

THE CHEMOSTAT.

Per Erik Strandberg
Supervisor: Stefan Rauch, Examiner: Magnus Herberthson

17th July 2003

About this text.

This report deals with the Chemostat. We carefully define the Chemostat and analyse it in all possible ways including looking at the nullclines, an invariant line, steady states, linearization etc. We use kinetics proposed by Monod in the 1950's, similar to the Michaelis-Menten kinetics in enzyme kinetics.

The report was originally written in a 3,5-credit course at LiTH¹ with Stefan Rauch as supervisor, and Magnus Herberthson as examiner in the spring of 2003 by me: Per Erik Strandberg, student at the Biotechnical Program. But I have later changed it to include some pictures and the optimization, for completeness. It is written with the help of \LaTeX .

The natural sequel to this report is a Bachelor of Arts final thesis in applied mathematics: "Mathematical Models of biological growth" at the moment being processed. Once it is complete it will be "published" at my homepage², where you also can find the latest version of this text:

Please send me feedback, comments, to: perst586@student.liu.se

¹Univeristy of Linköping, Sweden, the technical faculty.

²<http://www.midgard.liu.se/~b00perst/index.htm>

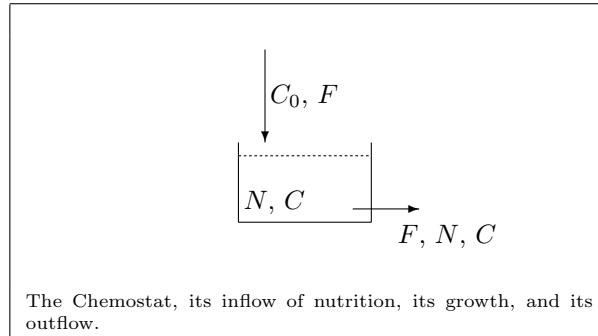
Contents

| | | |
|----------|-----------------------------------------------------------------|-----------|
| 1 | Introduction. | 3 |
| 2 | Two simple models of biological growth. | 4 |
| 2.1 | Exponential growth. | 4 |
| 2.2 | The logistic equation. | 4 |
| 3 | The chemostat equations. | 6 |
| 3.1 | Enter: The flow, F | 6 |
| 3.2 | The Michaelis-Menten-kinetics. | 6 |
| 3.3 | The dimensionless form of the chemostat. | 7 |
| 4 | Analysing the Chemostat equations. | 9 |
| 4.1 | Equilibrium solutions of the chemostat. | 9 |
| 4.2 | The parameters α_1 and α_2 | 9 |
| 4.3 | The null clines of the Chemostat. | 10 |
| 4.4 | The Linear stability around the two equilibrium points. | 10 |
| 4.5 | The invariant line. | 11 |
| 4.6 | Optimization of the Chemostat. | 12 |
| 5 | The “semi-permeable” model. | 14 |
| 5.1 | Explaining the semi-permeable model. | 14 |
| 5.2 | The dimensionless form of the semi-permeable model. | 14 |
| 5.3 | Steady-states, and the null-clines. | 15 |
| 5.4 | A stability-analysis. | 15 |
| 6 | Review. | 16 |

1 Introduction.

The chemostat is a device used for harvesting bacteria³. A chemostat is made of two main parts; a nutrient reservoir, and a growth-chamber, reactor, in which the bacteria reproduce.

Via an inflow from the reservoir fresh nutrition is added and from an outflow bacteria are harvested.



Section 2: We start our journey by looking at some simple models of biological growth: the exponential growth and the logistic equation.

Section 3: Here we will derive the chemostat equations. We will look at kinetics and reduce the number of parameters.

Section 4: In analysing the chemostat equations we look at equilibrium solutions, null clines, linearized equations, we also find an invariant line.

Section 5: In this section an other model, very similar to the chemostat is investigated, allowing us to use the tools created in earlier sections.

Section 6: A review.

The Appendix: Some mathematical tools are explained in the Appendix. A matlab m-file is also displayed.

³Bacteria, yeast, other micro-organisms, or products/chemicals made by them.

2 Two simple models of biological growth.

As a theoretical background we will look at what can be considered a chemostat without in- or out-flow, meaning: $F_{in} = F_{out} = 0 \neq F(t)$.

2.1 Exponential growth.

An extremely simple model could be $\frac{dN}{dt} = k \cdot N$ corresponding to (birth-death) of bacteria, with $k = const > 0$, giving

$$N(t) = N_0 e^{kt} \quad (1)$$

This is truly a too simple model. To limit the production of organisms we introduce the variable C describing the concentration of nutrient⁴, into the dynamic equations.

2.2 The logistic equation.

Let us assume that $\frac{dN}{dt} = k \cdot N$, with $k = k(C) = k \cdot C$, and that $\frac{dC}{dt} = -\alpha k C N$, meaning that each individual produces k units of offspring per time unit, for example 1.13. With $\alpha = const > 0$ we could mean that each produced unit of offspring requires α units of nutrition. This model is in correspondence with our intuition; CN could be interpreted as how often bacteria and food “meet” (giving the bacteria an opportunity to reproduce and consume).

We get a system of ODE's:

$$\begin{cases} \frac{dN}{dt} = kCN & (a) \\ \frac{dC}{dt} = -\alpha kCN & (b) \end{cases}$$

Performing $\alpha(a) + (b)$ we get: $\frac{d}{dt}(C + \alpha N) = 0$, thus $(C + \alpha N)(t) = \text{constant}$. In particular with $t = 0$ and $N(0) = N_0 \approx 0$ (or at least small in comparison to a normal $N(t)$) we have $C(0) + \alpha N(0) \approx C_0$ since N_0 small $\Rightarrow C(t) = C_0 - \alpha N(t)$ giving us a reason to eliminate (b), and rewrite (a):

$$\frac{dN}{dt} = k \underbrace{(C_0 - \alpha N)}_{C_{old}(t)} N = \underbrace{kC_0}_{r>0} \left(1 - \underbrace{\frac{N}{C_0/\alpha}}_{B>0}\right) N = r \left(1 - \frac{N}{B}\right) N$$

By changing some factors we have reduced our system of ODE's to one single equation, called the logistic equation:

$$\frac{dN}{dt} = r \left(1 - \frac{N}{B}\right) N \quad (2)$$

Where $r(1 - \frac{N}{B})$ corresponds to our old k in (1), called an intrinsic⁵ growth-speed, and B corresponds to the carrying capacity. Similarly, by eliminating N instead of C, we quickly find that $\frac{dC}{dt} = -\alpha r (1 - \frac{C}{\alpha B}) C$, however, this term is not necessarily as interesting as the bacteria-term.

When analysing (2) we discover several interesting things:

⁴Concentration of nutrient or concentration of the limiting nutrient.

⁵Translated to Swedish “intrinsic” could be: “inre”, “inneboende”, “egentlig”, or “reell”.

For small N when $0 < N \ll B$ we can approximate (2) to (1), our model corresponds to observations of exponential growth for starting cultures.

The factor -NN corresponds to a crowding effect, inhibiting the reproduction rate.

The sign of (2) is important to analyse. Let us assume that $N \geq 0$. We also know that $r > 0$. Meaning that $(1 - \frac{N}{B})$ is what determines the sign of $\frac{dN}{dt}$.

$N = 0 \Rightarrow \frac{dN}{dt} = 0$, a trivial solution, there is no population;

$0 < N < B \Rightarrow (1 - \frac{N}{B}) > 0$, the population grows;

$N = B \Rightarrow \frac{dN}{dt} = 0$, constant population; and

$N > B \Rightarrow \frac{dN}{dt} < 0$, decreasing population.

We now know that the model corresponds to our intuition: a population at zero will not give rise of a population. But even the smallest population will grow. If ever $N=B$ we will get a constant population. Finally: if $N > B$, N will eventually diminish towards $N = B$. $N = 0$ and $N = B$ equilibrium solutions.

One solution to (2) is:

$$N(t) = \frac{N_0 B}{N_0 + (B - N_0)e^{-rt}}, \quad \text{if } 0 < N_0 < B \quad (3)$$

this is easy to control with derivation.

We have seen the birth of this well-known curve from a simple model, we will in the next section move on, introduce the in- and out-flow, and make an investigation of the creation of the chemostat.

3 The chemostat equations.

The purpose of the chemostat is to have a quasi-constant N and C , allowing us to harvest at a constant (non-stop) rate. We must adjust our logistic equation introducing the flow, in doing so, we will also define the units used in our growth-chamber.

We will also reduce the degrees of freedom of the Chemostat by introducing the dimensionless form.

3.1 Enter: The flow, F .

$F = F_{in} = F_{out}$: volume/time. With F_{in} comes C_0 : “mass”/volume⁶. In the reactor we have N : number, and C : mass/volume.

From (2) we add some reasonable terms corresponding to in- and out-flow of the nutrition-solution (thus concentration) and outflow of bacteria, giving us:

$$\left\{ \begin{array}{l} \frac{dN}{dt} = \overbrace{K(C)N}^{mod.} - \overbrace{F\frac{N}{V}}^{new} \\ \frac{dC}{dt} = -\alpha \overbrace{K(C)N}^{mod.} - \overbrace{F\frac{C}{V}}^{new} + F\frac{C_0}{V} \end{array} \right. \quad (4)$$

It seems reasonable to assume that N/V is an amount of the bacteria-density, multiplying it with F gives us the amount of bacteria being flushed away. Similar to N , $-FC/V$ corresponds to the outflow, and $+FC_0/V$ to the inflow of nutrition.

3.2 The Michaelis-Menten-kinetics.

Let us review our $K(C)$. Is it reasonable to have $K(C) = kC$? No, because bacteria can not, and will not, reproduce at infinite speed just because we insert them in a reactor with infinite concentration.⁷ So, let us introduce a little more natural reproduction-constant-function $K(C)$. One way to do this is to introduce the Michaelis-Menten-kinetics.

Experimental data and our common sense tells us that we want the reproduction-constant to be almost linear at small positive values for C , but we also want an upper limit for K so that: $K(C) \xrightarrow{C \rightarrow \infty} K_{max}$. We introduce the Michaelis-Menten-kinetics:

$$K(C) = K_{max} \frac{C}{K_n + C}$$

An analysis of $K(C)$ is needed, do we achieve our goals?

Small C 's give us $K(C) = C \frac{K_{max}}{K_n}$, if we can assume $C \ll K_n$, thus almost linear.

The maximum K , K_{max} , is never reached, no matter how great C gets. We have $K_n > 0 \Leftrightarrow K_n + C > C \Leftrightarrow K(C) < K_{max}, \forall C$.

⁶“Mass” could be moles, kilograms, molecules, etc.

⁷Infinite concentration is, by the way, also not realistic. . .

The limit $K(C) \xrightarrow{C \rightarrow \infty} K_{max}$ is what we wanted. And we can let K_{max} be the maximal fraction to multiply N with if there are great recourses.

Deriving $K(C)$ gives us $K'(C) = K_{max} \frac{K_n}{(K_n+C)^2} > 0$, something positive, we have asymptotical growth towards K_{max} .

The new constant K_n can be given an interesting meaning if introduced in $K(C)$: $K(K_n) = K_{max} \frac{K_n}{K_n+K_n} = \frac{1}{2} K_{max}$. It corresponds to the concentration at which $K = \frac{1}{2} K_{max}$

Summarized, the model can be described as:

$$\begin{cases} \frac{dN}{dt} = K_{max} \frac{C}{K_n+C} N - F \frac{N}{V} \\ \frac{dC}{dt} = -\alpha K_{max} \frac{C}{K_n+C} N - F \frac{C}{V} + F \frac{C_0}{V} \end{cases} \quad (5)$$

3.3 The dimensionless form of the chemostat.

A quick glance at our equations show that we have a number of variable constants: K_{max} , K_n , $\frac{F}{V}$, α , and C_0 . Each one of them is important and necessary, but is there a way for us to reduce them somehow? The answer is yes, and we will see that it is possible to eliminate three of our constants (we eliminate five of them and introduce two new ones, this is possible since we have five parameters, and three dimensions).

As the title of this subsection suggests, we will actually eliminate the dimensions/units of the equations, but first we must investigate our constants, what units do they invisibly carry around? We start by investigating the first relation:

$dim[\frac{dN}{dt}] = \frac{number}{time}$ (here we assume $dim[N] = number$ and $dim[t] = time$), thus: $dim[\frac{K_{max}NC}{(K_n+C)}] = \frac{number}{time}$. With $dim[C] = \frac{mass}{volume}$ we get $dim[K_n] = \frac{mass}{volume}$ in order to keep $K_n + C$ meaningful, only allowing $dim[K_{max}] = \frac{1}{time}$.

Our second relation rewards us with $dim[\frac{dC}{dt}] = \frac{mass}{volume \cdot time}$, and since we know that $dim[C] = \frac{mass}{volume}$, we get $dim[C_0] = \frac{mass}{volume}$. And with the above relations we force $dim[\alpha] = \frac{mass}{volume \cdot number}$!

And now, to simplify things we replace C , N , and t with $C \cdot \hat{C}$, $N \cdot \hat{N}$, and $t \cdot \hat{t}$. Where \hat{C} , \hat{N} and \hat{t} corresponds to the unit-dimension, whatever they may be.⁸ Our beautiful (5) will now for a moment be replaced with:

$$\begin{cases} \frac{dN}{dt} \cdot \frac{\hat{N}}{\hat{t}} = K_{max} \frac{C\hat{C}}{K_n+C\hat{C}} N\hat{N} - F \frac{N\hat{N}}{V} \\ \frac{dC}{dt} \cdot \frac{\hat{C}}{\hat{t}} = -\alpha K_{max} \frac{C\hat{C}}{K_n+C\hat{C}} N\hat{N} - F \frac{C\hat{C}}{V} + F \frac{C_0}{V} \end{cases}$$

Now, to eliminate the dimensions, we multiply the dN -row with \hat{t}/\hat{N} , and the dC -row with \hat{t}/\hat{C} , rewarding us with...

$$\begin{cases} \frac{dN}{dt} = K_{max} \hat{t} \frac{C\hat{C}}{K_n+C\hat{C}} N - F \frac{N\hat{t}}{V} \\ \frac{dC}{dt} = -\alpha K_{max} \frac{N\hat{N}\hat{t}C}{K_n+C\hat{C}} - F \frac{C\hat{t}}{V} + F \frac{C_0\hat{t}}{V\hat{C}} \end{cases}$$

⁸Note that \hat{t} could be a second, a year, 3.25489677 minutes, etc, \hat{N} could be one, twelve or 22.5553 bacteria, and \hat{C} could typically be: mol/l, molecules/mm³ or 3.333 lb/gallon.

... allowing us to insert $\hat{t} = \frac{V}{F}$, $\hat{C} = K_n$, $\hat{N} = \frac{\hat{C}}{\alpha K_{max} \hat{t}} = \frac{K_n F}{\alpha K_{max} V}$, and replace $\alpha_1 = \hat{t} K_{max} = \frac{V}{F} K_{max}$ and $\alpha_2 = \frac{C_0}{\hat{C}} = \frac{C_0}{K_n} = \frac{\hat{t} F C_0}{V \hat{C}}$. These, mysterious replacements will reward us with:

$$\begin{cases} \frac{dN}{dt} = \alpha_1 \left(\frac{C}{1+C} \right) N - N \\ \frac{dC}{dt} = - \left(\frac{C}{1+C} \right) N - C + \alpha_2 \end{cases} \quad (6)$$

Showing that the Chemostat can be reduced to a system with only two degrees of freedom; α_1 , α_2 being the parameters. Now, the best thing for an experimentalist would be to find two analytically correct functions: $N(N, C)$ and $C(N, C)$, but because of (6)'s non-linearity we have little hope of finding them. Instead we will analyse them and draw conclusions from this.

4 Analysing the Chemostat equations.

When analysing the Chemostat we will find equilibrium solutions, null-clines, investigate the parameters α_1 and α_2 in detail, look at the linearization and the invariance line.

4.1 Equilibrium solutions of the chemostat.

To be able to find equilibrium solutions we use our recently found relations letting them equal zero, giving us:

$$\begin{cases} \frac{dN}{dt} = \alpha_1 \left(\frac{C}{1+C} \right) N - N = 0 \\ \frac{dC}{dt} = - \left(\frac{C}{1+C} \right) N - C + \alpha_2 = 0 \end{cases} \Rightarrow \begin{cases} 0 = \alpha_1 \left(\frac{C}{1+C} \right) N - N \\ 0 = - \left(\frac{C}{1+C} \right) N - C + \alpha_2 \end{cases}$$

In trying to solve the first relation we quickly find a trivial solution: $N = 0$. Inserting this in the second relation give us $C = \alpha_2$ thus an equilibrium solution is: $(\bar{N}_0, \bar{C}_0) = (0, \alpha_2)$, so maybe α_2 is a kind of stock-nutrient-concentration.

The other, the non-trivial, solution of the first line is a little more inspiring. We quickly transform it a little: $N = \alpha_1 \left(\frac{C}{1+C} \right) N \Rightarrow 1 = \alpha_1 \left(\frac{C}{1+C} \right) \Rightarrow (1+C) = \alpha_1 C \Rightarrow 1 = \alpha_1 C - C \Rightarrow 1 = C(\alpha_1 - 1) \Rightarrow \frac{1}{\alpha_1 - 1} = C$.

Combining this with the second line, we get:

$$\begin{aligned} 0 &= - \left(\frac{\frac{1}{\alpha_1 - 1}}{1 + \frac{1}{\alpha_1 - 1}} \right) N - \frac{1}{\alpha_1 - 1} + \alpha_2 = - \frac{1}{\alpha_1 - 1 + 1} N - \frac{1}{\alpha_1 - 1} + \alpha_2 = \\ &= - \frac{1}{\alpha_1} N - \frac{1}{\alpha_1 - 1} + \alpha_2 = 0 \Leftrightarrow \frac{1}{\alpha_1} N = \alpha_2 - \frac{1}{\alpha_1 - 1} \Leftrightarrow \\ N &= \alpha_1 \left(\alpha_2 - \frac{1}{\alpha_1 - 1} \right) \end{aligned}$$

With our second pair we have two solutions:

$$\begin{aligned} (\bar{N}_0, \bar{C}_0) &= (0, \alpha_2) \\ (\bar{N}_1, \bar{C}_1) &= \left(\alpha_1 \left(\alpha_2 - \frac{1}{\alpha_1 - 1} \right), \frac{1}{\alpha_1 - 1} \right) \end{aligned} \tag{7}$$

4.2 The parameters α_1 and α_2 .

Now is the time to discuss the two parameters, what are reasonable values? When do α_1 and α_2 give us an equation without physical meaning? Can they be given an intuitive meaning?

We saw that $\alpha_1 = \frac{K_{max}}{F/V}$. Giving us the hint that α_1 could be interpreted as a kind of dimensionless reproduction-rate, or even more interestingly: as a maximum reproduction-rate multiplied by the inverse of a flushing factor.

Combining our intuition with the solutions we found above, we notice: $\bar{C}_1 = \frac{1}{\alpha_1 - 1}$ for any population to exist, giving us: $\alpha_1 > 1$, and according to our guess, we must have a fraction larger than one to multiply N with each unit-time (small values would quickly eliminate it). Meaning that in the competition of reproduction and flushing, reproduction has to be the winner.

From the trivial solution we notice that $\bar{C}_0 = \alpha_2 = \frac{C_0}{K_n}$ seems to be some kind of stock nutrient. But as we will see, this is one way of dealing with α_2 . Another way of looking at this parameter is to see it as an inverse number of K_n . We saw that a small K_n meant that we reached K_{max} at a lower C. So a small K_n means a large α_2 , and vice versa.

Looking at our non-trivial solution again we notice that $\bar{N}_1 = \alpha_2 - \frac{1}{\alpha_1 - 1} > 0$ is needed for the population to exist. Requiring $\alpha_2 > \frac{1}{\alpha_1 - 1}$. (Thus $\alpha_2 > 0$, this seems pretty realistic: a concentration can not be negative.) Here we can see that for small $(\alpha_1 - 1)$ (large flushing or weak reproduction) we need α_2 to be large (strong flushing or weak reproduction, requires more food in order to reproduce faster), and a growing α_1 allows α_2 to be smaller. This seems logical; if it is easier to reproduce, you don't need as much food...

4.3 The null clines of the Chemostat.

A good tool to use in investigating the phase-portrait is the null-clines; where $\frac{dN}{dt} = \dot{N} = 0$, or $\frac{dC}{dt} = \dot{C} = 0$.⁹

Let us begin with the N-relation: $0 = \dot{N} = \alpha_1 \left(\frac{C}{1+C}\right)N - N$, we notice one line: $N = 0$, and continue with the rest: $\alpha_1 \left(\frac{C}{1+C}\right) - 1 = 0 \Rightarrow C = \frac{1}{\alpha_1 - 1}$.

Continuing with the null clines for C: $0 = \dot{C} = -\left(\frac{C}{1+C}\right)N - C + \alpha_2 = 0$ After some elementary work, we get: $N = \frac{(\alpha_2 - C)(1+C)}{C}$. Our two null-clines are:

$$\begin{cases} \dot{N} = 0 \Rightarrow (N = 0 \text{ or } C = \frac{1}{\alpha_1 - 1}) \\ \dot{C} = 0 \Rightarrow N = \frac{(\alpha_2 - C)(1+C)}{C} \end{cases}$$

The null clines are easy to draw, and by drawing some vectors in the right places, we can get a pretty good idea of how a state wanders around in the (N,C)-plane.

4.4 The Linear stability around the two equilibrium points.

We have found two equilibrium solutions in the positive quadrant of the (N,C)-plane: $(\bar{N}_0, \bar{C}_0) = (0, \alpha_2)$ and $(\bar{N}_1, \bar{C}_1) = \left(\alpha_1 \left(\alpha_2 - \frac{1}{\alpha_1 - 1}\right), \frac{1}{\alpha_1 - 1}\right)$. Around these points, we want to know how the Chemostat responds to a small disturbance, do we wander away from them or do we fall back into them if we try to move away. The question we want to answer is: are the solutions stable?

In order to analyse the Chemostat's behaviour at the stationary points we will use the stability-conditions described in the Appendix.

With some derivation, we notice:

$$\mathbf{A} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} = \begin{pmatrix} \alpha_1 \frac{C}{1+C} - 1 & \frac{\alpha_1 N}{(1+C)^2} \\ -\frac{C}{1+C} & -\frac{N}{(1+C)^2} - 1 \end{pmatrix}$$

Evaluating this at the trivial equilibrium point $(\bar{N}_0, \bar{C}_0) = (0, \alpha_2)$ we get:

$$\mathbf{A} = \begin{pmatrix} \frac{\alpha_1 \alpha_2}{1+\alpha_2} - 1 & 0 \\ -\frac{\alpha_2}{1+\alpha_2} & -1 \end{pmatrix} \Rightarrow \begin{cases} tr(\mathbf{A}) = \frac{\alpha_1 \alpha_2}{1+\alpha_2} - 2 \\ det(\mathbf{A}) = -\frac{\alpha_1 \alpha_2}{1+\alpha_2} + 1 \end{cases}$$

We know (or else we take a quick glance in Appendix A) that we have two conditions for stability around an equilibrium point: $tr(\mathbf{A}) < 0$ and $det(\mathbf{A}) > 0$. We will notice that our second condition: $-\frac{\alpha_1 \alpha_2}{1+\alpha_2} + 1 > 0 \Leftrightarrow 1 > \frac{\alpha_1 \alpha_2}{1+\alpha_2}$ is in

⁹We could just as well investigate the five-cline or π -cline, and get similar information. But by convention we investigate the null-clines.

conflict with the earlier condition $\alpha_2 > \frac{1}{\alpha_1 - 1} \Leftrightarrow 1 < \frac{\alpha_1 \alpha_2}{1 + \alpha_2}$. So this steady state is not stable.

The other equilibrium point, $(\bar{N}_1, \bar{C}_1) = \left(\alpha_1 \left(\alpha_2 - \frac{1}{\alpha_1 - 1} \right), \frac{1}{\alpha_1 - 1} \right)$, requires a more delicate touch, therefore we will, to lighten up the display, rename the term $\frac{\bar{N}_1}{(\bar{C}_1 + 1)^2} = \sigma$ and remember that $\sigma > 0$. Now we get:

$$\mathbf{A} = \begin{pmatrix} 0 & \sigma \alpha_1 \\ -\frac{1}{\alpha_1} & -\sigma - 1 \end{pmatrix} \Rightarrow \begin{cases} \text{tr}(\mathbf{A}) = -\sigma - 1 < 0. \\ \det(\mathbf{A}) = \sigma > 0. \end{cases}$$

The non-trivial equilibrium point is thus stable. We also note that: $-4 \det(\mathbf{A}) + \text{tr}(\mathbf{A})^2 = -4\sigma + \sigma^2 + 2\sigma + 1 = \sigma^2 - 2\sigma + 1 = (\sigma - 1)^2 > 0$. So that solutions near this point are not acting like spirals, but tend to go more straight-forward towards (\bar{N}_1, \bar{C}_1) , since we have eigenvalues that are real.

4.5 The invariant line.

In this subsection we will investigate the line: $N = -\alpha_1 C + \alpha_1 \alpha_2$, and discover that this line intersects both of our equilibrium solutions, that no condition, initially on it can get away from it, and that all solutions tends to approach it.

All solutions end up on the invariant line.

$$(6) : \begin{cases} \frac{dN}{dt} = \alpha_1 \left(\frac{C}{1+C} \right) N - N & (a) \\ \frac{dC}{dt} = -\left(\frac{C}{1+C} \right) N - C + \alpha_2 & (b) \end{cases}$$

We perform $(a) + \alpha_1(b)$ and get the ODE: $\frac{d}{dt}(N + \alpha_1 C)(t) = \alpha_1 \alpha_2 - (N + \alpha_1 C)(t)$. We can look at this relation as an ODE with one function $(N + \alpha_1 C)(t)$. One solution is: $(N + \alpha_1 C)(t) = K e^{-t} + \alpha_1 \alpha_2$. One nice property of $(N + \alpha_1 C)(t)$ is that $(N + \alpha_1 C)(t) \xrightarrow{t \rightarrow \infty} \alpha_1 \alpha_2$.

Thus when $t \rightarrow \infty$ we have $N - \alpha_1 C = \alpha_1 \alpha_2 \Leftrightarrow N = -\alpha_1 C + \alpha_1 \alpha_2$, all solutions wandering in the (N,C)-plane will eventually end up on this line.

We also notice that putting $N = 0$ will give $C = \alpha_2$, the trivial equilibrium point. and $C = 0$ give us $N = \alpha_1 \alpha_2$. You can also easily verify that this line passes through the non-trivial equilibrium point as well.

The invariance line is the elongation of one of the eigenvectors.

We remember that

$$\mathbf{A} = \begin{pmatrix} 0 & \sigma \alpha_1 \\ -\frac{1}{\alpha_1} & -\sigma - 1 \end{pmatrix}, \quad \sigma = \frac{\bar{N}_1}{(\bar{C}_1 + 1)^2} > 0,$$

now, assume that a solution has the form:

$$\begin{pmatrix} N(t) \\ C(t) \end{pmatrix} = \mathbf{X}(t) = \mathbf{v} e^{\lambda t}$$

When deriving this and looking at our linearization we get: $\mathbf{A} \mathbf{v} e^{\lambda t} = \lambda \mathbf{v} e^{\lambda t}$, and when using the classic secular equation to find the eigenvalues and eigenvectors we get:

$$(\mathbf{A} - \mathbf{I}\lambda) \mathbf{v} = 0 \Rightarrow 0 = \det(\mathbf{A} - \mathbf{I}\lambda) = \det \begin{pmatrix} -\lambda & \alpha_1 \sigma \\ -\frac{1}{\alpha_1} & -\sigma - 1 - \lambda \end{pmatrix}$$

$$\Rightarrow \lambda(\sigma + 1 + \lambda) + \sigma = 0 \Rightarrow \lambda_1 = -1, \text{ and } \lambda_2 = -\sigma.$$

We had expected real, negative eigenvalues, thanks to our earlier analysis. But now we must find a pair of eigenvectors. We insert our eigenvalues in $(\mathbf{A} - \mathbf{I}\lambda)\mathbf{v} = 0$:

$$(\mathbf{A} - \mathbf{I}\lambda_1)\mathbf{v}_1 = \begin{pmatrix} 1 & \alpha_1\sigma \\ -\frac{1}{\alpha_1} & -\sigma \end{pmatrix} \begin{pmatrix} v_{11} \\ v_{12} \end{pmatrix} = 0 \Rightarrow \mathbf{v}_1 = \begin{pmatrix} \alpha_1\sigma \\ -1 \end{pmatrix}$$

$$(\mathbf{A} - \mathbf{I}\lambda_2)\mathbf{v}_2 = \begin{pmatrix} \sigma & \alpha_1\sigma \\ -\frac{1}{\alpha_1} & -1 \end{pmatrix} \begin{pmatrix} v_{21} \\ v_{22} \end{pmatrix} = 0 \Rightarrow \mathbf{v}_2 = \begin{pmatrix} \alpha_1 \\ -1 \end{pmatrix}$$

By elongating the eigenvector \mathbf{v}_2 in positive and negative directions from (\bar{N}_1, \bar{C}_1) we can easily verify that this is the same line as $N = -\alpha_1 C + \alpha_1 \alpha_2$. Thus a state starting on the invariant line can not move away from it.

An observation.

Imagine you are looking at the phaseplane of the chemostat. If you have an arbitrary initial condition in the positive quadrant and let it move around as time passes. Now imagine a second solution and let them move simultaneously. It is possible to show that one of them can not cross the path of another, since their motion is depending on where they are and not where they came from.

The invariance line: conclusions.

We can now conclude that the invariance line can be seen as a barrier for the solutions. No solution above it can get below it and vice versa. This gives us an indication in drawing a phase portrait, and we can see that, indeed, the solutions near the non-trivial equilibrium solution can not vander around in spirals.

4.6 Optimization of the Chemostat.

Now we will leave the dimensionless form and use a general model. We will adapt it to fit the Chemostat, and express the steadystates in a different way.¹⁰ The model is now:

$$\begin{cases} \frac{dN}{dt} = \mu N - \frac{F}{V}N \\ \frac{dC}{dt} = -\alpha\mu N - \frac{F}{V}C + \frac{F}{V}C_0 \end{cases}$$

Where μ is a general rate-expression. Here we can replace the cumbersome $\frac{F}{V}$ with D , as in dilution coefficient. Simplifying it to:

$$\begin{cases} \frac{dN}{dt} = \mu N - DN \\ \frac{dC}{dt} = -\alpha\mu N - DC + DC_0 \end{cases}$$

If we ignore the trivial steady state and focus on the nontrivial steadystate (with dropped indexes: (\bar{N}, \bar{C})), we find $D = \mu$ if we let $\frac{dN}{dt} = 0$, simplifying the relation $\frac{dC}{dt} = 0 = -\alpha D\bar{N} - D\bar{C} + DC_0 \Leftrightarrow \bar{N} = \frac{1}{\alpha}(C_0 - \bar{C})$.

Now, we will use Michaelis-Menten kinetics for μ . We let $D = \mu = K_{max} \frac{\bar{C}}{K_S + \bar{C}}$
 $\Leftrightarrow \bar{C} = \frac{DK_S}{K_{max} - D}$, and now we can find an expression for \bar{N} with dimensions:

¹⁰We will do so since many of the parameters we changed in finding the dimensionless form includes the dilution coefficient D , and we need to compute $\frac{d}{dD}(D\bar{N})$

$\bar{N} = \frac{1}{\alpha}(C_0 - \frac{DK_S}{K_{max}-D})$. We are easily convinced that this expression multiplied with D is how to measure the amount of productivity, if we assume that productivity is growth-associated, or if we are interested in the bacteria in itself (as in yeast-production, etc.).

So we have $N_{out} = \bar{N}D$, we want to maximize this, and find an optimum. Let us derive: $\frac{d}{dD}N_{out} = \frac{d}{dD}(\frac{1}{\alpha}(DC_0 - \frac{D^2K_S}{K_{max}-D})) = \frac{1}{\alpha}(C_0 - \frac{2DK_S(K_{max}-D)+D^2K_S}{(K_{max}-D)^2}) \Leftrightarrow$
 $C_0(K_{max}-D)^2 = -D^2K_S + 2DK_SK_{max} \Leftrightarrow D^2(C_0 + K_S) - 2DK_{max}(C_0 + K_S) + C_0K_{max}^2 = 0 \Leftrightarrow (D - K_{max})^2 + K_{max}^2(-1 + \frac{C_0}{C_0+K_S}) = 0 \Leftrightarrow$
 $D = K_{max}(1 \pm \sqrt{\frac{-C_0+C_0+K_S}{C_0+K_S}}) = K_{max}(1 \pm \sqrt{\frac{K_S}{C_0+K_S}})$, but we saw earlier that $D = \mu$, so there is no way D could be greater than K_{max} , leaving us the only possible solution: $D_{max} = K_{max}(1 - \sqrt{\frac{K_S}{C_0+K_S}}) \Rightarrow$
 $N_{out,max} = \frac{1}{\alpha}(C_0 + K_S - \sqrt{K_S(C_0 + K_S)})$.

5 The “semi-permeable” model.

We will investigate a hypothetical growth-chamber somewhat similar to the chemostat.¹¹ In this growth-chamber bacteria and the stock-nutrient are kept in the same chamber with a semi-permeable membrane dividing them. The stock-nutrient concentration is kept constant. The micro-organisms have mortality μ .

5.1 Explaining the semi-permeable model.

We are given the equations:

$$\begin{cases} \frac{dN}{dt} = K_{max}(\frac{C}{K_n+C})N - \mu N & (a) \\ \frac{dC}{dt} = -\alpha K_{max}(\frac{C}{K_n+C})N + D(C_0 - C) & (b) \end{cases}$$

Now we want to know what each term means. In (a) we have a positive contribution to N and a negative one. The positive one, we remember from the chemostat, is the reproduction term. And $-\mu$ corresponds to the fraction of N that dies each time unit.

(b) includes two terms: the first term is consumption of C, α units of concentration are required to produce a unit of N, like in the chemostat, the next term corresponds to increase of C thanks to diffusion from the undrainable stock. If there is a big difference in concentration, we will have a larger inflow of C.

5.2 The dimensionless form of the semi-permeable model.

The units of the first line: $dim[\frac{dN}{dt}] = \frac{number}{time}$, $dim[N] = number$ and $dim[C] = \frac{mass}{volume}$, imply that $dim[K_{max}] = dim[\mu] = \frac{1}{time}$ and that $dim[K_n] = \frac{mass}{volume}$.

Continuing with the second line we get: $dim[\frac{dC}{dt}] = \frac{mass}{volume \cdot time}$ implying that $dim[D] = \frac{1}{time}$ and $dim[\alpha] = \frac{mass}{volume \cdot number}$.

We, as before, replace N , t and C with $N\hat{N}$, $t\hat{t}$ and $C\hat{C}$. After multiplying with $(\frac{\hat{N}}{t})^{-1}$ and $(\frac{\hat{C}}{t})^{-1}$ respectively we replace $K_n = \hat{C}$, $\hat{N} = \frac{\hat{C}}{\alpha K_{max}\hat{t}}$, $\alpha_1 = \hat{t}K_{max}$ and $\alpha_2 = \frac{C_0}{K_n}$ we get:

$$\begin{cases} \frac{dN}{dt} = \alpha_1 \frac{NC}{1+C} - \mu\hat{t}N \\ \frac{dC}{dt} = -\frac{NC}{1+C} + D\hat{t}(\alpha_2 - C) \end{cases}$$

We now wish that $D\hat{t} = \mu\hat{t} = 1$ but we must allow $D \neq \mu$ so we let $\mu\hat{t} = 1$ and $D\hat{t} = \delta$ giving us an equation very similar to the chemostat:

$$\begin{cases} \frac{dN}{dt} = \alpha_1(\frac{C}{1+C})N - N \\ \frac{dC}{dt} = -(\frac{C}{1+C})N + \delta(\alpha_2 - C) \end{cases} \quad (8)$$

We have reduced the number of parameters from six (K_{max} , K_n , μ , D , α and C_0) to three (α_1 , α_2 and δ) using our three dimensions. Here α_1 , α_2 are the exact same thing as in the chemostat model. We have one new parameter δ that needs some explaining: we notice $dim[\delta] = dim[D\hat{t}]$ but we know that $dim[\frac{dC}{dt}] = dim[D(C_0 - C)] = \frac{\hat{C}}{\hat{t}} \Rightarrow dim[D] = \frac{1}{\hat{t}} \Rightarrow dim[\delta] = 1$.

¹¹From [1], page 154, problem 14.

5.3 Steady-states, and the null-clines.

The null clines from $\dot{N} = 0$ are of course the same as for the chemostat: $N = 0$, or $C = \frac{1}{\alpha_1 - 1}$. With $N = 0$ we find that the trivial equilibrium solution is the same: $(\bar{N}_0, \bar{C}_0) = (0, \alpha_2)$.

Investigating the null cline from $\dot{C} = 0$ we get $N = \delta \frac{(C_0 - C)(C + 1)}{C}$. Giving positive N's if $C > C_0$, $N = 0$ if $C = C_0$ (or if $C = -1$), and negative N's if $C < C_0$.

Now, to find the non-trivial equilibrium solution, we insert $C = \frac{1}{\alpha_1 - 1}$ in the second null-cline: $N = \delta \alpha_1 (\alpha_1 - 1) (\alpha_2 - \frac{1}{\alpha_1 - 1})$

The equilibrium points and null-clines are thus:

$$\begin{cases} (\bar{N}_0, \bar{C}_0) = (0, \alpha_2) \\ (\bar{N}_1, \bar{C}_1) = \left(\delta \alpha_1 (\alpha_1 - 1) (\alpha_2 - \frac{1}{\alpha_1 - 1}), \frac{1}{\alpha_1 - 1} \right) \end{cases}$$

$$\begin{cases} \dot{N} = 0 & \Leftrightarrow (N = 0) \text{ or } (C = \frac{1}{\alpha_1 - 1}) \\ \dot{C} = 0 & \Leftrightarrow N = \delta \frac{(C_0 - C)(C + 1)}{C} \end{cases}$$

With this, we can now quite easily draw a phase-portrait.

5.4 A stability-analysis.

We use the tools given to us and find that $\mathbf{A} = \begin{pmatrix} \alpha_1 \frac{C}{1+C} - 1 & \alpha_1 \frac{N}{(1+C)^2} \\ -\frac{C}{1+C} & -\frac{N}{(1+C)^2} - \delta \end{pmatrix}$.

Taking a look at the trivial steady-state, we notice:

$$\mathbf{A}(\bar{N}_0, \bar{C}_0) = \begin{pmatrix} \frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 1 & 0 \\ -\frac{\alpha_2}{1 + \alpha_2} & -\delta \end{pmatrix} \Rightarrow \det(\mathbf{A}) = -\delta \left(\frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 1 \right)$$

We notice the same problem as for the chemostats trivial equilibrium point: $\det(\mathbf{A}) < 0$ because $1 < \frac{\alpha_1 \alpha_2}{1 + \alpha_2}$ as we saw earlier.

But if we investigate the non-trivial steady-state with $\sigma = \frac{\bar{N}_1}{(1 + \bar{C}_1)^2}$, we get:

$$\mathbf{A}(\bar{N}, \bar{C}) = \begin{pmatrix} 0 & \alpha_1 \sigma \\ -\frac{1}{\alpha_1} & -\sigma - \delta \end{pmatrix} \Rightarrow \begin{cases} \text{tr}(\mathbf{A}(\bar{N}, \bar{C})) & = -\sigma - \delta < 0 \\ \det(\mathbf{A}(\bar{N}, \bar{C})) & = +\sigma > 0 \end{cases}$$

The conditions for stability are fulfilled, the non-trivial steady-state is stable.

We remember the condition for real eigenvalues: $-4\det(\mathbf{A}) + \text{tr}(\mathbf{A})^2 > 0$. Renaming $\sigma = b \cdot \delta$ we get the condition $\delta > \frac{4b}{b+1}$ for real eigenvalues or $\delta < \frac{4b}{b+1}$ for complex ones.

6 Review.

Let us now take a look back and compare our models a bit. We first looked at the case where $\frac{dN}{dt} = k \cdot N$ giving us exponential growth: $N(t) = N_0 e^{kt}$. In introducing the nutrient concentration we got: $\begin{cases} \frac{dN}{dt} = kCN \\ \frac{dC}{dt} = -\alpha kCN \end{cases}$ giving us the logistic equation (and a similar case for C): $\frac{dN}{dt} = r(1 - \frac{N}{B})N$.

To derive the chemostat, we introduced the in and out-flow, we found two steady states and investigated the linearized stability. In the similar model, the semi-permeable model, we found almost the same thing. Results of our analysis are summarized in the table below.

| | Chemostat | Semi-permeable |
|--------------------------|-----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| \dot{N} | $\alpha_1(\frac{C}{1+C})N - N$ | $\alpha_1(\frac{C}{1+C})N - N$ |
| \dot{C} | $-(\frac{C}{1+C})N - C + \alpha_2$ | $-(\frac{C}{1+C})N + \delta(\alpha_2 - C)$ |
| Parameters. | $\alpha_1 = \frac{V}{F}K_{max}, \alpha_2 = \frac{C_0}{K_n}$ | $\alpha_1 = \frac{V}{F}K_{max}, \alpha_2 = \frac{C_0}{K_n}, \delta = D\hat{t}$ |
| Constraints. | $\alpha_1 > 1, \alpha_2 > \frac{1}{\alpha_1 - 1}$ | $\alpha_1 > 1, \alpha_2 > \frac{1}{\alpha_1 - 1}, \delta > 0$ |
| (\bar{N}_0, \bar{C}_0) | $(0, \alpha_2)$ | $(0, \alpha_2)$ |
| \mathbf{A}_0 | $\begin{pmatrix} \frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 1 & 0 \\ -\frac{\alpha_2}{1 + \alpha_2} & -1 \end{pmatrix}$ | $\begin{pmatrix} \frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 1 & 0 \\ -\frac{\alpha_2}{1 + \alpha_2} & -\delta \end{pmatrix}$ |
| $det(\mathbf{A}_0)$ | $-\frac{\alpha_1 \alpha_2}{1 + \alpha_2} + 1$ | $\delta(-\frac{\alpha_1 \alpha_2}{1 + \alpha_2} + 1)$ |
| $tr(\mathbf{A}_0)$ | $\frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 2$ | $\frac{\alpha_1 \alpha_2}{1 + \alpha_2} - 1 - \delta$ |
| Stable? | No. | No. |
| (\bar{N}_1, \bar{C}_1) | $(\alpha_1(\alpha_2 - \frac{1}{\alpha_1 - 1}), \frac{1}{\alpha_1 - 1})$ | $(\alpha_1 \delta(\alpha_1 - 1)(\alpha_2 - \frac{1}{\alpha_1 - 1}), \frac{1}{\alpha_1 - 1})$ |
| \mathbf{A}_1 | $\begin{pmatrix} 0 & \sigma \alpha_1 \\ -\frac{1}{\alpha_1} & -\sigma - 1 \end{pmatrix}$ | $\begin{pmatrix} 0 & \sigma \alpha_1 \\ -\frac{1}{\alpha_1} & -\sigma - \delta \end{pmatrix}$ |
| $det(\mathbf{A}_1)$ | σ | σ |
| $tr(\mathbf{A}_1)$ | $-\sigma - 1$ | $-\sigma - \delta$ |
| Stable? | Yes. | Yes. |

The two models are very similar. The difference is in an extra parameter δ for the semi-permeable case.

APPENDIX A: The Linearization, Stability, and Eigenvectors.

Some cumbersome, initially non-trivial, mathematical texts explaining the linearization, the stability of a linearized system, and the beginning of the invariant line, are put here to lighten up the main text.

The Linearization.

In general, for a one-variable function we can, by Taylor-expanding it around x , get $F(X + x) = F(X) + F'(X) \cdot x + O(x^2)$ if x is small in comparison to X we get: $F(X + x) \approx F(X) + F'(X) \cdot x$. We can call this the linearization of F if we include only the constant and the linear terms.

For two two-variable functions $F(N + n, C + c)$ and $G(N + n, C + c)$:

$$\begin{cases} F(N + n, C + c) = F(N, C) + F'_N(N, C)n + F'_C(N, C)c + O(n + c^2) \\ G(N + n, C + c) = G(N, C) + G'_N(N, C)n + G'_C(N, C)c + O(n + c^2) \end{cases}$$

If we now let...

$$\begin{cases} \frac{dN}{dt} = F(N + n, C + c), & \text{with } F(N, C) = 0 \\ \frac{dC}{dt} = G(N + n, C + c), & \text{with } C(N, C) = 0 \end{cases}$$

... we, by looking at the linearization, get...

$$\begin{cases} F(N + n, C + c) \approx F'_N(N, C)n + F'_C(N, C)c = a_{11}n + a_{12}c \\ G(N + n, C + c) \approx G'_N(N, C)n + G'_C(N, C)c = a_{21}n + a_{22}c \end{cases}$$

... allowing us to use the convenient notation: $\frac{d}{dt}\mathbf{X} = \mathbf{A}\mathbf{X} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} \mathbf{X}$, often used when looking at the chemostat or other dynamical systems of similar mathematical form.

The Stability.

Now, let us use our linearization and look at some conditions needed for the linearization to be stable: $\mathbf{X} = \mathbf{A}e^{\lambda t} \Rightarrow \frac{d}{dt}\mathbf{X} = \lambda\mathbf{A}e^{\lambda t} = \mathbf{A}\mathbf{v}e^{\lambda t}$. Eliminating the exponential in the two last terms, and treating it a little rewards us with a well-known equation: $\det(\mathbf{A} - \lambda\mathbf{I}) = 0$. Treating this equation a little leads us some interesting constraints:

$$\lambda = \frac{a_{11} + a_{22}}{2} \pm \frac{\sqrt{4(a_{12}a_{21} - a_{11}a_{22}) + (a_{11} + a_{22})^2}}{2} \Leftrightarrow$$

$$\lambda = \frac{\text{tr}(\mathbf{A})}{2} \pm \frac{\sqrt{-4\det(\mathbf{A}) + \text{tr}(\mathbf{A})^2}}{2}$$

Now, in order to have stable solutions, we must have $\lambda_{1,2} < 0$, forcing at least $\text{tr}(\mathbf{A}) < 0$ (otherwise, the solution with plus will have a positive real part).

Now, looking at this first solution with plus, we notice the following: $\lambda_1 < 0 \Leftrightarrow$

$$\frac{\text{tr}(\mathbf{A})}{2} + \frac{\sqrt{-4\det(\mathbf{A}) + \text{tr}(\mathbf{A})^2}}{2} < 0 \Leftrightarrow \text{tr}(\mathbf{A}) < -\sqrt{-4\det(\mathbf{A}) + \text{tr}(\mathbf{A})^2}$$

Now, when squaring the two sides, we multiply with something negative on both sides, changing the relation:

$$tr(\mathbf{A})^2 > -4det(\mathbf{A}) + tr(\mathbf{A})^2 \Leftrightarrow 0 < det(\mathbf{A})$$

Thus, for us to not have a positive real part in our exponentials (giving us stable solutions), we have to have: $tr(\mathbf{A}) < 0$ and $det(\mathbf{A}) > 0$. Allowing us to simply look at our linearization to know a lot of our how our system behaves near an equilibrium point.

Worth noting is also if $\sqrt{-4det(\mathbf{A}) + tr(\mathbf{A})^2}$ is real or complex. If a λ has a negative real part and no complex part in an equilibrium-point, this point could be considered to be a stable node because the exponentials include only negative real numbers.

If λ contains some complex parts we can easily discover that the pair of λ 's must be complex-conjugated and that the exponentials give rise of a spiral-like motion in the (N,C)-plane around the equilibrium-point. We call the point a stable spiral if $tr(\mathbf{A}) < 0$.

The Eigenvectors.

Let us return to the relation: $\lambda \mathbf{A} e^{\lambda t} = \mathbf{v} \mathbf{A} e^{\lambda t}$, and let us assume it gives us with the eigenvectors \mathbf{v}_1 and \mathbf{v}_2 , so that we have the solution:

$\mathbf{X} = C_1 \cdot \mathbf{v}_1 e^{\lambda_1 t} + C_2 \cdot \mathbf{v}_2 e^{\lambda_2 t}$ where C_1 and C_2 are constants. If we have the initial condition $\mathbf{X}_0 = \mathbf{v}_1 \cdot K$, it is clear that $C_1 = K$ and $C_2 = 0$.

The conclusions we can draw is that if we are close to an equilibrium-point, on the positive or negative elongation of an eigenvector, we can not leave this line (for a linearized system). This will be most useful when discussing the invariant line of the Chemostat.

APPENDIX B:

A Matlab chemostat.m file.

```

function chemostat(alfa1, alfa2, np0, cp0)
%
%CHEMOSTAT Displays a phaseportrait, null clines and an Euler-path
% of a Chemostat.
% CHEMOSTAT(alfa1, alfa2, np0, cp0) will run if
% alfa1 > 1 , thus there is a reproduction.
% alfa2 > 1/(alfa1 -1) , thus there is sufficient stock-nutrition.
% np0 > 0 , you can not have a nonpositive population.
% cp0 > 0 , you can not have a nonpositive concentration.
%
% The blue arrows represent the vectorfield.
% The black lines are two of the three nullclines.
% The black dotted line is the invariance-line (no solution crosses it).
% The red line is a standard Eulerpath, starting in *, with
% equidistant (in time) +'s .
%
% Try the following:
% chemostat( 2, 4, .1, .1) Meaning: initially an "empty" reactor.
% chemostat(1.5, 7, .1, 7) Meaning: initially stock concentration
% and "no" bacteria.
% chemostat(1.1, 20, .1, 20) Meaning: strong flushing, initially
% stock concentration and "no" bacteria.
% chemostat(20, .06, .01, .01) Meaning: low flushing, initially
% "empty" reactor.
%
% by Per Erik Strandberg, 2003, TATM91, LiTH.

% Start-condition:
if ((alfa1>1) & (alfa2> 1/(alfa1 -1)) & (cp0>0) & (np0>0)),

hold off

% The non-trivial equilibrium-solution:
nbar=alfa1*(alfa2-(1/(alfa1-1)));
cbar=(1/(alfa1-1));
plot(nbar,cbar,'o')
hold on

% The vector-field:
[nn,cc]=meshgrid(0.01*nbar : (2.99*nbar/15) : 3*nbar , 0.01*cbar :
(2.99*cbar/15) : 3*cbar);
dn= alfa1*nn.*cc./(cc+1)-nn;
dc= -nn.*cc./(cc+1)-cc+alfa2;
quiver(nn,cc,dn,dc, .5)

% The c-null cline:

```

```

ccc=[cbar/10: 3*cbar/100 :cbar*3];
nmn = (alfa2-ccc) .* (1+ccc) ./ ccc;
plot(nmn,ccc,'k')

% One of the n-null clines:
n5=[0 3*nbar];
c5=[(1/(alfa1-1)) (1/(alfa1-1))];
plot(n5,c5,'k')

% The Invariance-line:
c_inv=[cbar/10: 3*cbar/100 :cbar*3];
n_inv=alfa1*alfa2 - alfa1*c_inv;
plot(n_inv,c_inv,':k')

% The Euler-path:
np=[1:1:1000];
cp=[1:1:1000];
np(1)=np0;
cp(1)=cp0;
i=1;

while i < 1000,
    np(i+1)=np(i)+0.05*(alfa1*np(i)*cp(i)/(cp(i)+1)-np(i));
    cp(i+1)=cp(i)+0.05*((-1)*np(i)*cp(i)/(cp(i)+1)-cp(i)+alfa2);
    i=i+1;
end
plot(np,cp,'r')
plot(np(1), cp(1),'r*')

plot(np( 200), cp( 200), 'r+')
plot(np( 400), cp( 400), 'r+')
plot(np( 600), cp( 600), 'r+')
plot(np( 800), cp( 800), 'r+')
plot(np(1000), cp(1000), 'r+')

axis([0 3*nbar 0 3*cbar])

disp(' ')
disp(' CHEMOSTAT.M by Per Erik Strandberg, 2003, TATM91, LiTH. Finished OK. ')
disp(' ')

% The illegal indata case:
else
    disp(' ')
    disp(' CHEMOSTAT.M by Per Erik Strandberg, 2003, TATM91, LiTH. ')
    disp(' Did not Finish OK. (You used illegal indata. )')
    disp(' For syntax help type: help chemostat .')
    disp(' ')
end

```

References

- [1] Leah Edelstein-Keshet: *Mathematical Models in Biology*, McGraw Hill, Inc. (1988)
- [2] H. W. Blanch, D. S. Clark: *Biochemical Engineering*, Marcel Dekker (1997)