REJUVENATION RESEARCH
Volume 12, Number 5, 2009

DOI: 10.1089/rej.2009.0979

PERSONAL PROFILE

Interview with Leonid A. Gavrilov, Ph.D. and Natalia Gavrilova, Ph.D.

Editor's note: The interview series in *Rejuvenation Research* is a unique and, I believe, highly valuable feature of the journal, giving readers insights into the thinking and motivation of some of the most influential movers and shakers in the many disciplines—not only scientific[1–6] but also political, sociological,[7,8] ethical[9] and more—that impinge on the crusade to defeat aging. This issue's interview features two demographers who have been the most proactive in their field in terms of advocacy for the combating of aging. Given the widespread concern that success against aging would exacerbate overpopulation problems, high-quality communication between the fields of demography and biomedical gerontology is an essential component of the social and ethical context of cutting-edge science (especially biotechnology)–a debate that, as I[10–18] and others[19–24] have noted recently, is essential if we are to develop effective interventions against aging with all possible speed.

Leonid A. Gavrilov, Ph.D., and Natalia S. Gavrilova, Ph.D., are Research Associates at the Center on Aging, National Opinion Research Center, University of Chicago. Leonid Gavrilov received his Master's degree in chemistry, with a specialization in mathematical modeling and chemical kinetics, and his Ph.D. in genetics from Moscow State University, Russia. Natalia Gavrilova received her Master's degree in chemistry and her Ph.D. in anthropology and demography from Moscow State University, Russia. Later she received a second Master's degree in computer science from the University of Chicago. They are co-authors of over 100 scientific publications on aging and longevity studies, including their book, The Biology of Life Span: A Quantitative Approach, *(Harwood 1991). Drs. Gavrilov and Gavrilova are Fellows of the Gerontological Society of America (GSA), members of the Population Association of America (PAA), and serve as expert referees and editorial board members for numerous scientific journals. Dr. Gavrilova is a research grant proposal reviewer for the U.S. National Institutes of Health (NIH).*

How, in general, can demographers contribute to the effort to develop medical treatments to combat aging?

There are several ways in which human population studies could be very useful for efforts to extend healthy lifespan. First, there is the area of biodemography, a science that integrates biological knowledge with demographic approaches in an attempt to understand the dynamics of vital events in human populations, including mortality and longevity.[25–28] Looking back at the history of science, we can see that such important health findings as the discovery of the long-term harmful effects of smoking, hypertension, high cholesterol levels, and hyperglycemia all resulted from statistical/epidemiological studies on human populations. These significant findings from population studies have served as a guide and justification for subsequent development of specific medical treatments and health policies, which have already saved many human lives.

Looking forward to the future of biodemographic studies, we anticipate the "unraveling of the secrets of human longevity" with the discovery of determinants for exceptional human survival that allow some individuals to delay dramatically many diseases of aging and to live remarkably healthy long lives—sometimes beyond 100 years. When we determine why some people are so resilient to aging, these findings could lead to the identification and confirmation of therapeutic and preventive strategies and health policies to combat aging. To make this a reality we have developed a research project called the Biodemography of Exceptional Longevity, which was recently awarded a grant from the U.S. National Institute on Aging (NIA). Some preliminary findings have already published.[29–31] We continually update information about the progress of this research project on our scientific website entitled Unraveling the Secrets of Human Longevity' (http://longevity-science.org/). We also welcome comments and public discussion at our blog, Longevity Science (http://longevity-science.blogspot.com/).

Second of value is traditional demography, which provides tools for making demographic projections for different scenarios of life extension. This is important because a common objection against starting a large-scale biomedical war on aging is the fear of catastrophic population consequences—that is, overpopulation. This fear is only exacerbated by the fact that no detailed demographic projections for a radical life extension scenario have yet been published. What would happen to population numbers if aging-related deaths were significantly postponed or even eliminated? Is it possible to have a sustainable population dynamic in a future, hypothetical nonaging society? These are important questions that could be answered through traditional demographic studies.

Recently, we have completed a new study that explores different demographic scenarios and population projections, with the goal of clarifying the demographic consequences of a successful biomedical war on aging. The results of this study, which was supported by the Methuselah Foundation and the SENS Foundation, were presented at the SENS4 conference in Cambridge, United Kingdom, this past September, and will be published shortly.[32] In brief, we found that defeating aging, the joy of parenting, and sustainable population size are not mutually exclusive. This is an important point, because it can change the current public perception that life extension necessarily leads to overpopulation. Amazingly, on our return trip to the United States from SENS4, the passport control officer asked us exactly this same question about overpopulation during the interview about the purpose of our international travel! This example indicates how deeply the fear of overpopulation penetrates the fabric of modern society, and hence the importance of demographic studies on this topic.

Predictions of future trends in longevity have always been notoriously incorrect. Is this because reliable indicators of future trends do not exist or because those indicators are not recognized as useful by those making the predictions?

It is true that predicting longevity trends remains a challenging task. Moreover, our own analyses of Russian mortality data convinced us that a significant long-term drop in life expectancy can occur even in developed countries without any major wars.[33–35] Thus, there is a significant uncertainty not only concerning the pace of further longevity increase, but even the direction of future changes in life expectancy. This does not mean, in our opinion, that longevity predictions could not be improved further by finding more reliable indicators of future trends. Perhaps the emphasis should shift from traditional extrapolations of current mortality trends to deeper analyses of expert judgments on future mortality risks as well as emerging opportunities in the biomedical sciences.

You have spearheaded the application of reliability theory to the modeling of aging and mortality. Reliability theory is designed to describe the behavior of man-made machines, which differ from living organisms in that they do not incorporate significant in-built self-repair machinery. To what extent do you feel that this difference diminishes the applicability of reliability theory to living organisms?

Thank you for your kind use of the term "spearheading." Yes, we first started to apply reliability theory to the problem of biological aging more than 30 years ago, as early as 1978,[36,37] and since that time the reliability theory of aging and longevity has become well known in the scientific literature.[38–44] In answer to your question on the applicability of reliability theory to living organisms, it is useful to consider separately two different topics: (1) the applicability of reliability theory as a general concept; and (2) the applicability of our particular mathematical models that are based on reliability theory.

In discussing the first topic, it is important to note that reliability theory is a general theory about systems failure. It allows researchers to predict the age-related failure kinetics for a system of given architecture (reliability structure) and given reliability of its components. Although historically it was initially applied to describe the behavior of man-made machines, nothing in this general mathematical theory prevents us from taking into account the built-in self-repair machinery. Therefore, there is nothing fundamentally wrong with applying reliability theory to living organisms, or, more generally, applying mathematics to living organisms.

With regard to the second topic, it was our initial intent to find the simplest explanation for the major facts about aging and mortality, including the very origin of aging, the Gompertz law of mortality, the compensation law of mortality, and late-life mortality deceleration. We were interested in understanding the first principles and fundamental explanations of aging before trying to create a comprehensive model that would take into account all the complexities of living organisms. Therefore, in our models we have focused on the accumulation of unrepaired damage as the final outcome of the damage versus repair process, which leads to an age-related decrease in systems redundancy (e.g., a decrease in numbers of functional cells). When these intentionally simplified models, based on a minimum number of assumptions, gave us some general understanding of the nature of the aging process and mortality laws, it opened the way to build upon this knowledge to create a more detailed and complex model of aging. This challenge is open to anyone with the time to pursue it.

Another interesting feature of biological systems is that they are formed in evolution during a severe struggle for survival—a biological arms race with numerous infectious agents and predators. As a result, these systems have many potentially harmful defense mechanisms that may be useful for short-term survival in hostile, wild environments, but are not conducive for longevity in a protected environment. An example of this would be the inflammatory response. So the analogy between living organisms and man-made machines is most appropriate for man-made military machines that are overloaded by weaponry and ammunition at the expense of their durability. Such machines could last much longer in a protected environment if the many dangerous fighting devices designed for combat were removed. The same is true for living organisms; loss of some functions through introduced mutations or other interventions often leads to increased species longevity in a protected environment. This observation is sometimes interpreted as proof that aging is a programmed process, while in fact it simply means that organisms were selected by Nature for survival in a wild hostile environment, rather than for longevity in protected laboratory conditions.

Recently you developed novel software to describe the demographic consequences of therapies that genuinely reverse, rather than merely retard the advance of biological age (i.e., the life-long accumulation of the "damage" that causes age-related ill-health when it becomes sufficiently abundant). Were you surprised at the predictions that this scenario yielded?

Yes, we were surprised by some of our own findings. For example, consider the "worst-case" scenario (for overpopulation), that being physical immortality, or no deaths at all. What would happen to population numbers in that case? Common sense and intuition would predict a demographic catastrophe if immortal people were to continue to reproduce; that is what we initially believed too. However, a deeper mathematical analysis leads to paradoxical results. If parents produce less than two children on average, so that each next generation is smaller by some common ratio ($R < 1$), then even if everybody were immortal, the size of the population over time would not be infinite; instead it would be just $1/(1-R)$ times larger than the initial population. For example, one-child reproduction practices ($R = 0.5$) would only lead to a doubling of the total immortal population, because $1/(1–0.5) = 2$. In other words, a population of immortal reproducing organisms can grow indefinitely in time, but not necessarily indefinitely in size, because asymptotic growth is possible.[32] The beauty of this finding is that it does not require any complex calculations and questionable assumptions, but rather follows directly from the calculus and the fact that infinite geometric series converge when the absolute value of the common ratio (R) is less than one. The startling conclusion is that fears of overpopulation based on lay common sense and uneducated intuition are, in fact, grossly exaggerated. It came as a great surprise to us that just a bit of clear thinking and simple mathematics can make such a difference in resolving a problem.

Demographic predictions are of immense importance in determining economic and social policy, in view of the impact of factors such as dependency ratio on the relative economic viability of different policies. Thus, it seems essential that policy-makers and other opinion-formers take demographers' work seriously. What can be done to encourage influential people to understand the importance of such predictions and to act on them?

To increase the impact of demographic predictions on economic and social policy, it is important to have a very active and persistent strategic outreach program. In other words, we need to stimulate demographers to publish more reader-friendly articles in high-profile publications, to organize more joint conferences of demographers with policy-makers and other opinion-formers, and to arrange more public meetings and discussions between demographers and influential people. Such a strategic outreach program could become successful with the support of foundations led by wealthy visionaries such as Peter Thiel, Bill Gates, or Larry Ellison, for example.

It might also be helpful to strengthen the demographic component in current antiaging research programs, such as the Science Against Aging program, which was recently developed by Science for Life Extension, an international foundation.[45]

What factors in the industrialized world do you think most strongly influence the following: (1) The number of children women have; and (2) the average age at which women have their first child? How do you think these factors would be altered by the advent of therapies that combat aging, including menopause?

We believe that the key variable most strongly influencing fertility in the industrialized world is the "opportunity cost" of having a child. This is the cost of childbearing in terms of time and resources, and, most importantly, the intensity of competition between this choice and other opportunities in life. For example, a demanding job could prevent some career-oriented women from having a child before they have established themselves. The risk of losing a partner could be another opportunity cost, particularly for unmarried couples, cohabitating without a strong commitment. The desire to have a flexible lifestyle (primarily at younger ages), or concerns about the health consequences of childbearing (particularly at older ages) represent other examples of the perceived opportunity costs of having a child.

With the advent of therapies that combat aging, including menopause, the pressure on women to have a child "before it is too late" may decrease. However, we have to make sure that with these new therapies the children born to older parents will be as healthy as those born to younger parents. Our own studies, as well as the abundant biomedical literature, indicate that currently both advanced paternal and maternal age at the time of conceiving a child can have significant negative effects on a child's health and longevity. Therefore, at this time, it is better to avoid delayed parenting.[31,46–48]

References

1. Harrison DE. An interview with David E. Harrison, Ph.D. Interview by Vicki Glaser. Rejuvenation Res 2007;10:417–423.
2. Kedes L. Genomics prize—the X PRIZE Foundation. Interview by Vicki Glaser. Rejuvenation Res 2007;10:237–242.
3. Sinclair DA. Interview with David A. Sinclair, Ph.D. Interview by Vicki Glaser. Rejuvenation Res 2008;11:265–268.
4. Jaenisch R. Interview with Rudolf Jaenisch, M.D. Interview by Vicki Glaser. Rejuvenation Res 2008;11:849–850.
5. Blackburn E. Interview with Elizabeth Blackburn, Ph.D. Interview by Vicki Glaser. Rejuvenation Res 2008;11:701–705.
6. Warwick K. Interview with Kevin Warwick, D.Sc. Interview by Vicki Glaser. Rejuvenation Res 2008;11:1079–1082.
7. Butler RN. Interview with Robert Butler, M.D. Interview by Vicki Glaser. Rejuvenation Res 2008;11:977–980.

8. Glenn PF, Collins MR. The Glenn Foundation for Medical Research, Santa Barbara, CA: Interview with Paul F. Glenn and Mark R. Collins. Rejuvenation Res 2007;10:651–656.
9. Harris J. Interview with John Harris. Interview by Vicki Glaser. Rejuvenation Res 2007;10:107–111.
10. de Grey ADNJ. Aging and airborne HIV: A reassuring analogy. Rejuvenation Res 2007;10:1–3.
11. de Grey ADNJ. The case for prioritizing research on late-onset life-extension interventions in mammals. Rejuvenation Res 2007;10:257–259.
12. de Grey ADNJ. The need to debalkanize gerontology: A case study. Rejuvenation Res 2007;10:431–434.
13. de Grey ADNJ. Cautionary tales of the unexpected. Rejuvenation Res 2008;11:989–990.
14. de Grey ADNJ. Combating the Tithonus error: What works? Rejuvenation Res 2008;11:713–715.
15. de Grey ADNJ. Curiosity is addictive, and this is not an entirely good thing. Rejuvenation Res 2008;11:1–3.
16. de Grey ADNJ. Long live the unreasonable man. Rejuvenation Res 2008;11:541–542.
17. de Grey ADNJ. Man, machines, manufacturing, and maintenance: Merits of a much-maligned metaphor. Rejuvenation Res 2008;11:277–279.
18. de Grey ADNJ. Trans-simianism and truthiness: Hints of progress in the debate on whether aging is good. Rejuvenation Res 2008;11:857–859.
19. Farrelly C. Sufficiency, justice, and the pursuit of health extension. Rejuvenation Res 2007;10:513–520.
20. Stock G, Callahan D. Debate: the effects of life extension. Rejuvenation Res 2007;10:407–416.
21. Wilkes R. SENS: An engineer's point of view on feasibility and bioethics dialogue. Rejuvenation Res 2007;10:235–236.
22. Warner HR. Making the political case for biogerontology funding: A view from the trenches. Rejuvenation Res 2008; 11:485–488.
23. Ehni HJ, Marckmann G. The normative dimensions of extending the human lifespan by age-related biomedical innovations. Rejuvenation Res 2008;11:965–969.
24. Hynek P. The hyper-commons: How open science prizes can expand and level the medical research playing field. Rejuvenation Res 2008;11:1065–1072.
25. Curtsinger JW, Gavrilova NS, Gavrilov LA. Biodemography of Aging and Age-Specific Mortality in *Drosophila melanogaster*. In: Masoro EJ, Austad SN (eds), Handbook of the Biology of Aging, 6th edition. Academic Press, 2006, pp 261–288.
26. Gavrilov LA, Gavrilova NS, Olshansky SJ, Carnes BA. Genealogical data and biodemography of human longevity. Social Biol 2002;49:160–173.
27. Gavrilov LA, Gavrilova NS Biodemographic study of familial determinants of human longevity. Population: An English Selection 2001;13:197–222.
28. Gavrilova NS, Gavrilov LA. Data resources for biodemographic studies on familial clustering of human longevity. Demog Res 1999;1:1–48.
29. Gavrilova NS, Gavrilov LA. Can exceptional longevity be predicted? Contingencies (Journal of the American Academy of Actuaries) 2008; July/August:82–88.
30. Gavrilova NS, Gavrilov LA Physical and socioeconomic characteristics at young age as predictors of survival to 100: a study of a new historical data resource (U.S. WWI draft cards). In: Living to 100 and Beyond: Survival at Advanced Ages [online monograph]. The Society of Actuaries, 2008.
31. Gavrilova NS, Gavrilov LA. Search for predictors of exceptional human longevity: using computerized genealogies and Internet resources for human longevity studies. N Am Actuarial J 2007;11:49–67.
32. Gavrilov LA, Gavrilova NS. Demographic consequences of defeating aging. Rejuvenation Res 2009;12:S29–S30.
33. Gavrilova NS, Semyonova VG, Dubrovina E, Evdokushkina GN, Ivanova AE, Gavrilov LA. Russian mortality crisis and the quality of vital statistics. Populat Res Policy Rev 2008;27: 551–574.
34. Gavrilova NS, Gavrilov LA, Semyonova VG, Evdokushkina GN, Ivanova AE. Patterns of violent crime in Russia. In: Pridemore WA (ed), Ruling Russia: Law, Crime, and Justice in a Changing Society. Rowman & Littlefield Publ., Inc., 2005, pp 117–145.
35. Gavrilova NS, Semyonova VG, Evdokushkina GN, Gavrilov LA. The response of violent mortality to economic crisis in Russia. Populat Res Policy Rev 2000;19:397–419.
36. Gavrilov LA. A mathematical model of the aging of animals. Proc Acad Sci USSR [Doklady Akademii Nauk SSSR] 1978; 238:490–492.
37. Gavrilov LA, Gavrilova NS, Yaguzhinsky LS. The main regularities of animal aging and death viewed in terms of reliability theory. J Gen Biol [Zhurnal Obschey Biologii] 1978;39:734–742.
38. Gavrilov LA, Gavrilova NS. Reliability theory of aging and longevity. In: Masoro EJ and Austad SN (eds), Handbook of the Biology of Aging, 6th edition. Academic Press, New York, 2006, pp 3–42.
39. Gavrilov LA, Gavrilova NS. Models of systems failure in aging. In: Conn PM (ed), Handbook of Models for Human Aging. Academic Press, New York, 2006, pp 45–68.
40. Gavrilov LA, Gavrilova NS. Why we fall apart. engineering's reliability theory explains human aging. IEEE Spectrum 2004;41:30–35.
41. Gavrilov LA, Gavrilova NS. The reliability-engineering approach to the problem of biological aging. Ann NY Acad Sci 2004;1019:509–512.
42. Gavrilov LA, Gavrilova NS. The quest for a general theory of aging and longevity. Science's SAGE KE 2003;2003:1–10.
43. Gavrilov LA, Gavrilova NS. The reliability theory of aging and longevity. J Theor Biol 2001;213:527–545.
44. Gavrilov LA, Gavrilova NS. The Biology of Life Span: A Quantitative Approach. Harwood Academic Publisher, 1991.
45. Science Against Aging. International Foundation of Science for Life Extension 2009. Published online at www.scienceagainstaging.org/Books/Program_ENG_06_2009_razv.pdf/.
46. Gavrilov LA, Gavrilova NS. Early-life programming of aging and longevity: the idea of high initial damage load (the HIDL hypothesis). Ann NY Acad Sci 2004;1019: 496–501.
47. Gavrilov LA, Gavrilova NS. Early-life factors modulating lifespan. In: Rattan SIS (ed), Modulating Aging and Longevity. Kluwer Academic Publishers, Dordrecht, 2003, pp 27–50.
48. Gavrilov LA, Gavrilova NS. Human longevity and parental age at conception. In: Robine J-M, et al. (eds), Sex and Longevity: Sexuality, Gender, Reproduction, Parenthood. Springer-Verlag, Munich, 2000, pp 7–31.

—Interview by Vicki Glaser