MUTATION-SELECTION BALANCE IN BIODEMOGRAPHY

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ABSTRACT:

What evolutionary principles underlie rises in mortality with age? Mutation accumulation mdediated by mutation-selection balance is among the oldest answers to this question. A new mathematical model for mutation-selection balance has been developed jointly with David Steinsaltz and Steve Evans. This paper applies that model to controversial cases in biodemography, including proposals for explaining Gompertz hazard functions, for dealing with the breakdown known as the "Wall of Death" and for incorporating social support and resource constaints into the evolutionary theory of senescence.

SUMMARY:

The idea that senescence in higher organisms might be partly driven by the accumlation of deleterious genetic alleles with age-specific effects concentrated at higher ages, subject to weakening pressure from natural selection, goes back to writings by Sir Peter Medawar from 1952. W. D. Hamilton (1966) gave expressions for linear approximations to the declining force of natural selection in terms of derivatives of the intrinsic rate of natural increase with respect to perturbations in age-specific elements of schedules for survival and fertility. Hamilton's expressions were later put to work in approximate expressions for equilibrium mean hazard functions and fertility schedules maintained by the competing processes of ongoing mutation and natural selection. Brian Charlesworth's book Evolution in Age Structured Populations (Second Edition, 1994) gives a wide-ranging account of these age-specific applications. In parallel, a huge literature of largely age-independent rigorous mathematical theory surrounding mutation-selection balance has been created, summed up by Buerger (2000).

In a paper recently accepted for publication in Advances in Applied Mathematics, David Steinsaltz, Steve Evans, and I have developed a mathematical model for mutation selection balance which allows a rigorous treatment of the age-specific models, including those in use by Charlesworth (2001) and other biodemographers. This model is an infinite population, infinite sites model in continuous time with haploid inheritance and no recombination. The paper also lays the groundwork for a parallel model with diploid inheritance and free recombination. Theorems in the paper give closed-form expressions for finite-time and limiting solutions, so that full probability distributions for the mix of age-specific hazard functions present at equilibrium in a heterogeneous population can be computed. Under certain linearity conditions, these distributions are Poisson distributions and the mean hazard functions can be computed from Hamilton-style derivatives. In the more general case where linearity conditions do not hold, the model produces non-Poissonian distributions and solutions for mean hazard functions inaccessible with traditional methods.

The paper by Steinsaltz, Evans, and myself for Advances in Applied Mathematics is fairly abstract. In the present paper, I shall work out actual distributions for examples of hazard function models maintained by mutation-selection balance in several settings of importance to biodemographers. First are the models put forward by Charlesworth (2001) as a possible explanation for the ubiquitous occurrence of Gompertzian hazard functions. An early analysis of these models and their implications restricted to stylized cases has been given in a previous paper (Wachter, 2003). Now that non-linear theory is available, the present paper will give a fuller discussion. It turns out that restrictive assumptions are required to maintain the Gompertzian character of the solutions.

A well-known limitation of traditional applications of the ideas of mutation accumulation is the unrealistic prediction of a "Wall of Death" as hazard rates go to infinity. Usual treatments see this model breakdown occurring at the age at which the force of natural selection goes to zero, typically at the end of reproduction. Approaches which emphasize nurturant contributions to descendant survival beyond the ages of biological reproduction are partly motivated by the need to avoid this phenomenon. The new mathematical model shows that the Wall of Death is not tied precisely to the end of reproduction but to the violation of a particular inequality. This result imposes stricter conditions on the properties of models designed to avoid the phenomenon.

One of the current frontiers of biodemography is the need to develop models which take into account social support, resource transfers, and resource constraints in the prediction of the shapes and properties of schedules of fertility and mortality. Both optimization theory and mutation accumulation theory are being explored. Ideas in this context based on mutation-selection have received wide attention, including work published by Lee (2003). The present paper analyzes the limitations placed on such models by the general theory of mutation-selection balance.

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