ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Department of Computer Science
ETH Zürich

Synthetic Biology

Assignment #01

Stephanie Fingerhuth, Lorenzo Gatti

Friday 23rd March, 2012

0.1 The model

The model for a two protein network can be given by the system of equations:

$$\frac{dx}{dt} = f(y) - d_1 x \tag{0.1a}$$

$$\frac{dy}{dt} = g(x) - d_2 y \tag{0.1b}$$

where x and y are the concentration of the two proteins, f and g are "repression functions" and d_1, d_2 are positive constant describing the protein decay.

$$f(y) = \frac{k_1}{1 + [Y]^n} \tag{0.2a}$$

$$g(x) = \frac{k_2}{1 + [X]} \tag{0.2b}$$

The level of repression of $[X]$ in a "mixed" circuit model is described by a Hill function [Cherry and Adler, 2000], which models cooperativity of binding between two different molecular species. Cooperativity magnitude is described by the Hill coefficient n. Using the conditions for a change in the number of steady states derived from nullclines analysis:

$$d_1[X] = \frac{k_1}{1 + [Y]^n} * \frac{1}{d_1} = \frac{k_1'}{1 + [Y]^n} \tag{0.3a}$$

$$y_1 = \sqrt[n]{\frac{k_1'}{d_1[X]} - 1} \tag{0.3b}$$

$$d_2[Y] = \frac{k_2}{1 + [X]} * \frac{1}{d_2} = \frac{k_2'}{1 + [X]^n} \tag{0.3c}$$

$$y_2 = \frac{k_2'}{1 + [X]} \tag{0.3d}$$

with $k_1' = \frac{k_1}{d_1}$ and $k_2' = \frac{k_2}{d_2}$.

The equations 0.3a and 0.3d are solved as functions of $f(x)$ in the form $y = f(x)$.

0.2 Nullcline plots

The analysis performed in graphs 0.1 shows the existence of multiple steady states depending on which parameters are chosen. Multiple steady states are the necessary condition to have a switch. The purpose of the switch is to obtain a consisting change in the concentration of a certain protein. The graph 0.1b shows transverse nullclines.
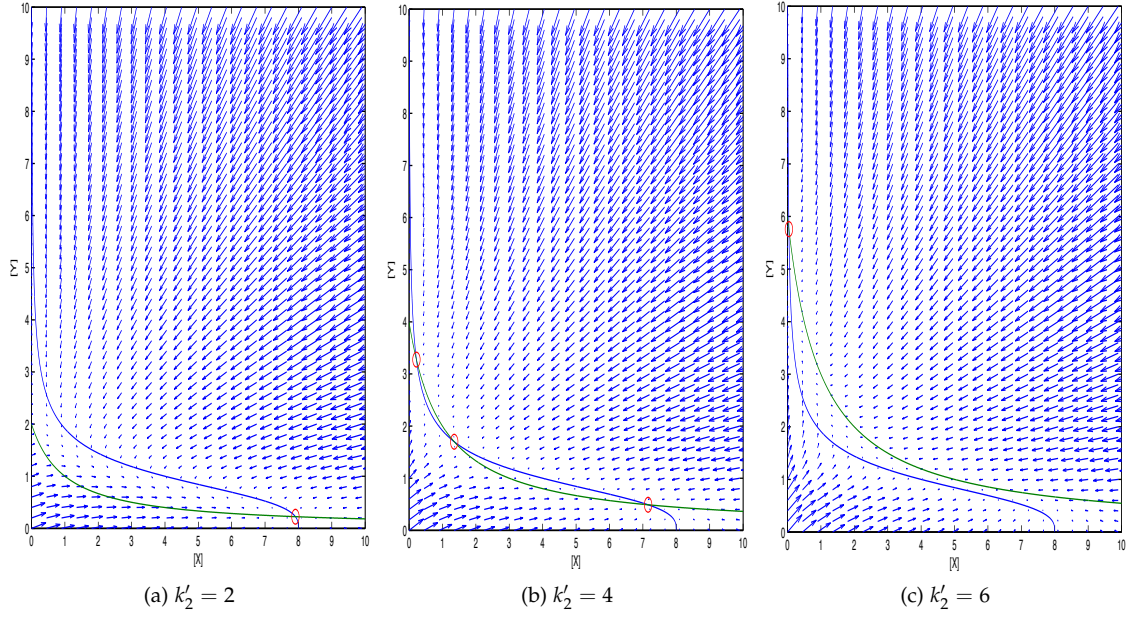

(a) $k_2' = 2$ (b) $k_2' = 4$ (c) $k_2' = 6$

Figure 0.1: Nullclines plots for the parametres $n = 3$, $k_1' = 8$, $k_2' = \{2, 4, 6\}$

Intersection of functions lines are circled in red. These points represent the steady state at different values of the parameter k_2. In the graph 0.1a we can distinguish only one point at high concentration of protein Y as well as in the graph 0.1c where the steady state is reached at high concentration of X. The major difference is visible in the graph 0.1b where we clearly confirm a possible switch, due to the presence of three steady state points.

0.3 Analytic expressions for k_1' and k_2'

According to Matlab *solve* function for the equations:

$$e1 : x = \frac{k_1'}{(1+y^3)} \tag{0.4a}$$

$$e2 : y = \frac{k2}{(1+x)} \tag{0.4b}$$

$$e3 : \delta\left(\frac{k_1}{(1+y^3)}, y\right) * \delta\left(\frac{k_2}{(1+x)}, x\right) = 1 \tag{0.4c}$$

we retrieve three solutions:

$$k_1' = \frac{(3 * x^2)}{(2 * x - 1)} \tag{0.5a}$$

$$k_2' = \left(\frac{(x+1)}{(2 * x - 1)} \right)^{\frac{1}{3}} * (x + 1) \tag{0.5b}$$

$$y = \left(\frac{(x+1)}{(2 * x - 1)} \right)^{\frac{1}{3}} \tag{0.5c}$$
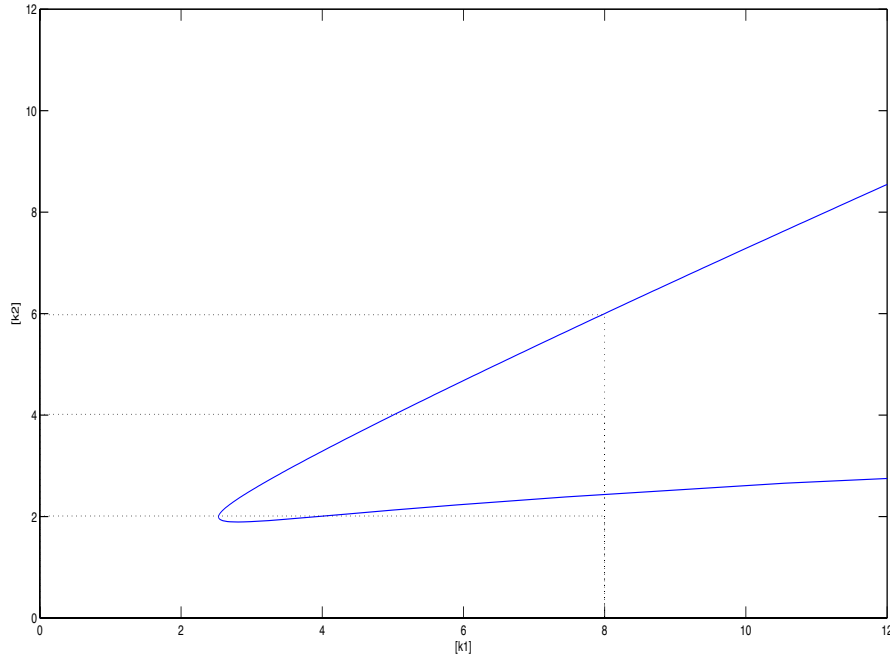
0.4 Bifurcation diagram

Figure 0.2: Values of the parameter k_1' and k_2' needed for a working switch for particular values of the exponent n in the Hill function.

In bifurcation diagram the region delimited by the graph is the bistable region. Only in this region switches are possible. From this diagram one can see clearly that $k_2' = 2$ is completely outside the bistable region, whereas $k_2' = 4$ lies inside. This corresponds to the nullclines analyses in plot 0.1. There we could find a possible switch for $k_2' = 4$ but not for $k_2' = 2$. Even though $k_2' = 6$ seems to be in the bistable region here, we can see from graph 0.1c that there are no possible switches.

0.5 synthbio_script_01.m

```
1  %###########################################################
2  %## Synth Bio Project 01 ##
3  %###########################################################
4  %# Author: Stephanie Fingerhuth, Lorenzo Gatti
5  %# Date: 09-Mar-2012  v.0.0.1
6  %# Update: 10-Mar-2012 v.0.1.1
7  %# Usage:
8  %# Parametres:
9  %# Output:
10 %#
11 %# TODO: Add comments [DONE]
12 %#
13 %###########################################################
14
15 %#######################################
16 % Problem [B]
17 %#######################################
18 % Solving equation with given parametres:
19 % n=3, k1p = 8; k2p = {2,4,6}
20
21 % Initialization of variables
22 n = 3;
23 k1 = 8;
24 k2 = [2 4 6];
25 x_val = [0:0.01:10];
26
27 % Defining the range of X and Y
28
29 [vf_x, vf_y] = meshgrid(0:0.45:15,0:0.20:10);
30
31 % Plotting solutions on a graph
32 for i=1:length(k2)
33
34     % Plotting the vector field
35     quiver(vf_x, vf_y,dx(k1, n, vf_x, vf_y), dy(k2(i), vf_x, vf_y), 2);
36
37     hold on;
38
39     % Find intersection points for the defined functions (X,Y)
40     [xi, yi] = polyxpoly(x_val, nx(k1, n, x_val), x_val, ny(x_val, k2(i)));
41
42     % Plotting the nulclines
43     plot(x_val, nx(k1, n, x_val), x_val, ny(x_val, k2(i)));
44
45     % Plot intersection of graphs
46     plot(xi, yi, 'or', 'MarkerSize',10);
47
48     xlabel('[X]');
49     ylabel('[Y]');
50
51     % Setting the new axis
52     axis([0 max(x_val) 0 10]);
53
54     hold off;
55
56     % Export graph in a pdf file
57     print('-dpdf', ['plot_B' num2str(i)]);
58 end
59
60 %#######################################
61 % Problem [C]
62 %#######################################
63
64 % Defining the equations to solve
65
66 e1 = 'x␣=␣k1/(1+y^3)';
67 e2 = 'y␣=␣k2/(1+x)';
68 e3 = 'diff(k1/(1+y^3),␣y)*diff(k2/(1+x),x)␣=1';
69
70 % Solving system of equations
71
72 S = solve(e1, e2, e3, 'y', 'k1', 'k2');
73
74 % Retriving first solution for each variable
75
```

```
76  k1 = S.k1(1);
77  k2 = S.k2(1);
78  y = S.y(1);
79
80  % Defining the range of X
81
82  x = [0:0.01:5];
83
84  % Solve the equations in the range of x
85
86  k1_solv = x.*subs(k1);
87  k2_solv = x.*subs(k2);
88
89  %#########################################
90  % Problem [D]
91  %#########################################
92
93  % Plotting of the solutions from the previous step
94
95  plot(k1_solv, k2_solv);
96  xlabel('[k1]');
97  ylabel('[k2]');
98
99  % Setting the new axis
100
101 axis([0 max(k1_solv) 0 max(k2_solv)]);
102
103 % Export graph in a pdf file
104 print('-dpdf', 'plot_D0');
```

Listing 1: ./synthbio_script_01.m

0.6 dx.m

```
1  function [ dx ] = dx( k1, n, x, y )
2
3      dx = (k1./(1+(y.^n))) - x;
4
5  end
```

Listing 2: ./dx.m

0.7 dy.m

```
1  function [ dy ] = dy( k2, x, y )
2
3      dy = (k2./(1+x))-y;
4
5  end
```

Listing 3: ./dy.m

0.8 nx.m

```
1
2  function [ y ] = nx( k1, n, x )
3
4      y = nthroot((k1-x)./x, n);
5
6  end
```

Listing 4: ./nx.m

0.9 ny.m

```matlab
function [ y ] = ny( x, k2 )

    y = k2./(1+x);

end
```

Listing 5: ./ny.m

Bibliography

Joshua L Cherry and Frederick R Adler. How to make a biological switch. *Journal of Theoretical Biology*, 203(2):117 – 133, 2000. ISSN 0022-5193. doi: 10.1006/jtbi.2000.1068. URL http://www.sciencedirect.com/science/article/pii/S0022519300910683.