**Effect of Network Configuration on the Aging Process in the Reliability Model of Cellular Aging**

Palpasa Manandhar 1, Hong Qin 2,

1 Department of Mathematics, 2 Department of Biology, Spelman College

**Abstract**

Aging can be quantitatively defined as the increasing risk of dying over time. A key distinction between biological aging and non-biological aging is the dynamics of the aging process. Increasing rate of mortality over time follows exponential function in biological aging versus Weibull functions in non-biological aging. Cellular aging can be studied through the reliability framework based on gene networks. Here, we study the influence of network configurations on the dynamics of aging process. We compare three types of networks – networks with degree distributions of constants (lattice network), Poisson distribution and power-law distribution. We then evaluate the heterogeneity of the aging process using the coefficient of variation (CV). Preliminary results show that CV of the aging process in lattice networks with constant connecting degrees is lower than networks with Poisson distributed degrees, suggesting that Poisson networks are more robust for aging than lattice networks. This somewhat counter-intuitive finding suggests an important role of randomness in the emergence of aging from gene networks.

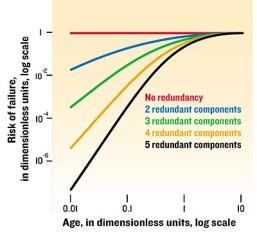
**-------old writing from previous years ----------**

**Introduction**

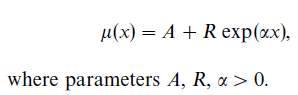
Aging is defined as the increasing chance of failure with time. In the reliability model of cellular aging, components are considered functionally redundant, if one fails, the entire system does not die, because the components are connected in parallel. The system will only die when all of the components fail.

**Figure 1. Redundancy of a system’s components leads to aging.**

Machines with more redundancy in their systems begin life with a lower risk of failure than those with less redundancy.



Redundancy decreases initial risk of failure/death and increases lifespan. In the human body, the cells that make up organs represent the components, and the organs represent the system. The individual components can either have the same failure rate (homogeneous) or different failure rates (heterogeneous). We are also studying the impact of varying functional modules and heterogeneous components on the emergence of biological aging characteristics, using R. R is software for statistical computing and graphics. Using R, we attempted to give rise to the Gompertz model.



**Gompertz Law of Mortality**

**Time**

**Log of Failure Rate**

**Figure 2. (a) Gompertz model equation and parameters (b) Exponential increase of failure with age according to Gompertz model**

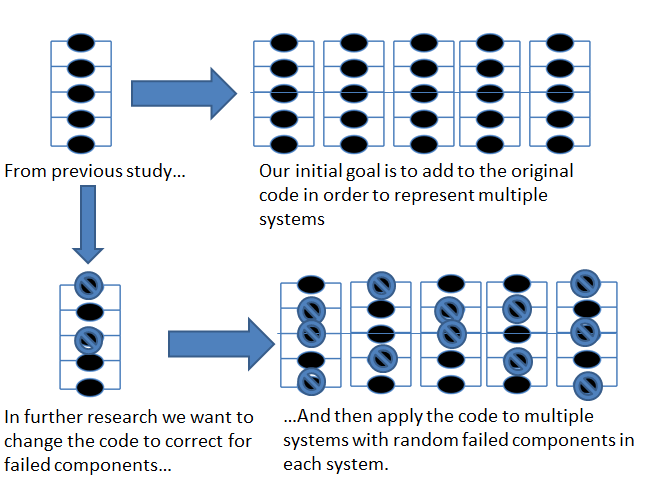
**Methods and Model**

R statistical programming language and environment was used to build a reliability mode. This model simulates the application of non-constant failure rates to the random, redundant components of a system.

Possion was used to simulate the initial defects in a system (the number of failed components). When a system already has several defects, and the probability that a component is functional is near zero, the simulation can give rise to the Gompertz model. Poisson model is a discreet probability model used to count variables with the assumption that the conditional means equal the conditional variances.

The codes used exhibited the method by which the lifespan of 15 systems with an original 50 components (can be altered in the code) was simulated with exponential failure rates applied. Further, the life span of the entire system was simulated for the total number of systems.

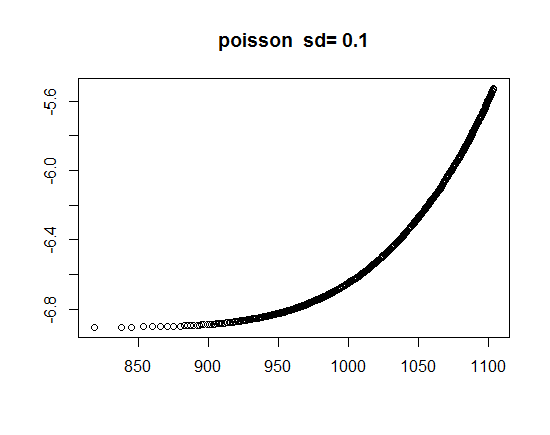
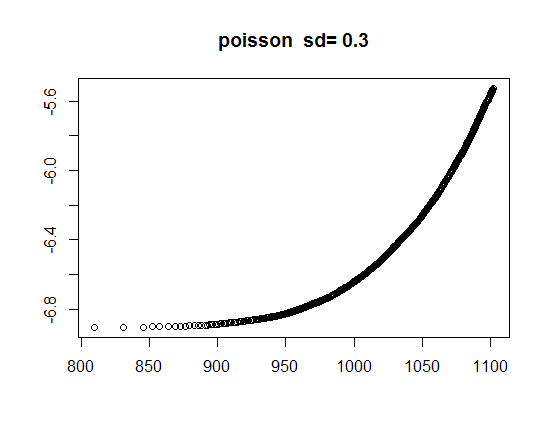
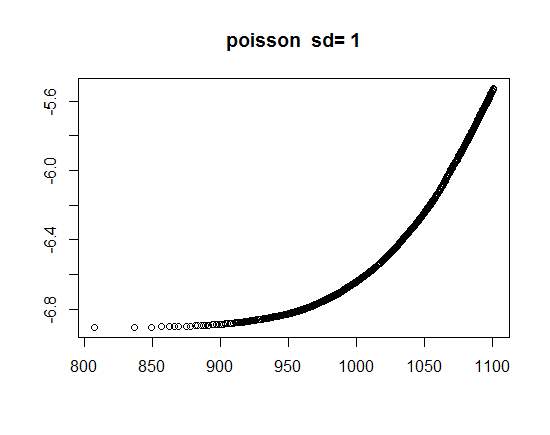
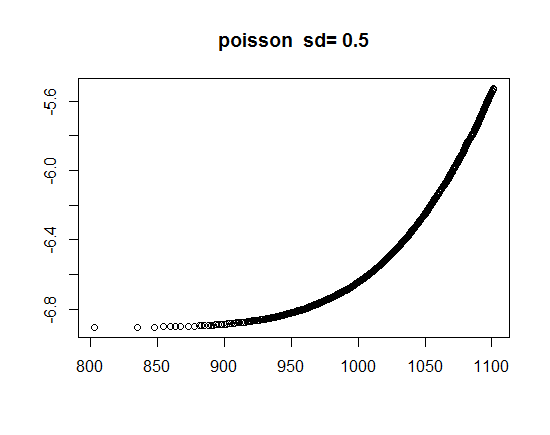
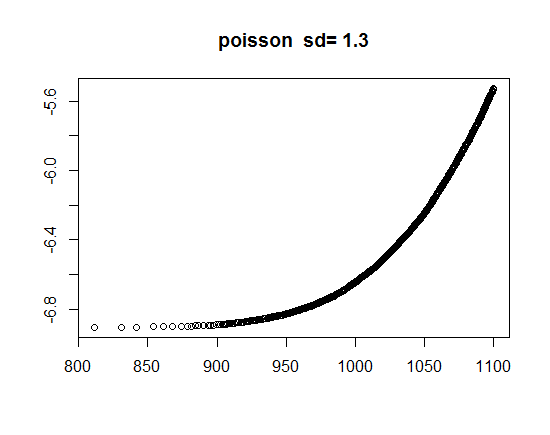
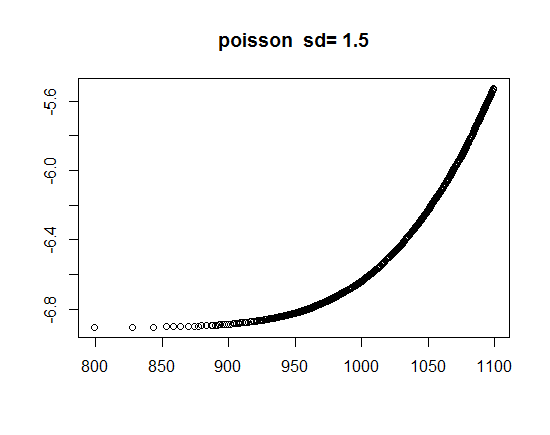
Poisson model – discreet probability model used to count variables with the assumption that the conditional means equal the conditional variances.

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**Figure 3. Diagram of past, present, and future simulations**

**Results**

**Graphs 1-5. Increasing rate of failure with respect to age (time)**

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Time

Failure Rate

Failure Rate

Failure Rate

Failure Rate

Failure Rate

Failure Rate

Time

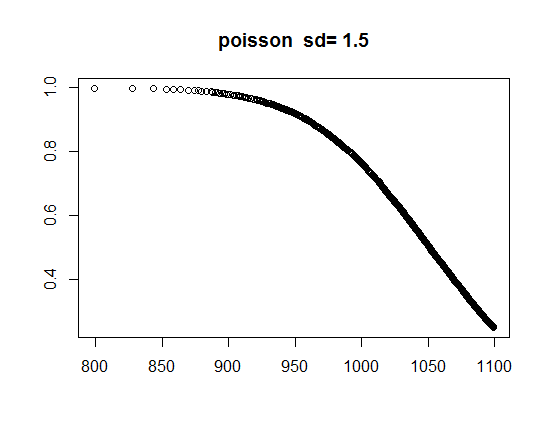
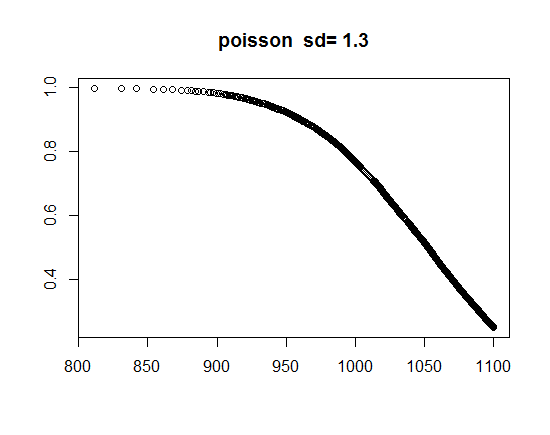
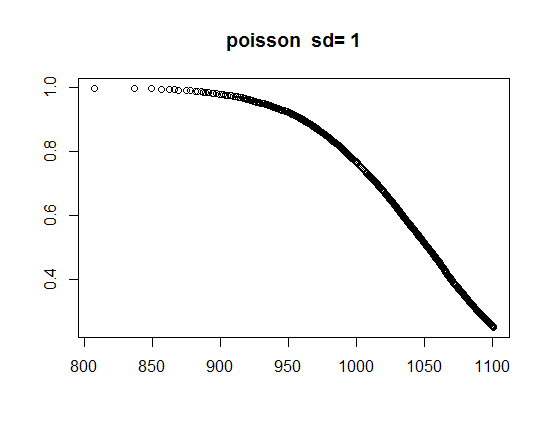
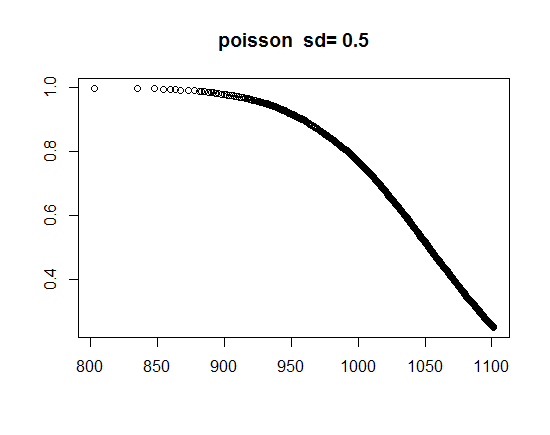
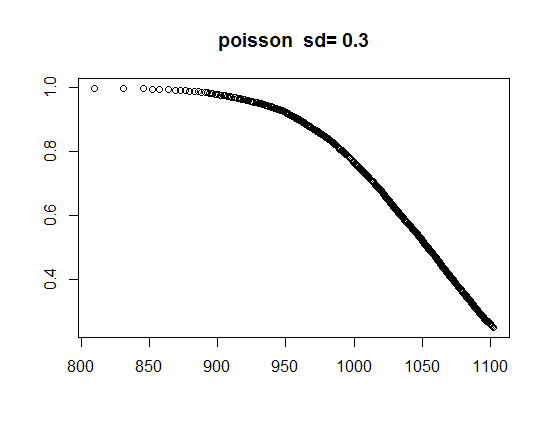
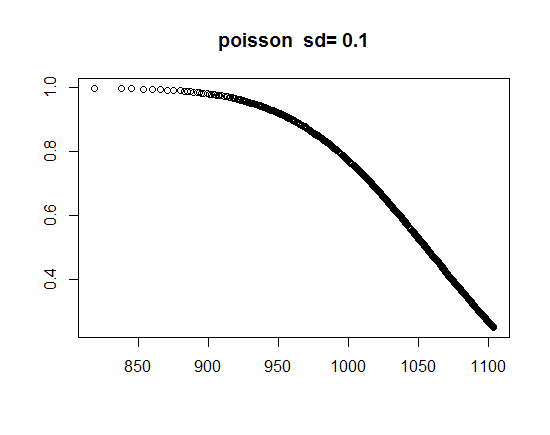
Time

Time

Time

Time

**Graphs 6-10. Exponentially decreasing viability with respect to age (time)**

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**Discussion, Conclusions and Future Work**

Simulations have shown that heterogeneity and initial defects simulated by poisson model can reproduce the exponentially increasing failure rates as dictated by the Gompertz Law of Mortality, the key biological feature of aging. Previous results show a correlation between standard deviation and the rate of aging. However, in recent experiments, the effect is not seen because the majority of the fluctuation comes from the poisson model as well as the noise added being too small.

We would like to simulate the leveling-off of the Reliability model which represents the late-life mortality deceleration and plateaus. This is a direct result of *redundancy exhaustion* in old age. In order to do that, a second population and repair mechanism must be introduced.

**References**

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**Supplemental Information**

R code provided in “Supplemental R code 1”