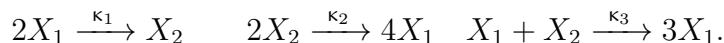


7. EXERCISE LIST. TUESDAY WEEK 2

**Exercise 7.1.** Consider the networks in Exercise 4.1 and show that they do not satisfy the assumptions to apply the multistationarity theorem based on the Brouwer degree seen in the lecture (conservativity + absence of boundary steady states in relevant stoichiometric compatibility classes). This exercise should be done by hand.

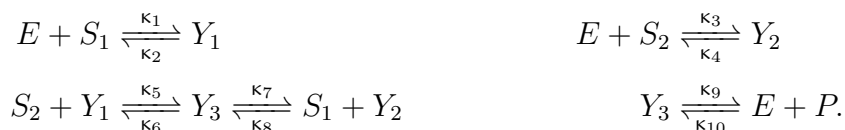
**Exercise 7.2.** Consider the network



This exercise should be done by hand.

- (1) Show that the network is conservative and has no boundary steady states in stoichiometric compatibility classes that intersect the positive orthant.
- (2) If  $N$  is the stoichiometric matrix constructed using the order of reactions indicated by the labels, show that the **nonnegative kernel**  $\ker(N) \cap \mathbb{R}_{\geq 0}^3$  is generated by the vectors  $(1, 0, 1)$  and  $(2, 1, 0)$ .
- (3) Use the theorem via Brouwer degree and the parametrization in terms of  $\lambda$  and  $h$  to show that the network is not multistationary.

**Exercise 7.3.** Consider the following network from Exercise 4.3, which is not injective:



Show that the network satisfies the assumptions of the multistationarity theorem via Brouwer degree and use it to conclude that the network is not multistationary. (You need to use software for this exercise – see the example files in Maple or SAGEMath).

**Exercise 7.4.** Consider the following network, which considers the phosphorylation of two substrates  $S, P$  such that both the kinase and phosphatase are shared:



Use the theorem of multistationarity via Brouwer degree to conclude that the network exhibits multistationarity for some total amounts if and only if

$$(\kappa_3\kappa_{12} - \kappa_6\kappa_9) \left( \kappa_1\kappa_3\kappa_{10}\kappa_{12}(\kappa_9 + \kappa_8)(\kappa_6 + \kappa_5) - \kappa_4\kappa_6\kappa_7\kappa_9(\kappa_{12} + \kappa_{11})(\kappa_3 + \kappa_2) \right) < 0.$$

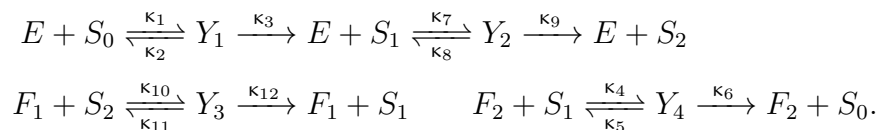
You need to find a parametrization of the positive steady state variety. The network is a PTM network and admits such one in terms of the concentrations of  $E, F, S_0, P_0$ . (You need to use software for this exercise).

The condition can be rewritten in a more meaningful way as

$$(\kappa_3\kappa_{12} - \kappa_6\kappa_9) \left( \kappa_3\kappa_{12} \frac{\kappa_1}{\kappa_3 + \kappa_2} \cdot \frac{\kappa_{10}}{\kappa_{12} + \kappa_{11}} - \kappa_6\kappa_9 \frac{\kappa_4}{\kappa_6 + \kappa_5} \cdot \frac{\kappa_7}{\kappa_9 + \kappa_8} \right) < 0.$$

Note that each of the quotients is the inverse of the Michaelis-Menten of one of the enzymes (this sentence might not make any sense to you, in that case, ignore it!).

**Exercise 7.5.** Consider the following network, which is a modification of the 2-site phosphorylation network, in which the two dephosphorylation events are catalyzed by different phosphatases:



Show that the network satisfies the assumptions of the multistationarity theorem via Brouwer degree and use it to conclude that the network is multistationary. Additionally, show that for all choices of reaction rate constants, there exist total amounts for which the network is multistationary. (To this end, you need to find a parametrization of the positive steady state variety. Note that the network is a PTM network and hence admits such one). You need to use software for this exercise.

**Exercise 7.6.** Let  $C \in \mathbb{R}^{s \times (s+1)}$  be a uniform matrix (with all maximal minors  $\neq 0$ ) of rank  $s$ . For any  $i = 1, \dots, s+1$ , set  $\lambda_i = (-1)^i \det(C(i))$ , where  $C(i)$  is the square submatrix of  $C$  obtained by deleting the  $i$ -th column.

Prove that  $C \cdot \lambda = 0$  and that the linear system  $C \cdot x = 0$  has a positive solution  $x \in \mathbb{R}_{>0}^{s+1}$  if and only if  $\lambda_i > 0$  for any  $i = 1, \dots, s+1$  or  $\lambda_i < 0$  for any  $i$  (that is, if and only if the signs of the determinants  $\det(C(i))$  alternate as  $i$  goes from 1 to  $s+1$ ).

We suggest that you reread the definition of a simplex positively decorated by a matrix  $C$ . Do you understand it now?

**Exercise 7.7.** Choose a few different values of  $c = (c_0, c_1, c_2, c_3) \in \mathbb{R}_{>0}^4$  and of  $h = (h_0, \dots, h_3) \in \mathbb{Z}_{\geq 0}^4$  inducing the subdivision  $[0, 1], [1, 2], [2, 3]$  of the interval  $[0, 3]$ . In each case, consider the polynomial  $f = t^{h_3} c_3 x^3 - t^{h_2} c_2 x^2 + t^{h_1} c_1 x - c_0 \in \mathbb{R}[t, x]$ . Compute the discriminant of  $f$  with respect to the  $x$  variable and its approximate positive roots (in the variable  $t$ ) using a CAS. Find  $t_0(c) > 0$  such that for any value of  $s \in (0, t_0(c))$ , the polynomial  $f(s, x)$  has 3 positive real roots. How do the values of the coefficients  $t_0(c)^{h_i} c_i$  vary as  $c$  and  $h$  vary?