Prelim ChemE 7770 ty369 $S|u|>0$

1. Convert $\langle n \rangle$ to $B = \langle m_c \rangle \hat{N}_c V$

a) $\hat{N}_c = 1 \times 10^8$ cells/mL $\quad \frac{gDW}{cell}$ $\quad 1\,mM = 1000 \frac{nmol}{mL}$

$\mu = \ln 2 / t_d$ doubling time

growth rate $\frac{1}{hr}$

Avg mass of an E. coli cell = 1 pg/cell. From online $\langle m_c \rangle$ (average) for E. coli $= 3 \times 10^{-13}$ gDW/cell

$$\langle n \rangle \left[\frac{\#\,copy}{cell}\right] / \left(\hat{N}_c \left[\frac{cells}{mL}\right] \cdot V[mL]\right) \cdot 1000 \left[\frac{nt}{copy}\right] \cdot \frac{1}{6.02\times10^{23}} \left[\frac{mol}{nt}\right] \cdot \frac{1}{3\times10^{-13}} \left[\frac{cell}{gDW}\right] \quad [=] \quad \frac{mol}{gDW} \text{ per cell}$$

e.g. $\langle n \rangle = 19$: Assume 1 mL

$$19 \frac{mRNA}{cell} \cdot 1\times10^{8} \frac{mL}{cell} \cdot \frac{1}{1\,mL} \cdot \frac{1}{6.02\times10^{23}} \frac{mol}{mRNA} \cdot \frac{1}{3\times10^{13}} \frac{cell}{gDW} = 1.05\times10^{-9} \frac{nmol}{gDW} \text{ per cell}$$

or $\quad B = 3\times10^{-13} \frac{gDW}{cell} \cdot 1\times10^{8} \frac{cells}{mL} \cdot 1\,mL = 3\times10^{-5}\,gDW$

$\langle n \rangle$ to mol: $\quad 19 \frac{mRNA}{cell} \cdot \frac{1}{6.02\times10^{23}} \frac{mol}{mRNA} \cdot \frac{10^9\,nmol}{1\,mol} = 3.156\times10^{-14} \frac{nmol}{cell}$

$$\frac{\langle n \rangle}{B} = \frac{3.156\times10^{-14} \frac{nmol}{cell}}{3\times10^{-5}\,gDW} = 1.05\times10^{-9} \frac{nmol}{gDW}/cell$$

Similarly the rest of the convert shows in matlab.

get converted values for each $\langle n \rangle$: 1.052×10^{-9}, 1.163×10^{-9}, 2.27×10^{-9}, 3.710×10^{-9}, 4.762×10^{-9}, 5.15×10^{-9}, 5.150×10^{-9}

$\left[\frac{nmol}{gDW}\right]$ per cell

1b. Derive gain for k_x

$$\dot{m}_i = r_{x,i}\bar{u}_i - (\mu + \theta_{m,i}) m_i$$

pseudo S.S. $\dot{m}_i = 0$: $\quad 0 = r_{xi}\bar{u}_i - (\mu + \theta_{m,i}) m_i^*$

$$m_i^* = \frac{r_{xi}\bar{u}_i}{\mu + \theta_{mi}} = \underbrace{\frac{r_{xi}}{\mu + \theta_{mi}}}_{k_x(g,\theta)} \cdot \underbrace{\bar{u}_i}_{\bar{u}(I,K)}$$

$$\therefore k_x = \frac{r_{xi}}{\mu + \theta_{mi}}$$

From lecture $\quad r_x = k_E R_{rt} \left(\frac{g}{\tau_{x,i} k_{x,i} + (\tau_{x,i}+1) g}\right)$

$\rightarrow k_x = f(g, \theta_i)$ (constant)

$$\bar{u} = \frac{w_1 + w_2 F_I}{1 + w_1 + w_2 f_I}, \quad f_I = \frac{I^n}{K^n + I^n} \quad \text{(Hill)}$$

$\rightarrow \bar{u} = f(I, K)$ (constant)

R, θ constant

1c) estimate $k_x(g,k)$ & $u(I,\theta)$

$$k_x = \frac{r_{x,i}}{u+\theta_{mi}}$$ → nmol/gDW·hr

$u+\theta_{mi}$ → dilution & degradation.

m_i^* → concentration of mRNA nmol/gDW

$\bar{u}$ → dimensionless.

$$m_i^* = \frac{r_{xi}}{u+\theta_{mi}} \cdot \bar{u}_i$$

In lecture $$u(I) = \frac{w_1 + w_2 f_I}{H w_1 + w_2 f_I}$$

$$f_I = \frac{I^n}{k^n + I^n}.$$

Using Excel Solver for Data fitting, get estimates data:

$w_1 = 0.2$

$w_2 = 5000$

$k = 9$

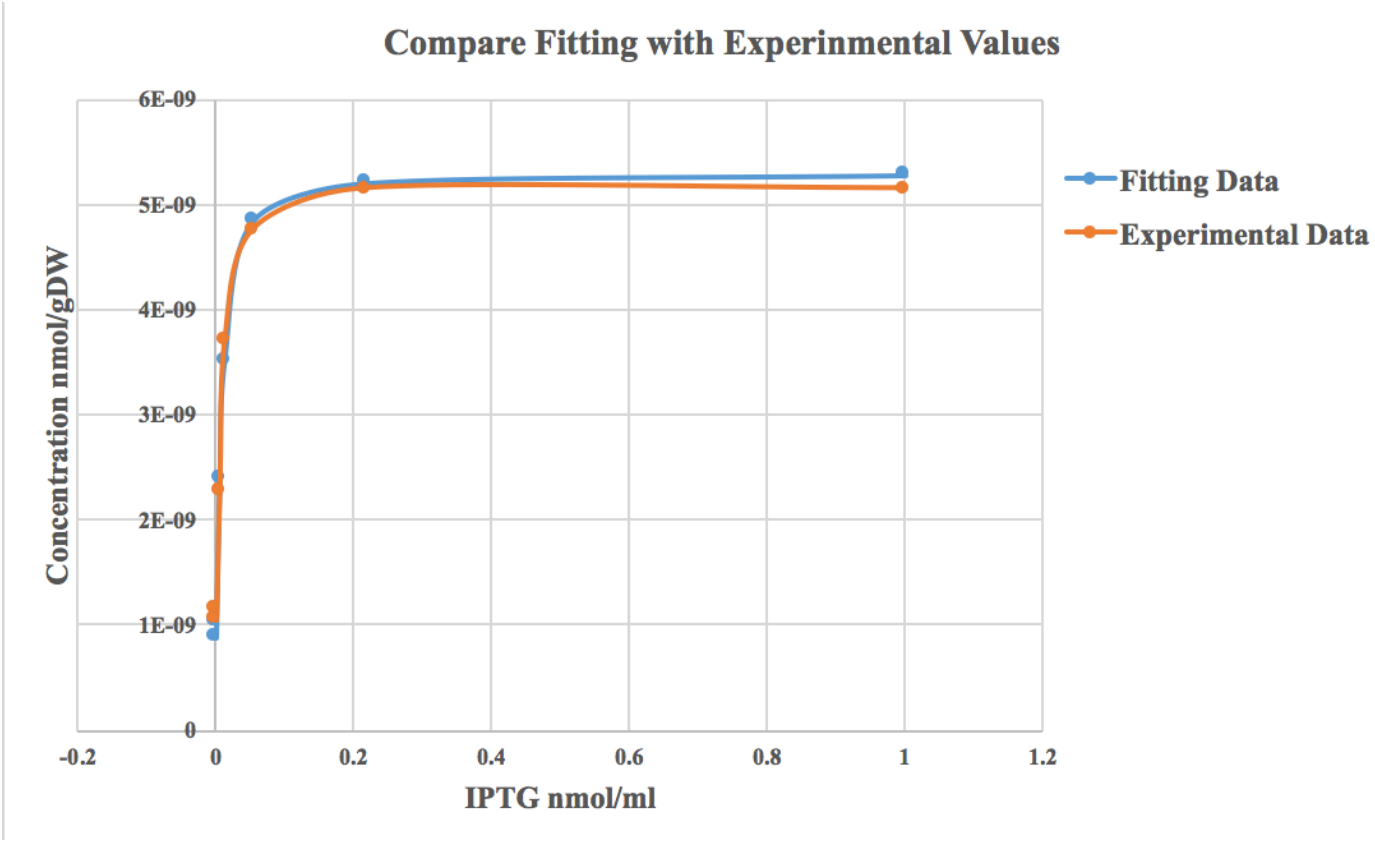
$k_x = 5.3 \times 10^{-9}$

$n = 1.2$

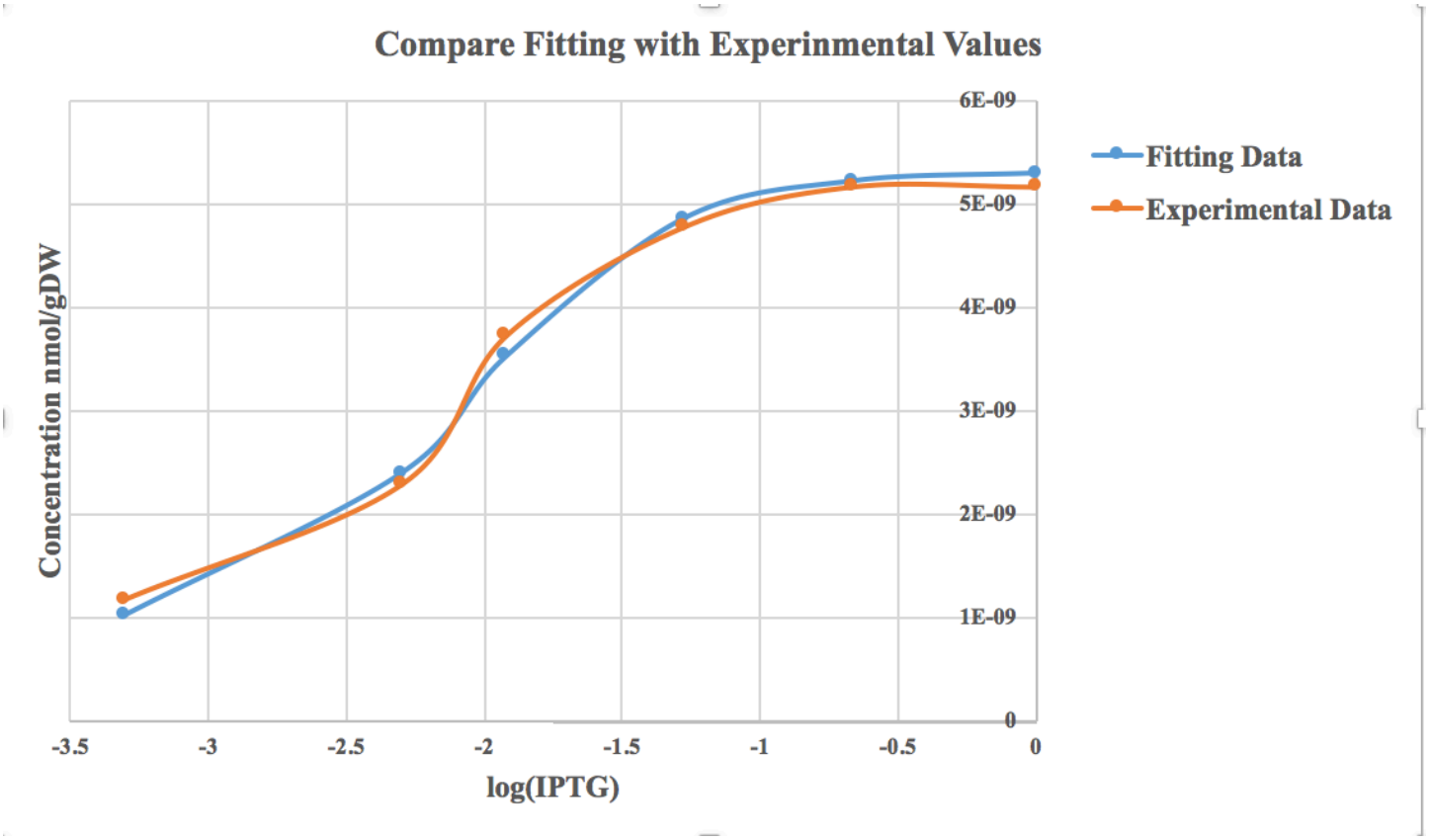
From Excel, it shows that the above parameter provide a fitting curve that make m^* consistent with the measured copy # as a function of IPTG concentration.

d). on the semilogx plot, it still shows the two set of data align. I consider the model is fair to estimate the concentration of m^* as a function of IPTG concentration

1d


Compare Fitting with Experinmental Values
Concentration nmol/gDW
6E-09
5E-09
4E-09
3E-09
2E-09
1E-09
0
-0.2
0
0.2
0.4
0.6
0.8
1
1.2
IPTG nmol/ml
Fitting Data
Experimental Data

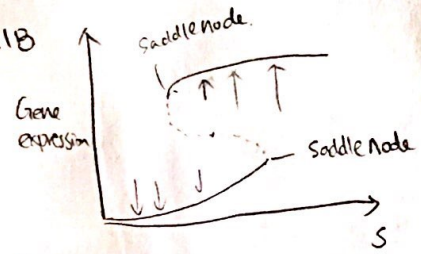
1d Semilogx Plot



2. AC-DC

a).

Fig.1B



for bistable switch

$$\frac{d\tilde{x}}{d\tilde{t}} = \frac{\tilde{\alpha}_x + \tilde{\beta}_x S}{1 + S + (\tilde{z}/\tilde{z}_x)^{n_{zx}}} - \tilde{\delta}_x \tilde{x} \quad (1)$$

$$\frac{d\tilde{z}}{d\tilde{t}} = \frac{\tilde{\alpha}_z}{1 + (\tilde{x}/\tilde{x}_z)^{n_{xz}}} - \tilde{\delta}_z \tilde{z} \quad (2)$$

where: $\tilde{x}$, $\tilde{z}$ are concentration of x, z protein

$\tilde{\alpha}_x$, $\tilde{\alpha}_z$ are production rate of x, z (basal production rate)

S is signal induced.

$\tilde{\beta}_x$ Production rate of S.

$\tilde{\delta}_x$ & $\tilde{\delta}_z$ are degradation rate of x & z

b). Eq.[3]-[6] from paper: $\delta_z = \frac{\tilde{\delta}_z}{\tilde{\delta}_x}$; $t = \tilde{t}\tilde{\delta}_x$; ↗ it should be $\tilde{\delta}_x$ instead of δ_x

$$\alpha_x = \frac{\tilde{\alpha}_x}{\tilde{\alpha}_z}, \quad \beta_x = \frac{\tilde{\beta}_x}{\tilde{\alpha}_z} ; \quad z_x = \frac{\tilde{z}_x \tilde{\delta}_x}{\tilde{\alpha}_z}, \quad x_y = \frac{\tilde{x}_y \tilde{\delta}_x}{\tilde{\alpha}_z}, \quad x_z = \frac{\tilde{x}_z \tilde{\delta}_x}{\tilde{\alpha}_z}$$

$$x = \frac{\tilde{x}\tilde{\delta}_x}{\tilde{\alpha}_z}, \quad z = \frac{\tilde{z}\tilde{\delta}_x}{\tilde{\alpha}_z}$$

Plug in ① ② in (2a)

→

2b. cont

①

$$\frac{d\hat{x}}{dt} = \frac{d(x\hat{\alpha}_z)\hat{\delta}_x}{\hat{\delta}_x\, dt} = \frac{\alpha_x \cdot \hat{\alpha}_z + \beta_x \hat{\alpha}_z S}{1 + S + \left(\frac{\hat{\alpha}_z \cdot z}{\hat{\delta}_x} \cdot \frac{\hat{\delta}_x}{z_x \hat{\alpha}_z}\right)^{n_{zx}}} - \frac{\hat{\delta}_x X \cdot \hat{\alpha}_z}{\hat{\delta}_x}$$

$$= \hat{\alpha}_z \frac{dx}{dt} = \frac{\hat{\alpha}_z(\alpha_x + \beta_x S)}{1 + S + \left(\frac{z}{z_x}\right)^{n_{zx}}} - \hat{\alpha}_z X$$

$$\Rightarrow \boxed{\frac{dx}{dt} = \frac{\alpha_x + \beta_x S}{1 + S + (z/z_x)^{n_{zx}}} - X ;}$$

similarly ② becomes: $\boxed{\frac{dz}{dt} = \frac{1}{1 + (x/x_z)^{n_{xz}}} - \delta_z z}$

c). Given $\alpha_x = 1.5$, $\beta_x = 5.0$, $z_x = 0.4$, $n_{zx} = 2.7$, $x_z = 1.5$, $n_{xz} = 2.7$, δ_z pick 1.0.

See matlab plots

the stable steady state part seems match the diagram in Fig 1B

d) See matlab codes for plots.

e). stable S.S, below Hopf

① I would select $S = 0.7$ S.S. of x, y, z are: $x_s = 0.0036$, $y_s = 2.015$, $z_s = 0.0029$

(See matlab for plots.)

cell 1 at S.S

cell 2 25% higher than S.S.

cell 3 25% lower than S.S.

the oscillation is incoherent for the change of S from 0.7 → 100

② S above the sadde node $S = 1010$ S.S. of x, y, z are:

Xs=2.9908
Ys=0.96595
Zs=0.01412

The oscillation is coherent for this case, (S from 1010 → 100) b/c the peaks can align each other for the 3 cells.

-c).

at S.S. $\frac{dx}{dt} = 0$, $\frac{dz}{dt} = 0$.

$$\frac{\alpha_x + \beta_x S}{1 + S + \left(\frac{z}{z_x}\right)^{n_{zx}}} - X = 0$$

$$\frac{1}{1 + \left(\frac{x}{x_z}\right)^{n_{xz}}} - \delta_z z = 0.$$

plug in $\alpha_x = 1.5$, $\beta_x = 5.0$, $z_x = 0.4$

$n_{zx} = 2.7$. $x_z = 1.5$ $n_{xz} = 2.7$

$\delta_z = 1.04$

$$\frac{1.5X + 5S}{1 + S + \left(\frac{z}{0.4}\right)^{2.7}} - X = 0 \quad ①$$

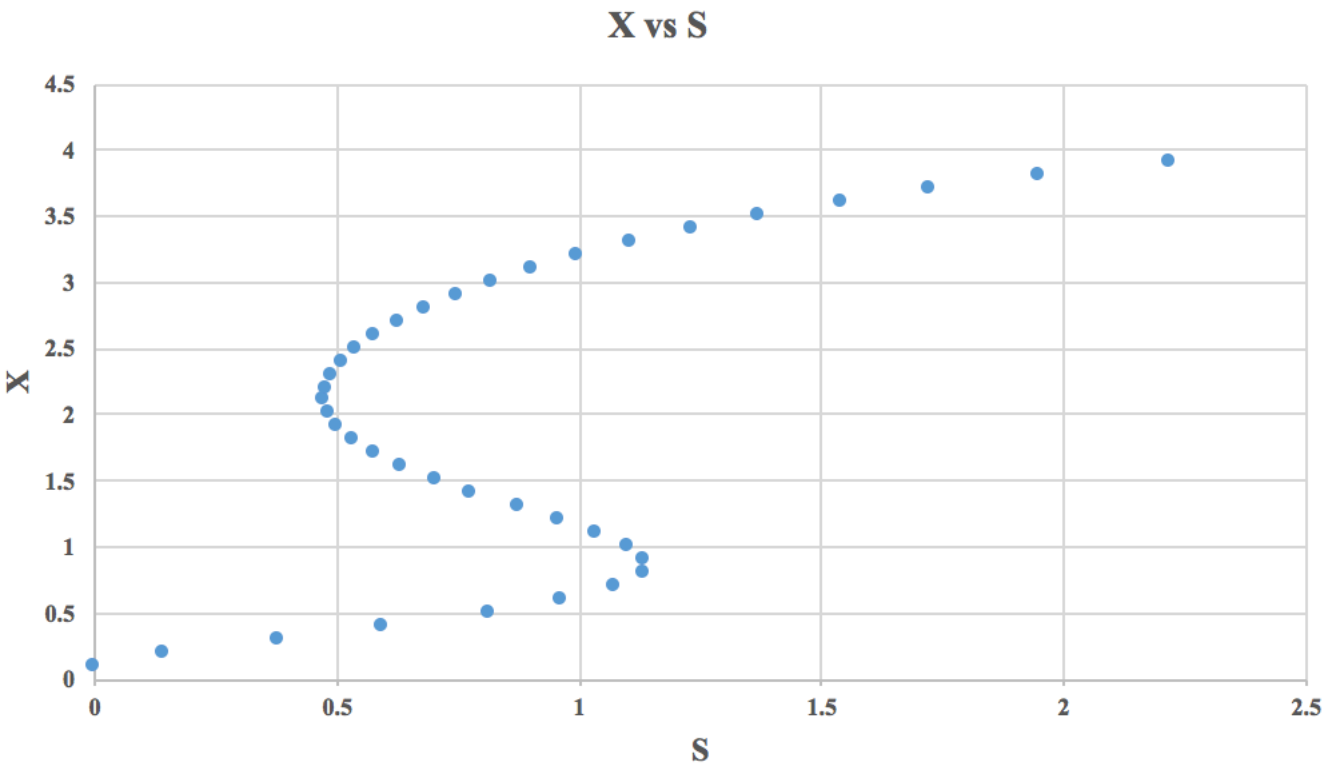
$$\frac{1}{1 + \left(\frac{x}{1.5}\right)^{2.7}} - 1.04\, z = 0. \quad ② \qquad z = \frac{1}{1.04\left(1 + \left(\frac{x}{1.5}\right)^{2.7}\right)}$$

11. plug ② in ①.

$$\frac{1.5 + 5S}{1 + S + \frac{1}{\left(0.4 \cdot 1.04\left(1 + \left(\frac{x}{1.5}\right)^{2.7}\right)\right)^{2.7}}} - X = 0.$$

Find X, S show on Excel on solver,

2c Plot, details in Excel sheet



The solid black lines in fig.1 are qualitatively reproducible. Details see Excel Sheet.

$x_1 = 1.5$, $x_2 = 1.5$

2 e). (un4

(1)

"Small initial diff. are amplified, resulting in lack of coherence of oscillations for a population of cells undergoing the bifurcation

- on contrast, cells pass thru the saddle-node bifurcation toward the limit cycle do so at expression levels that are far from those associated with the attractive oscillatory regime. They have the same initial phase, and stochastic trajectories are canalized together toward the oscillatory state.

f). No. See matlab plots. the peaks are not aligned.

doesn't show coherent result from 105 → 100.

Table of Contents

ChemE 7770 Prelim

```
clear all; close all; clc;
```

1a).

```
n=[19 21 41 67 86 93 93];
m=3*1e-13;%gDW/cell
Nc=1e8;%cells/ml
V=1; % assume 1ml
B=m.*Nc.*V;
nmol=n.*(6.02.*1e23).^(-1).*1e9;
convert=nmol./B;
display(convert)
```

```
convert =

   1.0e-08 *

    0.1052    0.1163    0.2270    0.3710    0.4762    0.5150    0.5150
```

2a 2b See hand-written part

2c

```
clear all;
tspan=linspace(0,30,50);
Y0=[10e-4 10e-4];
Sarray=linspace(10e-2,3.5);
% Increase S to a large number but still have the same trend, so I
 pick 3.5
% to enable zoom in at the region.
for i=1:length(Sarray)
    S=Sarray(i);
```

```
[t,Y]=ode45(@(t,Y)ACDC(t,Y,S),tspan,Y0);
A(:,i)=Y(:,1);
B(:,i)=Y(:,2);
end

% figure (1)
% subplot(2,1,1)
% for j=1:size(A,1)
% plot(t,A(:,j));
% hold on
% title('2c. X vs Time');
% xlabel('Time, t');
% ylabel('X');
% end
% subplot(2,1,2)
% for j=1:size(A,1)
% plot(Sarray,A(j,:),'.');
% hold on
% title('2c. X vs S');
% xlabel('S');
% ylabel('X');
% end

% figure(2)
% plot(Sarray, A(size(A,1),:),'.');
% title('2c. X vs Time at S=3.5');
% xlabel('Time, t');
% ylabel('X');

fprintf('Matlab seems cannot show the swist part in between, I then
 use Excel to plot the middle parts.');
```

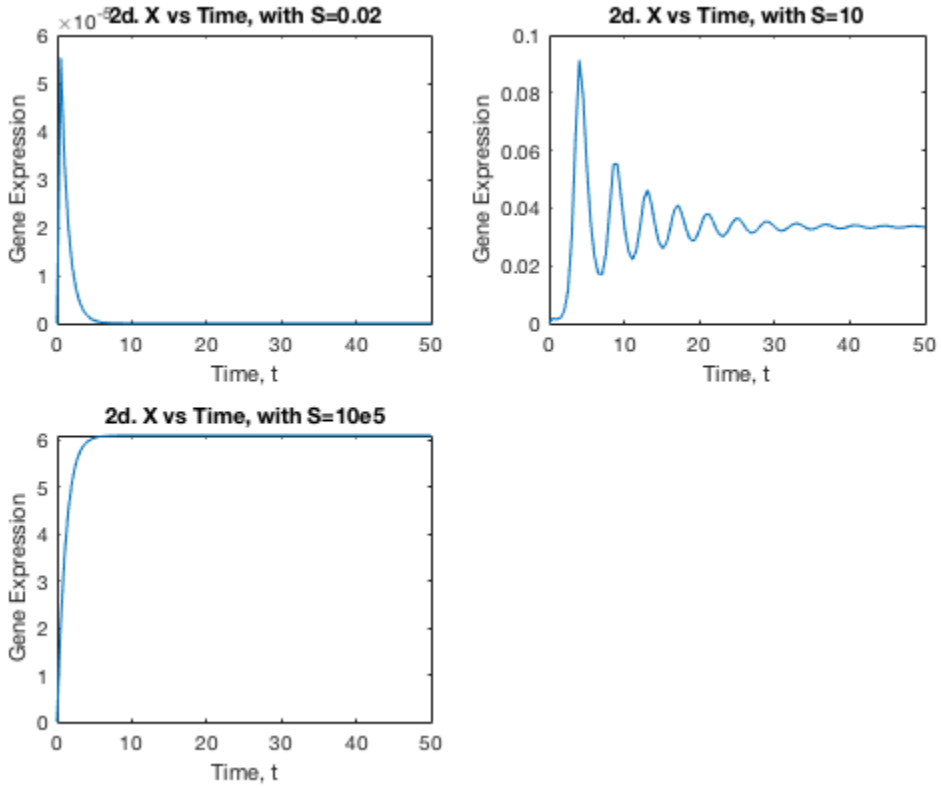
```
Matlab seems cannot show the swist part in between, I then use Excel
 to plot the middle parts.
```

2d

```
clear all;
tspan=linspace(0,50);
Y0=[0 0 0];
Sarray=[0.02 10 10e5];
for i=1:length(Sarray)
    S=Sarray(i);
[t,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan,Y0);
A(:,i)=Y(:,1);
B(:,i)=Y(:,2);
C(:,i)=Y(:,3);
end
% For X Y Z at different S, we can plot:
% plot(t,A(:,1),t,B(:,1),t,C(:,1))--> S=0.02;
% plot(t,A(:,2),t,B(:,2),t,C(:,2))--> S=10;
% plot(t,A(:,3),t,B(:,3),t,C(:,3))--> S=10e5;
```

```
figure (3)
subplot(2,2,1)
plot(t,A(:,1))
title('2d. X vs Time, with S=0.02');
xlabel('Time, t');
ylabel('Gene Expression');
subplot(2,2,2)
plot(t,A(:,2));
title('2d. X vs Time, with S=10');
xlabel('Time, t');
ylabel('Gene Expression');
subplot(2,2,3)
plot(t,A(:,3));
title('2d. X vs Time, with S=10e5');
xlabel('Time, t');
ylabel('Gene Expression');
disp('From the plots, it seems like the values approx. matches the
 value shown in Fig.2');
```

From the plots, it seems like the values approx. matches the value shown in Fig.2

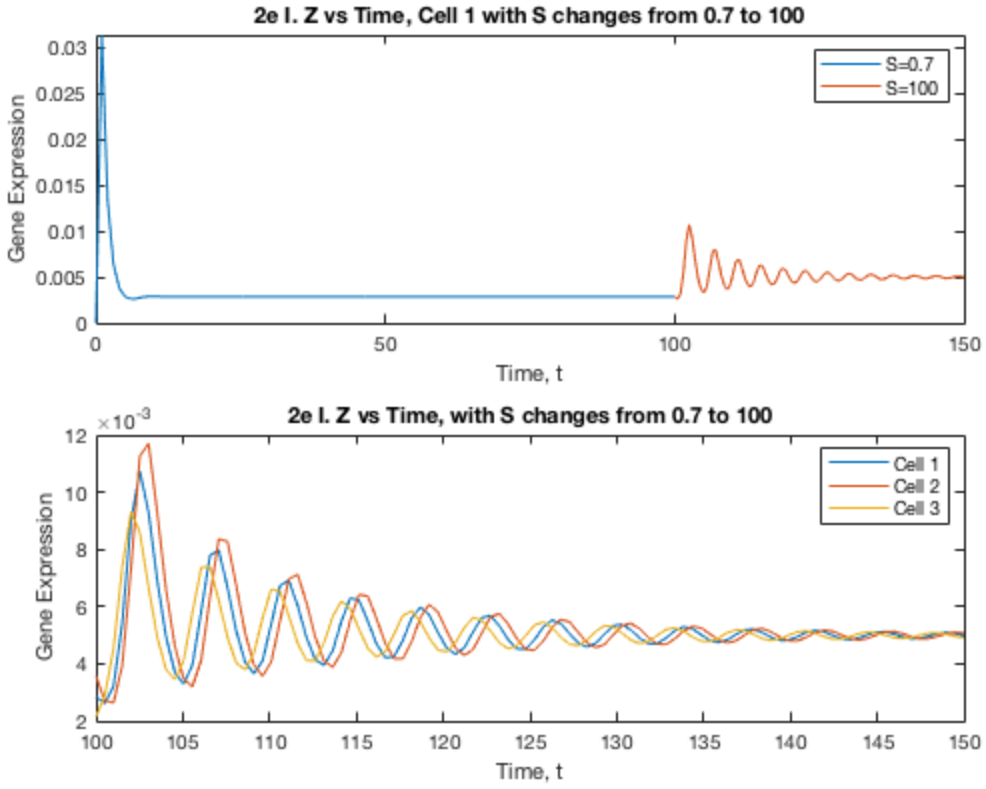


2e) I. S: 0.7-->100

```
clear all;
tspan=linspace(0,100);
```

```
tspan2=linspace(100,150);
Y0=[0 0 0];
S=0.7;
[t,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan,Y0);
A=Y;
S=100;
Y01=[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y01);
B=Y;
Y02=1.25.*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y02);
C=Y;
Y03=(1-0.25).*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y03);
D=Y;
s=['S=0.7, steady state values for X Y Z: ',num2str(Y01)];
disp(s);

figure (4) % Plot of Z vs time with S change to 100
subplot(2,1,1)
plot(t,A(:,3),t2,B(:,3));
title('2e I. Z vs Time, Cell 1 with S changes from 0.7 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('S=0.7','S=100');

subplot(2,1,2)
plot(t2,B(:,3),t2,C(:,3),t2,D(:,3));
title('2e I. Z vs Time, with S changes from 0.7 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('Cell 1','Cell 2','Cell 3');
```

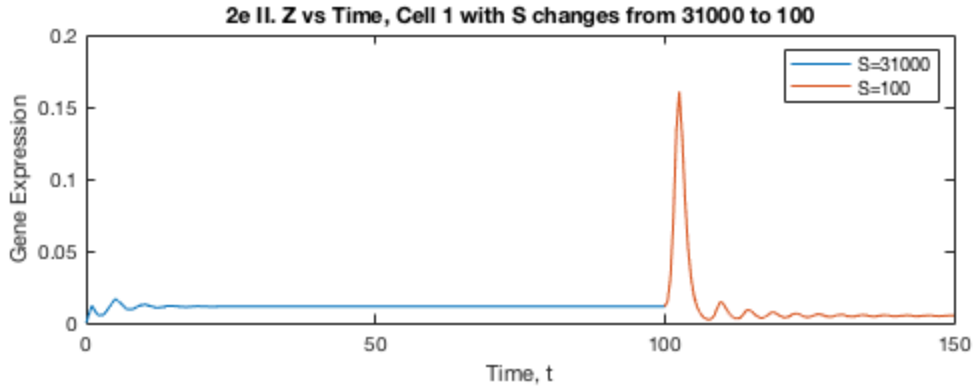
```
S=0.7, steady state values for X Y Z: 0.0035866      2.0152
 0.0028568
```

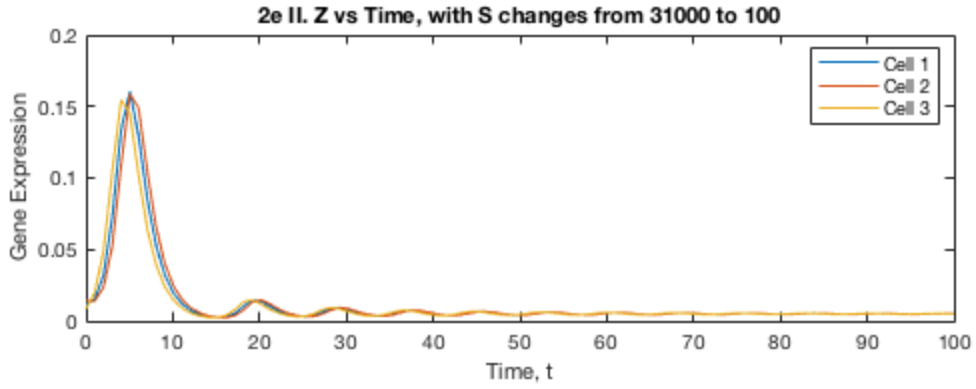


2e II. S: 31000-->100

```
clear all;
tspan=linspace(0,100);
tspan2=linspace(100,150);
Y0=[0 0 0];
S=31000;
[t,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan,Y0);
A=Y;
S=100;
Y01=[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y01);
B=Y;
Y02=1.25.*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y02);
C=Y;
Y03=(1-0.25).*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y03);
D=Y;
s=['S=31000, steady state values for X Y Z: ',num2str(Y01)];
disp(s);

figure (6)
subplot(2,1,1)
plot(t,A(:,3),t2,B(:,3));
```

```
title('2e II. Z vs Time, Cell 1 with S changes from 31000 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('S=31000','S=100');

subplot(2,1,2)
plot(t,B(:,3),t,C(:,3),t,D(:,3));
title('2e II. Z vs Time, with S changes from 31000 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('Cell 1','Cell 2','Cell 3');

% Explanation from the paper: "This difference in behavior is a
 consequence of the different
% initial gene expression states in relation to oscillatory spiral
 center. In a Hopf bifurcation,
% oscillations arise through an attracting spiral losing its stability
 and becoming a repulsing spiral.
% Hence, oscillations originating from a Hopf bifurcation start their
 transient close to the unstable
% spiral center, and a small variation in the initial condition can
 lead to a substantial difference in the
% final oscillation phase. Small initial differences are amplified,
 resulting in lack of coherence of
% oscillations for a population of cells undergoing the bifurcation.
 By contrast, cells passing
% through the saddle-node bifurcation toward the limit cycle do so at
 expression levels that are far from
% those associated with the attracting oscillatory regime.
 Consequently, they have the
% same initial phase, and stochastic trajectories are canalized
 together toward the oscillatory state."

S=31000, steady state values for X Y Z: 2.9908     0.96595     0.011412
```



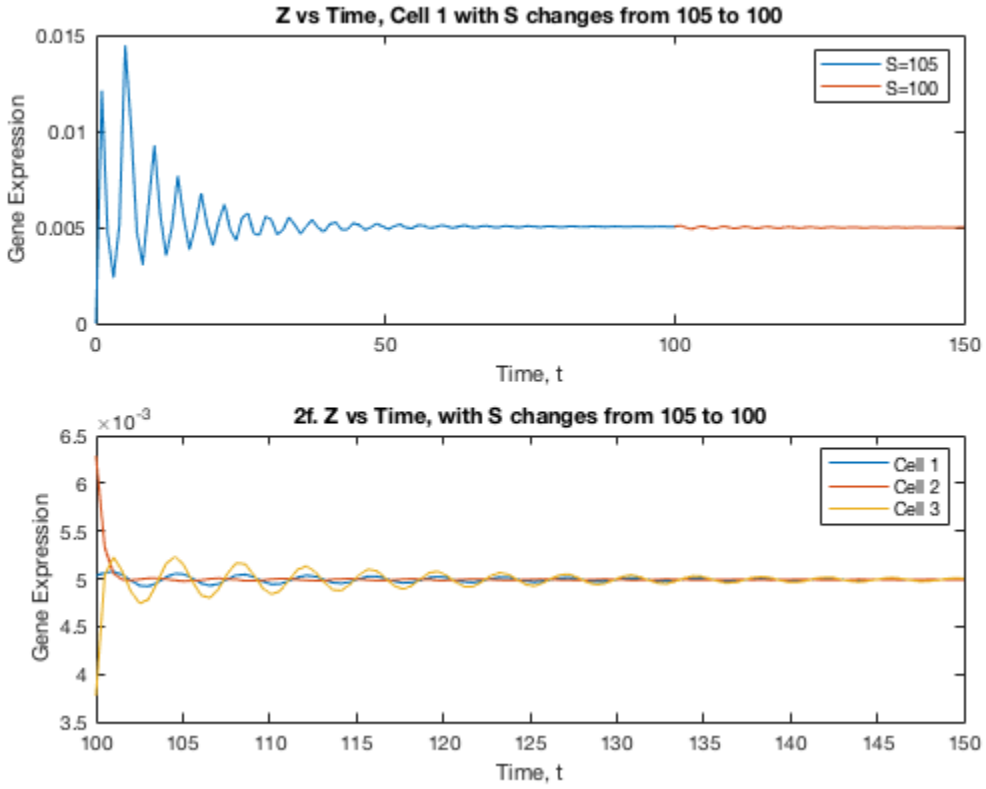


2f

```
clear all;
tspan=linspace(0,100);
Y0=[0 0 0];
%Sarray=[0.7 100 31000];
tspan2=linspace(100,150);
S=105;
[t,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan,Y0);
A=Y;
S=100;
Y01=[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y01);
B=Y;
Y02=1.25.*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y02);
C=Y;
Y03=(1-0.25).*[A(end,1) A(end,2) A(end,3)];
[t2,Y]=ode45(@(t,Y)ACDC2(t,Y,S),tspan2,Y03);
D=Y;
s=['S=105, steady state values for X Y Z: ',num2str(Y01)];
disp(s);

figure (6)
subplot(2,1,1)
```

```
plot(t,A(:,3),t2,B(:,3));
title('Z vs Time, Cell 1 with S changes from 105 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('S=105','S=100');

subplot(2,1,2)
plot(t2,B(:,3),t2,C(:,3),t2,D(:,3));
title('2f. Z vs Time, with S changes from 105 to 100');
xlabel('Time, t');
ylabel('Gene Expression');
legend('Cell 1','Cell 2','Cell 3');
```

S=105, steady state values for X Y Z: 0.13 1.5143 0.0050305



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