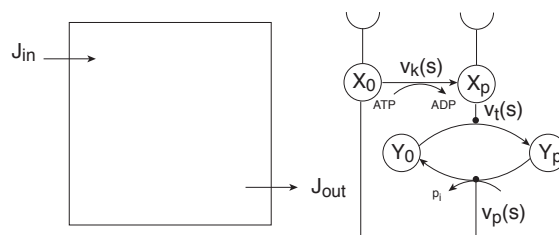


Physics of Behavior

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Exercise 4

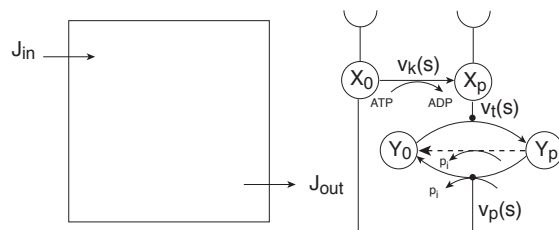
1. A bifunctional component provides a robust input-output relationship. (this is a review of lecture on robustness by bi-functional components). The receptor X catalyzes two opposing reactions: phosphorylating Y at one catalytic site on the receptor, and de-phosphorylating Y at a different catalytic site. Thus, the opposing kinase and phosphatase activities are rolled up into the same protein, instead of being separated on two different proteins. One way to solve this example is to write down several mass-action equations for the system, and find their fixed-point. An easier way to obtain the input-output relations presents itself when we view the system as a black box that breaks down ATP and releases phosphoryl groups back to the cytoplasm as inorganic phosphate (Pi). Consider the fluxes of phosphoryl into and out



of the system.

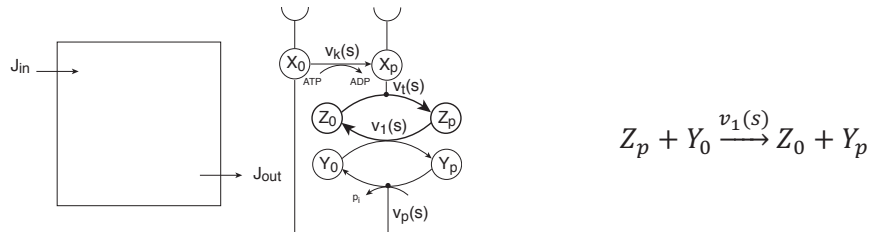
- Calculate the rate at which phosphoryl, p , enters the box, J_{in} , and exits J_{out} . Explain why J_{in} depends only on X_0 and J_{out} on X_0 and Y_p .
- Show that $Y_p = v_k(s)/v_p(s)$ at steady state provided there is enough protein Y . Explain why this resulting output level Y_p is robust to X and Y protein levels.
- What happens if total Y_T protein ($Y_0 + Y_p$) is below Y_p for a given value of s ?

2. Spontaneous dephosphorylation leads to small loss of robustness. In the EnvZ-OmpR circuit, Y_p can be spontaneously dephosphorylated without the action of X . The half-life of Y_p due to this reaction is ~ 90 minutes, compared to half-life of Y_p of seconds due to the dephosphorylation catalyzed by X .



- Write an equation for Y_p dynamics assuming the two-component mechanism also has a reaction of spontaneous dephosphorylation at rate ϵ .
- Use the black box approach to calculate the steady-state level of Y_p .
- Explain why robustness is lost only to order ϵ .

3. Use the black box to analyze a circuit that has an additional phosphor-transfer step (in bold). Here Z_p passes the phosphoryl to Y_0
- What is Y_p at steady state ?
 - Is it robust? Assume there are a lot of Z and Y proteins.



4. *The chemotaxis protein circuit.* We learned in class how attractant lowers the probability that motors turn CW and generate tumbling. Consider here other input alternatives.
- Repellent. Explain how the chemotaxis circuit responds to a step of repellent. Repellent binding increases receptor activity.
 - Reduction in attractant: Suppose attractant is removed in a step like manner. What is the response of the cells?

5. *Sensory adaptation.* Explain how the idea of exact adaptation applies to human senses: vision, hearing and smell. Are there senses which do not show exact adaptation? What might be the reason that some senses do and others do not show exact adaptation?

6. *Robust adaptation and Integral feedback.* The mapping of the Barkai-Leibler model and integral feedback is easiest to see from the equation.

$$\frac{dm}{dt} = v_B B(X_{st} - X^*)$$

The model becomes simpler when one uses the receptor binding constant K as a variable instead of m .

- Use the relations

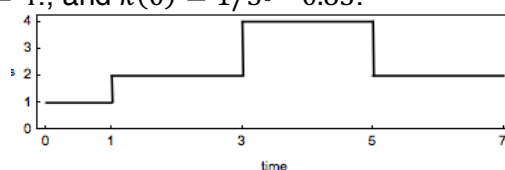
$$X^* = \frac{X_T}{1 + (s/K)^n}, \quad K = K_0 e^{\gamma m}$$

to show that the equation for K is:

$$\frac{dK}{dt} = c K (a_{st} - a), \quad a = \frac{1}{1 + \left(\frac{s}{K}\right)^n}$$

where $a = X^*/X_T$

- Simulate and plot the response when (i) $s = 1$ for a long time and then goes in a step-like way to $s = 2$, (ii) $s = 2$ goes to $s = 4$, and (iii) $s = 4$ goes to $s = 2$. Choose $n = 6$, $a_{st} = 1/4$, $c = 4$, and $k(0) = 1/3^6 \sim 0.83$.



c. Do you see adaptation?