MODELLERING AV DYNAMISKA SYSTEM

DATORSTÖDD RÄKNEÖVNING OCH INLUPP 3

1. **An introduction to modeling of bioreactors**
2. **Analysis and simulation of a Monod reactor**
3. **Analysis and simulation of a Haldane reactor**

Förberedelseuppgifter:
1. Läs igenom övningen noggrant.
1. Läs Kap 7.1-7.3 i kompendiet.
2. Lös teoriuppg (Exc P1-P3, P7, P10)

Namn	Handledarens kommentarer
Årskurs Inskrivningsår	
Utförd den	
Bonuspoäng Sign	

Innehåll

1   Introduction

In this laboratory work you will analyse and simulate two types of simple bioreactors. In the excercises you will apply concepts from the theory, for example, calculation of stationary values, linearization and phase portait.

2   An introduction to modeling of bioreactors

Below we will derive some simple models for bioreactors. Such models can help explain some fundamental properties of bioreactors and also give a suitable background for understanding more advanced models.

Bioreactors are used in many applications including industries concerned with food, beverages and pharmaceuticals. Another key application of bioreactors is in wastewater treatment. Biotechnology, which deals with the use of living organisms to manufacture valuable products, has had a long period of traditional fermentations (production of beer, wine, cheese etc.). The development of microbiology, around hundred years ago, expanded the use of bioreactors to produce primary metabolic products. In 1940's the large scale production of penicillin was a major breakthrough in biotechnology. Some 20 years ago, the computer technology started to make advanced process control possible. The development of genetic engineering have played a major role in creating the current progress in the field of biotechnology.

2.1   The specific growth rate

Many biochemical processes involves (batch) growth of microorganisms. In a batch process, microorganisms are added into a reactor containing substrate[1], one may (after some initial time delay) obtain an exponential growth phase (which may continue until the substrate is consumed).

Let $X(t)$ denote the concentration (mass/unit volume) of biomass (active microorganisms). An exponential growth can be expressed as

$$\frac{dX(t)}{dt} = \mu X \tag{2.1}$$

The parameter μ is denoted the *specific growth rate*, "rate of increase in cell concentration per unit cell concentration" ([1/time unit]).

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[1]Substrate is defined as the source of energy ("food"), it can be organic (for heterotrophic bacteria), inorganic (e.g. ammonia), or even light (for phototrophs).

2.1.1 The Monod function

Often the growth rate μ depends on the substrate concentration S. It is natural to assume that a low amount of substrate gives a low growth rate. If the substrate concentration increases the growth rate increases. For sufficiently high substrate levels though, the growth rate becomes saturated. The following empirical relation is often used and is commonly named the *Monod function*[2]

$$\mu(S) = \mu_{max} \frac{S}{K_S + S} \tag{2.2}$$

where

μ_{max} is the maximum specific growth rate
S is the concentration of substrate
K_S is the half saturation constant

The impact of the substrate concentration on the specific growth rate is shown in Figure 1.

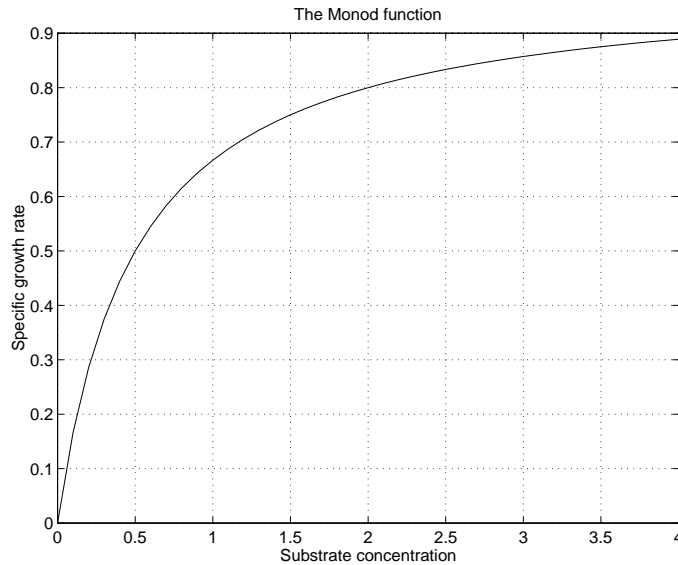
Figur 1: Illustration of the Monod function. The following parameters are used $K_S = 0.5$ and $\mu_{max} = 1$. Note that $S = K_S$ gives $\mu = 0.5\mu_{max}$.

2.1.2 The Haldane function

Some substrates have an inhibitory effect at high concentrations. That means that the growth rate starts to decrease if the substrate concentration becomes too high. The Monod function (2.2) does not account for any inhibitory effects. Substrate inhibition may be modeled by the *Haldane* law

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[2]It was initially proposed by Michaelis-Menton in 1913 (the relation is therefore also often called Michaelis-Menton law) and extended by Monod in 1942 to describe growth of microorganisms.

$$\mu(S) = \mu_o \frac{S}{K_1 + S + S^2/K_h} \tag{2.3}$$

The Haldane law will make $\mu(S)$ to decrease when S is sufficiently large due to the S^2 term in the denominator. It is seen that $\mu(S) \to 0$ as $S \to \infty$. The exact shape of the function is determined by the parameters μ_o, K_1, and K_h.

2.1.3   The Yield coefficient

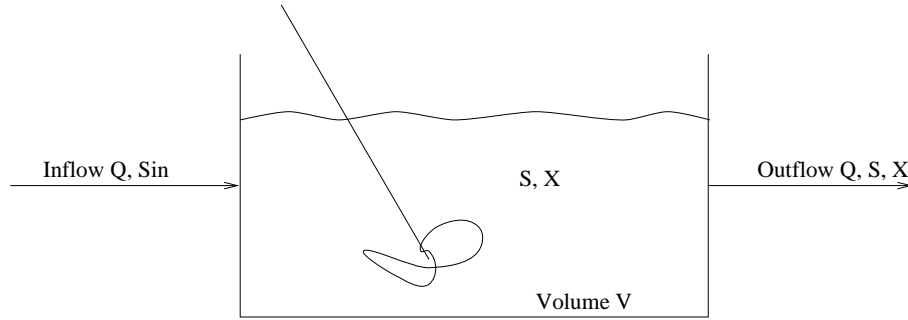As the microorganisms growth, substrate is used. This is commonly expressed as:

$$\frac{dX}{dt} = -Y\frac{dS}{dt} \tag{2.4}$$

where Y is the *yield coefficient* (utbyteskonstant), "the ratio of the mass of cells formed to the mass of substrate consumed". The yield coefficient can be expressed as

$$Y = -\frac{dX}{dS} \tag{2.5}$$

2.2   Microbial growth in a stirred tank reactor

We will consider the dynamics of a completely mixed tank reactor shown in Figure 2. See also example 2.1 in "Modellering av Dynamiska system". The influent flow rate Q [volume/time] is equal to the effluent (output) flow rate. Hence, the volume V is constant. The substrate concentration in the influent is denoted S_{in} [mass/volume]. The influent biomass concentration is assumed to be zero.

Figur 2: A completely mixed bioreactor.

The rate of accumulation of biomass is obtained from a mass balance. Assume that the biomass has a specific growth rate $\mu(S)$ (which for example may be given by (2.2)). The total amount of produced biomass per time unit in a reactor with volume V is $\mu(S)VX$, compare with (2.1). Since the reactor is completely mixed, the outflow concentration of biomass is equal to the concentration in the tank. The rate of change of biomass is then given as

$$V\frac{dX}{dt} = \mu(S)VX - QX \tag{2.6}$$

Now, define the *dilution rate* (utspädningshastighet)

$$D = \frac{Q}{V} \tag{2.7}$$

The model (2.6) can now be written in the following simple form

$$\frac{dX}{dt} = (\mu(S) - D)X \tag{2.8}$$

For the substrate consumption we assume that the yield coefficient is Y, see (2.4). Paralleling, the procedure above for the substrate mass balance gives

$$V\frac{dS}{dt} = QS_{in} - \frac{\mu(S)}{Y}VX - QS \tag{2.9}$$

Introducing the dilution rate (2.7) gives

$$\frac{dS}{dt} = -\frac{\mu(S)}{Y}X + D(S_{in} - S) \tag{2.10}$$

The model consisting of (2.8) and (2.10) form the basis for most bioreactors models. For physical reasons we also have $X \geq 0$ and $S \geq 0$.

2.2.1 Stationary points and wash-out

We will consider the basic bioreactor model (2.8) and (2.10) which is summarised below.

$$\frac{dX}{dt} = (\mu(S) - D)X \tag{2.11}$$

$$\frac{dS}{dt} = -\frac{\mu(S)}{Y}X + D(S_{in} - S) \tag{2.12}$$

In the following we assume that D and S_{in} are constant and we will derive the *stationary points* (also called equilibrium states or fixed points) of the model. The stationary points are found by solving $\frac{dX}{dt} = \frac{dS}{dt} = 0$. The stationary points are denoted[3] $\bar{X}$ and $\bar{S}$.

It is directly seen from (2.11) that a necessary condition for $\frac{dX}{dt} = 0$ is

$$\bar{X} = 0 \tag{2.13}$$

or

$$\mu(S) = D \tag{2.14}$$

The first condition (2.13) is known as *wash-out*. All biomass will disappear! In most cases the wash-out condition is undesirable and should be avoided. Wash out is typically obtained if D is too high (too much biomass is then taken out from the reactor and the reactor becomes "overloaded").

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[3]Note the difference in notation compared to the Compendium p 80.

Next we will consider the condition (2.14) when μ is a Monod function:

$$\mu(S) = \mu_{max} \frac{S}{K_S + S} \tag{2.15}$$

We then obtain

$$\mu_{max} \frac{\bar{S}}{K_S + \bar{S}} = D \tag{2.16}$$

Solving for $\bar{S}$ yields

$$\bar{S} = \frac{DK_S}{\mu_{max} - D} \tag{2.17}$$

Note that $\bar{S}$ does not depend on S_{in}! That means that during steady state the effluent substrate concentration from the reactor does not depend on the influent concentration of substrate (assuming the the specific growth rate can be modelled as a Monod function and that the influent biomass concentration is zero).

The steady state value of the biomass during non wash-out is obtained by solving (2.12) using $\frac{dS}{dt} = 0$ and $\mu(S) = D$. This gives

$$\bar{X} = Y(S_{in} - \bar{S}) \tag{2.18}$$

Hence, by first calculating $\bar{S}$ it is very easy to calculate $\bar{X}$ (assuming the yield and influent substrate to be known).

In order not to get a wash-out, we must have $\bar{X} > 0$. From (2.18) this gives the condition $S_{in} > \bar{S}$. By using (2.17) in this condition we can easily derive a condition on D so that wash-out is avoided.

2.2.2 State space description

The general form for a nonlinear state space description of order two is given by

$$\dot{x} = f(x, u)$$
$$x = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix}, \quad f(x, u) = \begin{bmatrix} f_1(x, u) \\ f_2(x, u) \end{bmatrix} \tag{2.19}$$

The model consisting of (2.8) and (2.10) can be written in the form (2.19) by defining $u = S_{in}$ and

$$x = \begin{bmatrix} X \\ S \end{bmatrix}, \quad f(x, u) = \begin{bmatrix} f_1(x, u) \\ f_2(x, u) \end{bmatrix} = \begin{bmatrix} \mu(S)x_1 - Dx_1 \\ -\frac{1}{Y}\mu(S)x_1 - Dx_2 + Du \end{bmatrix} \tag{2.20}$$

The model can be linearized around a *stationary point*, see further Chapter 7.1 "Modellering av Dynamiska System". The model (2.8) and (2.10) can also be written as

$$\dot{x}(t) = \begin{pmatrix} \mu(S) - D & 0 \\ -\frac{\mu(S)}{Y} & -D \end{pmatrix} x(t) + \begin{pmatrix} 0 \\ D \end{pmatrix} u \tag{2.21}$$

In the (not very realistic) case when $\mu(S) = \mu$ (a constant), the model (2.21) becomes linear, compare with equation (6.2) in "Modellering av Dynamiska system"

3 Analysis and simulation of a Monod reactor

3.1 The model

We will here consider the model described in Section 2.2 when the specific growth rate is a Monod function. For convenience we summarise the model equations below (see Section 2 for a derivation and definitions of involved variables):
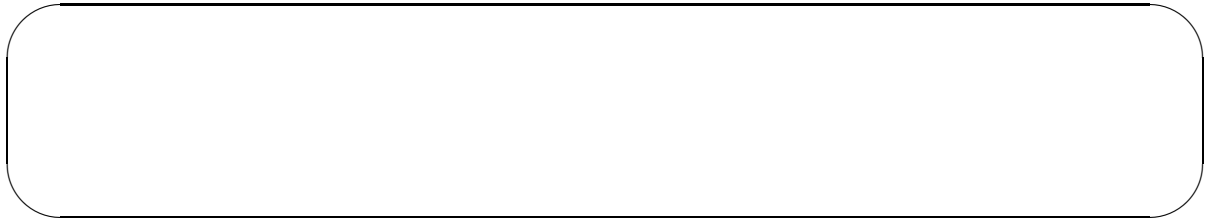
$$\frac{dX}{dt} = (\mu(S) - D)X \tag{3.1}$$

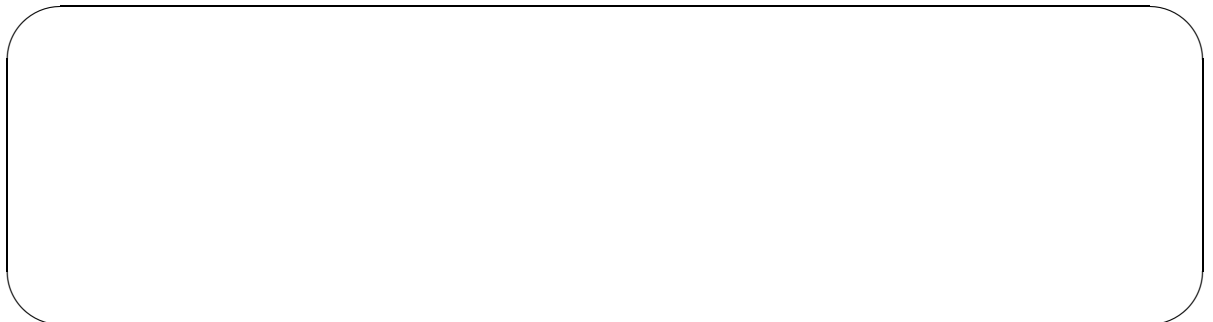$$\frac{dS}{dt} = -\frac{1}{Y}\mu(S)X + D(S_{in} - S) \tag{3.2}$$

$$\mu(S) = \mu_{max}\frac{S}{K_S + S} \tag{3.3}$$

3.2 Exercises

Exercise P1 The stationary values for the model (3.1)-(3.3) are given in the previous Section. Consider the wash-out case (all biomass is washed out from the reactor and $\bar{X} = 0$). What is the corresponding value for $\bar{S}$? Is the result natural?
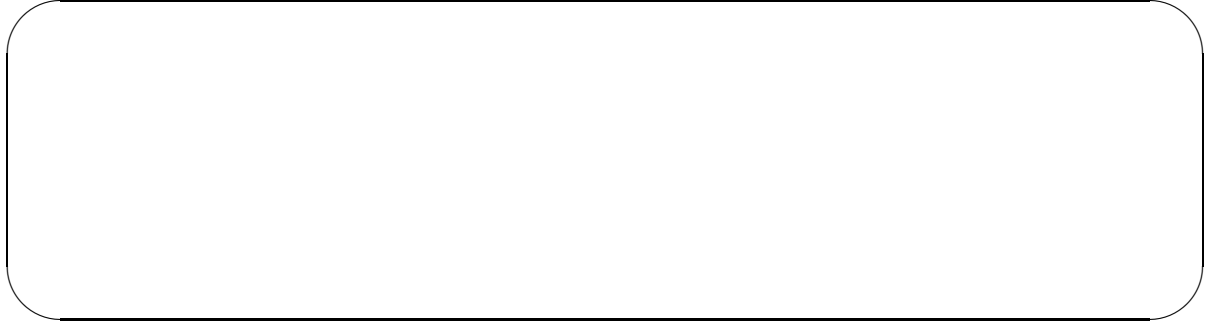
Exercise P2 Calculate a limit D_{lim} so that if $D < D_{lim}$ wash out will not occur.
Hint: The condition for *non* wash-out is that $S_{in} > \bar{S}$, where $\bar{S}$ is given in (2.17).

Exercise P3 Calculate numerically the stationary values $\bar{X}$, $\bar{S}$ and D_{lim} for the (non wash-out) case:

$$\mu_{max} = 2 \; [h^{-1}], \; K_S = 1.2 \; [mg/l], \; Y = 0.8, \; D = Q/V = 0.5 \; [h^{-1}], \; S_{in} = 1 \; [mg/l]$$

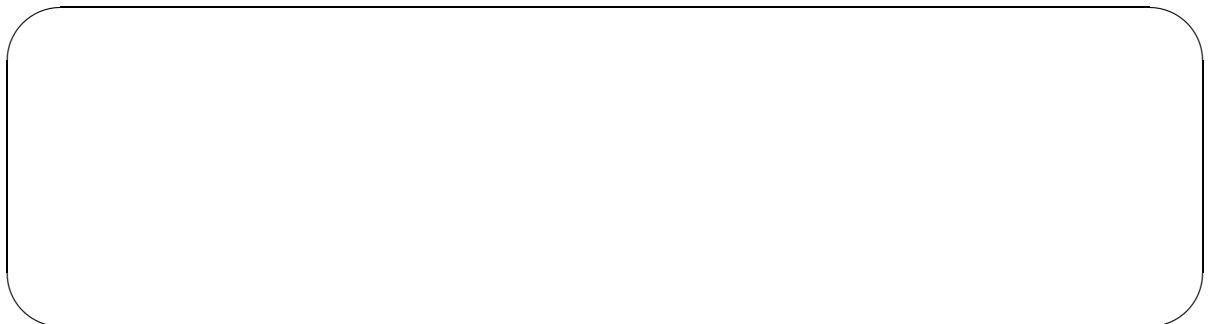Next the process will be simulated using a program written in Matlab.

1. Start the computer and log in.

2. Go to the Start menu and select StudentLabProg/DynSys/lab3 (this will copy the files to your working directory).

In Matlab, the model (3.1)-(3.3) is simulated by the m-file *growth* (just type *growth* followed by return).
The simulator has the default values given in Exercise P3. The initial[4] values are: $X(0) = 0.1$, $S(0) = 1.1$.
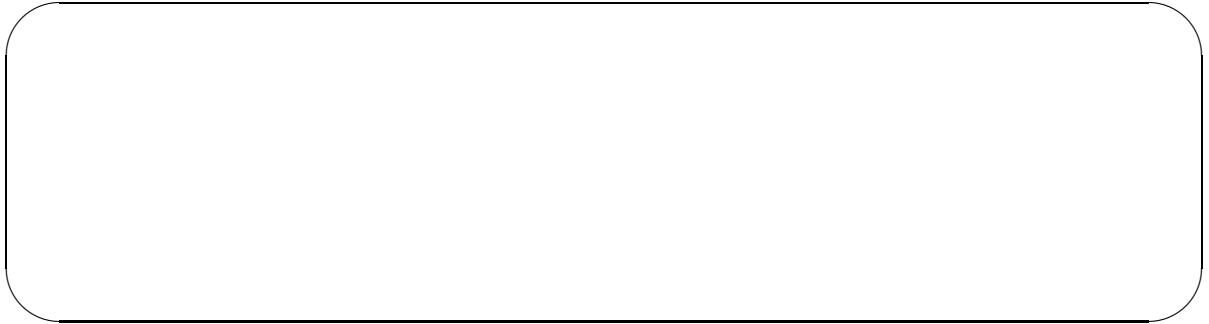The default simulation length T_{max} is 40 time units.

Exercise 4 Simulate the model (3.1)-(3.3) using the function *growth*. From the plot, estimate the stationary values of biomass and substrate. Compare the results with the calculated values in Exercise P3.
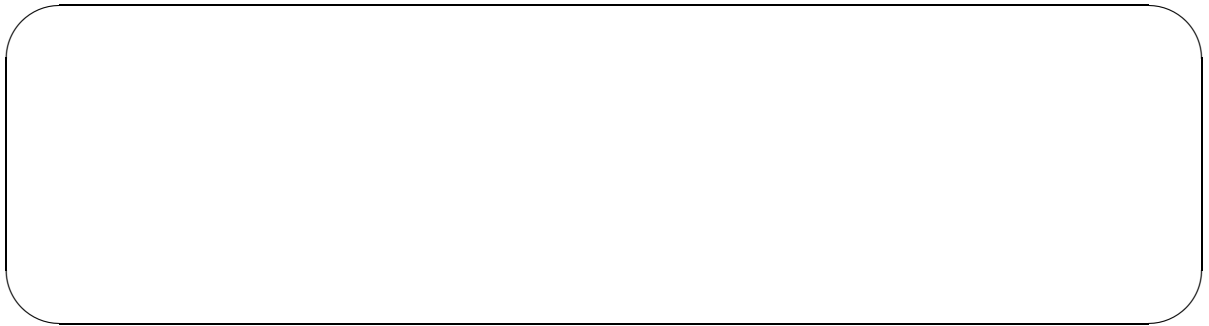
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[4]The concentrations at time t=0 in the reactor.

Exercise 5 Increase the value of D until wash-out is obtained. Note that by increasing the simulation time the accuracy of the estimate is increased. For what (approximate) value on D is wash-out obtained? Compare with the calculated value in Exercise P3. Compare also $\bar{S}$ during wash-out with the result in Exercise P1.

Exercise 6, Optional (frivillig) Check how the simulated biomass and substrate is affected by different values on μ_{max}, K_S, Y, S_{in} and $D = Q/V$

4 Analysis and simulation of a Haldane reactor

4.1 The model

In this section we will consider the same basic model as in the previous section but when the biomass specific growth rate is modeled with the Haldane kinetics (see Section 2.1.2). The model is summarised below

$$\frac{dX}{dt} = (\mu(S) - D)X$$

$$\tag{4.1}$$

$$\frac{dS}{dt} = -\frac{1}{Y}\mu(S)X + D(S_{in} - S)$$

$$\mu(S) = \mu_o\frac{S}{K_1 + S + S^2/K_h}$$

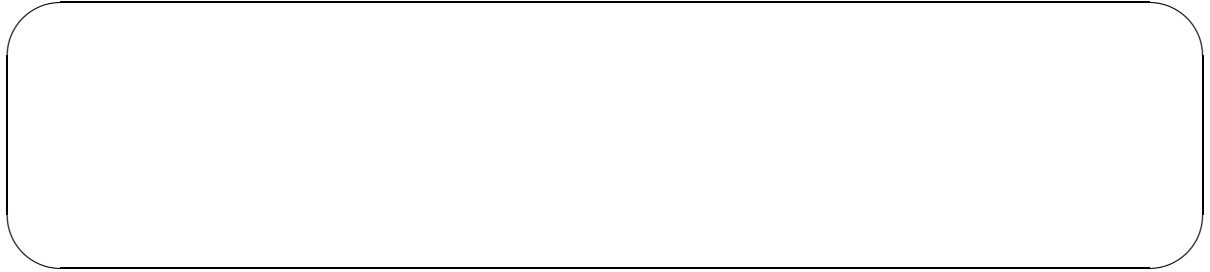$$\tag{4.2}$$

4.2 Exercises

Exercise P7 During non washout conditions (that is $\mu(S) = D$) the model (4.1) with the Haldane law (4.2) has two stationary points which we denote $(\bar{S}_1, \bar{X}_1)$ and $(\bar{S}_2, \bar{X}_2)$

Calculate (that is solve $\mu(S) = D$) $(\bar{S}_1, \bar{X}_1)$ and $(\bar{S}_2, \bar{X}_2)$ for the case:
$\mu_o = 1.5\ [h^{-1}]$, $K_1 = 1.2 [mg/l]$, $K_h = 2\ [mg/l]$, $Y = 0.8$, $D = Q/V = 0.5\ [h^{-1}]$, $S_{in} = 5$ $[mg/l]$.
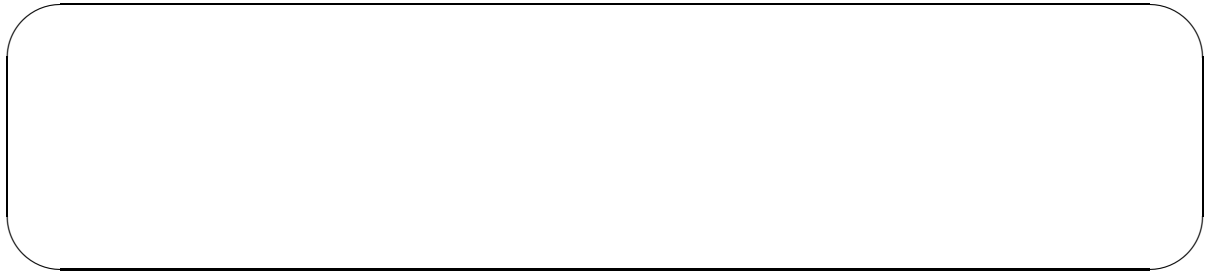
Hint: If your calculations are correct, one point should be $(\bar{S}, \bar{X}) = (0.735, 3.412)$.

Next the Haldane reactor will be simulated. This is done in Matlab, with the m-file *hald*. The simulator has the default values given in Exercise P7. The initial values are: $X(0) = 3$, $S(0) = 3$.

Exercise 8 Simulate the model (4.1)-(4.2) using the function *hald*. From the plot, estimate the stationary values of the substrate and biomass. Verify that one of the stationary points calculated in Exercise P7 is achieved.

Exercise 9 Play around with the simulator and (for example) check the stationary value of S for different input concentrations S_{in}. For what values of S_{in} do wash-out occurs?
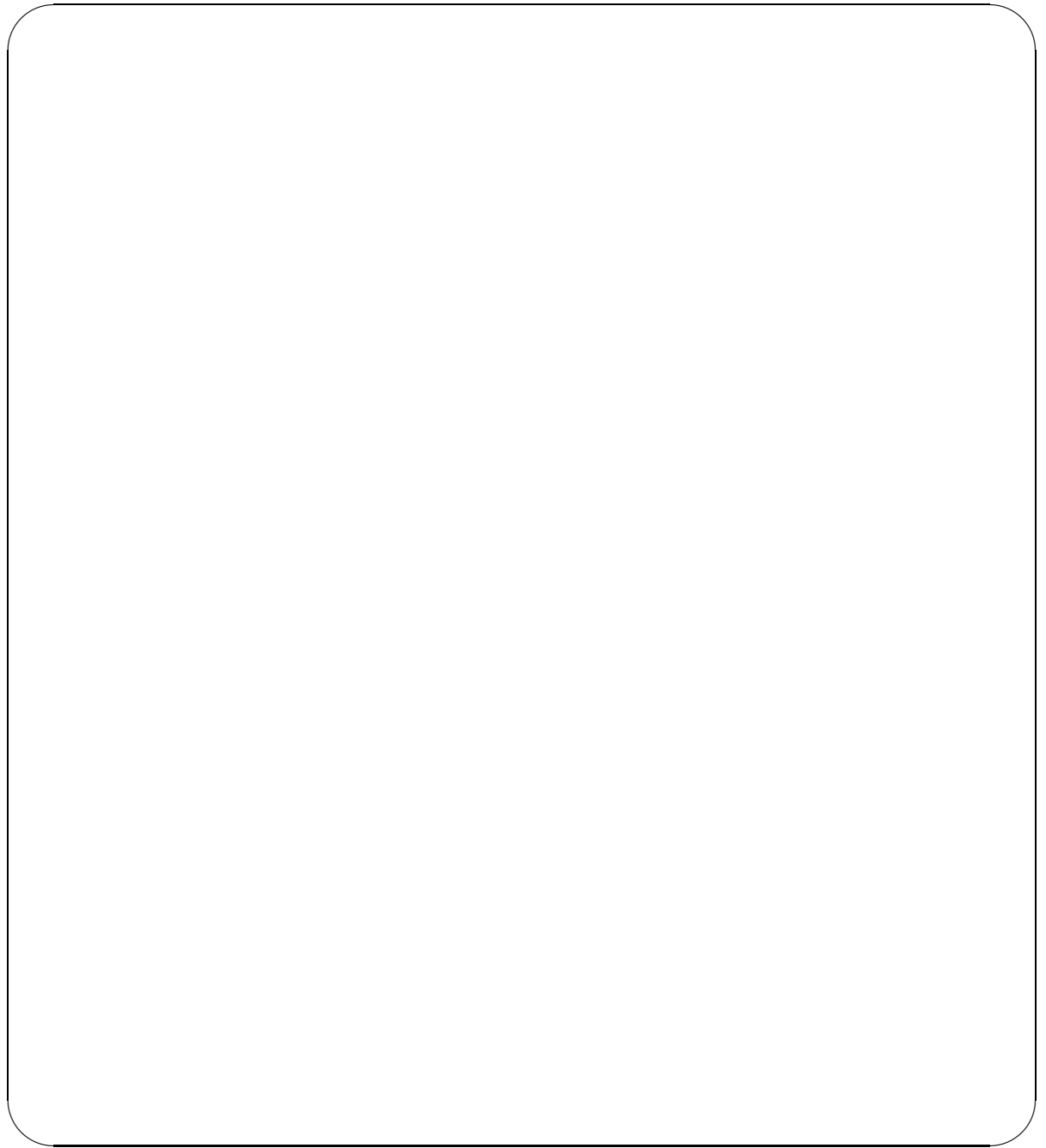
Exercise P10 You may have noticed from from the simulations that only one of the stationary (non wash-out) points was achieved. Maybe there is something "strange" with the other point?

In order to analyse this, linearise the system and evaluate the eigenvalues of the linearised system matrix for the two stationary points (the non wash-out case). Show that one stationary point is asymptotically stable stationary point while the other is unstable.
Hints:
You are encouraged to use Matlab when needed, for example to calculate eigenvalues (do *help eig* to get information).

Remark: It is possible to check stability for the two stationary points without using any numerical values. The characteristic equation will be on the form $s^2 + as + b$. The following holds:

All roots in the left half plane $<=>$ $a > 0$, $b > 0$.

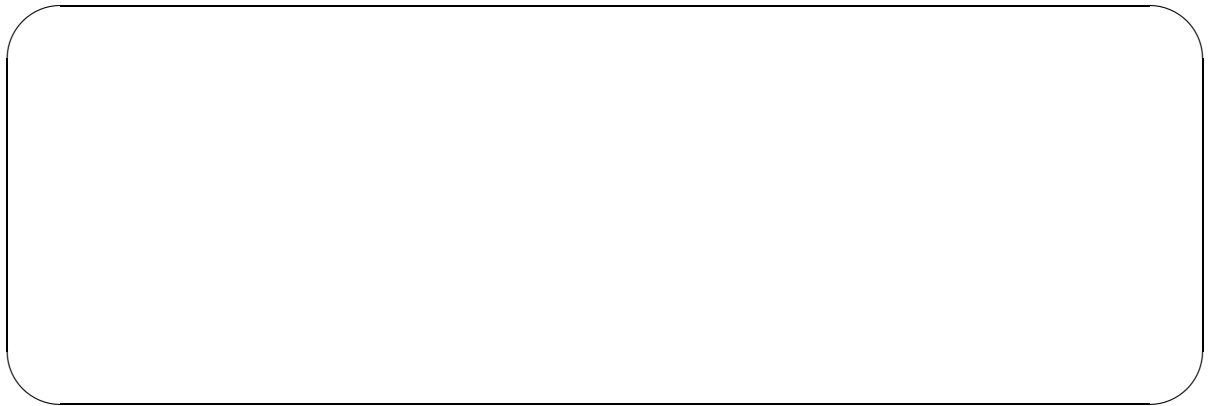In order to check if b is positive or negative the condition

$$0 < \bar{S}_1 < \sqrt{K_1 K_h} < \bar{S}_2$$

is the used for evaluating if $\frac{d\mu(S)}{dS}$ is positive or negative.

Exercise 11 The m-file *haldphase* plots the phase portrait for the system. Inspect the file (and the m-file that is called from the file)) and *describe* what it does. Use the m-file[5] to make a phase portrait, print it out, and make (by pen) appropriate arrows and mark the locations of the analysed stationary points. Also mark the wash-out point (which is also a stationary point).

Assume that it is known that $0 < S(0) < 6$, approximately what value on $X(0)$ is needed to prevent wash-out?

Submit (bifoga) the plot!.

Remark: For simple models like the one above, finding steady state solutions, linearisation and calculation of eigenvalues may be done analytically. For larger models these calculations are not possible to do by paper and pen. Many of these analyses (finding steady state values, linearisation) are possible to do in Matlab but the model needs to be created in Simulink which is an extension of Matlab where models are created by block diagrams.

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[5]You are free to modify the file, in case you want a higher resolution in the plot.