Systems medicine

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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

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

(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 $[RX]$ 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:

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

(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

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

(c) What are the values of the maximal removal capacity $\beta$, 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 $\eta$, 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 $\tau$?

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

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