CHEME5440 HW1

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Part 1

Using the model developed in Problem Set 1 the parameters in Table 1 were increased and decreased by 50%. Their observed effect was recorded below. Most of the parameters that affected mRNA concentration were part of the control function, u.

Table 1: Parameters changed in the transcription model and their observed effect on the graph of the steady state mRNA concentration

Parameter	Definition	Effects on mRNA Concentration
e_x	Average Elongation Rate	No Visible Effect
L	Average Gene Length	No Visible Effect
$K_x j$	Saturation Coefficient	No Visible Effect
k_I	Rate for Open Complex Formation	No Visible Effect
R_X, T	Concentration of RNAP	No Visible Effect
K_1	Binding Constant of RNAP without Inducer	Increase in parameter makes basal transcription rate increase at low inducer concentration. Decrease in parameter makes basal transcription rate decrease at low inducer concentration.

| Parameter	Definition	Effects on mRNA Concentration
K_2	Binding Constant of RNAP with Inducer	Increase in parameter makes the slope of the curve steeper in the middle part of the diagram. Decrease in parameters decreases the slope of the curve in the middle part of the diagram.
n	Cooperativity Constant	Increase in parameter makes the slope of the curve steeper in the middle part of the diagram. Decrease in parameters decreases the slope of the curve in the middle part of the diagram.
K_d	Binding Function for Inducer	No Visible Effect
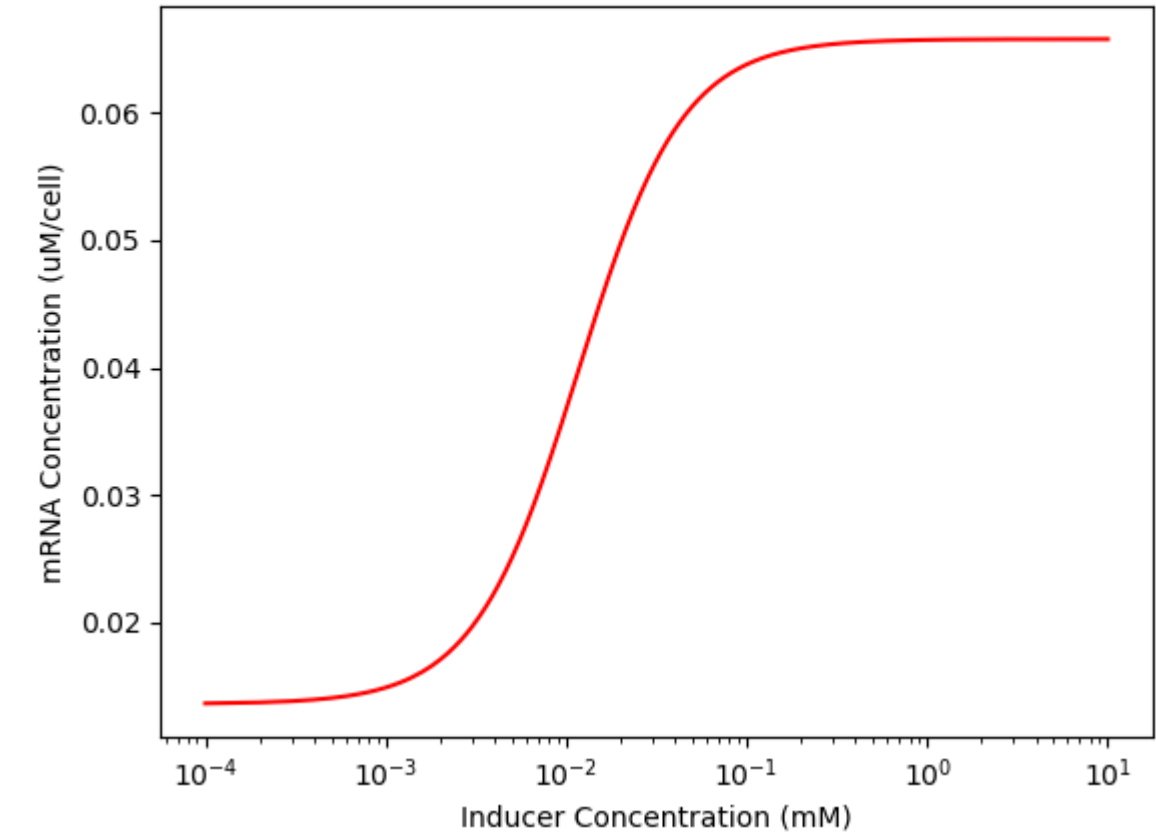
Figure 1: Concentration of steady state mRNA over a range of inducer concentrations.

Part 2

Part 2a

Mass Balances for mRNA, m_i and protein, p_i, were derived based on transcription/translation rate, degradation rate, and dilution rate.

For the mRNA balance and protein balances:

$$\frac{dm_i}{dt} = r_{x,i}u_{x,i} - (k_{x,d} - \mu)m_i$$

$$\frac{dp_i}{dt} = r_{L,i}u_{L,i} - (k_{L,d} - \mu)p_i$$

Note that since the first protein is outside the cell, there is no dilution term for m_1 and p_1. The system of 6 ODEs can be simplified as

$\frac{dx}{dt} = Ax - Sr$

where

$$A = \begin{pmatrix} -k_{x,d} & 0 & 0 & 0 & 0 & 0 \\ 0 & -k_{x,d} - \mu & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_{x,d} - \mu & 0 & 0 & 0 \\ 0 & 0 & 0 & -k_{L,d} & 0 & 0 \\ 0 & 0 & 0 & 0 & k_{L,d} - \mu & 0 \\ 0 & 0 & 0 & 0 & 0 & k_{L,d} - \mu \end{pmatrix}$$

$$x = \begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ p_1 \\ p_2 \\ p_3 \end{pmatrix}$$

$$S = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

$$x = \begin{pmatrix} r_{x,1}u_{x,1} \\ r_{x,2}u_{x,2} \\ r_{x,3}u_{x,3} \\ r_{L,1}u_{L,1} \\ r_{L,2}u_{L,2} \\ r_{L,3}u_{L,3} \end{pmatrix}$$

Where r_i are the kinetic transcription and translation rates and u_i are control functions for transcription and translation. The control function, u_i, is given as:

$$u_i = \frac{K_x + \sum K_{ij} f_{i,j}}{1 + K_x + \sum K_{ij} f_{i,j}}$$

Part 2b

Note: to run the code for `HW2.jl` the functions `RateTranslation.jl` and `RateTransription.jl` must be initialized by typing

```
include("RateTranslation.jl")
include("RateTransription.jl")
```

For all simulations of the memory circuit, the inducer concentration was set to 10 mM for 60 minutes, and set to zero after 50 minutes. These changes are reflected in the sharp drop in the mRNA charts at the 1 hour mark.

Functional Memory Circuit

In the functional memory circuit after the inducer is removed, the mRNA concentration for protein 1 drops dramatically, however, the mRNA concentrations remains at steady state as shown in Figure 3. Due to the mutual induction between protein 2 and 3, once they are inducer by protein 1, they remain in the cell as shown in Figure 4.
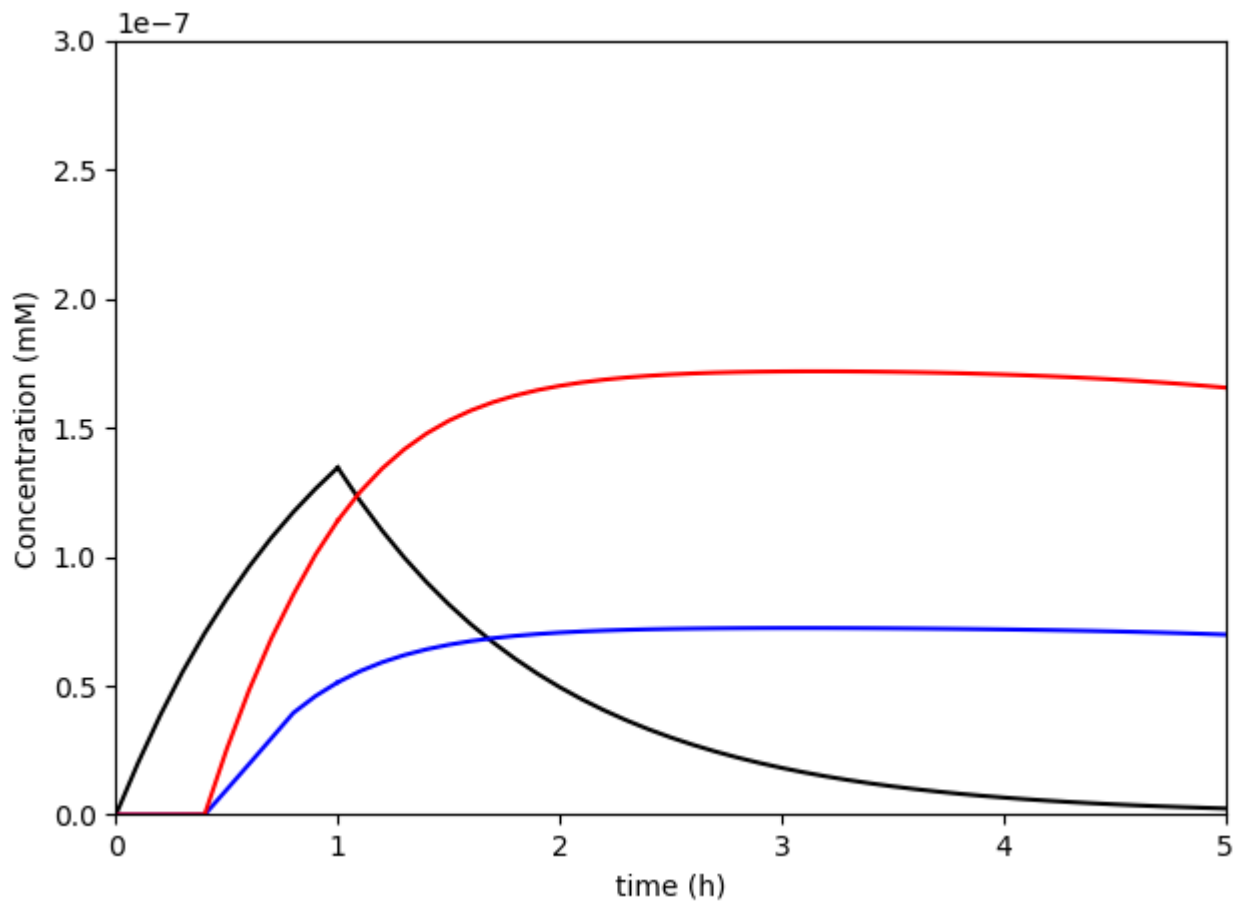
Figure 3: mRNA concentration as a function of time in the functional memory circuit. m_1 is in black, m_2 is in blue, m_3 is in red.
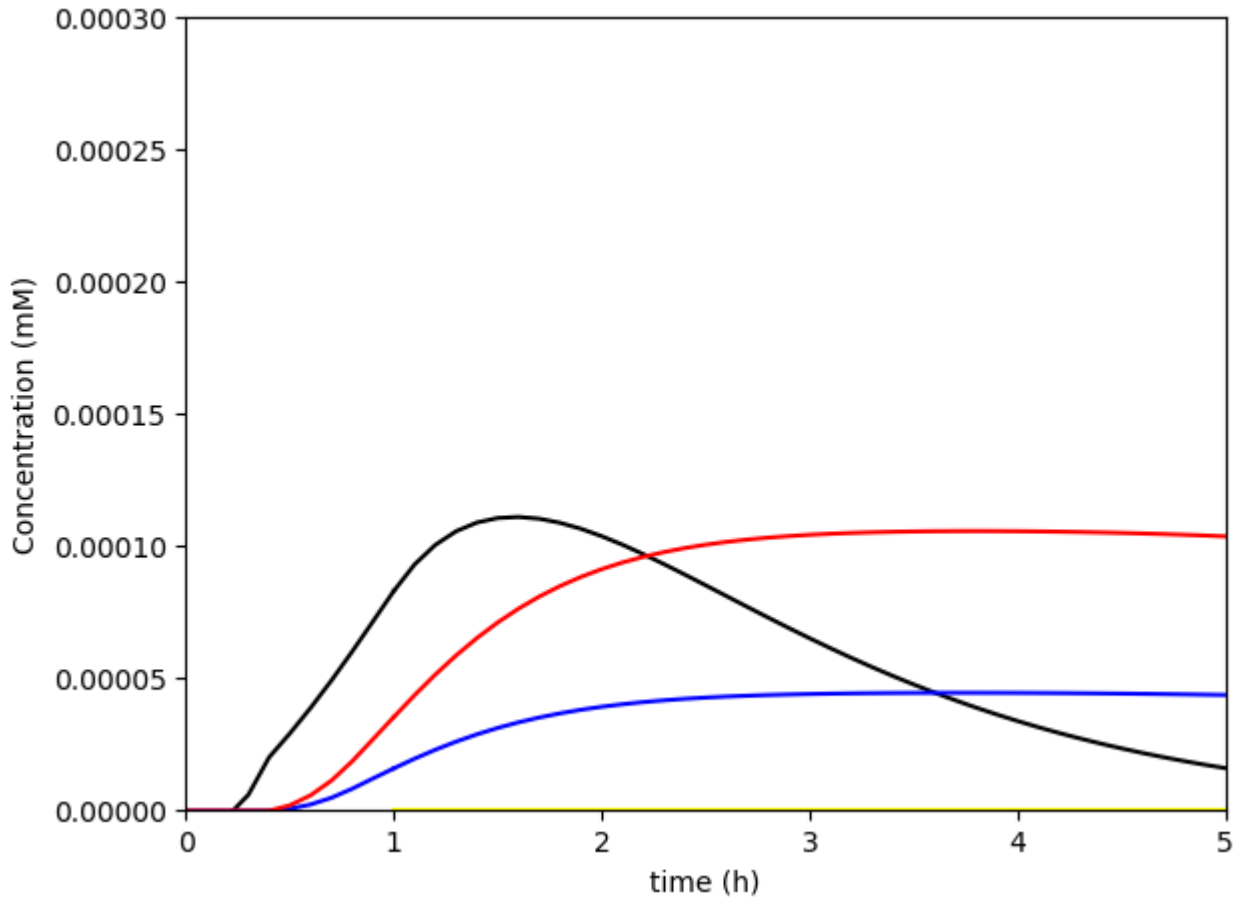
Figure 4: Protein concentration as a function of time in the functional memory circuit. p_1 is in black, p_2 is in blue, p_3 is in red.

Broken Memory Circuit

In the broken memory circuit, protein 2 does not induce protein 3 production. In this circuit, after the inducer is removed, the protein 1 concentration decreases, followed by the protein 3 concentration. protein 2 remains longest of the three because protein 3 continues to induce the production of protein 2. In this circuit, the induction of protein 3 by protein 2 is removed by setting

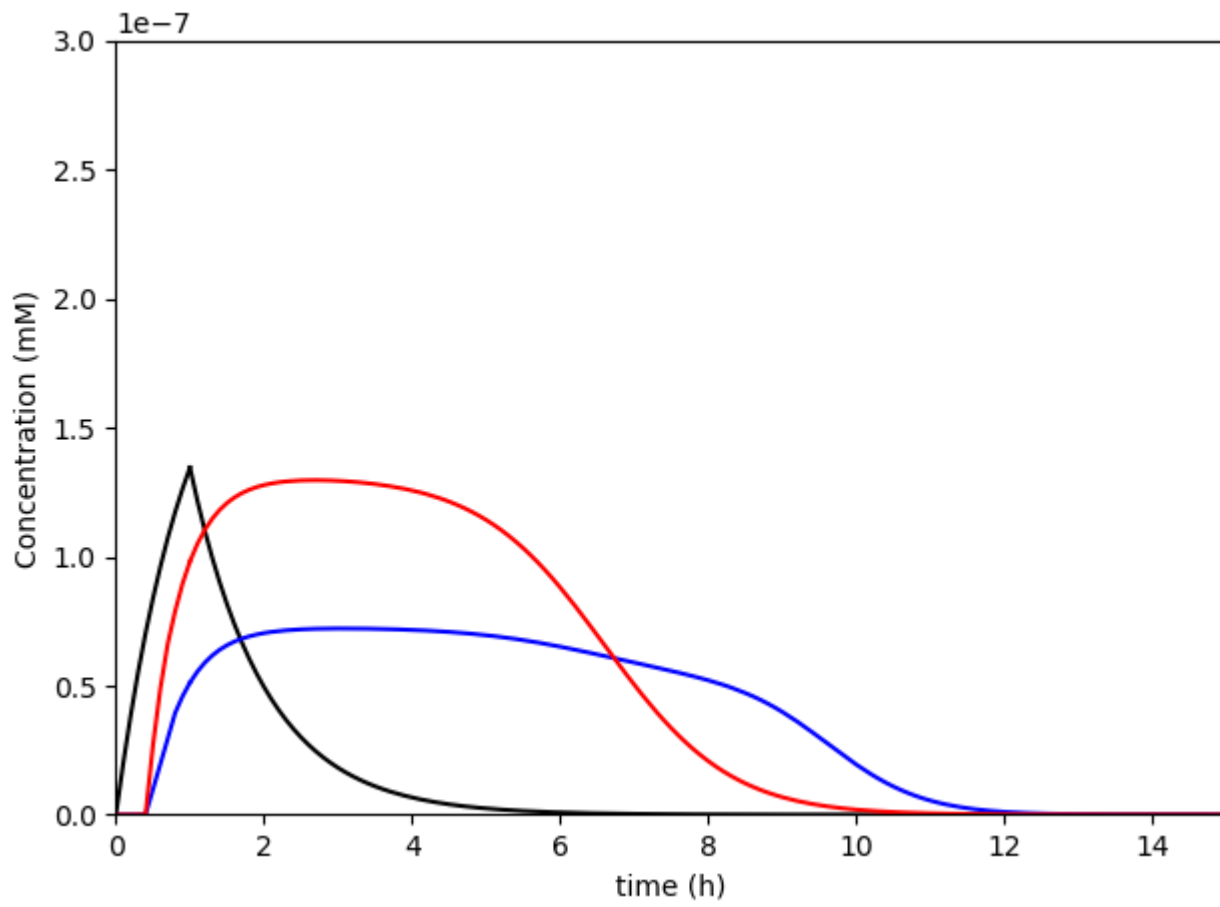$$f_{2,3} = \frac{(p_2)^n}{(K_d)^n + (p_2)^n} = 0$$

Figure 5: mRNA concentration as a function of time in the broken memory circuit. m_1 is in black, m_2 is in blue, m_3 is in red.
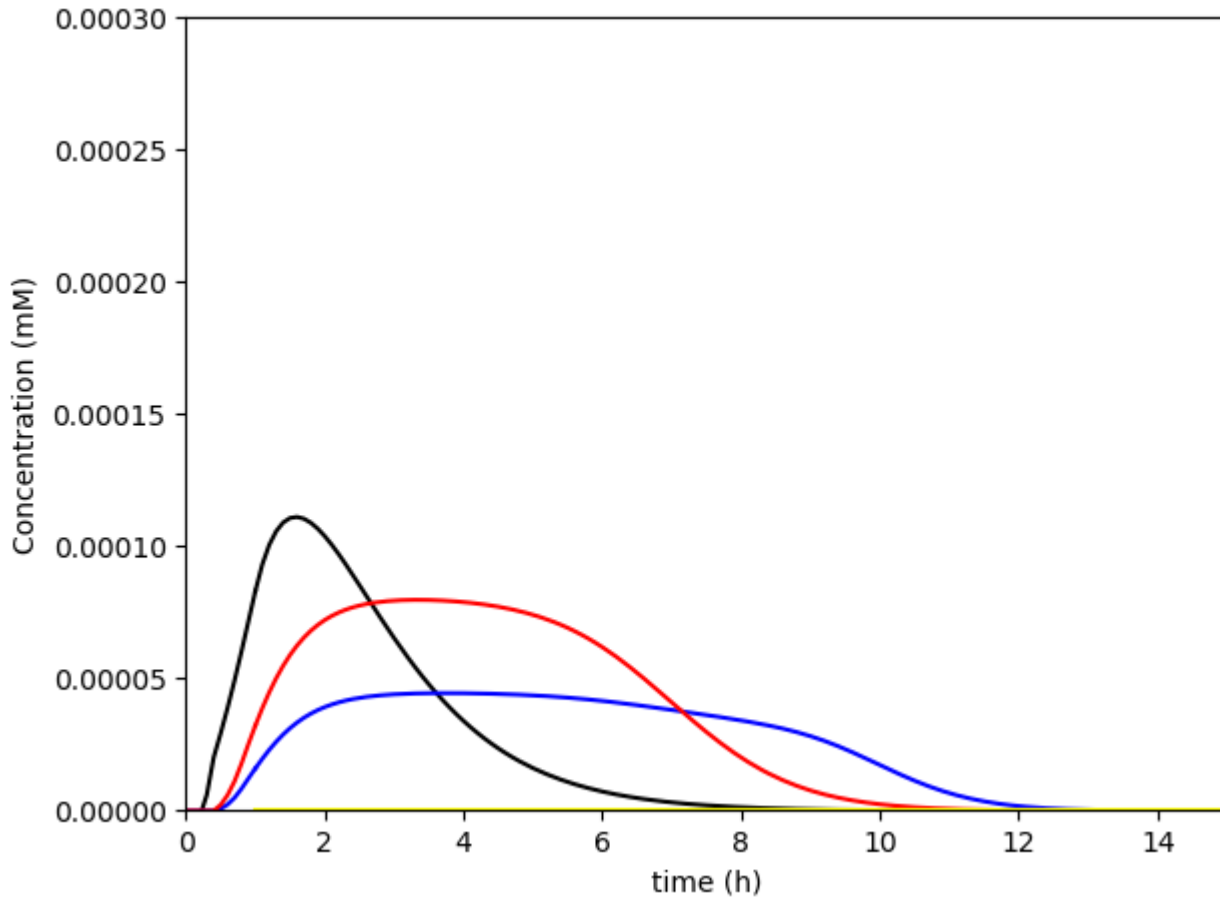
Figure 6: Protein concentration as a function of time in the broken memory circuit. p_1 is in black, p_2 is in blue, p_3 is in red.

Part 2c

In Part 2c, a discretization was used to approximate the solution achieved by the ODE solver in part 2b. The approximation is as follows:

$$x_{k+1} = A_{hat}x_k + S_{hat}r_k$$

where

$$A_{hat} = exp(A * \tau)$$

$$S_{hat} = A^{-1}[A_{hat} - I]S$$

Using this approximation, a solution of the same order of magnitude was determined as shown in the mRNA concentration and protein concentration shown in Figure 7 and 8.
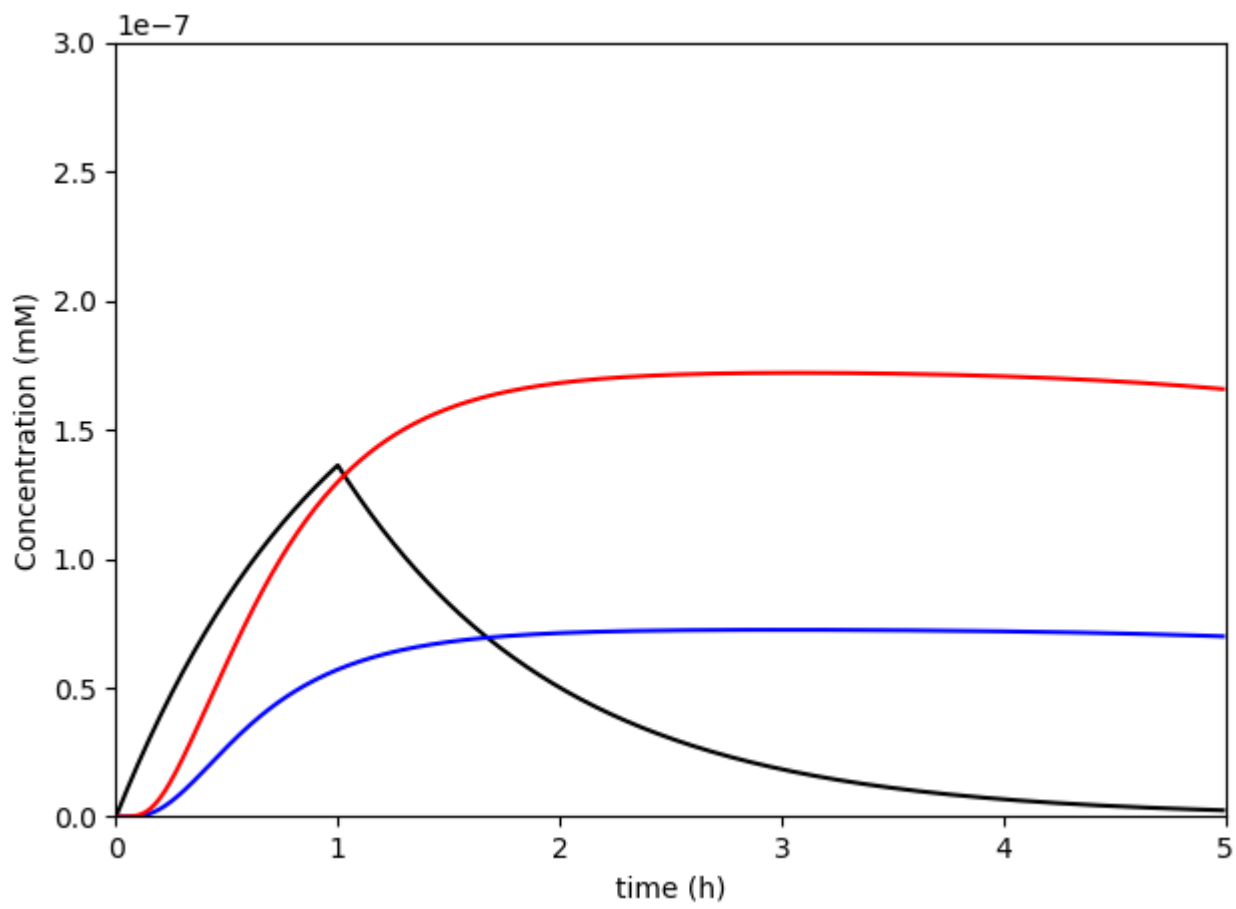
Figure 7: mRNA concentration as a function of time in the functional memory circuit. m_1 is in black, m_2 is in blue, m_3 is in red.
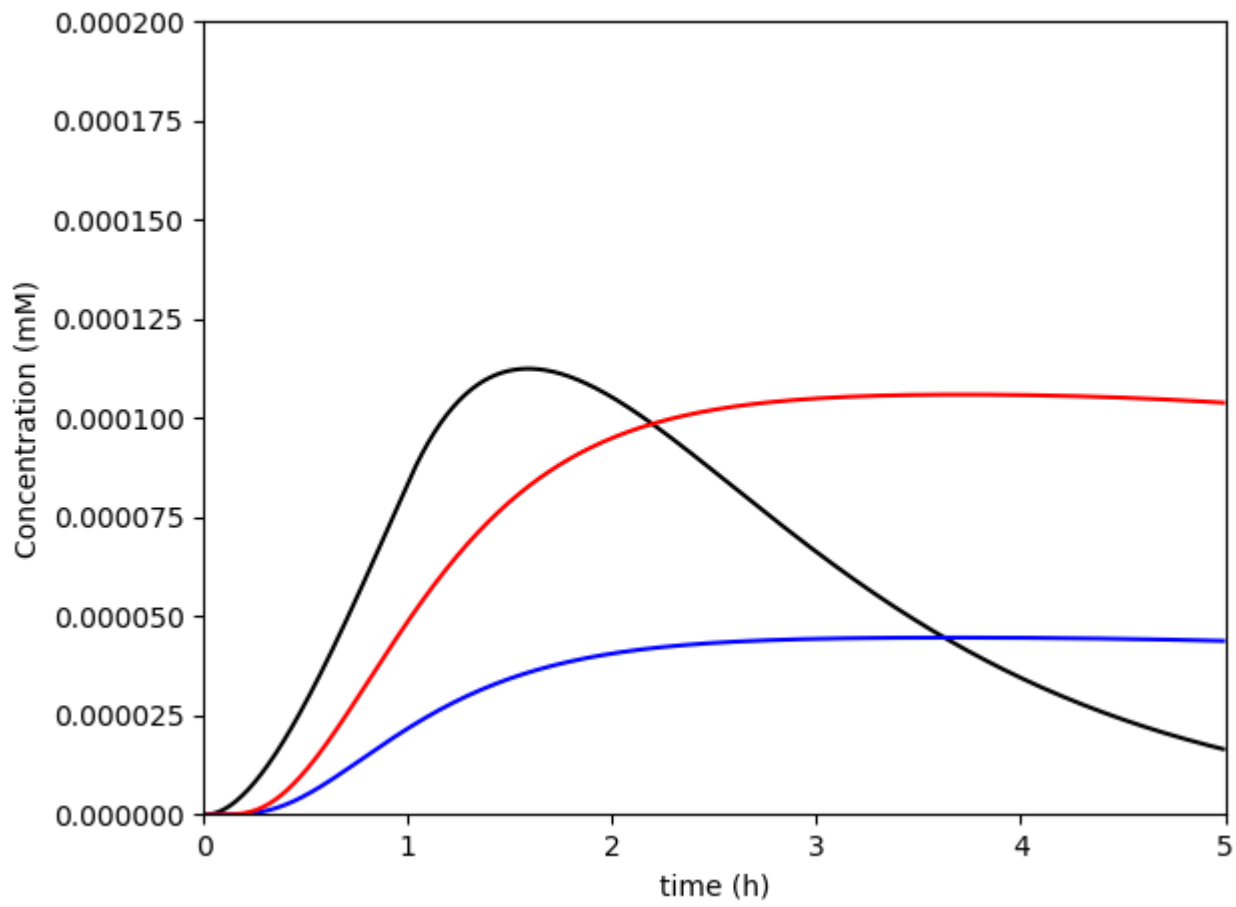
Figure 8: Protein concentration as a function of time in the functional memory circuit. p_1 is in black, p_2 is in blue, p_3 is in red.