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Life histories and the evolution of aging in bacteria and other single-celled organisms

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Abstract

The disposable soma theory of aging was developed to explore how differences in lifespans and aging rates could be linked to life history trade-offs. Although generally applied for multicellular organisms, it is also useful for exploring life history strategies of single-celled organisms such as bacteria. Motivated by recent research of aging in *E. coli*, we explore the effects of aging on the fitness of simple single-celled organisms. Starting from the Euler-Lotka equation, we propose a mathematical model to explore how a finite reproductive lifespan affects fitness and resource allocation in simple organisms. This model provides quantitative predictions that have the potential for direct comparison with experiment, providing an opportunity to test the disposable soma theory more directly.

Keywords: Bacteria; Life history; Mathematical model; Replicative senescence; Euler-Lotka equation

1. Introduction

Single-celled organisms, as well as any organisms where the soma and the germ line are not separate, were once expected to be immortal (Williams, 1957). Later it was observed that some asymmetrically dividing single-celled organisms, such as *Saccharomyces cerevisiae* (Mortimer and Johnston, 1959) and *Caulobacter crescentus* (Ackerman et al., 2003) age and die. Therefore, it was hypothesized that the distinction between organisms that age and those that do not depends upon asymmetry in reproduction (Partridge and Barton, 1993). Recent research by Stewart et al. (2005) indicates that even bacteria that appear to divide symmetrically, such as *Escherichia coli*, actually produce functionally asymmetric cells during cell division. They identified one of the cells as the aging parent cell that produces offspring that are ''rejuvenated,'' and found evidence that these older cells reproduce more slowly as they age, and may even stop reproducing.

Current theories of aging seek to combine principles of evolution with theories from physiology, microbiology, and genetics (Rauser et al., 2005). For instance, the mutation accumulation theory of aging hypothesizes that lethal genetic mutations which affect organisms late in life will not be selected against, because the force of selection decreases with age. Over time, these negative, late-acting mutations can accumulate, resulting in increased mortality as organisms age (Medawar, 1952). The antagonistic pleiotropy theory takes this a step further and hypothesizes that these late acting mutations may be selected for if they benefit an organism earlier in life (Williams, 1957; Hamilton, 1966, 1996). On the other hand, the reliability theory of aging and longevity hypothesizes that over time organisms wear out and eventually fail due to the loss of irreplaceable parts (Gavrilov and Gavrilova, 1991, 2001).

Another theory is the disposable soma theory of aging (Drenos and Kirkwood, 2005; Finch and Kirkwood, 2000; Kirkwood, 1981). This theory predicts that because organisms have a finite amount of energy to use for all life functions, there is a trade-off between repairing and maintaining the soma or reproducing. If energy is used to maintain the soma, there might not be enough energy to reproduce, and vice versa. We therefore expect that the optimal allocation strategy, which would maximize the representation of an organism's genes in future generations, will not be one that allows an organism to maintain the soma indefinitely.

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These theories make similar predictions about how aging and lifespan will evolve in response to extrinsic mortality. For instance, if an organism experiences high natural mortality, natural selection will result in greater investment in offspring than in soma. High natural mortality is also predicted to encourage earlier maturation, so an organism will be less likely to die before having an opportunity to reproduce. Organisms with low natural mortality are predicted to maintain the soma for longer, produce offspring less frequently, and experience longer lives. However, disposable soma theory also predicts how natural mortality is expected to influence life span and reproductive schedules, and gives insight into responses to aging in terms of allocation of resources for repair and maintenance.

2. Fitness models of bacteria and simple organisms

Quantitative models can be useful for exploring how evolutionary trade-offs shape aging and senescence in these simple organisms. In this paper we utilize a simple mathematical model to explore the effect of senescence, in the form of finite reproductive lifespan, on bacterial fitness and resource allocation. We first introduce a baseline model without aging to provide a point of reference with which to compare the model with aging, then present a model of life histories of simple organisms that includes aging.

2.1. The baseline model: population without aging

Various approaches are available for modeling life-history strategies (Charlesworth, 1980; Roff, 2002; Stearns, 1992). We use the Euler-Lotka equation to explore the effects of life history choices on fitness of single-celled organisms. Our selected measure of fitness is the intrinsic rate of natural increase, for populations living in a constant environment with age-dependent reproduction and mortality schedules, denoted by r. The Euler-Lotka equation in continuous time is given by:

$$1 = \int_0^\infty \mathrm{e}^{-rx} l_x b_x \mathrm{d}x. \tag{1}$$

Here the probability of surviving to age x is denoted as l_x and the rate of production of offspring by an individual of age x is b_x.

Before examining a model with aging, we review a baseline model that assumes infinite reproductive potential. Kirkwood (1981) proposed a simple model of bacterial fitness for cells that divide perfectly symmetrically, based upon (1), with appropriate choices of b_x and l_x for a clonally reproducing population. First, let l_x be an exponentially decreasing survival probability, $l_x = \mathrm{e}^{-mx}$, where m is the constant extrinsic mortality rate. The birth rate depends upon the doubling time, T. If an individual bacteria survives to time T, it divides. Since the division is perfectly symmetric, we cannot tell the difference between the two resulting cells. We therefore consider both of the cells to be identical offspring, and the original bacteria is essentially "dead" (rather like a semelparous organism). If the offspring have the same doubling time as the original cell, an appropriate "birth" rate would therefore be $b_x = 2\delta(x - T)$, where $\delta(\cdot)$ is the Dirac delta function.[1] With these expressions for l_x and b_x the Euler-Lotka Eq. (1) becomes:

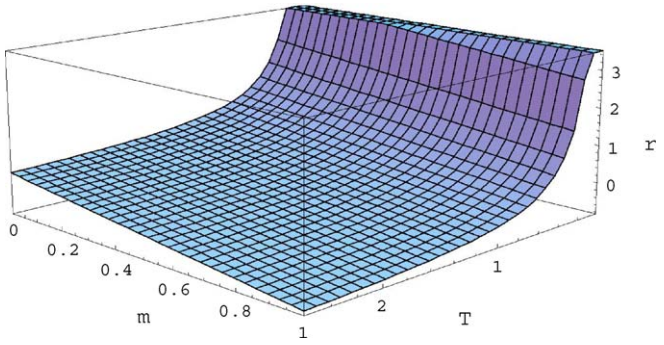

Fig. 1. The intrinsic rate of natural increase, r, as a function of the doubling time, T, and the mortality, m.

$$2\mathrm{e}^{-(m+r)T} = 1. \tag{2}$$

In Fig. 1, we show this functional relationship between fitness, r, mortality rate, m, and doubling time, T. As m and T increase, r decreases. As $T \to 0$, $r \to \infty$ regardless of the value of m. As m and T increase, r decreases.

Trade-offs between mortality and reproduction can be explored by examining how resource allocation impacts the mortality rate and doubling time of the bacteria. We denote the fraction of resources allocated for growth and reproduction by ρ, and the fraction allotted for maintenance/repair and survival by $1 - \rho$. Following Kirkwood (1981), we parameterize the mortality, m, and doubling time, T, in terms of ρ as:

$$T(\rho) = \frac{T_0}{\rho} \tag{3}$$

$$m(\rho) = \frac{m_0}{1 - \rho}. \tag{4}$$

Here, T_0 can be thought of as the minimum possible time it would take for the bacteria to reproduce if all of its resources are allocated to growth; m_0 is the minimum mortality of the bacteria if all resources are allocated to survival. Solving for r in (2) with the expressions for T and m in (3)–(4) yields:

$$r = \frac{\rho}{T_0} \ln 2 - \frac{m_0}{1 - \rho}. \tag{5}$$

[1] The Dirac delta function is defined as a unit impulse at some point x_0 such that:

$$\delta(x - x_0) = 0, \quad x \neq x_0$$
$$\int_{-\infty}^{\infty} \delta(x - x_0)\mathrm{d}x = 1,$$

and given an arbitrary function $f(x)$:

$$\int_{-\infty}^{\infty} f(x)\delta(x - x_0)\mathrm{d}x = f(x_0).$$