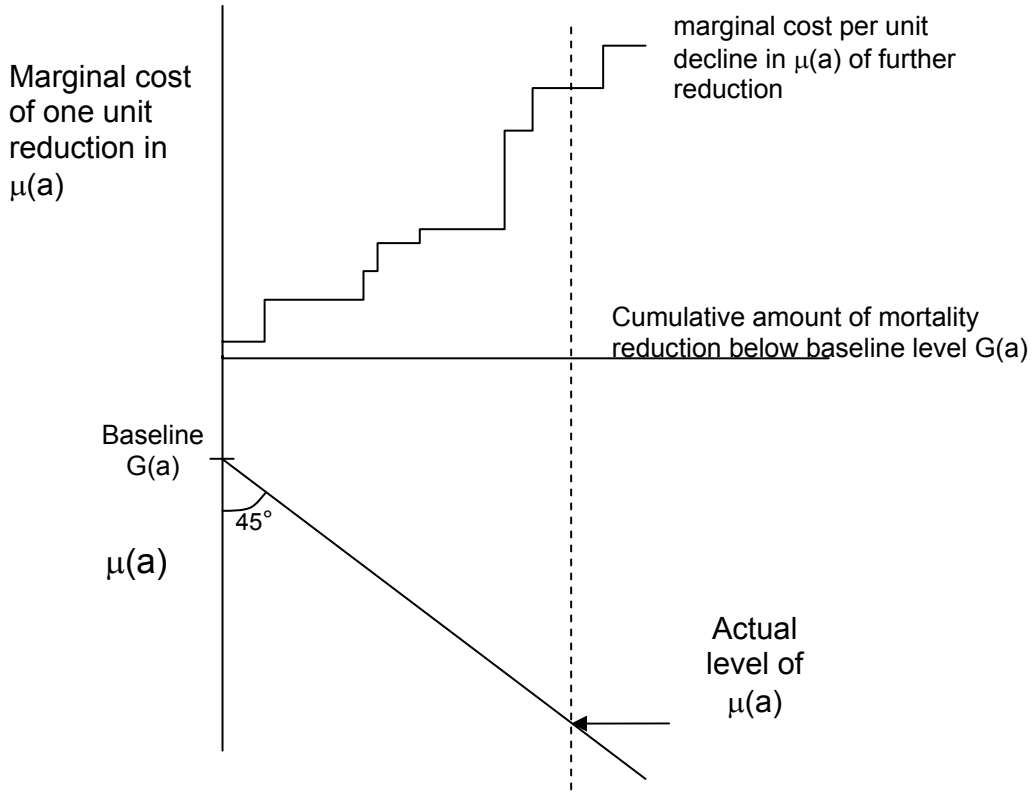
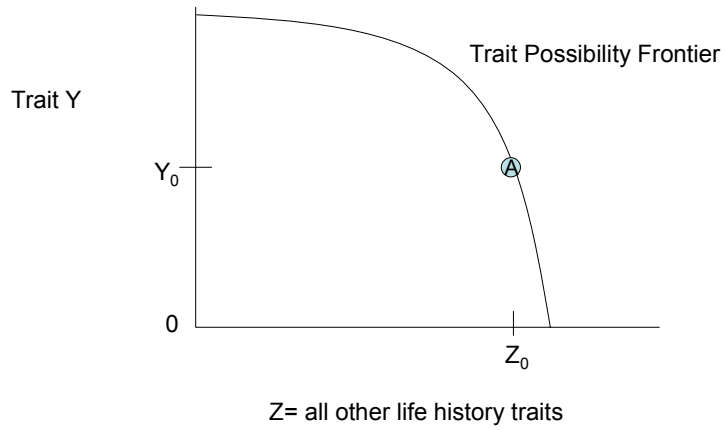


Figure 2. In an optimal life history, the marginal cost of further reducing mortality is higher when mortality is lower, because lower-cost mutations have already been exhausted.



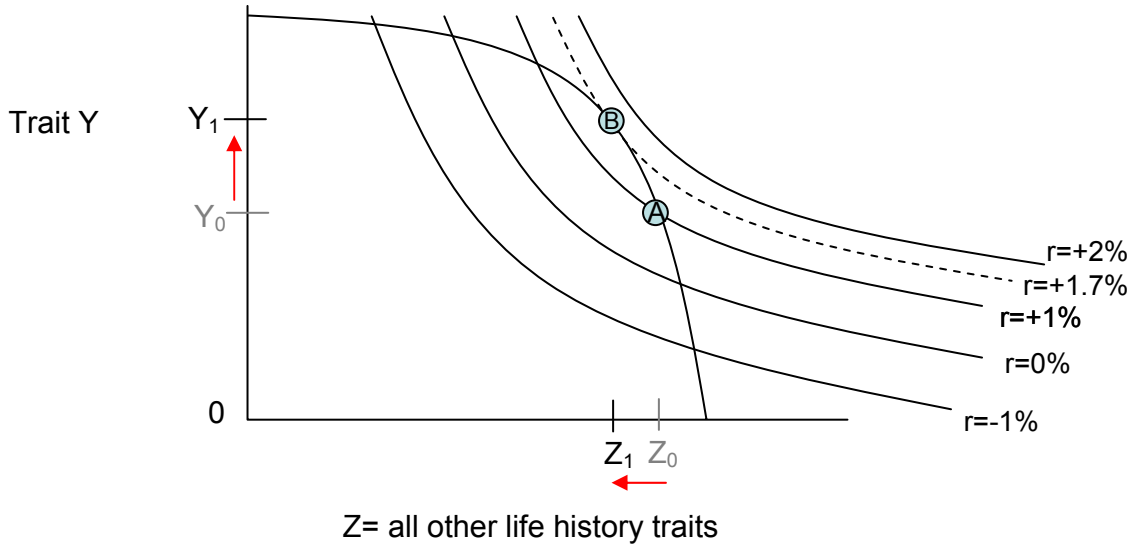
Note: The diagram shows a ranked series of mutations that reduce mortality at increasing marginal costs per unit reduction in mortality, each of which is used up after some varying amount of decline is achieved, hence the unequal horizontal lengths. The dashed vertical line locates the cumulative amount of mortality decline in the optimal life history relative to the baseline level G(a). Its intersection with the 45 degree line in the lower panel locates the optimal level of mortality at age a. The Hamilton weight for μ(a) must lie between the height of the penultimate and ultimate values of the marginal cost step function. Logical order of "using" mutations need not correspond to the actual order in which they would happen to be selected.

Figure 3. The Trait Possibility Frontier expresses the physiological, genetic, or resource tradeoff constraint between the two traits, and shows all points attainable through evolution, other things equal.



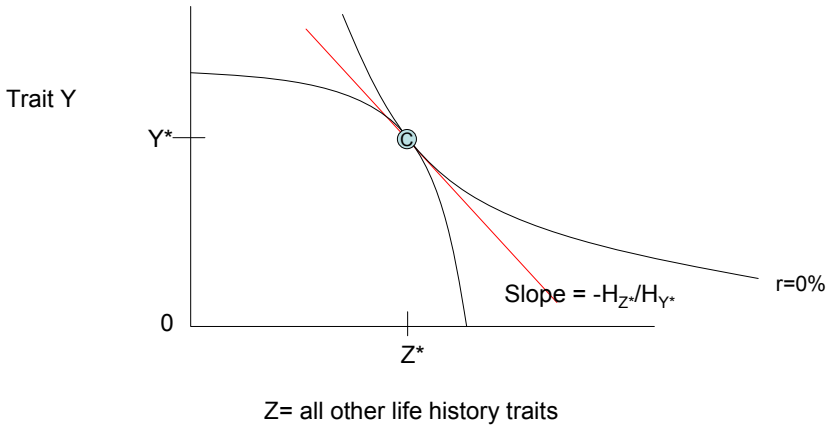
Note: Y is a given life history trait (some set of Leslie matrix elements). Z is a composite of all other life history traits. The frontier shows all combinations that are accessible through evolution given the same context that in which traits A are possible. The slope of the frontier gives the rate of tradeoff. For Y, when the slope is small the tradeoff cost is high, and conversely. The tradeoff cost increases at higher values of Y.

Figure 4. Fitness Isoquants (constant r contours) for traits Y and Z. The slope of the contour is the fitness tradeoff rate of Y and Z.



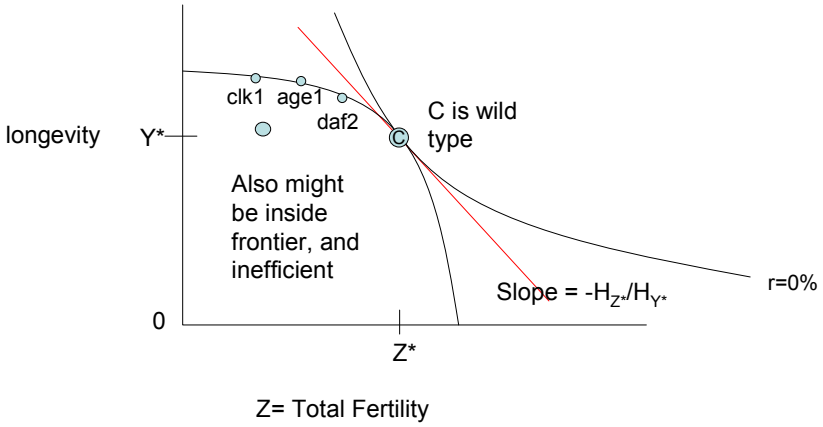
Note: A steep contour means that Z has a greater effect on r than does Y, because a small change in Z compensates a large change in Y, and conversely. A is the initial trait pair, lying on the r=1%/year contour. Natural selection will move the species along the trait possibility frontier to achieve the highest possible r, where the r=1.7% contour is tangent to the frontier, at B. Y and Z change accordingly to Y_1 and Z_1. However, population is growing so this optimum is not a long term equilibrium.

Figure 5. Increasing Density Shrinks the Trait Possibility Frontier Until It Is Tangent to the r=0 Isoquant (point C) at the Optimal Equilibrium.



Note: At C, the slope of the tangent to the two lines equals the ratio of the Hamilton weights, and the rate of physiological tradeoff between the two traits equals the rate of fitness tradeoff.

Figure 6. Several lab-induced mutations extend nematode lifespan, but at cost of reduced fertility. Even though shown on the frontier, they are not selected here because increased longevity has little effect on fitness (low Hamilton weight).



Note: The lab-induced mutations named daf2, clk1 and age1 have not been found in the wild. They can extend longevity substantially (e.g. by a factor of six or seven) but they reduce fertility.

Figure 7. If the Hamilton Weight for Trait A is Big, Trait A Will Have a More Favorable Value Than If Its Hamilton Weight Is Small, Other Things Equal (Same Trait Possibility Frontier and Same Hamilton Weight for Trait Z)

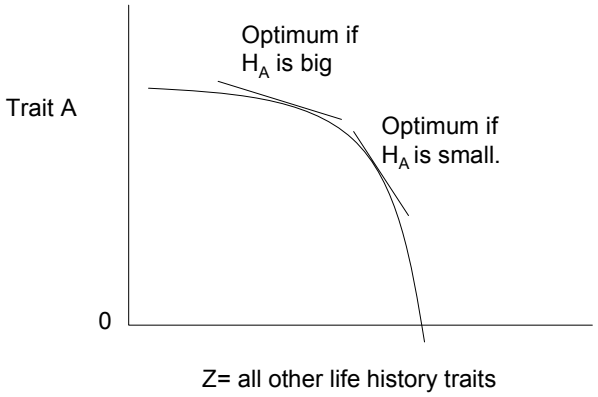
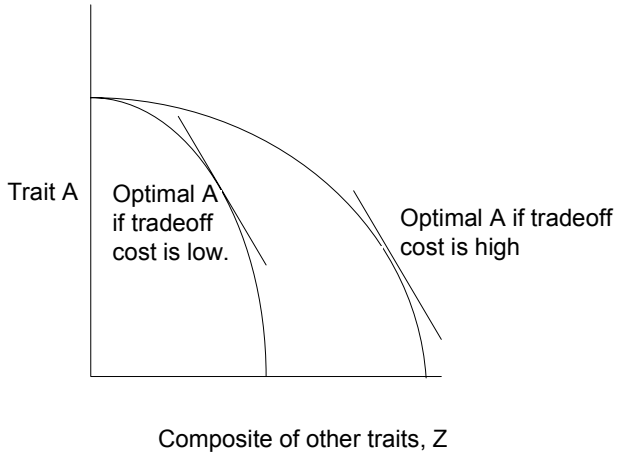
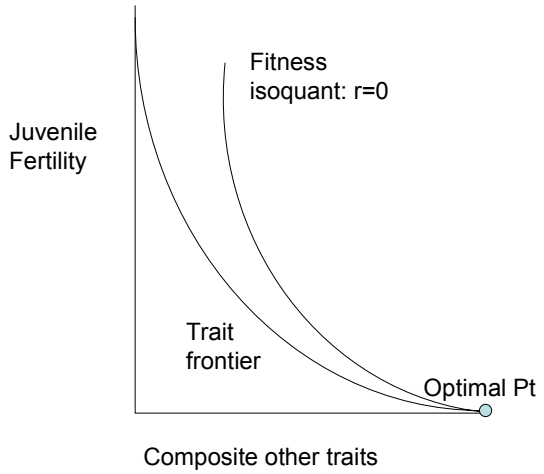


Figure 8. Trait A Could Have a Higher or Lower Favorable Value than Trait Z, Depending on the Shape of the Trait Possibility Frontier, For Given Hamilton Weights of A and Z.



Note: The trait possibility frontier that is closer to the origin indicates lower tradeoff costs for A than the other frontier, farther from the origin. With identical Hamilton weights, A will be higher given the first frontier.

Figure 9. The trait possibility frontier for mammalian juvenile fertility is concave, and optimum is at a corner where the equal slope condition is not met.



There would be huge fitness payoff to increasing fertility below age 15. However, because of high and concave tradeoff costs, the optimal life history as child fertility at 0. A corner solution: fitness slope does not equal tradeoff slope.

Figure 10. This trait tradeoff frontier has both increasing and diminishing returns, and a trait with a big Hamilton weight here has a low optimal value.

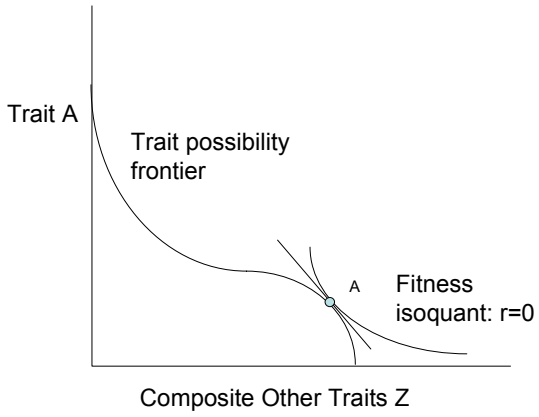


Figure 11. Mutation accumulation balance implies that a statistical trait equilibrium is reached at D, where the deficit in each trait relative to the optimal equilibrium at C is inversely proportional to the Hamilton weight for the trait, perhaps modified by differential rates of mutation. The displaced individual trait values shown by dashed arrows will lie on some negative growth rate isoquant. The solid arrow shows the displacement of the trait pair from the optimal equilibrium at C to D.

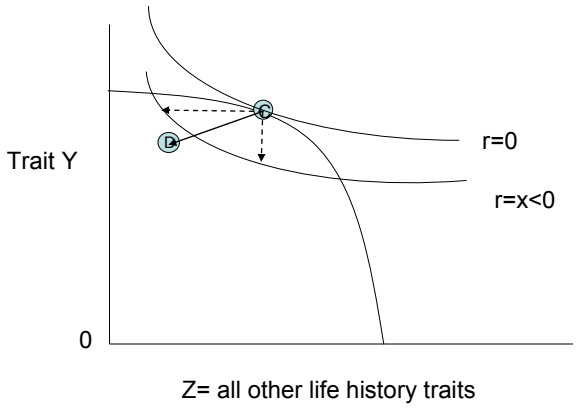


Figure 12. In mutation selection balance, the entire trait possibility frontier is shifted in towards the origin because although the initial frontier is physiologically possible, mutation accumulation makes its attainment through evolution impossible. Every point on the original frontier is now shifted in toward the origin in exactly the same way as the shift from C to D, as indicated by the dotted arrows, each identical to the arrow from C to D.

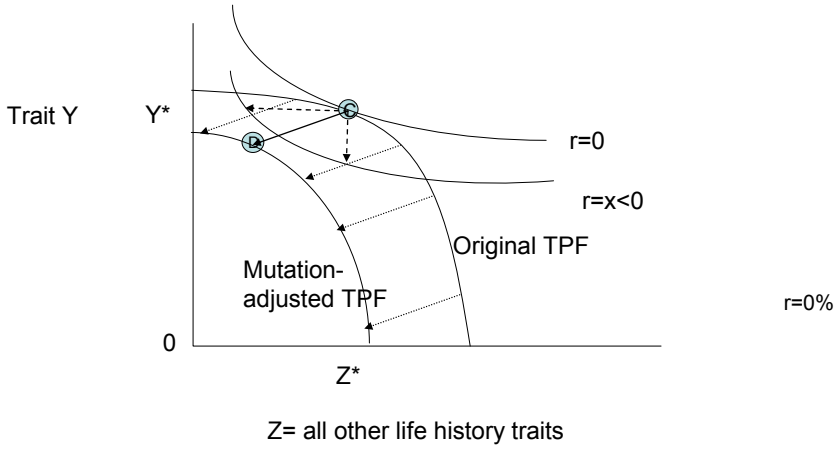


Figure 13. At D, the growth rate is negative. Population decline expands the mutation adjusted TPF proportionately outward until the trait mix at D, moving along the ray from the origin, reaches the zero growth isoquant at E.

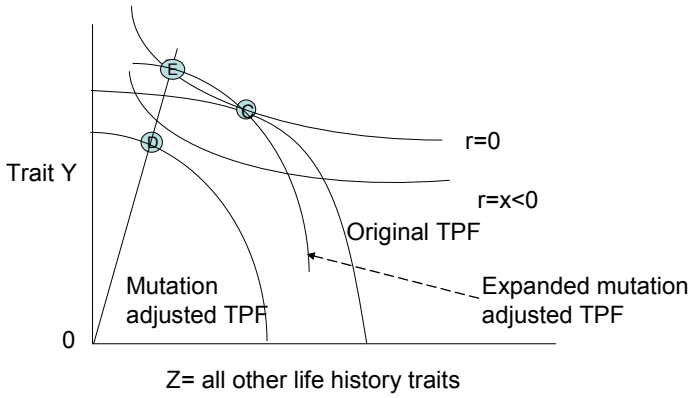


Figure 14. The trait mix at E does not maximize fitness. Natural selection moves the trait mix to the right around the TPF, achieving positive growth. Growth shrinks the TPF back toward the origin until a sustainable equilibrium is reached at F, where the mutation-adjusted TPF is tangent to the zero growth isoquant. The equilibrium trait mix at F lies between the optimal equilibrium trait mix at C, and the initial mutation-distorted trait mix at D and E.