

# Exercise sheet 1

## Systems Biology class 2014

March 19, 2014

Return by email to [jean.hausser@weizmann.ac.il](mailto:jean.hausser@weizmann.ac.il) until March 30th 2014 at the latest with [SB14] Exercise sheet 1 in the subject of the email.

### 1 Origin of the production-removal equation

In the class, we introduced the production-removal equation:

$$\frac{dX}{dt} = \beta - \alpha X \quad (1)$$

This exercise explains why the rate of protein removal,  $\alpha$ , is equal to the sum of the degradation rate  $\alpha_{deg}$  and the dilution rate  $\alpha_{dil}$ ,  $\alpha = \alpha_{deg} + \alpha_{dil}$ .

Consider a collection of cells, which contain a certain protein. Let  $P$  be the total number of molecules of this protein, summing up over all cells. The concentration of the protein is  $X = P/V$ , where  $V$  is the total volume of all cells. The protein is produced at a rate  $\beta$  per unit cell volume. It is actively degraded at rate  $\alpha_{deg}$ . Cells grow exponentially, such that cell volume produces new cell volume at rate  $\alpha_{dil}$ .

1. The differential equation describe the change in the total cell volume  $V$  is  $\frac{dV}{dt} = \alpha_{dil}V$ . Interpret this equation in words.
2. Write a differential equation for the rate of change the total protein:  $\frac{dP}{dt} = \dots$
3. Write a differential equation for the rate of change of protein concentration  $X = P/V$ . Compare to Equation 1.

### 2 Change in degradation/dilution

Protein  $X$  is at steady state, produced at a constant rate  $\beta$ , with degradation/dilution rate  $\alpha_0$ . The degradation/dilution rate suddenly changes to a new, lower value,  $\alpha_1$ . Solve for the dynamics  $X(t)$ , plot the dynamics, and calculate the response time.

Hint: the response time  $t_{1/2}$  is defined as the time necessary to reach half the regulation. Formally,  $X(t_{1/2}) = \frac{X_0 + X_{ss}}{2}$ .

### 3 Long lived mRNA

Consider a gene which is constantly activated, producing mRNA at rate  $\beta_m$ . The mRNA is long lived (not degraded), and produces  $\beta_p$  proteins per unit time. The protein is also long lived (not degraded).

1. Solve for the protein concentration as a function of time, starting from zero initial mRNA and protein, for the case where cells do not grow ( $\alpha_{dil} = 0$ ).
2. At time  $t_1$ , a drug is added to the cells that blocks transcription completely. At a later time,  $t_2$ , another drug is added that stops translation completely. Assuming that cells do not grow ( $\alpha_{dil} = 0$ ), solve and plot the resulting protein concentration as a function of time.
3. *optional*: solve for the protein concentration as a function of time, starting from zero initial mRNA and protein, for the case where cells grow at rate  $\alpha_{dil}$ . Plot the protein concentration as a function of time.