Exercise set 5 (covering lectures 9,10, 11)
Due July 25
Basic facts of aging
Aging and the saturation of damage removal
Age-related diseases

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) Solve and plot the survival function S when the hazard follows the following cases.
1. Constant hazard $h = h_0$
2. Linearly rising hazrd: $h(\tau) = \alpha\,\tau$
3. Gompertz law: $h(\tau) = b\,e^{\alpha\,\tau}$. In humans, empirical magnitude of the alpha-parameter is about $0.085\ year^{-1}$, implying a doubling of mortality every $log(2)/\alpha = 0.69/0.085 = 8$ years.

(d) 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?

2. **Disposable soma theory:**

(a) Use evolutionary thinking to explain the phenomenon of menopause, which happens in very few species including humans and elephants.

(b) A gene has 'antagonistic pleiotropy', meaning that it provides reproductive advantage to a young reproductive organism but reduces survival at old age. How would natural selection affect the genes frequency in the population?

(c) Consider the case of senecent cells. What type of biological mechanism such as production or removal of senescent cells might serve as a possible place to look for antagonistic pleiotropy?

3. Age-dependent reduction in repair capacity: Consider a process in which damage X is produced at a constant rate η, and removal does not saturate. Removal rate per cell drops with age τ. Production and removal rates are fast compared to the lifetime of the organism. This is an alternative model to the SR model discussed in the lecture. Its equation is:

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

(a) Explain the parameter. What is the steady-state damage X (assume $dX/dt = 0$)? Does it rise with age? Does it 'explode' at a certain age?

(b) What is the distribution of damage between individuals P(X) at age? Use the potential function and the Boltzmann-like approximation from the lecture. Are older individuals more different from each other than younger ones?

(c) What is the hazard, assuming that death occurs when a threshold is crossed, $X > Xc$? Is there a Gompertz law? Use the potential function and the Kramers approximation from the lecture.

(d) What biological processes might cause such a reduction in removal capacity?

4. Two diseases in the same person: Consider two age-related diseases with senescent-cell thresholds X_{c1} and X_{c2}. Suppose the two diseases can occur in the same person (the person is susceptible to both diseases).

(a) What would you expect about the timing of the diseases in the same person?

(b) How would you test this hypothesis? What are some confounding factors?