Homework-4

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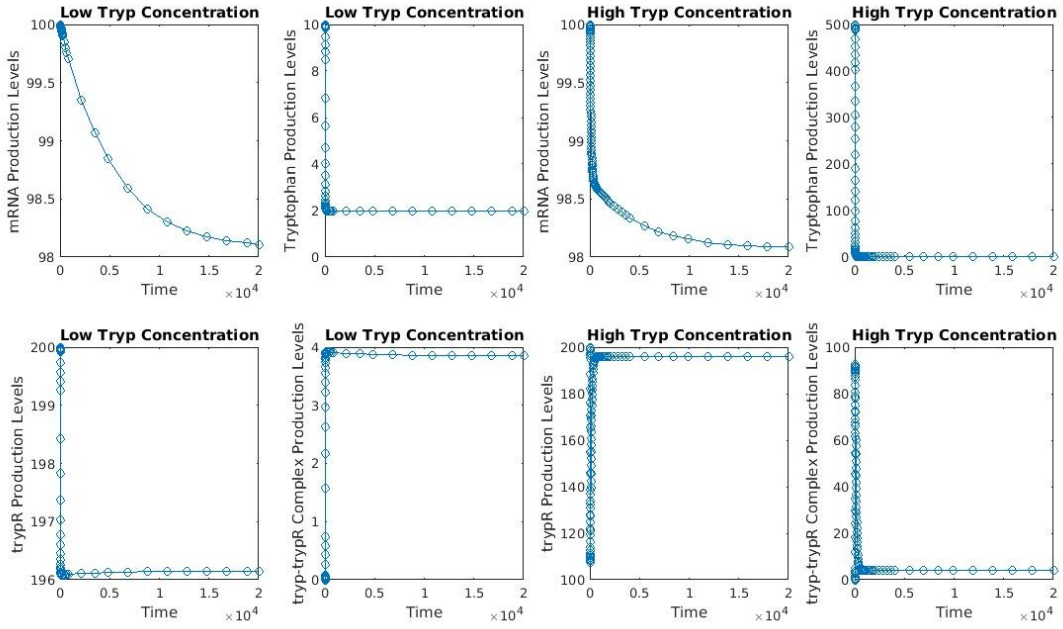
1.Answer-a) Matlab Code for tryptophan production ignoring feedback regulation through tryp-trypR binding:

```
% ODE for tryptophan production ignoring feedback regulation
function [t,y] = tryptophan()
    tspan = [0 20000];                                          % set time interval
    y1_0 = 100;                                                 % set mRNA initial concentration (in nM)
    y2_0 = 10;                                                  % set low initial tryptophan concentration = 10 nM
    y3_0 = 200;                                                 % set trypR initial concentration (in nM)
    y4_0 = 0;                                                   % set tryp-trypR initial concentration (in nM)
    [t,y] = ode15s( @tryptophan ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

    subplot(2, 4, 1);
    plot(t, y(:,1), '-o');
    xlabel('Time');
    ylabel('mRNA Production Levels');
    title('Low Tryp Concentration');
    subplot(2, 4, 2);
    plot(t, y(:,2), '-o');
    xlabel('Time');
    ylabel('Tryptophan Production Levels');
    title('Low Tryp Concentration');
    subplot(2, 4, 5);
    plot(t, y(:,3), '-o');
    xlabel('Time');
    ylabel('trypR Production Levels');
    title('Low Tryp Concentration');
    subplot(2, 4, 6);
    plot(t, y(:,4), '-o');
    xlabel('Time');
    ylabel('tryp-trypR Complex Production Levels');
    title('Low Tryp Concentration');

    S = 'Tryptophan Production Levels When Tryptophan Concentration Is Low (=10 nM)';
    disp(S);
    S1 = '       Time    Tryptophan Concentration (in nM)';
    disp(S1);
    disp([t, y(:,2)]);                                          % displays t and y(t)

    y2_0 = 500;                                                 % set high initial tryptophan concentration = 10 nM
    [t,y] = ode15s( @tryptophan ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

    subplot(2, 4, 3);
    plot(t, y(:,1), '-o');
    xlabel('Time');
    ylabel('mRNA Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 4);
    plot(t, y(:,2), '-o');
    xlabel('Time');
    ylabel('Tryptophan Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 7);
    plot(t, y(:,3), '-o');
    xlabel('Time');
    ylabel('trypR Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 8);
    plot(t, y(:,4), '-o');
```

```
    xlabel('Time');
    ylabel('tryp-trypR Complex Production Levels');
    title('High Tryp Concentration');

    S = 'Tryptophan Production Levels When Tryptophan Concentration Is High (=500 nM)';
    disp(S);
    S1 = '       Time    Tryptophan Concentration (in nM)';
    disp(S1);
    disp([t, y(:,2)]);                                          % displays t and y(t)
        function dydt = tryptophan(t,y)
            dydt = zeros(4,1); % a column vector
            Ks = 1e-2;                                         % gene transcription rate
            Kd = 2e-4;                                          % mRNA degradation rate
            alpha = 1e-3;                                       % tryp production effective kinetic constant
            Kloss = 5e-2;                                      % tryptophan loss (protein production / degradation ....)
            Kon = 1e-4;                                         % tryp-trypR binding
            Koff = 1e-2;                                       % tryp-trypR dissociation
            Ng = 2;

            dydt(1) = Ks*Ng*(1-y(4)/200) - Kd*y(1);            % y(1) --> mRNA
            dydt(2) = alpha*y(1) - Kloss*y(2);                 % y(2) --> tryptophan (tryp)
            dydt(3) = -Kon*y(2)*y(3) + Koff*y(4);              % y(3) --> trypR (repressor)
            dydt(4) = Kon*y(2)*y(3) - Koff*y(4);               % y(4) --> tryp-trypR complex
        end
end
```

Figure-1

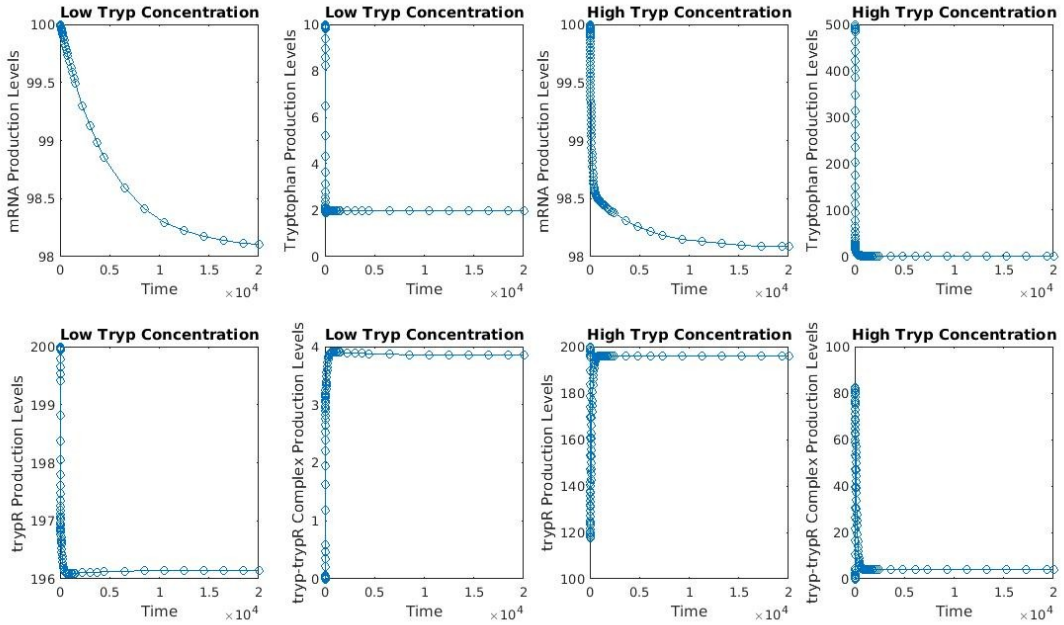


1.Answer-b) Matlab Code for tryptophan production including feedback regulation through tryp-trypR binding:

```
% ODE for tryptophan production with feedback regulation
function [t,y] = tryptophan1()
    tspan = [0 20000];                                          % set time interval
    y1_0 = 100;                                                 % set mRNA initial concentration (in nM)
    y2_0 = 10;                                                  % set low initial tryptophan concentration = 10 nM
    y3_0 = 200;                                                 % set trypR initial concentration (in nM)
    y4_0 = 0;                                                   % set tryp-trypR initial concentration (in nM)
    [t,y] = ode15s( @tryptophan1 ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

    subplot(2, 4, 1);
    plot(t, y(:,1), '-o');
    xlabel('Time');
    ylabel('mRNA Production Levels');
    title('Low Tryp Concentration');
```

```
    subplot(2, 4, 2);
    plot(t, y(:,2), '-o');
    xlabel('Time');
    ylabel('Tryptophan Production Levels');
    title('Low Tryp Concentration');
    subplot(2, 4, 5);
    plot(t, y(:,3), '-o');
    xlabel('Time');
    ylabel('trypR Production Levels');
    title('Low Tryp Concentration');
    subplot(2, 4, 6);
    plot(t, y(:,4), '-o');
    xlabel('Time');
    ylabel('tryp-trypR Complex Production Levels');
    title('Low Tryp Concentration');

    S = 'Tryptophan Production Levels When Tryptophan Concentration Is Low (=10 nM)';
    disp(S);
    S1 = '       Time    Tryptophan Concentration (in nM)';
    disp(S1);
    disp([t, y(:,2)]);                                          % displays t and y(t)

    y2_0 = 500;                                                  % set low initial tryptophan concentration = 10 nM
    [t,y] = ode15s( @tryptophan1 ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

    subplot(2, 4, 3);
    plot(t, y(:,1), '-o');
    xlabel('Time');
    ylabel('mRNA Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 4);
    plot(t, y(:,2), '-o');
    xlabel('Time');
    ylabel('Tryptophan Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 7);
    plot(t, y(:,3), '-o');
    xlabel('Time');
    ylabel('trypR Production Levels');
    title('High Tryp Concentration');
    subplot(2, 4, 8);
    plot(t, y(:,4), '-o');
    xlabel('Time');
    ylabel('tryp-trypR Complex Production Levels');
    title('High Tryp Concentration');

    S = 'Tryptophan Production Levels When Tryptophan Concentration Is High (=500 nM)';
    disp(S);
    S1 = '       Time    Tryptophan Concentration (in nM)';
    disp(S1);
    disp([t, y(:,2)]);                                          % displays t and y(t)
        function dydt = tryptophan1(t,y)
            dydt = zeros(4,1);                                   % a column vector
            Ks = 1e-2;                                           % gene transcription rate
            Kd = 2e-4;                                           % mRNA degradation rate
            alpha = 1e-3;                                        % tryp production effective kinetic constant
            kloss = 5e-2;                                        % tryptophan loss (protein production /
degradation ....)
            Kon = 1e-4;                                          % tryp-trypR binding
            Koff = 1e-2;                                         % tryp-trypR dissociation
            Ng = 2;

            dydt(1) = Ks*Ng*(1-y(4)/200) - Kd*y(1);              % y(1) --> mRNA
            dydt(2) = alpha*y(1) - kloss*y(2) - Kon*y(2)*y(3) + Koff*y(4);   % y(2) --> tryptophan (tryp)
            dydt(3) = (-Kon)*y(2)*y(3) + Koff*y(4);              % y(3) --> trypR (repressor)
            dydt(4) = Kon*y(2)*y(3) - Koff*y(4);                 % y(4) --> tryp-trypR complex
        end
end
```

Figure-2



Biological significance of the gene regulatory circuit (feedback regulation):
In Figure-2, the Tryptophan Concentration vs Time graphs for Low Tryptophan and High Tryptophan concentrations clearly show that when there is low tryp concentration, the cell proceeds to generate tryptophan in the medium with time. But when the tryp concentration is high (or when there is a rapid influx of tryptophan), the tryp concentration produced almost reaches zero, indicating that the cell has now stopped producing the tryptophan by initiating the feedback regulation process.

The significance of such a genetic-switch is that the cell has adapting abilities and can easily adapt to diverse environments, thus sustaining itself without any interference from any foreign matters that might affect its functioning.

Answer- (Challenge Problem)
Matlab Code for generating a plot for the mRNA production levels as a function of intracellular tryptophan level (to check if tryptophan operon functions as a genetic switch):

```
% mRNA production levels as a function of intracellular tryptophan level
function [t,y] = tryptophan2()
    tspan = [0 20000];                                          % set time interval
    y1_0 = 100;                                                 % set mRNA initial concentration (in nM)
    y2_0 = 10;                                                  % set low initial tryptophan concentration = 10 nM
    y3_0 = 200;                                                 % set trypR initial concentration (in nM)
    y4_0 = 0;                                                   % set tryp-trypR initial concentration (in nM)
    [t,y] = ode15s( @tryptophan2 ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

    subplot(2, 2, 1);
    plot(t, y(:,1), '-o');
    xlabel('Time');
    ylabel('mRNA Production Levels');
    title('Low Tryptophan Concentration');
    subplot(2, 2, 3);
    plot(y(:,2), y(:,1), '-o');
    xlabel('Tryptophan Production levels');
    ylabel('mRNA Production Levels');
    title('Low Tryptophan Concentration');
```

```
S = 'mRNA Production Levels When Tryptophan Concentration Is Low (=10 nM)';
disp(S);
S1 = '       Time  mRNA Concentration (in nM)';
disp(S1);
disp([t, y(:,1)]);                                          % displays t and y(t)

y2_0 = 500;                                                 % set low initial tryptophan concentration = 10 nM
[t,y] = ode15s( @tryptophan2 ,tspan ,[y1_0, y2_0, y3_0, y4_0]);  %tryptophan evaluates r.h.s. of the ode

subplot(2, 2, 2);
plot(t, y(:,1), '-o');
xlabel('Time');
ylabel('mRNA Production Levels');
title('High Tryptophan Concentration');
subplot(2, 2, 4);
plot(y(:,2), y(:,1), '-o');
xlabel('Tryptophan Production Levels');
ylabel('mRNA Production Levels');
title('High Tryptophan Concentration');

S = 'mRNA Production Levels When Tryptophan Concentration Is High (=500 nM)';
disp(S);
S1 = '       Time  mRNA Concentration (in nM)';
disp(S1);
disp([t, y(:,1)]);
    function dydt = tryptophan2(t,y)
        dydt = zeros(4,1);                                  % a column vector
        Ks = 1e-2;                                          % gene transcription rate
        Kd = 2e-4;                                          % mRNA degradation rate
        alpha = 1e-3;                                       % tryp production effective kinetic constant
        Kloss = 5e-2;                                       % tryptophan loss (protein production /
degradation ....)
        Kon = 1e-4;                                         % tryp-trypR binding
        Koff = 1e-2;                                        % tryp-trypR dissociation
        Ng = 2;

        dydt(1) = Ks*Ng*(1-y(4)/200) - Kd*y(1);             % y(1) --> mRNA
        dydt(2) = alpha*y(1) - Kloss*y(2) - Kon*y(2)*y(3) + Koff*y(4);   % y(2) --> tryptophan (tryp)
        dydt(3) = -Kon*y(2)*y(3) + Koff*y(4);               % y(3) --> trypR (repressor)
        dydt(4) = Kon*y(2)*y(3) - Koff*y(4);                % y(4) --> tryp-trypR complex
    end
end
```

Figure-3