Systems medicine

Uri Alon

Exercise 3.

6.1. **Survival and hazard functions:**

(a) Show that hazard, $h(\tau)$, defined as the probability of death per unit time, is related to survival $S(\tau)$ as follows

$$h(\tau) = -\frac{1}{S}\frac{dS(\tau)}{d\tau} = -\frac{dlogS(\tau)}{d\tau}$$

(b) Show that $S(\tau) = e^{-\int h(\tau)d\tau}$

(c) What is the survival function S when the hazard follows the Gompertz-law? Plot this survival function.

(d) What is the survival function if hazard is constant $h(\tau) = h_0$?

(e) A tree has a hazard function that drops with age, $h(\tau) = \frac{a}{1+b\tau}$. What is the survival function? Plot and compare to d and c. What might be a biological cause of such a decreasing hazard function?

6.2 **Removal of SnC based on saturating their own removal process:** SnC are removed by immune cells such as NK cells, which we will denote by R. There are a total of R_T removing cells in the body, and that this number does not change appreciably with age (as is indeed the case for NK cells in humans). The R cells meet SnCs, denoted X, at rate k_{on} to from a complex [R X] which can either fall apart at rate k_{off}, or end up killing the SnC at rate v. Thus,

$$R + X \rightleftharpoons [RX] \rightarrow R.$$

(a)Explain the following dynamic equation for the complex:

$$\frac{d[RX]}{dt} = k_{on}R\,X - (v + k_{off})[RX]$$

(b) Use the fact that R cells can be either free or in a complex, so that $R + [RX] = R_T$, to show that the removal rate of SnC is

$$removal = \frac{\beta X}{k+X}.$$

(c) What are the values of the maximal removal capacity β, and the half-way saturation point k in terms of $R_T, k_{on}\ k_{off}$, and v? Explain intuitively.

6.3 Age-dependent reduction in repair capacity: Consider a process in which damage is produced at a constant rate η, and removal does not saturate. Removal rate per cell drops with age,

$$\frac{dX}{dt} = \eta - (\beta - \beta_1 \tau)X + \sqrt{2\epsilon}\xi$$

(a) What is the mean damage X?

(b) What is the distribution P(X) at age τ?

(c) What is the ratio of mean and standard deviation of X: $< X >/\sigma$?

(d) Estimate the hazard, assuming that death occurs when $X > Xc$? Is there a Gompertz law?