Chapter XVIII
Mathematical Modeling of the Aging Process

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ABSTRACT

Aging is a complex biological phenomenon that practically affects all multicellular eukaryotes. It is manifested by an ever increasing mortality risk, which finally leads to the death of the organism. Modern hygiene and medicine has led to an amazing increase in average life expectancy over the last 150 years, but the underlying biochemical mechanisms of the aging process are still poorly understood. However, a better understanding of these mechanisms is increasingly important since the growing fraction of elderly people in the human population confronts our society with completely new and challenging problems. The aim of this chapter is to provide an overview of the aging process, discuss how it relates to system biological concepts, and explain how mathematical modeling can improve our understanding of biochemical processes involved in the aging process. We concentrate on the modeling of stochastic effects that become important when the number of involved entities (i.e., molecules, organelles, cells) is very small and the reaction rates are low. This is the case for the accumulation of defective mitochondria, which we describe mathematically in detail. In recent years several tools became available for stochastic modeling and we also provide a brief description of the most important of those tools. Of course, mitochondria are not the only target of modeling efforts in aging research. Therefore, the chapter concludes with a brief survey of other interesting computational models in this field of research.

WHAT IS AGING?

Looking at the enormous rise of average human lifespan over the last 150 years, one could get the impression that modern research actually has identified the relevant biochemical pathways involved in aging and has successfully reduced the pace of aging. Oeppen and Vaupel (2002) collected data on world wide life expectancy from studies going back to 1840. Figure 1 shows the life expectancy for males (squares) and females (circles) for the countries that had the highest life expectancy for the given year. Two points are remarkable. Firstly, there is an amazingly linear trend in life expectancy that corresponds to an increase of 3 months per year (!) and secondly there is no leveling off observable.

These impressive data suggest strongly that lifespan will also continue to rise in the next years, but it does not show that the actual aging rate has fallen during the last century. Aging can best be described as a gradual functional decline, leading to a constantly increasing risk to die within the next time interval (mortality). The Gompertz-Makeham equation (Gompertz, 1825; Makeham, 1867), $m(t) = I \cdot e^{Gt} + E$, describes how the exponential increase of mortality depends on intrinsic vulnerability (I), actuarial aging rate (G) and environmental risk (E). All living organisms have a base mortality caused by environmental risks, but it is the aging rate, G, which causes human mortality to double approx. every 8 years. From this equation we can derive the following expression for the survivorship function: $N(t) = e^{\frac{1}{G}\left(1-e^{Gt}\right)-Et}$.

Figure 1. Male (blue squares) and female (red circles) life expectancy in the world record holding country between 1840 and 2000 based on the annual data of countries world wide (reproduced with permission from Oeppen & Vaupel, 2002).