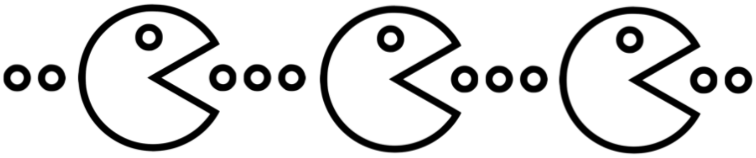
UNIVERSITY OF AMSTERDAM

MSc Mathematics
Master Thesis

GROWTH DYNAMICS OF CROSS-FEEDING MICROBES



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Examination date: November 2018

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Abstract

In this thesis we study microbial cross-feeding communities with nutrient-limited growth. Nutrient-limited growth means that an essential nutrient for some microbe species is scarce in the environment, which affects the growth rate of the species. In particular, we study the systems in which every species of microbes consumes an essential scarce nutrient that is produced by another species in a microbial community of multiple species. The focus lies on systems that are such that microbe concentrations can grow to infinity when time t approaches infinity and where the environment does not change over time; it is different per microbial community whether the growth rates of the species converge to the same rate or not.

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Introduction

A microorganism, or microbe, is a microscopic organism which may exist in a single-celled form or in a colony of cells.[1] The culture[2] of microorganisms is a method that has been used for millennia; yeast and bacteria are for example used as mixed cultures for the preparation of cheese, beer or bread. The technique has been known for so long and microbial forms of life are relatively simple, but profound analysis on the growth of microbial communities is experienced to be complex. If there is more known about the interaction between different species, one could obtain a better understanding of biological processes found in a natural environment. This could also give the (food) industry more insight for experiments with different cultures [1] [2].

The focus of this thesis is the growth dynamics of microbial communities when the growth of the species is limited due to a shortage of one or more nutrients. Jacques Monod set a foundation for the analysis on this subject, as he studied how growth rates are affected when there is a deficiency of one nutrient [3]. He found (for particular microorganisms and nutrients) that the total increase in concentration is proportional to the total intake of the limited concentration of the nutrient. Also, he discovered how to express the growth rate in the exponential growth phase in terms of the limiting nutrient. Even though these formulas come from empirical results, they are often accurate and thus widely used.

Over the years, scientists studied this same problem in the case of growing microbes inside a chemostat; based on Monod's growth curves, this could also be theoretically analyzed. A chemostat is a barrel to which a medium is continuously added, while liquid containing left-over nutrients, metabolic end products and microorganisms are continuously removed at the same rate to keep the volume constant [4]. In this *continuous culture*, the exponential growth of cells will be maintained because there will be no depletion of the limiting nutrient since it is continuously added and other conditions can be held in balance. This has the advantage that it can be both theoretically and experimentally analyzed to check if indeed the same outcome is obtained. Moreover, since in this case the volume is kept constant, the microbial concentrations in the chemostat are bounded (and possibly converge to an equilibrium). However, this continuous inflow of an essential nutrient

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[1] In this thesis, the words microbe, micro-organism or bacterium are used interchangeably.

[2] The term culture can be used for both the method as for the initial composition of species [1].

actually controls the growth of the species, hence the method thus describes more of an industrial way of modeling microbial communities [5] [6] [7].

In contrast to the continuous culture, the model that is studied in this thesis does not consider any controlled inflow of an essential nutrient but the essential nutrients are *only* produced by the microbes. The microbial cross-feeding process is initiated when fixed essential nutrient concentrations are added and the concentration of the nutrients in the environment during the process only relies on the consumption and production of the microbes, which is called a *batch culture* [4]. This means that the growth rate of some species actually depends on the production of the essential nutrient by some other species and not on some additional inflow. Some research is done covering this subject for the case that after some time the essential nutrients in the environment are completely consumed, hence for which the microbial concentrations are bounded, such as the recent article by *Kong et al.* [8].

In our case, we will consider the model in which the nutrient concentrations are not completely consumed after some time, but stay present in the environment. This should be possible if every essential nutrient is the product of at least one microbe species in the community. With the assumptions that the environment does not change over time in terms of pH-values, presence of inhibitory nutrients or scarcity of another essential nutrient, this means that the microbe concentrations can in theory grow infinitely large. Hence, the particular dynamics which are studied in this thesis are purely theoretical but could give a good indication of how the long-term behaviour is for microbial communities in large-scale environments. So unlike the aforementioned models in which the analyzed microbe concentrations are bounded, we will discuss in this thesis a model in which the microbe concentrations may grow to infinity when time approaches infinity. At the current time of writing, this type of system has not yet been studied.

We want to know for which conditions the microbe concentrations can grow infinitely large and we want to analyze the critical points at infinity: how can we obtain a model that shows what happens in the long term? What can be said about the concentrations of the different species when time t approaches infinity? The main question that ought to be proven to glue the pieces together is: do the growth rates of the different species converge to some steady state value? A model and an analysis are sought to represent and explain the dynamics of the community, which should also be extendable to higher-dimension and a more complex cross-feeding system.

The following gives a short overview of what will be discussed in the chapters.

- Chapter 2. By using the results of Monod we can model a two-species system in terms of a four-dimensional system of ordinary differential equations. The four-dimensional system can subsequently be simplified to a two-dimensional system of differential equations with some constraints for the initial conditions.

- Chapter 3. Since the microbe concentrations can infinitely large the critical points lie on infinity, so we want to compactify the space and observe the long-term dynamics. An intuitive choice for such compactification is to transform the space to a compact space in which the microbe concentrations x_1, x_2 are mapped to $z = \frac{x_1}{x_1+x_2}$, hence the fractional concentrations are considered. Phase portraits are easily obtained to get a visualization of the dynamics and to show how parameters influence the phase portraits. However, the transformation appears to be less practical for a mathematical analysis. The chapter is mainly based on numerical results and its purpose is to see what can be expected in the mathematical analysis.

- Chapter 4. A different compactification is introduced, known as the Poincaré transformation. The flow of the two-dimensional system on $\mathbb{R}^2$ will be projected onto the surface of the unit sphere. With this projection, the critical points at infinity are mapped onto the equator of the sphere. The dynamics on the sphere and the fixed points on the equator are mathematically analyzed. We will conclude that the non-trivial equilibrium points on the equator are degenerate, which makes the problem more complicated. By analyzing nullclines and other characteristic lines of the system, we shall find that there is one stable equilibrium on the equator (on the first octant).

- Chapter 5. An extension of the model to a community of n species with a "cyclic" cross-feeding topology is considered for which the Poincaré transformation is used again. We find that it is not necessary to go into detail of the dynamics on the sphere around and still discover a lot about the long-term behaviour by first considering only the nutrient dynamics to obtain a condition that ensures unbounded growth for all species. In fact, it can be proved that the growth rate of every species converges to the same value and their relative concentrations in this equilibrium can be obtained.

- Chapter 6. Three alternative cross-feeding topologies of a three-species microbial community is considered. The systems are obtained by considering different combinations of the consumed and produced nutrient of a species. For two of the three systems, we are able to use the same techniques as before to show the long-term behaviour. The third system is more complicated and the techniques introduced are not sufficient to prove how the system behaves in the long term.

2

Two-species cross-feeding system

This chapter is dedicated to introducing the two-species model with which will be worked, to give an intuitive understanding of the parameters that are used. The results of Monod are presented to show the relation between variables to obtain the main model of a two-species community.

2.1 Formulating the main model

Microbial growth is defined as the division of a micro-organism into two identical daughter cells. A microbe first increases in biomass and duplicates its DNA, and will subsequently split into two cells, both of which are genetically identical to the original cell. Mathematically speaking, if we start with one cell and if the number of these doubling events is denoted by n, then the number of cells after n doubling events is 2^n. If a constant number of events per unit time is assumed, we can write $n = (\text{doubling events}/\text{time}) \times \text{time} = r \cdot t$. It is convenient to rewrite this to the natural exponent: $2^n = 2^{rt} = e^{\ln(2^{rt})} = e^{\ln(2)rt} = e^{\mu t}$, where μ can be defined as the *growth rate*. Instead of the number of microbes of a species, we consider the concentration of the species which describes a continuous process. For a given beginning concentration x_0, the total concentration at a time t can then be given by $x(t) = x_0 e^{\mu t}$. The rate of change of the microbe concentration over time can then be expressed as $\frac{\mathrm{d}x(t)}{\mathrm{d}t} = \frac{\mathrm{d}x_0 e^{\mu t}}{\mathrm{d}t} = x_0 e^{\mu t}\mu = x(t)\mu$.

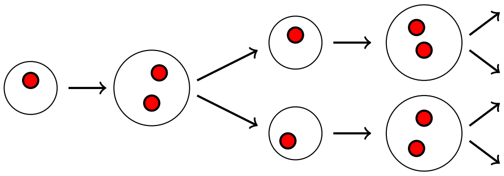

FIGURE 2.1 A cell divides itself into two identical duplicates.

The growth rate μ does not have to be constant over time, as it is affected by different factors; the concentration of a nutrient (required in order to grow) can be limited, the pH could change to some value where the microbes cannot grow, an inhibitor in the medium could slow down the growth, etc. Monod examined in his article *The growth of bacterial cultures* [3] how the growth evolves for different microbes in the presence of a limited concentration of an essential nutrient. He discovered that the variable growth rate that depends on the the growth-limiting nutrient m, denoted by $Q(m)$, can be expressed as follows:

$$Q(m) = V\frac{m}{K+m},$$

where V is the maximum growth rate, m is the concentration of the limiting nutrient and K is the concentration of the nutrient at which the rate is half the maximum growth rate.

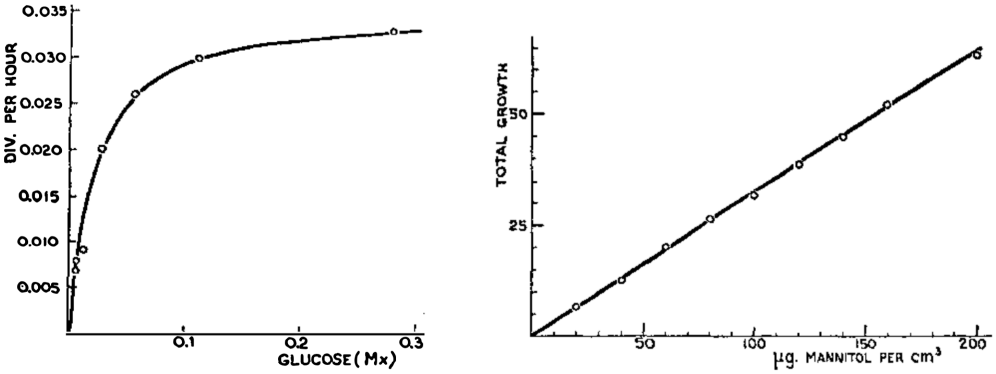

FIGURE 2.2 Monod found that the growth *rate* can be expressed in terms of the growth-limiting nutrient (l), and that the *total* growth is proportional to the total intake of the limiting nutrient (r). Figures from the article ”The growth of bacterial cultures” of Monod [3].

There are a lot of different systems one can study, but to be able to understand and analyze more complex systems, it is convenient to start with the most simple case; a cross-feeding community of two species in which each microbe consumes an (non-excessive) essential nutrient which is produced by the other microbe. The concentrations of the growth-limiting nutrients in the environment - hence the growth rates - thus depend on the production rates of these essential nutrients. The rates of change of the limiting nutrients are then given by the rate of the total production minus the rate of total consumption of the nutrients:

$$\begin{cases} \dot{x}_1 = Q_1(m_2)x_1, \\ \dot{x}_2 = Q_2(m_1)x_2, \\ \dot{m}_1 = p_{11}x_1 - c_{12}x_2, \\ \dot{m}_2 = p_{22}x_2 - c_{21}x_1, \end{cases} . \tag{2.1}$$

Here the concentration of microbes of species 1 (resp. 2) is denoted as x_1 (resp. x_2), and the concentration of the nutrient 1 (resp. 2) is denoted as m_1 (resp. m_2); the rate of producing nutrient 1 per unit concentration of species 1 is denoted by p_{11}, and the rate of consuming nutrient 2 per unit concentration of species 1 is denoted by c_{12}. Figure 2.3 shows a schematic interpretation of this system.

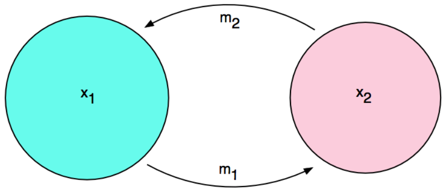

FIGURE 2.3 The microbial species 1 excretes (produces) a substance which is the growth-limiting nutrient for microbial species 2. Thus the increase in concentration (growth) of species 2 depends on the amount of substance produced by species 1.

Monod also described that the total intake of a limiting nutrient $\mathrm{d}s$ is proportional to the total change in growth $\mathrm{d}x$, that is, $\mathrm{d}x = C \cdot \mathrm{d}s$, C is defined as the yield of biomass on substrate s. Hence the growth rate is proportional to the consumption rate: $Q = \frac{\mathrm{d}x}{x\,\mathrm{d}t} = \frac{C \cdot \mathrm{d}s}{x\,\mathrm{d}t} = C \cdot c$, where c is the consumption rate. For convenience sake, I consider the inverse yield $H := \frac{1}{C}$, to leave out unnecessary division signs. Similarly, there will be more excretion when there is a faster growth rate, so that we should also consider that the production rate p is proportional to the growth rate [5] [7] [8]. Hence $G \cdot Q = p$, where G can be viewed as the yield in terms of number of created product per number of increased biomass. This means that we can substitute all the consumption and production rates in (2.1) so that the fundamental model governing the dynamics is as follows:

$$\boxed{\begin{cases} \dot{x}_1 = Q_1(m_2)x_1, \\ \dot{x}_2 = Q_2(m_1)x_2, \\ \dot{m}_1 = G_{11}Q_1(m_2)x_1 - H_{12}Q_2(m_1)x_2, \\ \dot{m}_2 = G_{22}Q_2(m_1)x_2 - H_{21}Q_1(m_2)x_1, \end{cases} \quad \text{where} \quad \begin{aligned} Q_1(m_2) &= V_1 \tfrac{m_2}{K_{12}+m_2}, \\ Q_2(m_1) &= V_2 \tfrac{m_1}{K_{21}+m_1}. \end{aligned}} \tag{2.2}$$

Our main focus lies on analyzing the behaviour of the growth rates in system (2.2) when the species have *unbounded growth*:

DEFINITION 2.1 A microbial species has unbounded growth if the microbe concentration grows to infinity when $t \to \infty$.

It is not clear yet from the equations for which parameter values or initial conditions we actually have unbounded growth. For the maximum growth rates V_1 and V_2 we would intuitively suspect that the microbe species with the smallest maximum growth rate would be an important factor in the system as this withholds the other from growing faster, since the production rate is growth rate dependent. This is indeed what we will find in the next chapters.

2.2 Simplification to a two-dimensional system

The assumption that both consumption and production rates are proportional to the growth rates is put to good use in this model. System (2.2) can be rewritten such that the following can be said:

THEOREM 2.2 *Assume that the cross-feeding community of two species is modeled by the four-dimensional system* (2.2). *This system can be written as a two-dimensional system governing the growth dynamics for both species:*

$$\begin{cases} \dot{x}_1 = V_1 \dfrac{m_2(x_1,x_2)}{K_{12}+m_2(x_1,x_2)} x_1 := V_1 \dfrac{G_{22}x_2 - H_{21}x_1 + C_2}{K_{12}+G_{22}x_2 - H_{21}x_1 + C_2} x_1, \\ \dot{x}_2 = V_2 \dfrac{m_1(x_1,x_2)}{K_{21}+m_1(x_1,x_2)} x_2 := V_2 \dfrac{G_{11}x_1 - H_{12}x_2 + C_1}{K_{21}+G_{11}x_1 - H_{12}x_2 + C_1} x_2, \end{cases} \tag{2.3}$$

where $C_i := -G_{ii}x_i(0) + H_{ij}x_j(0) + m_i(0)$ *for* $i,j \in \{1,2\}$ *and* $i \neq j$ *in the equations can attain any real value and can be seen as constraints of the initial conditions.*

Proof: Consider the rate of change of the nutrients in the environment, one sees that they are explicitly given by the rates of change of the microbe concentrations. That is, we can rewrite the system (2.2) to:

$$\begin{cases} \dot{x}_1 = Q_1(m_2)x_1, \\ \dot{x}_2 = Q_2(m_1)x_2, \\ \dot{m}_1 = G_{11}\dot{x}_1 - H_{12}\dot{x}_2, \\ \dot{m}_2 = G_{22}\dot{x}_2 - H_{21}\dot{x}_1. \end{cases} \tag{2.4}$$

If we integrate the derivatives of m_1 and m_2, the total concentrations of the nutrients can be explicitly given by the concentrations of the microbes (and initial conditions):

$$\begin{aligned} m_1 &= G_{11}x_1 - H_{12}x_2 + C_1, \\ m_2 &= G_{22}x_2 - H_{21}x_1 + C_2, \end{aligned} \tag{2.5}$$

where $C_1 = -G_{11}x_1(0) + H_{12}x_2(0) + m_1(0)$ and $C_2 = -G_{22}x_2(0) + H_{21}x_1(0) + m_2(0)$ depend on the initial microbe and nutrient concentrations. As m_1 and m_2 are now given in terms of x_1 and x_2, substitute m_i in the growth rates Q_i so that the growth dynamics (2.2) can be expressed in just x_1 and x_2. ■

Besides the advantage of this system just being defined in two variables, the downside is that the growth rate function is now analytically more complicated and some characteristics of the dynamics are less intuitive, but above all, the concentrations satisfy the conditions (2.5) at any time. This means that for given C_1 and C_2, only those initial conditions that satisfy (2.5) can be considered; to analyze trajectories with other initial conditions, the constants C_1 and C_2 should be adjusted accordingly. Also, the microbe concentrations can grow to infinity in which case one can not speak of equilibrium points, but of critical points at infinity.

We want to know what the long-term behaviour of the growth rates is when the species show unbounded growth. The following two chapters are dedicated to showing that the following conjecture holds.

CONJECTURE 2.3 *Let the microbial system be given by* (2.2). *For positive initial conditions the growth rates* Q_1 *and* Q_2 *converge to each other as* $t \to \infty$ *when the species have unbounded growth.*

Chapter 3 helps to support this conjecture by visualizing the system using phase portraits, and a mathematical proof is sought in Chapter 4. Not only do we want to prove this conjecture in a 2-dimensional system, the proof should also be extendable to a higher-dimensional system. These analyses should also give insight into the conditions for the presence of unbounded growth.

3

Fractional concentrations

Since the microbe concentrations can grow to infinity, the critical points of the system lie at infinity. To analyze what the long-term behaviour is like a compactification of the space is necessary; the fractional (or relative) concentrations are considered. The main interest in this chapter is gaining insight into whether these fractional concentrations converge at all, and if so, to which fractions and for which conditions. From these observations a hypothesis about the behaviour of the microbial community is made.

3.1 System of fractional concentrations

The microbe concentration of one species relative to the total microbe concentration of both species, hence the fractional concentration, is given by $z_i = \frac{x_i}{\sum x_j}$ for $i = 1, 2$. The transformation in this chapter is based on this transformed variable, which results in the following:

THEOREM 3.1 *The system of ODEs* (2.3) *can be transformed to a system defined on* $[0,1]^2$ *by the transformation* $z = \frac{x_1}{x_1+x_2}$ *and* $v = \frac{x_1+x_2}{1+x_1+x_2}$*, yielding the following system:*

$$\begin{cases} \dot{z} = z(Q_1 - Q_2)(1-z), \\ \dot{v} = v(1-v)(Q_1 z + Q_2(1-z)), \end{cases} \tag{3.1}$$

where Q_i *are the growth rates in terms of* z *and* v*.*

Proof: One can obtain the differential equation for z_i by substitution into the the short form of the growth equations (2.3):

$$\dot{z}_i \sum_j x_j + z_i \sum_j \dot{x}_j = \dot{\left(z_i \sum_j x_j \right)} = \dot{x}_i = Q_i x_i = Q_i z_i \sum_j x_j,$$

Rewrite this equation and substitute the derivatives $\dot{x}_i$ for $Q_i x_i$:

$$\dot{z}_i \sum_j x_j = Q_i z_i \sum_j x_j - z_i \sum_j \dot{x}_j = Q_i z_i \sum_j x_j - z_i \sum_j Q_j x_j = Q_i z_i \sum_j x_j - z_i \sum_j Q_j z_j \sum_k x_k.$$

The summations $\sum x_j$ can be cancelled out on both sides, as they are positive. Since z_1 depends on z_2 by the relation $z_1 = 1 - z_2$, the dynamics of one fractional concentration also describes the dynamics of the other. Set $z := z_1$ and substitute $z_2 = 1 - z$ into the differential equation so that the growth dynamics can be expressed in z:

$$\dot{z} = z(Q_1 - Q_2)(1 - z)z.$$

This form seems nice, but the growth rates Q_1 and Q_2 still depend on the summation $\sum x_j$, as explicitly shown for Q_1:

$$Q_1 = V_1 \frac{G_{22}(1-z)\sum x_j - H_{21} z \sum x_j + C_2}{k_{12} + G_{22}(1-z)\sum x_j - H_{21} z \sum x_j + C_2},$$

with the sum $\sum x_j$ possibly growing to infinity and whose behaviour is not yet described. Hence, write $s := \sum x_j$, so that substitution of $z = \frac{x_1}{s}$ into the growth equation (2.3) leads to the following:

$$\begin{aligned} \dot{s}z &= Q_1 s z - s\dot{z} = Q_1 s z - s(Q_1 - Q_2)(1-z)z \\ &= Q_1 s z - s Q_1 (1-z) z + s Q_2 (1-z) z = Q_1 s z^2 + s Q_2 (1-z) z. \end{aligned}$$

Thus the differential equation for s is defined as:

$$\dot{s} = s(Q_1 z + Q_2(1-z)).$$

So we now have a system of differential equations in z and s describing the growth dynamics of the original system. However, we have not yet dealt with the fact that this variable might grow to infinity for $t \to \infty$; by using the transformation $v := \frac{s}{1+s}$, the dynamics are mapped to a bounded set. The differential equation for this transformed variable is given as follows:

$$\dot{v} = \frac{(1+s)\dot{s} - \dot{s}s}{(1+s)^2} = \frac{\dot{s}}{(1+s)^2}.$$

Since the inverse transformation is denoted by $s = \frac{v}{1-v}$, one has $1 + s = 1 + \frac{v}{1-v} = \frac{1}{1-v}$. Hence $\dot{v}$ can be expressed as follows:

$$\dot{v} = \dot{s}(1-v)^2 = s(Q_1 z + Q_2(1-z))(1-v)^2 = v(1-v)(Q_1 z + Q_2(1-z)).$$

Ultimately, the growth rates Q_1, Q_2 are written in terms of z and v, as shown for Q_1:

$$Q_1(z,v) = V_1 \frac{G_{22}(1-z)\frac{v}{1-v} - H_{21}z\frac{v}{1-v} + C_2}{k_{12} + G_{22}(1-z)\frac{v}{1-v} - H_{21}z\frac{v}{1-v} + C_2}.$$

■

3.2 Phase plane analysis

From the two dimensional system of ODEs (3.1) a phase portrait can be obtained for chosen values of the parameters, so that the dynamics can be studied, see Figure 3.1. It is important to have these parameter values such that most of the characteristics of the behaviour are visualized, and such that they are biologically relevant (excluding mathematically special cases). Changing these parameters results in a different phase portrait and will be discussed in Section 3.3. We assume that the maximum growth rates satisfy $V_1 > V_2$. Since we fix C_1 and C_2 any point in the (z,v)-plane satisfies $m_1 = G_{11}x_1 - H_{12}x_2 + C_1$ and $m_2 = G_{22}x_2 - H_{21}x_1 + C_2$.

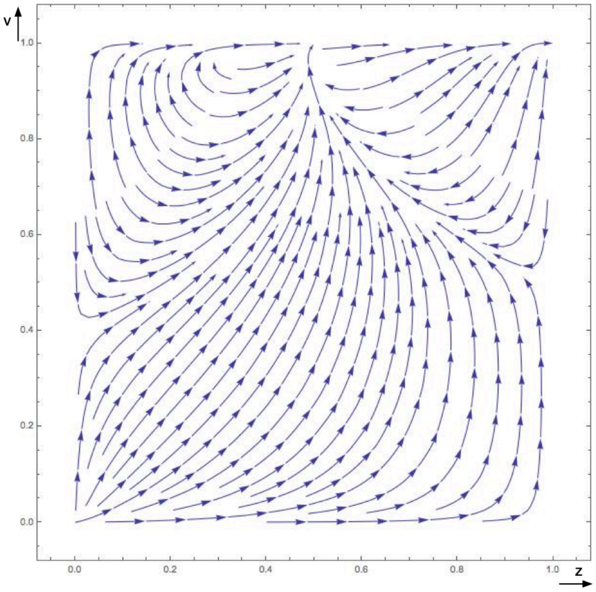

FIGURE 3.1 Example of a phase portrait on the (z,v)-plane, with maximum growth rates $V_1 = 10, V_2 = 7$ and the other parameters set to $G_{11} = 5, G_{22} = 1, H_{12} = 3, H_{21} = 1, K_{12} = 1, K_{21} = 3, C_1 = 2, C_2 = 1$.

In this plane, $v = 1$ corresponds to $\sum_i x_i \to \infty$ in the original system. We see that many trajectories converge to a certain point on the boundary $v = 1$. However, trajectories also seem to emerge from this same point towards the point $z = 1$ on the boundary $v = 1$. Moreover, considering these trajectories that converge to $(1,1)$, this would mean that the growth rate of one species is always bigger than the other so that eventually $z = \frac{x_1}{x_1+x_2} \to 1$. It is also unclear what really happens around the lines where the flow changes directions.

3.2.1 Biologically meaningful region

The reason of aforementioned odd behaviour is due to an additional restriction that should be taken into account. The plane shows the dynamics of the trajectories that satisfy the conditions $m_1 = G_{11}x_1 - H_{12}x_2 + C_1$ and $m_2 = G_{22}x_2 - H_{21}x_1 + C_2$, while not necessarily satisfying that m_i is positive. For a biologically meaningful trajectory, this should of course be the case.

THEOREM 3.2 *For the system* (3.1) *the region in* $[0,1]^2$ *in which is satisfied that the nutrient concentrations are positive, is enclosed by the curves*

$$v = \frac{C_1}{H_{12} - (G_{11} + H_{12})z + C_1}, \tag{3.2}$$

and

$$v = \frac{C_2}{(G_{22} + H_{21})z - G_{22} + C_2}. \tag{3.3}$$

Proof: The region of the pairs that satisfy the condition of positive nutrient concentrations, is deduced by the two expressions for the nutrient concentrations m_1 and m_2:

$$G_{11}x_1 - H_{12}x_2 + C_1 > 0, \quad G_{22}x_2 - H_{21}x_1 + C_2 > 0.$$

It is possible to express the variable x_2 in the variable x_1 and the parameter C_i:

$$x_2 < \frac{G_{11}x_1 + C_1}{H_{12}}, \quad x_2 > \frac{H_{21}x_1 - C_2}{G_{22}}$$

Suppose that both $C_i > 0$. Let us consider the upper bound for x_2, for which z satisfies:

$$z = \frac{x_1}{x_1 + x_2} > \frac{x_1}{x_1 + \frac{G_{11}x_1 + C_1}{H_{12}}} = \frac{H_{12}x_1}{(G_{11} + H_{12})x_1 + C_1}.$$

This inequality can be rewritten to an inequality of x_1 in terms of z:

$$x_1 < \frac{C_1 z}{H_{12} - (G_{11} + H_{12})z}.$$

Since v is increasing in $x_1 + x_2$, one can obtain the inequality for v by using the fact that by definition $x_1 + x_2 = \frac{x_1}{z}$:

$$v = \frac{x_1 + x_2}{1 + x_1 + x_2} = \frac{\frac{x_1}{z}}{1 + \frac{x_1}{z}} < \frac{\frac{C_1}{H_{12} - (G_{11} + H_{12})z}}{1 + \frac{C_1}{H_{12} - (G_{11} + H_{12})z}} = \frac{C_1}{H_{12} - (G_{11} + H_{12})z + C_1}. \tag{3.4}$$

This expression gives us explicitly the lower bound for z for different values of v, as shown in the left figure of Figure 3.2.

In the same way, the lower bound of x_2 can be considered, from which the second bound of the

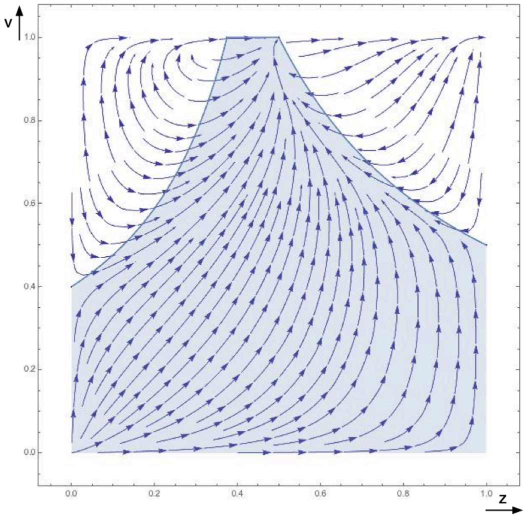

FIGURE 3.2 The marked region for which pairs (z, v) satisfy the restrictions.

region can be obtained:

$$v > \frac{C_2}{(G_{22} + H_{21})z - G_{22} + C_2}, \tag{3.5}$$

which will be called the upper bound (as it bounds z from above). ■

One can show that this region is invariant by considering the original system (2.2), for which we want to show that the concentrations cannot become negative when we start with non-negative values.

THEOREM 3.3 *The biologically meaningful region is an invariant region.*

Proof: Consider system (2.2) and suppose that $x_1, x_2, m_1, m_2 \geq 0$. As long as $m_1 \geq 0$ then $\dot{x}_2 = Q_2(m_1)x_2 \geq 0$, thus x_2 is non-decreasing; analogously for m_2 and x_1. Suppose that m_1 can become negative. By continuity, it should first reach $m_1 = 0$. However, $m_1 = 0$ yields $Q_2 = 0$ so that the derivative is $\dot{m}_1 = G_{11}Q_1x_1$, which can only be negative if m_2 is already negative (or $x_1 < 0$ but also then m_2 has to have been negative). Also for m_2 the same arguments show that it can only become negative if m_1 is already negative. So positive concentrations of the nutrients and microbes cannot become negative. Since the biologically meaningful region is the transformation of the region where $x_1, x_2, m_1, m_2 \geq 0$ in the original system, it proves the invariance. ■

3.2.2 Contour plot of nutrient concentration

From the plot of the restricted region, we see that the trajectories inside the region move towards a point to which also the bound of the region converges. As this bound is in fact the line on which $m_2 = 0$, it seems that the trajectories converges to a point where at least one nutrient depletes (and the growth rate converges to zero). This section will give insights into this oddity.

In the previous subsection, we studied the curves where the nutrient concentrations are equal to zero. Instead of considering zero, any other fixed value b for the concentration could be considered, so that the two conditions can be written for x_2:

$$x_2 = \frac{G_{11}x_1 + C_1 - b_1}{H_{12}}, \quad x_2 = \frac{H_{21}x_1 - C_2 + b_2}{G_{22}}.$$

The same rewriting to an expression of v in terms of z can be done (as in (3.2) and (3.3)), which results in the the expression of the curve on which $m_2 = b_2$:

$$v = \frac{C_2 - b_2}{(G_{22} + H_{21})z - G_{22} + C_2 - b_2}, \tag{3.6}$$

and the expression for the curve on which $m_1 = b_1$, being given by:

$$v = \frac{C_1 - b_1}{H_{12} - (G_{11} + H_{12})z + C_1 - b_1}. \tag{3.7}$$

One can observe that for the curves defined by (3.6), $v \to 1$ is satisfied if and only if $z \to \frac{G_{22}}{G_{22}+H_{21}}$. So this means that every curve on which $m_2 = b_2$ for any value $b_2 \in \mathbb{R}$ intersect the point $(z, v) = (\frac{G_{22}}{G_{22}+H_{21}}, 1)$. The same can be said about $m_1 = b_1$ for any $b_1 \in \mathbb{R}$ which intersects the other point in $v = 1$. The contour plots for the concentrations m_1 and m_2 expressed in z and v are shown in Figure 3.3.

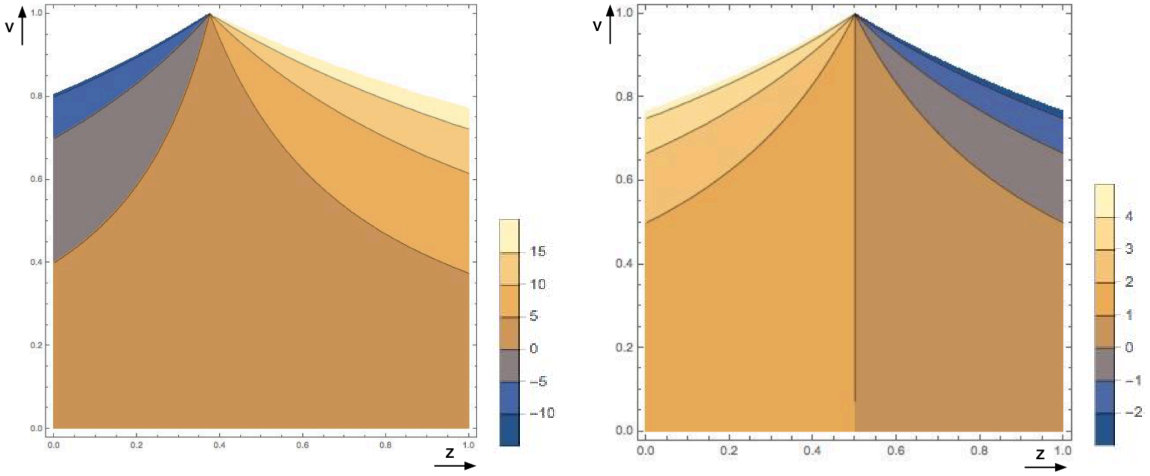

FIGURE 3.3 Contour plots for m_1 (left) and m_2 (right) for the same parameter settings the phase portraits, showing the values of these variables in the domain.

The observation that all these curves come together at the same point explains why the nutrient concentrations do not necessarily converge to zero even though the trajectories converge to the point which the curve $m_2 = 0$ intersects.

CLAIM 3.4 *For $i = 1, 2$, at the intersection point of the curves on which $m_i = b_i$ for $b_i \in \mathbb{R}$, the value of m_i is undefined.*

These plots also explain the behaviour in the upper corners where the arrows change direction (outside the meaningful region); this change of direction happens exactly on the curve where

$m_1 = -K_{21}$ and on the curve where $m_2 = -K_{12}$, for which the denominator in the growth rates are zero. Hence around each curve one of the growth rates changes from $-\infty$ to ∞. These curves obviously lie outside the biologically meaningful region, since the at least one nutrient concentration m_i is negative.

3.3 Long-term behaviour for adjusted parameters

In what way do the parameters influence the dynamics of the system? The phase portrait changes when a parameter is adjusted and these changes will be discussed in this subsection. The most important part is to analyze the bounds of the invariant region, as the dynamics inside the region do not seem to change much.

INFLUENCE OF C Recall that C_i is determined by initial conditions. However, since we fix C_i to draw the phase portraits, these parameters actually give a condition that the initial values should satisfy. The bounds of the biologically meaningful region are both the curve on which $m_1 = 0$ and the curve on which $m_2 = 0$. By viewing the equations for the bounds (3.4) and (3.5), one can see that a decrease in C_i gives the same result as an increase in b_i. Considering the contour plots of m_i in Figure 3.3, one can then see that an increase in C_1 makes the lower boundary of the invariant region move to the left, whereas an increase of C_2 makes the upper bound of the region move to the right.

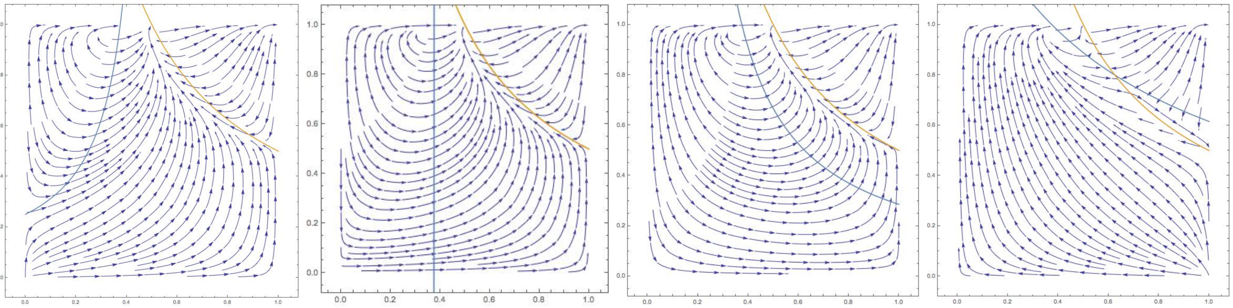

FIGURE 3.4 Several phase portraits for fixed value C_2 and varying C_1 (from positive to negative values). From the definition of C_i one should note that it is indeed biologically meaningful that this value may be negative. Note that the biologically meaningful region is the region in $[0,1]^2$ enclosed by the lower and upper bound for z.

INFLUENCE OF THE YIELDS For $v = 1$, the lower bound lies on $z = \frac{H_{12}}{G_{11}+H_{12}}$, while the upper bound lies on $z = \frac{G_{22}}{G_{22}+H21}$. Hence the lower bound is to the left of the upper bound if and only if

$$\frac{H_{12}}{G_{11}+H_{12}} \leq \frac{G_{22}}{G_{22}+H_{21}} \iff H_{12}(G_{22}+H_{21}) \leq G_{22}(G_{11}+H_{12}) \iff H_{12}H_{21} \leq G_{22}G_{11}$$
$$\iff 1 \leq \frac{G_{22}G_{11}}{H_{12}H_{21}}.$$

When this ratio is smaller than 1 the upper bound lies to the right of the lower bound in $v = 1$ so trajectories in the biologically meaningful region do not reach $v = 1$, hence the microbe concentrations then do not grow to infinity, see Figure 3.5. This is an important ratio which makes the difference whether the microbe concentrations can grow to infinity or not.

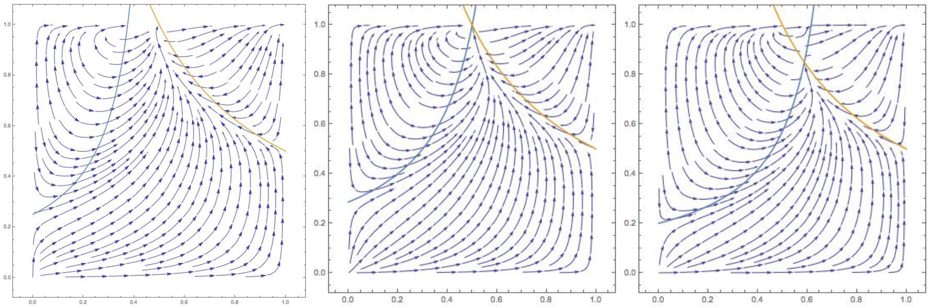

FIGURE 3.5 Decrease in the yields ratio also influences where v converges to, in these particular figures only the yields H_{12} and G_{11} were adjusted; adjusting the other two yields shifts the other bound. The right figure shows the case when the parameters are such that the microbe concentrations cannot grow infinitely large.

INFLUENCE OF THE MAXIMUM GROWTH RATE We assumed in this section that $V_1 > V_2$. One might deduce that if $V_1 < V_2$ the dynamics will change in such a way that all trajectories now converge to the lower bound of the invariant region in $v = 1$ instead of to the upper bound in the case of unbounded growth.

INFLUENCE OF K There are constants K_{ij} in the growth rates, which depends on the species and limiting nutrient used. This only changes the dynamics slightly, in particular when the nutrient concentrations are small; the constant K_{ij} influences the slope of the growth rate in such a way that for smaller K_{ij} the maximum growth is reached for a lower concentration of the nutrient.

INFLUENCE OF TYPE OF GROWTH RATE One can see that as long as the growth rate is a monotonically increasing bounded function of the nutrient, it will result in the same dynamics as seen above. Just like the the influence of K_{ij}, only the short-term behaviour is different, but since the total nutrient concentration always grows to infinity, one growth rate reaches its maximum which then limits the other growth rate.

From the aforementioned observations, one knows how the stream plot changes when parameters are adjusted. This kind of phase plane analysis shows heuristically the converging behaviour, but a cohesive algebraic proof is missing, so the following shall not yet be stated as a theorem; it will rather act as a guideline for the analysis done in the next chapter.

CLAIM 3.5 *Let the growth dynamics be given by the transformed system* (3.1) *and suppose that* $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ *and* $V_1 > V_2$. *In the biologically meaningful region, every trajectory converges to the point* $(z, v) = (\frac{G_{22}}{G_{22}+H_{21}}, 1)$. *Hence the proportion of the microbe concentrations will converge to*

$$\frac{x_1}{x_2} = \frac{z}{1-z} = \frac{\frac{G_{22}}{G_{22}+H_{21}}}{1 - \frac{G_{22}}{G_{22}+H_{21}}} = \frac{G_{22}}{G_{22} + H_{21} - G_{22}} = \frac{G_{22}}{H_{21}}.$$

3.4 Discussion on the fractional transformation

Compactifying the system by considering fractional concentrations of the microbes is an intuitive way of approaching the problem. The analysis performed was quite specific and rather computational. We could see exactly what the dynamics looked like and how the parameters influence the behaviour. The important results came from the plots that showed the biologically meaningful region (where the nutrient concentrations are positive) where we noticed that $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ is an important ratio that determines whether the trajectories can converge to $v = 1$, hence for which the microbe concentrations have unbounded growth. The contour plots of m_1 and m_2 showed the intersection of the lines on which $m_i = b_i$ for any $b_i \in \mathbb{R}$ on $v = 1$, giving that the nutrient concentration is not defined in this intersection. Since the equilibrium point in $v = 1$ to which the trajectories in the biologically meaningful region converge coincides with (at least) one of these intersections, (at least) one growth rate is not defined in the equilibrium point; hence it is not clear yet from these plots what the long-term behaviour of the growth rates is in the case of unbounded growth.

Instead of observing *what* happens, we want to know *why* it happens; what are the important factors of the system such that trajectories converge to a given point and which of the results will be useful for the analysis of a higher-dimensional system? A different transformation to compactify the system will be presented and a mathematical analysis will be performed in which the equilibrium points are attempted to be classified with linear stability analysis. Linear stability analysis could have also been done for the preceding transformation but we only show it for the following transformation since characteristics are more elegantly described and is therefore more appropriate for the higher-dimensional case. We can eventually compare the two transformations and discuss their similar characteristics.

4

Projection onto the sphere

We will perform in this chapter a different compactification of the two-dimensional system that was obtained in Chapter 2:

$$\begin{cases} \dot{x}_1 = V_1 \dfrac{m_2(x_1, x_2)}{K_{12} + m_2(x_1, x_2)} x_1 := V_1 \dfrac{G_{22}x_2 - H_{21}x_1 + C_2}{K_{12} + G_{22}x_2 - H_{21}x_1 + C_2} x_1, \\ \dot{x}_2 = V_2 \dfrac{m_1(x_1, x_2)}{K_{21} + m_1(x_1, x_2)} x_2 := V_2 \dfrac{G_{11}x_1 - H_{12}x_2 + C_1}{K_{21} + G_{11}x_1 - H_{12}x_2 + C_1} x_2, \end{cases} \tag{4.1}$$

An alternative approach of studying the behaviour of trajectories at infinity is by using the Poincaré sphere, introduced by Henri Poincaré in his article *Mémoire sur les courbes définies par une équation différentielle* [10]. A more readable version of this approach can be found in the book *Differential Equations and Dynamical Systems* [9]. There will be a projection from the center of the unit sphere $S^2 = \{(X, Y, Z) \in \mathbb{R} : X^2 + Y^2 + Z^2 = 1\}$ onto the (x_1, x_2)-plane, which lies tangent to S^2 at the north pole, as shown in Figure 4.1. The critical points at infinity are then mapped along the equator of the sphere, on $X^2 + Y^2 = 1$. The positive plane $(x_1 > 0, x_2 > 0)$ is mapped to the first octant; we will study the whole first octant instead of only the biologically meaningful region

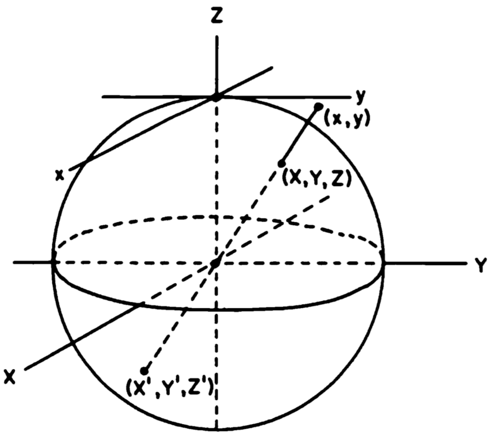

FIGURE 4.1 Projection of the (x, y)-plane onto the surface of the unit sphere. Figure from the book *Differential Equations and Dynamical Systems* [9].

on which we should be able to classify the equilibrium points by linear stability analysis. This then also gives information about biologically meaningful orbits.

We already observed in the previous chapter that there are lines in the plane on either side of which trajectories go in opposite directions. These are the lines where $Q_i \to \infty$ which are the singularities in the system that happen because the denominator goes to zero. One can eliminate the singularities from the system by multiplying both equations by the denominators of Q_i so that, setting

$$L[x_1, x_2] = (K_{21} + m_1(x_1, x_2)(K_{12} + m_2(x_1, x_2)),$$

the following system is obtained:

$$\begin{cases} L[x_1, x_2]\dot{x}_1 = p_1(x_1, x_2)x_1, \\ L[x_1, x_2]\dot{x}_2 = p_2(x_1, x_2)x_2, \end{cases} \tag{4.2}$$

where p and q are quadratic polynomials in x_1 and x_2 given by

$$p_1 = V_1 m_2(x_1, x_2)(K_{21} + m_1(x_1, x_2)),$$
$$p_2 = V_2 m_1(x_1, x_2)(K_{12} + m_2(x_1, x_2)).$$

Normally, when there is a constant α in front of the time derivative, one can substitute it inside the derivative by the time scale $t = \alpha\tau$. Then $\frac{\mathrm{d}z}{\mathrm{d}t} = \frac{\mathrm{d}z}{\mathrm{d}\tau}\frac{\mathrm{d}\tau}{\mathrm{d}t} = \frac{\mathrm{d}z}{\mathrm{d}\tau}\frac{1}{\alpha}$. Similarly, a non-constant can be taken into the time derivative, in such a way that $L[x_1, x_2]\,\mathrm{d}\tau = \mathrm{d}t$. In the scaled time derivative, the system is given by:

$$\begin{cases} x_1' = p_1(x_1, x_2)x_1, \\ x_2' = p_2(x_1, x_2)x_2. \end{cases} \tag{4.3}$$

The phase planes of (4.2) and (4.3) are actually the same, but orbits are traversed with different speed and (possibly) directions. At the positions in the plane where p_i is negative the derivative in scaled time τ will be of opposite sign as the the derivative in the original time t; hence the orbit is traversed in the opposite direction. The advantage of this is that the orbits do not change direction around the lines of singularity as we saw in the previous chapter. Note that p_i by definition can only be negative outside the biologically meaningful region.

4.1 Poincaré transformation

In order to have the planar dynamics projected onto the Poincaré sphere, the system undergoes the following transformation:

THEOREM 4.1 *Let the system of ODEs be given by* (4.3)*. By introducing the new variables* X, Y, Z *as* $x_1 = \frac{X}{Z},\ x_2 = \frac{Y}{Z},\ X^2 + Y^2 + Z^2 = 1$*, the system can be projected onto the unit sphere with the* *dynamics given by:*

$$\begin{cases} \dot{X} = XP_1 + X\left(-X^2P_1 - Y^2P_2\right), \\ \dot{Y} = YP_2 + Y\left(-X^2P_1 - Y^2P_2\right), \\ \dot{Z} = Z\left(-X^2P_1 - Y^2P_2\right). \end{cases} \tag{4.4}$$

where

$$\begin{aligned} P_1 &= V_1\Big(- H_{21}X + G_{22}Y + C_2Z\Big)\Big(G_{11}X - H_{12}Y + (C_1 + K_{21})Z\Big), \\ P_2 &= V_2\Big(- H_{21}X + G_{22}Y + (C_2 + K_{12})Z\Big)\Big(G_{11}X - H_{12}Y + C_1Z\Big). \end{aligned}$$

Proof: We will show this by considering a modified Poincaré transformation:

$$x_1 = \frac{X}{Z^\alpha},\ x_2 = \frac{Y}{Z^\beta},\ X^a + Y^b + Z^c = 1,$$

where α, β, a, b, c will be defined later. In some cases, different values for these parameters may give a projection from which more information about critical points can be obtained [11]. Substitute these variables into the equations (4.3):

$$\begin{aligned} \frac{Z^\alpha X' - \alpha Z^{\alpha-1}Z'X}{Z^{2\alpha}} &= x_1' = x_1p_1(x,y) = \frac{X}{Z^\alpha}p_1(\frac{X}{Z^\alpha}, \frac{Y}{Z^\alpha}), \\ \frac{Z^\beta Y' - \beta Z^{\beta-1}Z'Y}{Z^{2\beta}} &= \frac{Y}{Z^\beta}p_2(\frac{X}{Z^\beta}, \frac{Y}{Z^\beta}). \end{aligned}$$

Since p_1 and p_2 are quadratic polynomials, in order to remove the singularities, multiply the first equation by $Z^{3\alpha}$ and the second by $Z^{3\beta}$:

$$\begin{aligned} Z^{2\alpha}X' - \alpha Z^{2\alpha-1}Z'X &= XP_1(X, Y, Z^\alpha), \\ Z^{2\beta}Y' - \beta Z^{2\beta-1}Z'Y &= YP_2(X, Y, Z^\beta), \end{aligned}$$

where P_1 and P_2 are deduced from the multiplication of p and q with $Z^{2\alpha}$ and $Z^{2\beta}$ respectively:

$$\begin{aligned} Z^{2\alpha}p_1(\frac{X}{Z^\alpha}, \frac{Y}{Z^\alpha}) &= Z^{2\alpha}V_1(-H_{21}\frac{X}{Z^\alpha} + G_{22}\frac{Y}{Z^\alpha} + C_2)(G_{11}\frac{X}{Z\alpha} - H_{12}\frac{Y}{Z^\alpha} + (C_1 + K_{21})) \\ &= V_1(-H_{21}X + G_{22}Y + C_2Z^\alpha)(G_{11}X - H_{12}Y + (C_1 + K_{21})Z^\alpha) \\ &=: P_1(X, Y, Z^\alpha), \end{aligned}$$

and same for P_2. Choose α and β such that the exponents are the same, i.e., choose $\alpha = \beta$ (solving for Z' will then be easier):

$$Z^{2\alpha}X' - \alpha Z^{2\alpha-1}Z'X = XP_1(X, Y, Z^\alpha), \tag{4.5}$$

$$Z^{2\alpha}Y' - \alpha Z^{2\alpha-1}Z'Y = YP_2(X, Y, Z^\alpha). \tag{4.6}$$

The third condition is imposed to close the system, for which the derivative is given by:

$$aX^{a-1}X' + bY^{b-1}Y' + cZ^{c-1}Z' = 0. \tag{4.7}$$

To solve the equations (4.5)-(4.7) for Z', multiply the first by $-aX^{a-1}$, the second by $-bY^{b-1}$ and the third by $Z^{2\alpha}$, so that after cancellation of terms the sum of these becomes:

$$\begin{aligned}(\alpha a X^a + \alpha b Y^b + cZ^c)Z^{2\alpha-1}Z' &= \alpha a Z^{2\alpha-1}Z'X^a + \alpha b Z^{2\alpha-1}Z'Y^b + cZ^{c-1+2\alpha}Z' \\ &= -aX^aP_1 - bY^bP_2.\end{aligned}$$

To simplify the part inside the brackets by making use of the third constraint, we want to have that $\alpha a = \alpha b = c$, which implies that $a = b$ and $c = \alpha a$ and the equation writes to:

$$\alpha Z^{2\alpha-1}Z' = -X^aP_1 - Y^aP_2.$$

Comparing this expression with the equations (4.5) and (4.6), we see that it can be readily substituted to obtain expression for X' and Y' and Z':

$$\begin{aligned}Z^{2\alpha}X' &= XP_1(X, Y, Z^\alpha) + X(-X^aP_1 - Y^aP_2), \\ Z^{2\alpha}Y' &= YP_2(X, Y, Z^\alpha) + Y(-X^aP_1 - Y^aP_2), \\ Z^{2\alpha-1}Z' &= \frac{1}{\alpha}(-X^aP_1 - Y^aP_2).\end{aligned}$$

To have the same terms in front of the derivatives, multiply the third equation by Z, so that we can scale the time variable with $Z^{2\alpha}$ to obtain the desired equations in terms of α and a. It is clear that the choice for a and α does not really matter, as they do not make the system much different. In particular, there is no certain choice in these parameters so that there is *no* degeneracy of the fixed points on $Z = 0$.[1] So choose $a = b = c = 2$ and $\alpha = \beta = 1$, which is the standard Poincaré transformation. ■

REMARK *I chose in the beginning α and β to be equal. This simplified the derivation of the expression for Z', but could possibly exclude a more suitable choice of these parameters. Without loss of generality, suppose $\alpha < \beta$, then the equations become:*

$$\begin{aligned}Z^{2\alpha+2\beta}X' &= -X(-cP_1Z^{c+2\beta} + bP_2Y^bZ^{2\alpha}\alpha - bP_1Y^bZ^{2\beta}\beta), \\ Z^{2\alpha+2\beta}Y' &= -Y(-cP_2Z^{c+2\alpha} + aP_2X^aZ^{2\alpha}\alpha - aP_1Y^bZ^{2\beta}\beta), \\ Z^{2\alpha+2\beta}Z' &= -Z(bP_2Y^bZ^{2\alpha} + aP_1X^aZ^{2\beta}).\end{aligned}$$

The degeneracy happens at $Z = 0$ in the points where $P_1 = P_2 = 0$. We want the smallest exponent with respect to powers of Z in the three equations to be equal. However, the smallest term for Z'

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[1] More on the presence of non-hyperbolic equilibra in the next subsection.

will be $Z^{2\alpha+1}$, whereas the smallest term for the other two equations is at most $Z^{2\alpha}$. Since these terms do not coincide, it is not possible to choose α in such a way that the smallest exponent for Z are equal for the equations. Hence, if we would divide out Z^{2a}, there will always remain a term Z in front of the expression for Z', whereas the other two expressions then have terms independent of Z. One can see that both $Z = 0$ and $P_1 = P_2 = 0$ give that $Z' = 0$; this is what gives the complication when considering linear stability analysis in Section 4.2. The non-trivial equilibrium points happen to lie on the points where $Z = 0$ and $P_1 = P_2 = 0$; the derivative to any variable (X, Y, Z) of the expression for Z' evaluated in these points will equal zero. See Theorem 4.4.

In this system, $Z \to 0$ corresponds to $x, y \to \infty$ in the original system, which indeed occurs as we are looking at the unbounded growth case. The equilibria for positive X, Y, Z can be obtained by considering the different combinations of fixed points of the three variables; there are in the positive octant $X, Y, Z \geq 0$ three trivial equilibria:

$$(X = 0, Y = 1, Z = 0), (X = 1, Y = 0, Z = 0), (X = 0, Y = 0, Z = 1),$$

and several non-trivial equilibria given in terms of P_1 and P_2:

$$(X = 0, P_2 = 0), (Y = 0, P_1 = 0), (P_1 = 0, P_2 = 0).$$

The exact points of the equilibria implicitly defined by $(P_1 = 0, P_2 = 0)$ will be derived in the next section. First, some properties of these lines are shown in the following subsection.

4.1.1 The first octant and properties on it

In this subsection, we will have a closer look at some of the properties of the functions P_1 and P_2 on the first octant which are necessary for further analysis on stability of equilibrium points. From the definition of P_1 and P_2 one can see that each function is a product of two functions. For simplicity, define the following:

DEFINITION 4.2 Let the functions $\mathcal{M}_1$ and $\mathcal{M}_2$ be defined as follows:

$$\mathcal{M}_1 = G_{11}X - H_{12}Y + C_1 Z, \quad \mathcal{M}_2 = G_{22}Y - H_{21}X + C_2 Z.$$

The functions P_1 and P_2 can be written in terms of $\mathcal{M}_1$ and $\mathcal{M}_2$:

$$P_1 = V_1 \mathcal{M}_2(\mathcal{M}_1 + K_{21}Z), \quad P_2 = V_2(\mathcal{M}_2 + K_{12}Z)\mathcal{M}_1.$$

From the definition of $\mathcal{M}_1$ and $\mathcal{M}_2$ one can see that these functions are influenced by the yield parameters and (especially) by the parameters C_1 and C_2. For example, the point $\mathcal{M}_2 = 0$ on $Y = 0$ can be expressed as $\frac{X}{Z} = \frac{C_2}{H_{21}}$; if $C_2 > 0$ this point lies on $X > 0$ (on the positive hemisphere), but if $C_2 < 0$ this point lies on $X < 0$ (on the positive hemisphere). One might observe from

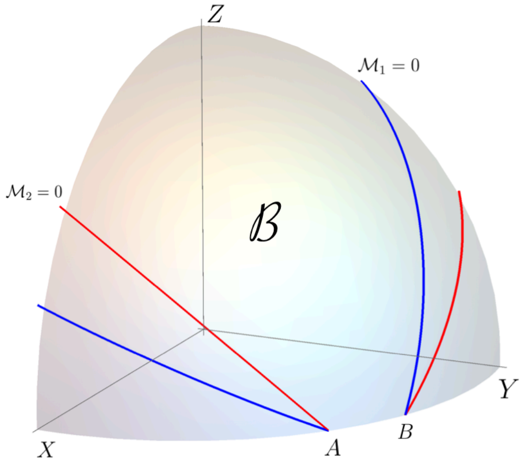

FIGURE 4.2 The red and blue lines are the zeroes for P_1 and P_2 respectively for $C_1, C_2 > 0$ and $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. Proposition 4.3 shows that in $\mathcal{B}$ both $P_1 > 0$ and $P_2 > 0$.

Figure 4.2 that in the latter case it is possible that $\mathcal{M}_2 = 0$ and $\mathcal{M}_1 = 0$ intersect in the first octant, hence a new equilibrium point arises (since in this intersection $P_1 = P_2 = 0$). Considering this, we start with the assumption that $C_1, C_2 > 0$.

The intersections $P_1 = P_2 = 0$ on the equator can be explicitly given by:

$$A := \{(X,Y,Z) \in S^2 : Z = 0, \frac{X}{Y} = \frac{G_{22}}{H_{21}}\},$$
$$B := \{(X,Y,Z) \in S^2 : Z = 0, \frac{X}{Y} = \frac{H_{12}}{G_{11}}\}.$$

One can see that the lines $P_1 = 0$ and $P_2 = 0$ through A in fact only intersect in A (in the first octant) since they are given by $\mathcal{M}_2 = 0$ and $\mathcal{M}_2 = -K_{12}Z$, hence only equal in $Z = 0$ (since $K_{12} \neq 0$). The same is true for the zeroes of P_1 and P_2 through B.

Finally, we see that for the ratio $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ point A is to the left of point B on the equator. Hence for $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ the only intersection of the lines $P_1 = 0$ and $P_2 = 0$ is on the equator (note how there would be more intersections when A moves to the right of B), thus we also start with assuming this condition.

Finally, denote $\mathcal{B}$ as the region that is enclosed by $\mathcal{M}_1 = 0$ and $\mathcal{M}_2 = 0$ as depicted in the Figure 4.2.

PROPOSITION 4.3 *P_1 is positive in the region enclosed by its zeroes $P_1 = 0$ and negative outside. P_2 is positive in the region enclosed by its zeroes $P_2 = 0$ and negative outside. Hence in the interior of the region $\mathcal{B}$ both P_1 and P_2 are positive.*

Proof: On $Z = 0$, $\mathcal{M}_1 > 0 \iff G_{11}X > H_{12}Y$ and $\mathcal{M}_2 > 0 \iff G_{22}Y > H_{21}X$. One can see that these conditions are exactly the points A and B; between these points on the equator both functions $\mathcal{M}_1$ and $\mathcal{M}_2$ are positive. This implies that P_1 and P_2 are positive on the equator between A and B. We can furthermore deduce that to the left of A we have $\mathcal{M}_1 > 0$ and $\mathcal{M}_2 < 0$, whereas to the right of B we have $\mathcal{M}_1 < 0$ and $\mathcal{M}_2 > 0$. Hence outside the interval between A and B on the equator we have that both $P_1 < 0$ and $P_2 < 0$.

From the signs of the functions P_1 and P_2 on the equator we can derive the signs of P_1 and P_2 on the first octant enclosed by their respective zeroes $P_1 = 0$ and $P_2 = 0$. ■

REMARK (Assumptions) *In the following analysis we assume that both* $C_1 > 0$ *and* $C_2 > 0$ *and that* $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. *As before, we also assume that* $V_1 > V_2$.

4.2 Projection onto tangent planes

The flow can again be projected onto planes tangent to S^2 so that equilibria are more easily classified. If the surface is projected onto the plane $X = 1$, then in any neighbourhood of a critical point on the equator the flow is topologically equivalent to the flow defined on the plane $X = 1$, except on the points $(0, \pm 1, 0)$ [9]. In particular, all of the equilibrium points on $X = 0$ are projected to ∞. To be able to classify all equilibrium points on the sphere, we consider both projections onto $X = 1$ and onto $Y = 1$. Points on the equator of the sphere will be denoted by the fraction $\frac{X}{Y}$, which is unique on the positive octant. In this way, one can immediately obtain the actual relative microbial fraction when a trajectory on the sphere converges to a point, since $\frac{X}{Y} = \frac{\frac{X}{Z}}{\frac{Y}{Z}} = \frac{x_1}{x_2}$. Moreover, the points on the equator are in general more easily expressed using fractions.

4.2.1 Projection onto X=1

The projection onto the plane $X = 1$ is done by setting $X = 1$ in the system of equations. This also means that there is no change in the X direction, so that the system on this plane can be given

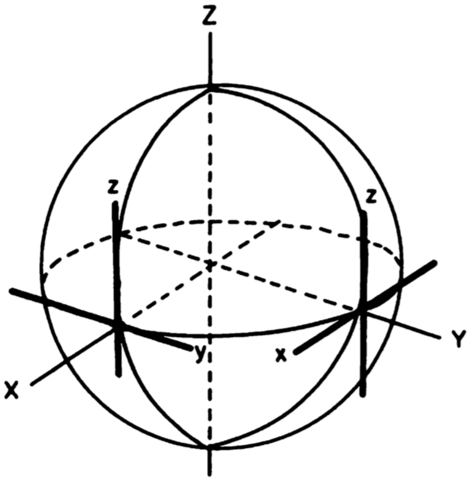

FIGURE 4.3 Projection of the dynamics on the surface of the sphere onto planes tangent to the sphere. The flows on the tangent planes are topologically equivalent to the flows on the sphere. Figure from the book *Differential Equations and Dynamical Systems* [9].

in the variables y and z:

$$\begin{cases} \dot{y} = y(P_2 - P_1 - y^2 P_2), \\ \dot{z} = z(-P_1 - y^2 P_2), \end{cases} \tag{4.8}$$

where now

$$\begin{aligned} P_1 &= V_1(-H_{21} + G_{22}y + C_2 z)(G_{11} - H_{12}y + (C_1 + K_{21})z), \\ P_2 &= V_2(-H_{21} + G_{22}y + (C_2 + K_{12})z)(G_{11} - H_{12}y + C_1 z). \end{aligned}$$

Using the same letters P_1 and P_2 on this plane should not be confusing in the context of the lower-case variables y and z. The equilibria in this system are denoted by:

$$(y = 0, z = 0), (y = 0, P_1 = 0), (P_1 = 0, P_2 = 0).$$

The points A and B on the sphere (on the equator on which $P_1 = P_2 = 0$) are mapped to $(y, z) = (\frac{H_{21}}{G_{22}}, 0)$ and $(y, z) = (\frac{G_{11}}{H_{12}}, 0)$ respectively.

4.2.1.1 Linear stability analysis gives no information on the equator

In this subsection we want to classify the equilibrium points on the plane on which the flow is projected with linear stability analysis. However, we will find that for the non-trivial equilibria it is not possible to do so. To summarize the classifications a figure is made with the classified equilibrium points in the next section. The Jacobian matrix is given by

$$J = \begin{bmatrix} P_2 - P_1 - y^2 P_2 + Y(P_{2y} - P_{1y} - y^2 P_{2y} - 2yP_2) & y(P_{2z} - P_{1z} - y^2 P_{2z}) \\ z(-P_{1y} - y^2 P_{2y} - 2yP_2) & -P_1 - y^2 P_2 + z(-P_{1z} - y^2 P_{2z}) \end{bmatrix}.$$

Evaluating the Jacobian at the trivial equilibrium $(y = 0, z = 0)$ gives:

$$J\big|_{(y=0,z=0)} = \begin{bmatrix} P_2 - P_1\big|_{(y=0,z=0)} & 0 \\ 0 & -P_1\big|_{(y=0,z=0)} \end{bmatrix}.$$

With the assumption of $V_1 > V_2$, one can easily obtain that in this equilibrium

$$P_1\big|_{(y=0,z=0)} = -V_1 H_{21} G_{11} < -V_2 H_{21} G_{11} = P_2\big|_{(y=0,z=0)} < 0,$$

so that $P_2 - P_1\big|_{(y=0,z=0)} > 0$. So this equilibrium has two positive eigenvalues, hence it is an unstable node.

The Jacobian at $(y = 0, P_1 = 0)$ yields

$$J = \begin{bmatrix} P_2\Big|_{(y=0,P_1=0)} & 0 \\ -zP_{1y}\Big|_{(y=0,P_1=0)} & -zP_{1z}\Big|_{(y=0,P_1=0)} \end{bmatrix}.$$

In this equilibrium $P_2\Big|_{(y=0,P_1=0)} = V_2(G_{11} + \frac{H_{21}C_1}{C_2})(-H_{21} + \frac{H_{21}(C_2+K_{21})}{C_2}) > 0$, which can also be obtained from the fact the this point lies in the region where $P_2 > 0$. On the other hand $-zP_{1Z}\Big|_{(y=0,P_1=0)} = -zV_1(C_2G_{11} + H_{21}(C_1 + K_{21}))$, which is negative on the positive hemisphere $z > 0$. So this equilibrium is a saddle point.

The non-trivial equilibria A and B are given by $P_1 = P_2 = 0$. Since there are two equilibria, we start with equilibrium A. The Jacobian in this point is:

$$J = \begin{bmatrix} \frac{H_{21}(-G_{22}G_{11}+H_{21}H_{12})(G_{22}^2(V_1-V_2)+H_{21}^2V_2)}{G_{22}^3} & \frac{H_{21}(-G_{22}G_{11}+H_{21}H_{12})(G_{22}^3V_1+(H_{21}^2-G_{22}^2)V_2(C_2+K_{12}))}{G_{22}^3} \\ 0 & 0 \end{bmatrix}.$$

The zero row implies that there is a zero eigenvalue. The non-zero eigenvalue is given by $\frac{H_{21}(-G_{22}G_{11}+H_{21}H_{12})(G_{22}^2(V_1-V_2)+a^2V_2)}{G_{22}^3}$, which is negative since $-G_{22}G_{11} + H_{21}H_{12} < 0$; its eigenvector is $(1, 0)^\top$. Since this is a non-hyperbolic equilibrium in a non-linear system, one can not state anything about the type of equilibrium.

In the equilibrium B, where the other pair of $P_1 = 0$ and $P_2 = 0$ intersect, the Jacobian is given by:

$$J = \begin{bmatrix} \frac{G_{11}(G_{22}G_{11}-H_{21}H_{12})(H_{12}^2(V_1-V_2)+G_{11}^2V_2)}{H_{12}^3} & \frac{-G_{11}(G_{22}G_{11}+H_{21}H_{12})((G_{11}^2-H_{12}^2)(C_2+K_{12}))V_2-H_{12}^3V_1)}{H_{12}^3} \\ 0 & 0 \end{bmatrix}.$$

Again there is one zero eigenvalue; the other eigenvalue is positive, since $G_{22}G_{11} - H_{21}H_{12} > 0$, again with eigenvector $(1, 0)^\top$. The following theorem shows why these zero rows in the Jacobain are obtained for the points A and B.

THEOREM 4.4 *The non-trivial equilibrium points A and B of system* (4.4) *on the equator of the sphere are non-hyperbolic.*

Proof: The flow on the sphere is topologically equivalent to the projected flow onto the tangent plane $X = 1$, and is given by the equations of the form:

$$\begin{cases} \dot{y} = yf(y, z), \\ \dot{z} = zg(y, z), \end{cases}$$

where the Jacobian of this system is given by

$$J = \begin{bmatrix} f + yf_y & yf_z \\ zg_y & g + zg_z \end{bmatrix}.$$

The equilibrium points A and B in the projection lie on $z = 0$ where $P_1 = P_2 = 0$. However, on $P_1 = P_2 = 0$ the function $g(y,z) := -P_1 - y^2P_2$ equals zero. Hence the Jacobian evaluated at the point where $z = 0$ and $P_1 = P_2 = 0$ always has the second row as zero row, showing that these equilibrium points on the projection are non-hyperbolic. ■

4.2.1.2 Nullcline through the non-hyperbolic equilibria

To still be able to deduce some general properties of the system, we can consider the nullclines through the equilibrium points A and B. For z there is a trivial nullcline and a non-trivial nullcline and for y there is one non-trivial nullcline going through the equilibria. This being said, firstly it is not clear if each non-trivial nullcline in each equilibrium consists of just a single curve or whether there are multiple nullclines in the plane that intersect the equilibrium point and secondly it is difficult to obtain how these nullclines lie in the plane since they are implicitly given in terms of P_1 and P_2.

To show that the non-trivial nullclines for y and z each consist of exactly one continuous curve, we make use of the following theorem.

THEOREM 4.5 (Implicit Function Theorem) *Let $f : R^{n+m} \to R^m$ be a continuously differentiable function, and let R^{n+m} have coordinates $(\mathbf{x}, \mathbf{y})$. Fix a point $(\mathbf{a}, \mathbf{b}) = (a_1, \ldots, a_n, b_1, \ldots, b_m)$ with $f(\mathbf{a}, \mathbf{b}) = \mathbf{0}$. If the Jacobian matrix $J_{f,\mathbf{y}}(\mathbf{a}, \mathbf{b}) = [(\partial f_i/\partial y_j)(\mathbf{a}, \mathbf{b})]$ is invertible, then there exists an open set U of R^n containing $\mathbf{a}$ such that there exists a unique continuously differentiable function $g : U \to R^m$ such that*

$$g(\mathbf{a}) = \mathbf{b} \quad \textit{and} \quad f(\mathbf{x}, g(\mathbf{x})) = 0 \quad \textit{for all } \mathbf{x} \in U.$$

Denote $f : \mathbb{R}^2 \to \mathbb{R}$ where $(y,z) \mapsto -P_1(y,z) - y^2P_2(y,z)$, which describes the non-trivial nullcline for z when the function is set equal to zero. In this case, the desired Jacobian matrix is 1×1 and given by

$$-P_{1z} - y^2 P_{2z}\Big|_{(\frac{H_{21}}{G_{22}},0)} = (H_{12}H_{21} - G_{11}G_{22})\frac{H_{21}^2C_2V_1 + G_{22}^2(C_2 + K_{12})V_2}{G_{22}^3},$$

which is non-zero as $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ (hence invertible). The implicit function theorem tells us that in a neighbourhood of the point $y = \frac{H_{21}}{G_{22}}$, a unique continuously differentiable function exists on which the function f is zero. That is, there is a unique line in the (y,z)-plane intersecting the equilibrium $(\frac{H_{21}}{G_{22}}, 0)$ on which $-P_1 - y^2P_2 = 0$ is satisfied.

The same can be done for the function $h : \mathbb{R}^2 \to \mathbb{R} : (y, z) \mapsto P_2(y, z) - P(y, z) - y^2 P_2(y, z)$, which describes the y nullcline when h is set equal to zero. In this case it is easier to obtain a function from a neighbourhood of $z = 0$ to y. The derivative to y in the point $(\frac{H_{21}}{G_{22}}, 0)$ is given by:

$$P_{2y} - P_{1y} - 2yP_2 - y^2 P_{2y}\Big|_{(\frac{H_{21}}{G_{22}},0)} = (H_{12}H_{21} - G_{11}G_{22})\frac{G_{22}^2(V_1 - V_2) + H_{21}^2 V_2}{G_{22}^2},$$

which is also non-zero. So there is a neighbourhood around the point $z = 0$ such that there is a continuously differentiable function on which f is zero, hence the nullcline through $(\frac{H_{21}}{G_{22}}, 0)$ is a unique line.

The same can be done for the non-trivial nullclines through the equilibrium point B in which also both the y and z nullclines are unique curves. We will now show where these nullclines lie in the plane relative to each other and the corresponding dynamics on the nullclines. A sketch of the following results are drawn in Figure 4.4.

- **EQUATOR.** On $z = 0$ there is $\dot{z} = 0$. Observe that $z = 0$ yields $V_2 P_1 = V_1 P_2$, so that $P_1 > 0 \iff P_2 > 0 \iff P_1 > P_2$ since $V_1 > V_2$. In Proposition 4.3 we showed that in between A and B we have that $P_1 > 0$. Since for $y > 0$ we have $\dot{y} < 0 \iff P_2 - P_1 < y^2 P_2$, whose left-hand side is negative and right-handside is positive in between A and B by the aforementioned arguments. This also agrees with the non-zero eigenvalues and eigenvectors of the trivial equilibria we found.

- **NON-TRIVIAL z NULLCLINE.** The non-trivial nullcline of z goes through the points that satisfy $P_1 = -y^2 P_2$, which can only occur if P_1 and P_2 have opposite signs. Consider the equilibrium A. From Figure 4.2 we know how the lines $P_1 = 0$ and $P_2 = 0$ lie with respect to each other. By Proposition 4.3 P_1 is positive only in the area enclosed by the red lines ($P_1 = 0$) and similarly, P_2 is positive only in the area enclosed by the blue lines ($P_2 = 0$). From this observation, one can deduce the region where $P_1 < 0$ and $P_2 > 0$, in which the nullcline lies. The same can be said about the nullcline through B. On the nullclines we have $\dot{y} = yP_2$. The nullcline through A goes through the region where $P_2 > 0$ hence on which $\dot{y} > 0$, whereas the nullcline through B goes through the area where $P_2 < 0$ hence on which $\dot{y} < 0$.

- **NON-TRIVIAL y NULLCLINE.** Since we locally know the position of the non-trivial nullcline of z and its corresponding y direction, we can now easily obtain how the y nullclines lie around the equilibrium points. Considering the direction on the non-trivial z nullcline and on the equator, one can see that the direction should y direction must change somewhere in the region. This direction changes on the nullcline where $y = 0$, from which roughly the position in the plane can be drawn.

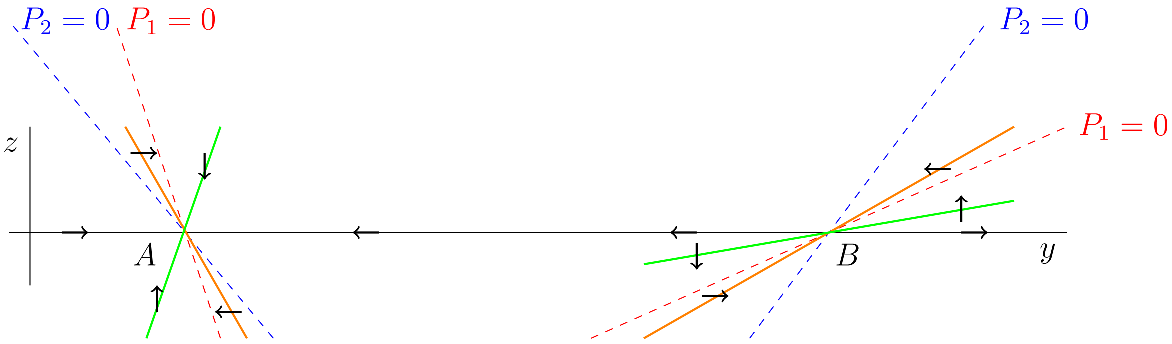

FIGURE 4.4 A sketch of the dynamics of the projected flow on the tangent plane around the two non-trivial equilibria on the equator. The orange lines indicate the nullclines of z and the green lines indicate the nullclines of y. From this figure one obtains that A is a stable equilibrium and B is an unstable equilibrium.

4.2.2 Projection onto Y=1

The important equilibria on the sphere where $Y = 0$ could not be classified when the projection onto $X = 1$ was considered. Hence, if the flow on the surface is projected onto $Y = 1$, the system is given by:

$$\begin{cases} \dot{x} = x(P_1 - x^2 P_1 - P_2), \\ \dot{z} = z(-x^2 P_1 - P_2), \end{cases}$$

where inside P_1 and P_2 now Y is set to 1. The fixed points are given by

$$\begin{aligned} &(x = 0, z = 0), \\ &(x = 0, P_2 = 0), \\ &(P_1 = 0, P_2 = 0). \end{aligned}$$

The only equilibria of interest are the first two, since the last has already been analyzed in the other projection. The Jacobian is given by:

$$J = \begin{bmatrix} P_1 - P_2 - x^2 P_1 + x(P_{1x} - P_{2x} - x^2 P_{1x} - 2xP_1) & x(P_{1z} - P_{2z} - x^2 P_{1z}) \\ z(-2xP_1 - x^2 P_{1x} - P_{2x}) & -x^2 P_1 - P_2 + z(-x^2 P_{1z} - P_{2z}) \end{bmatrix}.$$

Evaluated in the equilibrium point $(x = 0, z = 0)$, the Jacobian is given by:

$$J = \begin{bmatrix} P_1 - P_2\big|_{(x=0,z=0)} & 0 \\ 0 & -P_2\big|_{(x=0,z=0)} \end{bmatrix}.$$

Also in this equilibrium $P_1\big|_{(x=0,z=0)} < P_2\big|_{(x=0,z=0)} < 0$, so that there is one negative eigenvalue with eigenvector $(1, 0)^\top$ and one positive eigenvalue with eigenvector $(0, 1)^\top$.

The Jacobian in the second equilibrium, $(x=0, P_2=0)$ is given by

$$J = \begin{bmatrix} P_1\big|_{(x=0,P_2=0)} & 0 \\ -zP_{2x}\big|_{(x=0,P_2=0)} & -zP_{2z}\big|_{(x=0,P_2=0)} \end{bmatrix}.$$

The point satisfying $P_2 = 0$ in $x = 0$ is given by $z = \frac{H_{12}}{C_1}$. In this point, $P_1\big|_{(x=0,P_2=0)} > 0$, and $P_{2z} = V_2(G_{22}G_{11} + H_{12}(C_2 + K_{12}) > 0$, so that there is one positive and one negative eigenvalue.

4.3 General dynamics on the sphere

As mentioned, the flow on the projection onto a tangent plane is topologically equivalent to the flow on the sphere (except for the points being projected to infinity). So from the information of the projections, the dynamics around the equilibrium points can be shown on the sphere itself (see Figure 4.5). From the system of equations (4.4) it is easily observed that the first octant is an invariant region. To show that all trajectories in the first octant converge to A, we will prove the non-existence of periodic orbits. The easiest way to show it in this case is by an implication of a theorem from index theory, as described by S. H. Strogatz [12]. Without going into detail, the statement about periodic orbits is as follows:

PROPOSITION 4.6 *There is always at least one equilibrium point inside any closed orbit in the phase plane.*

The possibility of periodic orbits inside the region $X, Y, Z > 0$ is ruled out by this statement since there are no equilibrium points inside this region. There are also no periodic orbits possible around the equilibrium points on $X = 0$, $Y = 0$ or $Z = 0$ since these are nullclines that give

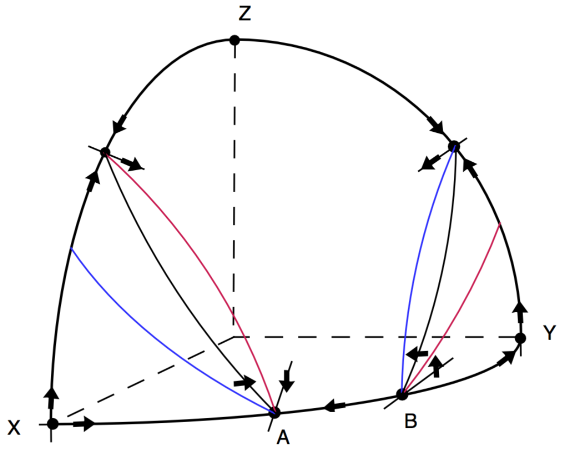

FIGURE 4.5 Schematic figure of the behaviour of the flow around the equilibrium points, obtained by classifiable equilibrium points and nullclines. All trajectories move towards A, hence being the only stable equilibrium point.

straight-line orbits. So the only attractor in the first octant is the stable equilibrium A, hence all trajectories in $X, Y, Z > 0$ converge to this point. Convergence towards the equilibrium point A on one hand implies that $\dot{X} \to 0$ and $\dot{Y} \to 0$ so that in the limit $t \to \infty$ we have $\dot{\left(\frac{X}{Y}\right)} = 0$, but on the other hand implies that $\frac{X}{Y} \to \frac{G_{22}}{H_{21}}$, so that for $t \to \infty$:

$$0 \leftarrow \dot{\left(\frac{X}{Y}\right)} = \frac{\dot{X}Y - X\dot{Y}}{Y^2} = \frac{X(P_1 - P_2)}{Y} = \frac{G_{22}}{H_{21}}(P_1 - P_2).$$

Thus for $t \to \infty$ we have $P_1 - P_2 \to 0$, which is equivalent to $Q_1 - Q_2 \to 0$ (easy proof). This analysis partly proves Conjecture 2.3, since we made the assumption that $C_1, C_2 > 0$.

THEOREM 4.7 *Let the microbial system be given by* (4.1), *with the parameters such that* $V_1 > V_2$ *and* $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. *For positive initial conditions that satisfy* $C_1 > 0$ *and* $C_2 > 0$, *the growth rates* Q_1 *and* Q_2 *converge to each other as* $t \to \infty$.

Moreover, since we know exactly where the point A lies on the equator, the following can be stated about the value of growth rate in the limit and the convergence of the relative fraction of the microbe concentrations.

COROLLARY 4.8 *Let the microbial system of ODEs be given by* (4.1) *with* $V_1 > V_2$ *and* $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. *Then orbits with positive initial conditions that satisfy the conditions for* $C_1 > 0$ *and* $C_2 > 0$, *the growth rates converge to* V_2 *and the relative fraction* $\frac{x_1}{x_2}$ *converges to* $\frac{G_{22}}{H_{21}}$. *Hence, the nutrient concentration that grows to infinity is the one that is consumed by the species with the lowest growth rate.*

Proof: From Theorem 5.3, we obtain that $m_1 + m_2 \to \infty$ as $t \to \infty$. Recall that the growth rates Q_1 and Q_2 are monotone increasing functions with upper bound V_1 and V_2 respectively. So when $m_1 + m_2 \to \infty$, $Q_1 - Q_2 \to 0$ is satisfied if and only if $m_1 \to \infty$ and $m_2 \to m_2^*$ for a certain constant m_2^* for which $Q_1(m_2^*) = V_2$. In this case $Q_1 \to V_2$ and $Q_2 \to V_2$.

Since for $t \to \infty$ every trajectory converges to A given by $\frac{X}{Y} = \frac{G_{22}}{H_{21}}$, the relative fraction of the microbe concentrations converges to this ratio:

$$\frac{x_1}{x_2} = \frac{\frac{X}{Z}}{\frac{Y}{Z}} = \frac{X}{Y} \to \frac{G_{22}}{H_{21}}.$$

■

This analysis is only for the parameters that satisfy the conditions $C_1, C_2 > 0$ and $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. However, since the analysis is quite laborious it is not practical to analyze the system for different parameter settings. The length of this analysis is mostly due to the important equilibrium points on the equator being non-hyperbolic. If these were in fact hyperbolic, we could much faster obtain their stability for any parameter values. As mentioned, new equilibrium points might arise and bifurcations may occur when we change parameter values, which will also not make the analysis easier.

We end this analysis by mentioning that Figure 4.5 shows the unanswered behaviour that was observed in the phase portrait of Chapter 3, namely: the lines $\mathcal{M}_2 = 0$ and $\mathcal{M}_1 = K_{21}Z$ intersect the equilibrium point A. Hence on A we have that both $\mathcal{M}_2 = 0$ and $\mathcal{M}_1 = 0$ (since $Z = 0$), which implies $P_1 = P_2 = 0$. At first sight, this would suggest that all the meaningful trajectories converge to the point where eventually the growth rates are zero. However, the following proposition shows that in the case that the microbe concentrations grow to infinity for $t \to \infty$ the fraction $\frac{X}{Y}$ should always go to this point if $Q_1 \not\to V_1$.

PROPOSITION 4.9 *Let $Q_1(m_2)$ be the growth rate with $m_2 = G_{22}x_2 - H_{21}x_1 + C_2$ and suppose that $x_1, x_2 \to \infty$ for $t \to \infty$. If $Q_1 \not\to V_1$ then $\frac{x_1}{x_2} \to \frac{G_{22}}{H_{21}}$ for $t \to \infty$.*

Proof: $Q_1 \not\to V_1$ is equivalent to $m_2 \not\to \infty$ (since Q_1 is an increasing function in m_2 with upper bound V_1). One can rewrite $m_2 = G_{22}x_2 - H_{21}x_1 + C_2$ to $\frac{x_1}{x_2} = \frac{G_{22}}{H_{21}} + \frac{C_2 - m_2}{H_{21}x_2}$. Since $x_2 \to \infty$ and $m_2 < \infty$ for $t \to \infty$, one obtains that $\lim_{t\to\infty} \frac{x_1}{x_2} = \frac{G_{22}}{H_{21}}$. ■

This proves that in the case of unbounded growth, any growth rate Q_1 smaller than V_1 can only be attained if the microbial relative fraction converges towards this specific point for $t \to \infty$. Hence the growth rate for Q_1 is undefined for this point on the equator, as it could attain any value. This is exactly what was also observed in the contour plots of the nutrient concentrations in Chapter 3. So it is important to keep in mind that it is an asymptotic convergence towards this point and the trajectories do no reach this point for finite time.

4.4 Discussion on the Poincaré approach

We transformed the system to a compact system using the Poincaré transformation. For parameter values $C_1, C_2 > 0$ and $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ linear stability analysis was performed and we obtained that the important equilibrium points on the equator were non-hyperbolic. This is not specifically caused by the Poincaré transformation, but rather by the nature of this system. L. Perko, in his book on differential equations [9], shows that a much simpler system already gives these kind of improper nodes at the equator, though definitely not all systems show this peculiarity after the transformation. Moreover, the two non-trivial equilibria would also be found as non-hyperbolic when doing linear stability analysis on the fractional system of Chapter 3 (which is not showcased). By showing how certain nullclines lie on the sphere and what the direction of the trajectories are on these lines, one could eventually observe where all trajectories converge to on the first octant of the sphere for $V_1 > V_2$. This unique stable equilibrium was specifically given by the ratio $\frac{X}{Y} = \frac{G_{22}}{H_{21}}$. In this case, the nutrient concentration m_1 grows to infinity, whereas the nutrient concentration m_2 converges to some constant. Because the analysis was quite laborious we did not analyze the system for other parameter values than the ones considered. However, the parameter values do have a big influence on the dynamics as they alter the lines $P_1 = 0$ and $P_2 = 0$, for which bifurcations may occur and new equilibrium points may arise.

For positive values C_1, C_2 and $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ one can show the phase portrait and some trajectories on the sphere for certain parameter values, given in Figure 4.6. The image is obtained by projecting the two-dimensional stream plot of X and Y (with Z in the equations substituted for $\sqrt{1-X^2-Y^2}$) onto the sphere. This two-dimensional system is defined on the disk $X^2+Y^2 \leq 1$ and trajectories with unbounded growth move towards the boundary of this disk, clearly showing exactly the same behaviour. One might notice that the proof in the next chapter for n species could also be done when the disk is considered, as the whole classification of equilibrium points is omitted.

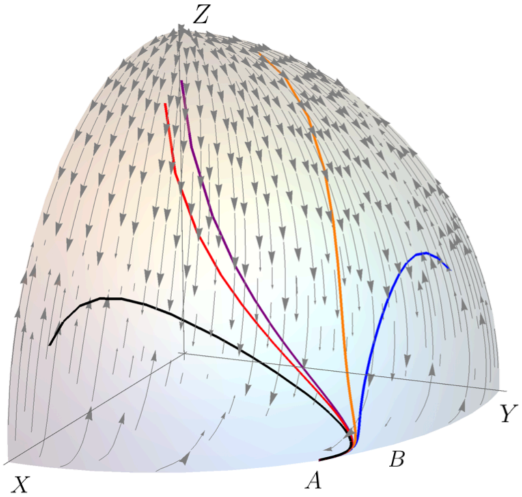

FIGURE 4.6 This figure is made by projecting the stream plot of the planar dynamics of (X, Y) onto the sphere; the reason for the low density of trajectories around $Z = 0$ is due to this projection and the built-in restriction of number of trajectories in *Mathematica*.

Even though the linear stability analysis for which the transformation to the sphere was intended did not work out, this transformation has some advantages compared to the fractional approach. The expressions for the lines on which $P_1 = 0$ or $P_2 = 0$ are more straight-forward, as they are implicitly expressed by planes in $\mathbb{R}^3$ intersecting the sphere; in particular, $\mathcal{M}_1 = 0$ and $\mathcal{M}_2 = 0$ each gives the boundary of the biologically meaningful region and implies $P_2 = 0$ and $P_1 = 0$ respectively. In the fractional approach we already noticed that the lines enclosing the biologically meaningful region were expressed as hyperbolic function in z, which is obviously less easy to work with than planes, especially for higher dimensions. Also, the points on the equator expressed as fractions $\frac{X}{Y}$ coincide exactly with the fractions of interest, namely $\frac{x_1}{x_2}$, so results are more easily interpreted on the sphere (compare to the point in Claim 3.5).

In the next chapter we will find where this ratio $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ comes from and see that this condition indeed plays an important role for the unbounded growth.

5

General cyclic cross-feeding system

In the previous two chapters two different approaches were presented of transforming the unbounded system to a compactly defined system. We noticed in both Chapter 3 and Chapter 4 that some condition exists for the yield parameters given by $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ that has an influence on the long-term behaviour of the dynamics. In this chapter we will show how this condition can be derived without observing it from figures. With this condition it is actually relatively easy to show the long-term behaviour of a generalized system of n species. So we will show the derivation of the condition $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$ for the two-species system for a better understanding of the proof of the condition for a generalized model for n species. Subsequently, only for the generalized system the long-term behaviour will be shown for which we obtain similar results as observed in the previous chapters.

5.1 Influence of yield parameters on the nutrient dynamics

Consider again the main model we obtained before rewriting it to a two-dimensional system:

$$\begin{cases} \dot{x}_1 = Q_1(m_2)x_1, \\ \dot{x}_2 = Q_2(m_1)x_2, \\ \dot{m}_1 = G_{11}Q_1(m_2)x_1 - H_{12}Q_2(m_1)x_2, \\ \dot{m}_2 = G_{22}Q_2(m_1)x_2 - H_{21}Q_1(m_2)x_1, \end{cases}$$

We should focus on the dynamics of the nutrient concentrations since depletion of the nutrients of course implies that the microbes will eventually not be able to grow, whereas the microbes keep growing if there is a positive nutrient concentration in the environment; so when *do* they deplete? The following proposition sets a foundation for the understanding of these dynamics:

PROPOSITION 5.1 *Suppose the system of ODEs is given by* (2.2). *Then* $m_1 \to 0 \iff m_2 \to 0.$

Proof: Suppose that $m_1 \to 0$. Then by definition also $Q_2(m_1) \to 0$. One can rewrite $\dot{x}_2 = Q_2x_2$ to $\frac{\dot{x}_2}{x_2} = Q_2$, where the left-hand side is in fact $\frac{\mathrm{d}}{\mathrm{d}t}\ln x_2$. Since $Q_2 \to 0$, this derivative converges to zero, hence $\ln x_2$ converges to some constant which implies that x_2 converges to a certain constant; hence $Q_2 x_2 \to 0$. From this, we see that for t large enough $m_1 \to 0$ gives that the expression for $\dot{m}_2$ becomes $\dot{m}_2 = -H_{21} Q_1 x_1$. Since $x_1 > 0$ and non-decreasing, $\dot{m}_2$ is negative as long as $m_2 > 0$ (since then $Q_1(m_2) > 0$); hence m_2 decreases to zero. ■

This proposition turns out to be important to prove long-term behaviour of the nutrient dynamics.

PROPOSITION 5.2 *If the initial condition of one nutrient concentration is zero while the other is non-zero, then the former nutrient concentration also becomes positive.*

Proof: Suppose $m_1 = 0$ and $m_2 > 0$. Then $Q_1(m_2) > 0$, hence by proportionality of the production rate to the growth rate, the nutrient will be produced so that $m_1 > 0$. ■

REMARK (Positive initial concentrations) *One nutrient present in the environment is enough to start the cross-feeding behaviour. However, as the non-zero concentration becomes positive instantaneously, it is convenient to consider that the initial conditions of the nutrients are positive.*

The major influence on the dynamics of the nutrient concentrations is in fact the choice for the yield parameters. A condition for the yield parameters ensures whether there will be depletion of the nutrients or not.

THEOREM 5.3 *Suppose there are two cross-feeding microbe species whose behaviour is defined by* (2.2)*, with positive initial conditions. Then the sum of nutrient concentrations grows to infinity for* $t \to \infty$*, if the yield parameters satisfy the ratio:*

$$R := \frac{G_{11} G_{22}}{H_{12} H_{21}} > 1.$$

$R < 1$ *implies that the nutrients will deplete (all concentrations converge to zero), and the special case* $R = 1$ *implies that the nutrient concentrations do not converge to zero and are bounded from above.*

Proof: Consider the dynamics of the nutrients in (2.2) again:

$$\begin{aligned} \dot{m}_1 &= G_{11} Q_1 x_1 - H_{12} Q_2 x_2, \\ \dot{m}_2 &= G_{22} Q_2 x_2 - H_{21} Q_1 x_1. \end{aligned}$$

Multiply the first equation by G_{22} and the second by H_{12}, and add them up to obtain:

$$G_{22} \dot{m}_1 + H_{12} \dot{m}_2 = (G_{11} G_{22} - H_{21} H_{12}) Q_1 x_1. \tag{5.1}$$

Write $R := \frac{G_{11} G_{22}}{H_{21} H_{12}}$. One can view the left-hand side to be the derivative of the whole (weighted) sum: $(G_{22} m_1 + H_{12} m_2)$. On the right-hand side of (5.1), $x_1 > 0$, $Q_1 \geq 0$ and $Q_1 \not\to 0$ as long as $m_2 \not\to 0$.

For $R > 1$, the derivative on the left-hand side is at least non-negative, hence the weighted sum of the nutrient concentrations is at least non-decreasing. Moreover, by Proposition 5.1, it is not possible that $m_2 \to 0$ individually, so that $Q_1 \not\to 0$. Hence the derivative of the weighted sum does not converge to zero, implying that this weighted sum is always increasing and thus grows to infinity over time; therefore, also the actual sum of nutrients grows to infinity, $m_1 + m_2 \to \infty$.

When $R < 1$, the weighted sum decreases and keeps decreasing until *both* nutrient concentrations reach zero, implied by Proposition 5.1, in which case $Q_1 \to 0$.

The special case $R = 1$ implies that the right-hand side is always zero. Hence, m_1 and m_2 can vary, but only such that the weighted sum stays the same over time. Thus in that case the concentrations are bounded, but again, none may individually converge to zero. ■

By Proposition 5.1 either both nutrients deplete or none does. So if $R > 1$ the sum of nutrient concentrations increases, hence both concentrations do not deplete so that the the microbe concentrations keep increasing.

COROLLARY 5.4 *For $R \geq 1$, there is unbounded growth; for $R < 1$ the microbe concentrations are bounded.*

Proof: When the nutrient concentrations do not converge to zero ($R \geq 1$) the growth rates will not converge to zero, which implies that the microbe concentrations have unbounded growth.

When nutrient concentrations do converge to zero ($R < 1$) we can bound the microbe concentrations from above. One can substitute $\dot{x}_1$ for $Q_1 x_1$ in equation (5.1) and integrate to obtain $G_{22}m_1 + H_{12}m_2 = (G_{11}G_{22} - H_{21}H_{12})x_1 + C$, where C is the integration constant. Since the left-hand side can not be negative and the term $(G_{11}G_{22} - H_{21}H_{12})x_1$ is negative and non-increasing, we see that this term must be bounded from below $(G_{11}G_{22} - H_{21}H_{12})x_1 \geq -C$. Hence x_1 is bounded from above by $\frac{-C}{G_{11}G_{22}-H_{21}H_{12}} > 0$. From this also the bound of x_2 follows. ■

REMARK (Biological interpretation) *How can the result of Theorem 5.3 be biologically interpreted? Consider the ratio R in terms of production and consumption rates:*

$$\begin{aligned} R &= \frac{p_{11} \cdot p_{22}}{c_{21} \cdot c_{12}} \\ &= \frac{\textit{prod. of nutrient } 1 \textit{ by unit concentr. microbe } 1/\textit{ unit of time}}{\textit{cons. of nutrient } 2 \textit{ by unit concentr. microbe } 1/\textit{ unit of time}} \\ &\quad \times \frac{\textit{prod. of nutrient } 2 \textit{ by unit concentr. microbe } 2/\textit{ unit of time}}{\textit{cons. of nutrient } 1 \textit{ by unit concentr. microbe } 2/\textit{ unit of time}} \\ &= \left(\frac{\textit{prod. of nutrient } 1}{\textit{cons. of nutrient } 2} \textit{ by unit concentr. microbe } 1 \right) \\ &\quad \times \left(\frac{\textit{prod. of nutrient } 2}{\textit{cons. of nutrient } 1} \textit{ by unit concentr. microbe } 2 \right). \end{aligned}$$

This gives essentially the efficiency rates per unit concentration of the microbes of turning the consumed nutrient concentration into produced nutrient concentration. The production and con-

sumption rates fluctuate, but since R is fixed, these ratios always multiply up to a certain constant. In the case of $R > 1$ this means that even though one species can be inefficient, the other species has such an efficiency ratio that the overall efficiency of the system is "positive". In this case, the total production is bigger than the total consumption by a unit concentration of species 1 and 2.

5.2 Generalized system

The results of unbounded growth implied by the yield ratio is really important: if we know that the yield parameters satisfy the condition then unbounded growth is ensured, so that for every microbial community with positive initial conditions the microbe concentrations grow to ∞ as time t approaches ∞. To obtain additional results of the long-term behaviour we will again need to perform and analyze the Poincaré transformation. With this transformation certain important functions are more easily defined compared to the fractional approach of Chapter 3.

First, the generalizations of the statements made at the beginning of this chapter are discussed to show when unbounded growth is ensured. To prove the convergence of the growth rates, the Poincaré transformation will be done to be able to show what happens in the *biologically meaningful region* on the $n+1$-dimensional sphere. In the case of unbounded growth trajectories on the sphere move towards $Z = 0$, so the dynamics for trajectories on $Z = 0$ are studied which will give essential information about the trajectories in the biologically meaningful region converging to $Z = 0$. Figure 4.2 of the sphere with its characteristic lines can be kept in mind for the intuition of the analysis; additionally, the equator of the four-dimensional sphere is visualized to get a better idea of the dynamics on the equator in general.

The general system that shows the same characteristics as the one previously studied, should have a cyclic topology:

DEFINITION 5.5 A cross-feeding community of microbial species is said to have a cyclic topology if every species produces its own unique nutrient and if every produced nutrient is the unique growth-limiting nutrient for exactly one other species in the community.

One can schematically order the microbes of such a community so that a cycle can be formed where every microbe consumes the nutrient produced by its neighbour. Consider the system of n microbe species having a cyclic cross-feeding topology such that species 1 consumes the product of species 2, which on its turn consumes the product of species 3, et cetera, so that the system can be written as follows:

$$\begin{cases} \dot{x}_i = Q_i(m_\iota)x_i, \\ \dot{m}_\iota = G_{\iota\iota}Q_\iota x_\iota - H_{\iota i}Q_i x_i, \end{cases} \qquad \text{for all } i = 1, \dots, n \text{ and } \iota := (i \mod n) + 1 \tag{5.2}$$

where $Q_i(m_\iota) = V_i \frac{m_\iota}{K_{i\iota} + m_\iota}$. We assume that none of the maximum growth rates V_i are equal.

REMARK *The relation between i and ι as defined in* (5.2) *will be used throughout this section.*

Hence ι is always the $+1$ increment of i in a formula. To have a cycle, we want that species n consumes the product of species 1; this particular transition makes the system more complicated notation-wise, hence the ι.

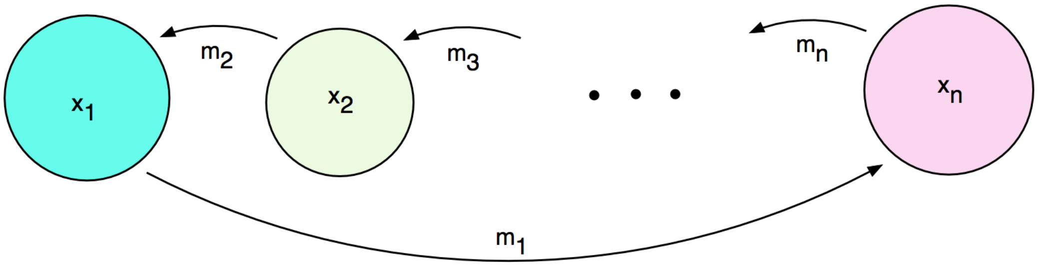

FIGURE 5.1 Schematic figure for n species with a cyclic cross-feeding topology, visualizing system (5.2).

5.2.1 Behaviour of nutrients affects growth dynamics

The dynamics for the growth depend on dynamics of the nutrient concentrations. The following proposition shows that there is either no depletion or total depletion of the nutrients.

PROPOSITION 5.6 *Let the system be given by* (5.2). *The following equivalence holds for* $i, j \in \{1, \dots, n\}$*:* $\exists i \; m_i \to 0 \iff \forall j \; m_j \to 0$.

Proof: Follow exactly the same proof of Theorem 5.1 and repeat it to show that starting from $m_i \to 0$ for some $i \in \{1, \dots, n\}$, every consecutive m_ι should converge to zero as well. ■

As previously mentioned, it is convenient to only suppose positive initial conditions, since at least one positive nutrient concentration ensures that all the other nutrient concentrations will be positive, by the proportionality of the production rates to the growth rate, thus also to consumption rate. We can now prove the following theorem, which gives a condition for the yield parameters to satisfy so that the nutrients do not deplete.

THEOREM 5.7 *Let the dynamics of a cyclic cross-feeding microbe community be defined by* (5.2). *For positive initial concentrations, the sum of nutrient concentrations* $\sum_{1 \le i \le n} m_i$ *grows to infinity for* $t \to \infty$ *if the yield parameters satisfy the ratio:*

$$R := \frac{\prod_i G_{ii}}{\prod_i H_{\iota i}} > 1.$$

Proof: We consider only the derivatives of the nutrient concentrations in terms of the derivatives of the microbe concentrations for simplicity (instead of $Q_i x_i$):

$$\dot{m}_\iota = G_{\iota\iota} \dot{x}_\iota - H_{\iota i} \dot{x}_i, \text{ for all } i \in \{1, \dots, n\}.$$

One can write them below each other in exactly the following order:

$$\begin{aligned}\dot{m}_2 &= G_{22}\dot{x}_2 - H_{21}\dot{x}_1,\\ \dot{m}_3 &= G_{33}\dot{x}_3 - H_{32}\dot{x}_2,\\ &\vdots\\ \dot{m}_n &= G_{nn}\dot{x}_n - H_{n(n-1)}\dot{x}_{n-1},\\ \dot{m}_1 &= G_{11}\dot{x}_1 - H_{1n}\dot{x}_n.\end{aligned}$$

To write the summation of these equations of $\dot{m}_j$ only in terms of, say, $\dot{x}_1$, we need to eliminate the other $\dot{x}_i, \forall i \neq 1$ out of the summation. Notice how each term $\dot{x}_i$ can be eliminated by the following equation. Starting from the top, to eliminate $\dot{x}_2$, one needs to multiply the first equation by H_{32} and the second by G_{22}:

$$\begin{aligned}H_{32}\dot{m}_2 &= H_{32}G_{22}\dot{x}_2 - H_{32}H_{21}\dot{x}_1,\\ G_{22}\dot{m}_3 &= G_{22}G_{33}\dot{x}_3 - G_{22}H_{32}\dot{x}_2.\end{aligned}$$

This will also affect how all the following equations should be multiplied to eliminate the other $\dot{x}_i$; notice that the elimination of $\dot{x}_3$ with the third equation can only be done when this equation is multiplied by $G_{22}G_{33}$ *and* the equation for $\dot{m}_3$ is multiplied by H_{43}:

$$\begin{aligned}H_{43}G_{22}\dot{m}_3 &= H_{43}G_{22}G_{33}\dot{x}_3 - H_{43}G_{22}H_{32}\dot{x}_2,\\ G_{22}G_{33}\dot{m}_4 &= G_{22}G_{33}G_{44}\dot{x}_4 - G_{22}G_{33}H_{43}\dot{x}_3.\end{aligned}$$

This last multiplication clearly affects the first elimination, as the second equation now has an extra term H_{43}, so the first equation $\dot{m}_2$ should also be multiplied by H_{43}.

One can see that when the equations are written in this order, the multiplications of G_{ii} affects all the following eliminations, and the multiplications of $H_{\iota i}$ affects all the previous eliminations. Hence any $\dot{m}_k$ should be multiplied with all G_{ii} above it and all $H_{\iota i}$ below it in the array. Summing up all these multiplied equations then leads to:

$$\sum_{k=1}^{n}\prod_{i=2}^{k}G_{ii}\prod_{i=k+1}^{n}H_{\iota i}\,\dot{m}_\kappa = \left(\prod_{i=1}^{n}G_{ii} - \prod_{i=1}^{n}H_{\iota i}\right)\dot{x}_1. \tag{5.3}$$

Recall that $\iota := (i \mod n) + 1$ and in the same way κ is defined as $\kappa := (k \mod n) + 1$. Once again we see that the right-hand side is non-negative if and only if $R := \frac{\prod_{i=1}^{n} G_{ii}}{\prod_{i=1}^{n} H_{ji}} \geq 1$.

Write the sum of derivatives on the left-hand side in (5.3) as the derivative of the sum. Then this derivative is negative if $R < 1$, zero if $R = 1$ and positive if $R > 1$, since $\dot{x}_i$ is non-negative; hence the sum does not converge to zero if $R \geq 1$. Note that for $R \geq 1$ it is the *sum* that does not converge to zero, not the individual m_i; nevertheless, from Proposition 5.6 none of the nutrients can individually converge to zero. Then in particular $m_1 \not\to 0$ which means that $Q_1 \not\to 0$, hence the right-hand side of (5.3) does not converge to zero since $\dot{x}_1 = Q_1 x_1 \not\to 0$. So for $R > 1$ derivative of the weighted sum of nutrients is positive and does not converge to zero, thus the sum of the nutrients grows to infinity for $t \to \infty$. ■

We omit the case $R = 1$, as this is only a special case which biologically does not occur, but also where some of the following results does not hold. For $R < 1$, similar to the proof of Corollary 5.4 one can prove that the concentrations are bounded by first showing the upper bound for x_1 for all time t, from which the upper bounds for all time t for the other microbe concentrations follow.

By Proposition 5.6 either all nutrients deplete or none does, so that for $R > 1$ none of the nutrients deplete (as the sum increases).

COROLLARY 5.8 *For $R > 1$ (and positive initial conditions), unbounded growth for all species is ensured.*

5.2.2 Poincaré transformation of the system

The transformation of a system of a higher dimensions to the Poincaré sphere is quite similar to the original two-dimensional system transformation. First rewrite the system (5.2) by substituting the nutrient concentrations m_i by their expressions in the microbe concentrations x_i and initial conditions C_i. Multiply every equation of $\dot{x}_i$ by every denominator of the growth rates to remove the singularities of the growth rates from the system, and scale the time variable (see start of Chapter 4) so that the system can be written as:

$$\begin{cases} x_i' = p_i(\mathbf{x}) x_i, \qquad \text{for all } 1 \leq i \leq n, \end{cases} \tag{5.4}$$

where p_i is a polynomial of degree n defined as

$$p_i(\mathbf{x}) = V_i \prod_{k=1}^{n} (m_\kappa(\mathbf{x}) + \mathbb{1}_{\{k \neq i\}} K_{k\kappa}),$$

or, with the functions $m_\kappa(\mathbf{x})$ written out:

$$p_i(\mathbf{x}) = V_i \prod_{k=1}^{n} (G_{\kappa\kappa} x_\kappa - H_{\kappa k} x_k + C_\kappa + \mathbb{1}_{\{k \neq i\}} K_{k\kappa}),$$

where again $\kappa = (k \mod n) + 1$ and with $\mathbb{1}_{k \neq i}$ being the indicator function that equals 0 if $k = i$ and 1 otherwise. An example of the function p_1 for the three-dimensional case then yields:

$$p_1(\mathbf{x}) = V_1 \prod_{k=1}^{3} m_2(\mathbf{x})(m_3(\mathbf{x}) + K_{23})(m_1(\mathbf{x}) + K_{31}).$$

To transform the system to the $(n+1)$-dimensional Poincaré sphere, introduce the variables as follows:

$$x_i = \frac{X_i}{Z} \text{ for } 1 \leq i \leq n, \sum_{1 \leq i \leq n} X_i^2 + Z^2 = 1.$$

Following the approach in Section 4.1, the system (5.4) can be rewritten in the new variables, which gives after multiplication of Z^{n+1} (as p_i are polynomials of degree n):

$$\begin{cases} Z^n X_i' - Z^{n-1} Z' X_i = X_i P_i(X_1, \dots, X_n, Z) & \text{for all } 1 \leq i \leq n, \\ \sum_{i=1}^n X_i X_i' + Z Z' = 0, \end{cases}$$

with

$$P_i(X_1, \dots, X_n, Z) = V_i \prod_{k=1}^{n} (G_{\kappa\kappa} X_\kappa - H_{\kappa k} X_k + (C_\kappa + \mathbb{1}_{\{k \neq i\}} K_{k\kappa}) Z). \tag{5.5}$$

Multiply equation i by $-X_i$ for all $i \in \{1, \dots, n\}$, and the last equation by Z^n, so that the summation over these expressions gives:

$$Z^{n-1} Z' = -\sum_i X_i^2 P_i(X_1, \dots, X_n, Z).$$

Thus substituting this expression for $Z^{n-1}Z'$ in the other equations and scaling the time derivative to remove the Z^n term in front of the derivatives, gives:

$$\begin{cases} \dot{X}_i = X_i P_i + X_i(-\sum_i X_i^2 P_i) & \text{for all } 1 \leq i \leq n, \\ \dot{Z} = -Z \sum_i X_i^2 P_i, \end{cases} \tag{5.6}$$

where the arguments for P_i are dropped for simplicity.

5.3 The biologically meaningful region

Since we are only considering the part on the surface of the sphere where the actual microbe concentrations are non-negative, we define the following for simplicity:

DEFINITION 5.9 The part on the surface of the sphere for which $X_i \geq 0 \, \forall i \in \{1, \dots, n\}$ and $Z \geq 0$ is denoted as the *positive octant*. The part on this positive octant on $Z = 0$ will be denoted as the *positive equator*.

In the previous section a simplification was done by writing the nutrient concentrations in terms of the microbe concentrations and some constant C_i. In the general case, the values for C_i can be any value from $\mathbb{R}$. Now, our main interest are the points on the sphere that give non-negative nutrient concentrations; the biologically meaningful region. The following functions are introduced, as they give more information regarding this region.

DEFINITION 5.10 Let the functions $\mathcal{M}_i$ be defined as follows:

$$\mathcal{M}_\iota = G_{\iota\iota}X_\iota - H_{\iota i}X_i + C_\iota Z \qquad 1 \leq i \leq n \text{ and } \iota = (i \mod n) + 1.$$

The functions P_i can be written in terms of $\mathcal{M}_i$:

$$P_i = V_i \prod_{k=1}^{n} (\mathcal{M}_\kappa + \mathbb{1}_{\{k \neq i\}} K_{k\kappa} Z) \qquad 1 \leq i \leq n \text{ and } \kappa = (k \mod n) + 1.$$

Compare $\mathcal{M}_i$ with the expression for the nutrient concentration m_i to see their similarity that is emphasized by the following proposition (trivial proof).

PROPOSITION 5.11 *For $i \in \{1, \ldots, n\}$ and $Z > 0$ is satisfied: $\mathcal{M}_i \geq 0 \iff m_i \geq 0$.*

DEFINITION 5.12 (Biologically meaningful region) The biologically meaningful region on the sphere, denoted by $\mathcal{B}$, can be defined as the region on the sphere for $X_i \geq 0 \; \forall i \in \{1, \ldots, n\}$ and $Z \geq 0$, where $\mathcal{M}_i \geq 0$ for all $i \in \{1, \ldots, n\}$. That is,

$$\mathcal{B} := \Big\{(X_1, \ldots, X_n, Z) \in S^n : \mathcal{M}_i \geq 0 \; \forall i \in \{1, \ldots, n\}\Big\} \tag{5.7}$$

The Poincaré transformation projects $\mathbb{R}^n$ onto the sphere S^n defined in $\mathbb{R}^{n+1}$ and the region $\mathcal{B}$ is just a part of this sphere. However, for example, we want to speak about the points on the sphere that encloses this region $\mathcal{B}$. The topological notion of boundary of the region $\mathcal{B}$ on the sphere with respect to $\mathbb{R}^{n+1}$ would be given by the set itself (5.7). Hence, topologically speaking, the boundary will be with respect to the *sphere* itself (with the subspace topology of $\mathbb{R}^{n+1}$), so that the notion of the boundary of $\mathcal{B}$ now has the intended meaning. Similarly, the interior of the region $\mathcal{B}$ should be taken with respect to the sphere.

Also, the region on the positive octant on $Z = 0$ in which $\mathcal{M}_i \geq 0 \; \forall i \in \{1, \ldots, n\}$ shall be considered; note that the equator is now actually an n-dimensional sphere. In particular, the set that is enclosing this region is analyzed. It seems again intuitive to call this set the boundary of this region, but again topologically speaking the notion of *this* boundary of this set should be taken with respect to the equator, which is the n-dimensional sphere S^{n-1} given by $\sum_{i \leq 1 \leq n} X_i^2 = 1$. In the same way the interior of $\mathcal{E}$ is taken with respect to the equator.

From the context there should be no ambiguity about the definition of the boundary, interior and closure of a given set, hence with respect to which set will generally be omitted.

DEFINITION 5.13 Let $\partial\mathcal{B}$ denote the boundary (w.r.t. the sphere) of the region $\mathcal{B}$. Also, let $\mathcal{E}$ define the set on the positive equator in which $\mathcal{M}_i \geq 0$ for all $i \in \{1, \ldots, n\}$ and subsequently, let $\partial\mathcal{E} \subset \mathcal{E}$ denote its boundary (w.r.t. the equator).

From the definition of $\mathcal{M}_i$ one can see that $\mathcal{M}_i = 0$ is a hyperplane through the origin. The biologically meaningful region on the sphere is then actually the region enclosed by hyperplanes $\mathcal{M}_i = 0$ for all $1 \leq i \leq n$ (or, the intersection of the regions $\mathcal{M}_i \geq 0$ for all $1 \leq i \leq n$) intersected by the sphere. It is quite hard to think of a sphere in $n+1$ dimensions being intersected by a hyperplanes. However, to what extent do we really need to know how these hyperplanes intersect the sphere? We can state the following theorems about the properties of the biologically meaningful region.

PROPOSITION 5.14 *For $R > 1$, $\mathcal{E}$ exists and is contained inside the* interior *of the positive equator. Moreover, the interior of $\mathcal{E}$ is non-empty.*

Proof: $\mathcal{E}$ is defined as the set on the sphere on $Z = 0$ where $\mathcal{M}_i \geq 0 \; \forall i$. This can be expressed in terms of X_i (by writing out the definition of $\mathcal{M}_i$):

$$\frac{G_{\iota\iota}}{H_{\iota i}} X_\iota \geq X_i \qquad \text{for all } 1 \leq i \leq n.$$

Considering this conditions for each i, the following should be satisfied:

$$\frac{G_{22}}{H_{21}} \cdots \frac{G_{nn}}{H_{n(n-1)}} \frac{G_{11}}{H_{1n}} X_1 \geq \frac{G_{22}}{H_{21}} \cdots \frac{G_{nn}}{H_{n(n-1)}} X_n \geq \ldots \geq \frac{G_{22}}{H_{21}} \frac{G_{33}}{H_{32}} X_3 \geq \frac{G_{22}}{H_{21}} X_2 \geq X_1, \tag{5.8}$$

which is satisfied since $R = \prod_i \frac{G_{\iota\iota}}{H_{\iota i}} > 1$.

One sees from the inequality that some point with $X_i = 0$ or $X_i = 1$ for some $1 \leq i \leq n$ cannot lie in $\mathcal{E}$, as it would then violate the inequality (also, $X_i = 0$ or $X_i = 1$ for all $1 \leq i \leq n$ is not possible by the spherical property).

Since $\mathcal{E}$ is strictly contained inside the positive equator, on the boundary $\partial\mathcal{E}$ holds $\mathcal{M}_i = 0$ for some $i \in \{1, \ldots, n\}$. Hence, write the inequality (5.8) with strictly greater signs, which is defined for a set that is contained inside the interior of $\mathcal{E}$ (we will see later that this set should exactly be

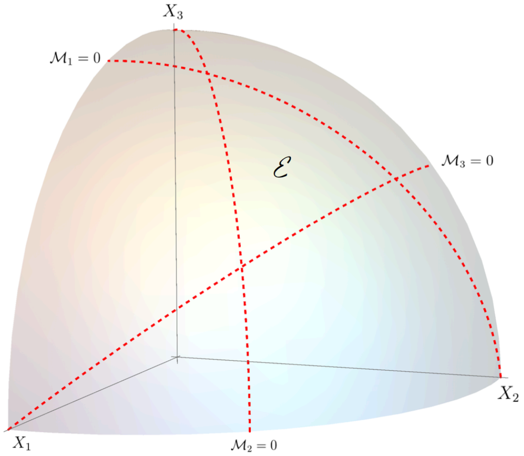

FIGURE 5.2 For a 4-dimensional sphere $X_1^2+X_3^2+X_3^2+Z^2 = 1$ the part where $Z = 0$, defined as the equator, is a 3-dimensional sphere given by $X_1^2 + X_3^2 + X_3^2 = 1$. Hence this figure shows in fact the *positive* equator $(X_1, X_2, X_3 > 0)$ of the 4-dimensional sphere. The region $\mathcal{E}$ is enclosed by the lines on which $\mathcal{M}_i = 0$ for $i \in \{1, 2, 3\}$. Moreover, since the region lies in the interior of the positive octant $(X_1, X_2, X_3 > 0)$, the boundary of the region in this type of system is exactly given by these lines.

the interior). This strict inequality is still satisfied since $R > 1$. ■

We can now deduce that the biologically meaningful region indeed exists on the sphere for meaningful parameters (i.e., yield parameters are positive and C_i is finite).

THEOREM 5.15 *For $R > 1$ the biological meaningful region $\mathcal{B}$ is non-empty and its subset on $Z > 0$ is non-empty.*

Proof: On $Z = 0$ the biologically meaningful region $\mathcal{B}$ coincides with $\mathcal{E}$, thus is not empty by the previous result. When the coordinates are not restricted to the sphere $\mathcal{M}_i = 0$ are hyperplanes through the origin. Since their intersection with the sphere encloses a non-empty region on $Z = 0$ in which $\mathcal{M}_i > 0$ for all $1 \leq i \leq n$, one can induce that because of their relatively simple structure this enclosed region is not only restricted to $Z = 0$, but also for $Z > 0$. That is, since the yield parameters are non-zero and C_i is finite, there is no such plane $\mathcal{M}_i = 0$ that coincides exactly with the plane $Z = 0$ for which the region could indeed be only restricted to $Z = 0$. ■

5.3.1 Properties of the functions in the biologically meaningful region

From the relation of the functions $\mathcal{M}_i$ with respect to the function P_i and the growth rate Q_i some properties can be deduced for different parts of the biologically meaningful region. These results will be important for the following analysis, since the functions P_i tell much about the dynamics and steady states of the system. Pay attention to if they are stated for $Z \neq 0$ or for $Z = 0$.

PROPOSITION 5.16 *In the interior of $\mathcal{E}$ we have $\mathcal{M}_i > 0$ all $1 \leq i \leq n$. On the boundary $\partial\mathcal{E}$ we have $\mathcal{M}_i = 0$ for some $1 \leq i \leq n$.*

Proof: For every $i \in \{1, \ldots, n\}$ the hyperplane $\mathcal{M}_i = 0$ divides the space $\mathbb{R}^{n+1}$ into two subsets; $\mathcal{M}_i > 0$ and $\mathcal{M}_i < 0$. Hence in the *interior* of the region on the equator for which $\mathcal{M}_i \geq 0\ \forall i$, it is not possible that there is an $i \in \{1, \ldots n\}$ such that $\mathcal{M}_i = 0$. Since this set lies strictly contained inside the positive equator, on the boundary we have $\mathcal{M}_i = 0$ for some $1 \leq i \leq n$. ■

About the interior of the biologically meaningful region $\mathcal{B}$ we can state the same using the same proof.

PROPOSITION 5.17 *In the interior of $\mathcal{B}$ we have $\mathcal{M}_i > 0$ all $1 \leq i \leq n$.*

Since P_i is defined in terms of $\mathcal{M}_j$, we can deduce from Proposition 5.17 the following.

COROLLARY 5.18 *In the interior of $\mathcal{B}$ we have $P_i > 0$ for all $1 \leq i \leq n$.*

Statements about behaviour on $\mathcal{E}$ will be done using the following properties.

PROPOSITION 5.19 *On $Z = 0$, the polynomials P_i are equal up to multiplication by the maximum growth rates:*

$$P_i = \frac{V_i}{V_k} P_k \quad \text{for all } i, k \in \{1, \ldots, n\}.$$

This implies that in $Z = 0$ the zeroes of these polynomials coincide:

$$P_i = 0 \iff P_k = 0 \quad \textit{for all } i, k \in \{1, \ldots, n\},$$

and that $P_i = P_k$ holds if and only if they equal zero (or if all V_i are equal, which is not biologically relevant).

Proof: From Definition 5.10 one can see that the functions P_i on $Z = 0$ are defined by:

$$P_i = V_i \prod_{k=1}^{n} \mathcal{M}_\kappa \qquad 1 \leq i \leq n \text{ and } \kappa = (k \mod n) + 1.$$

So the functions P_i only differ from each other by the term V_i. The statements follow from this observation. ■

We can now prove that the biologically meaningful region is an invariant region.

THEOREM 5.20 *The biologically meaningful region is an invariant region.*

Proof: Consider system (5.2) and suppose that $x_i \geq 0$ and $m_i \geq 0$ for $1 \leq i \leq n$ and $\sum_i x_i < \infty$. As long as $m_\iota \geq 0$ then $\dot{x}_i = Q_i(m_\iota)x_i \geq 0$, thus x_i is non-decreasing.

If m_ι for some $\iota \in \{1, \ldots, n\}$ should become negative, by continuity it should go through $m_\iota = 0$. However, on $m_\iota = 0$ we have $Q_i(m_\iota) = 0$, hence the expression becomes $\dot{m}_\iota = G_{\iota\iota} Q_\iota x_\iota$ which can only be negative if the argument of Q_ι is already negative (or has been negative so that $x_\iota < 0$). So a nutrient concentration can only become negative if an other nutrient concentration is already negative. Since this holds for any nutrient, non-negative concentrations (of both microbes and nutrients) cannot become negative.

The only part of the biological meaningful region $\mathcal{B}$ that is not included in this proof is the boundary on $Z = 0$ as this corresponds to $\sum_i x_i = \infty$. However, one can see that $\dot{Z} = 0$ on $Z = 0$ and that $\mathcal{M}_i = 0$ for some i implies $P_i = 0 \,\forall i$, which gives $X_i = 0 \,\forall 1 \leq i \leq n$. Hence trajectories cannot move to negative Z nor to negative values of $\mathcal{M}_i$ for some i on $Z = 0$. ■

Finally, to stress the fact that one should be careful making statements for points on $\mathcal{E}$ (which lies on $Z = 0$); compare the following two propositions. The proofs are left for the reader as the statements easily follow from the definition $\mathcal{M}_i$ and the definition of P_i.

PROPOSITION 5.21 *On $Z \neq 0$ for every $i \in \{1, \ldots, n\}$ and corresponding ι satisfies: $\mathcal{M}_\iota = 0$ is equivalent to $Q_i = 0$ (growth rate of species i) and implies $P_i = 0$.*

PROPOSITION 5.22 *On $Z = 0$, $\mathcal{M}_\iota = 0$ implies $P_i = 0$, but not necessarily that $Q_i = 0$ for any $i \in \{1, \ldots, n\}$.*

5.4 Convergence in the biologically meaningful region

The important regions are defined and we know several properties inside these regions, so now we can look at the behaviour of trajectories inside these regions. For the yield ratio $R > 1$ as defined in Theorem 5.7 we know that there is unbounded growth, in which case $\sum_i x_i \to \infty$ as $t \to \infty$. A simple but important deduction is the following:

PROPOSITION 5.23 *Unbounded growth implies that the trajectories in the biologically meaningful region on the Poincaré sphere converge towards* $Z = 0$.

Proof: Unbounded growth means that $\sum_i x_i \to \infty$ as $t \to \infty$ for positive initial concentrations. This implies that on the Poincaré sphere we have $\frac{1}{Z} \geq \frac{1}{Z}\sum_i X_i = \sum_i \frac{X_i}{Z} = \sum_i x_i \to \infty$, hence $Z \to 0$. So every trajectory in the *interior* of biologically meaningful region (where initial concentrations are positive) must converge to $Z = 0$ if there is unbounded growth implied by $R > 1$.

■

To know whether the trajectories converge to an equilibrium on $Z = 0$ we first show where the equilibrium points lie in the biologically meaningful region on $Z = 0$, i.e., the equilibrium points in $\mathcal{E}$.

THEOREM 5.24 (Equilibrium points on the equator) *For* $R > 1$, *the collection of equilibrium points on* $\mathcal{E}$ *is exactly* $\partial\mathcal{E}$, *which are the points for which holds* $\mathcal{M}_i = 0$ *for any* $i \in \{1, \ldots, n\}$. *This collection does not lie anywhere on* $X_i = 0$ *or* $X_i = 1$ *for any* $i \in \{1, \ldots, n\}$.

Proof: Suppose $R > 1$, then by previous propositions, $\mathcal{E}$ exists, coincides with the subset of $\mathcal{B}$ on $Z = 0$ and lies strictly inside the positive equator ($X_i > 0\ \forall i$). Hence, on $\mathcal{E}$ the equilibrium points are given by $P_i = P_k$ for every $i, k \in \{1, \ldots, n\}$, since $Z = 0$ already gives the steady state $\dot{Z} = 0$. Proposition 5.19 states that on $Z = 0$ we have $P_i = P_k$ if and only if they are zero and in particular, this happens only if $\mathcal{M}_i = 0$ for some $i \in \{1, \ldots, n\}$, giving that the collection of equilibrium points on $\mathcal{E}$ is exactly $\partial\mathcal{E}$ by Proposition 5.16. Since $\mathcal{E}$ is a closed set, its boundary $\partial\mathcal{E}$ is also strictly contained inside the positive equator.

■

The statement about the boundary not lying on $X_i = 0$ or $X_i = 1$ for any $i \in \{1, \ldots, n\}$ maybe seems not essential but is quite important, since *if* some point of the boundary of the meaningful region did lie on $X_i = 0$ or $X_i = 1$ for some i, then convergence towards the boundary would not necessarily imply convergence to the same growth rates. For example; convergence to the point on the equator for which $X_i = 0$ for all but one $i \in \{1, \ldots, n\}$, would imply that there is one dominant species that keeps on growing faster than all the others. We will encounter a similar kind of results in the next chapter.

5.4.1 Convergence towards equilibrium points on the equator

In this last subsection we can show the actual convergence. In the case of unbounded growth all trajectories move towards $\mathcal{E}$ for $t \to \infty$, since trajectories should converge towards $Z = 0$ and stay inside the invariant region $\mathcal{B}$. So they either could move towards the boundary $\partial\mathcal{E}$, which is an equilibrium, or move towards the interior of $\mathcal{E}$. In this section we show how the dynamics roughly are in the interior of $\mathcal{E}$, hence we analyze the dynamics *on* the equator. This will show that on the interior of $\mathcal{E}$ trajectories move towards the boundary, hence towards an equilibrium point (since the boundary $\partial\mathcal{E}$ consists of equilibrium points). Then trajectories in the interior of the biologically meaningful region converging *towards* $\mathcal{E}$ will eventually have similar dynamics as *on* the interior of $\mathcal{E}$. The following lemma tells that on the interior of $\mathcal{E}$, there is at least one variable that is always decreasing.

PROPOSITION 5.25 *Let the Poincaré dynamics be given by* (5.6) *for* $R > 1$. *Let* $k = \arg\min_i V_i$. *On the interior of* $\mathcal{E}$ X_k *has no steady states and* $\dot{X}_k < 0$.

Proof: Consider the interior of $\mathcal{E}$, on which $P_i > 0\ \forall i$ by Proposition 5.18. Since $X_k = 0$ is not contained in $\mathcal{E}$ by Proposition 5.14 the only steady states of X_k in $\mathcal{E}$ are given by $P_k = \sum_i X_i^2 P_i$. However, by Proposition 5.19 every P_i is proportional to P_k, hence one can write the following inequality by using $V_i > V_k$ for some i:

$$\sum_i X_i^2 P_i = \sum_i X_i^2 \frac{V_i}{V_k} P_k > \sum_i X_i^2 P_k = P_k.$$

So the condition $P_k = \sum_i X_i^2 P_i$ for the steady state is never satisfied in the interior of $\mathcal{E}$. Moreover, $\sum_i X_i^2 P_i > P_k$ implies $\dot{X}_k < 0$, hence X_k decreases in the interior of $\mathcal{E}$. ■

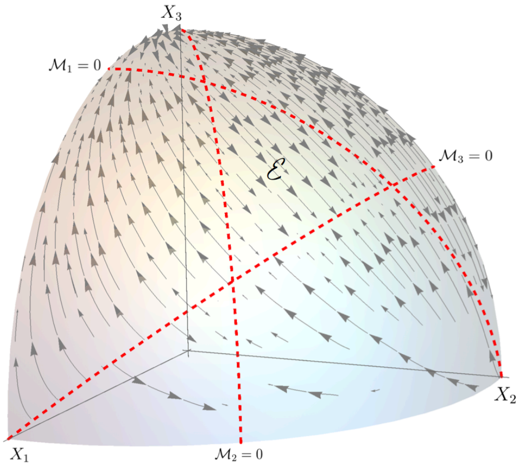

FIGURE 5.3 The dynamics on the (positive) equator of a 4-dimensional sphere can be visualized. In this particular figure, the parameters were such that V_3 was the smallest maximum growth rate, in which can be seen that indeed $\dot{X}_3 < 0$ inside $\mathcal{E}$. This figure is made by projecting the stream plot of the planar dynamics of (X_1, X_2) onto the sphere.

As we showed that on the interior of $\mathcal{E}$ the variable X_k decreases and the only steady states of X_k are at the boundary, this implies that this variable will end up at the boundary of the (compact) region on which in fact *every* variable is stationary. This lemma hence excludes the existence of any sort of limit cycle on the equator. Figure 5.3 shows an example of dynamics on the equator of a four-dimensional sphere. The hypothesis of the convergence of the growth rates to the same rate can now be proved:

THEOREM 5.26 *Let the system of equations on the Poincaré sphere be given by* (5.6). *Assume that* $R > 1$. *Then every trajectory in the interior of* $\mathcal{B}$ *converges to a point where all growth rates are equal.*

Proof: In $\mathcal{B}$, all trajectories move towards the equator $Z = 0$, in particular, to $\mathcal{E}$. From Proposition 5.25, we can deduce that the trajectories tending towards the interior of the region, eventually also converge to the boundary. On the whole boundary $\partial\mathcal{E}$ $P_i = 0$ $\forall i \in \{1, \dots, n\}$ (since $\mathcal{M}_i = 0$ for some $i \in \{1, \dots, n\}$), thus convergence of one variable towards the boundary implies that the derivatives of all the variables converge to zero. So every trajectory (eventually) converges towards the boundary, hence towards an equilibrium, with this equilibrium point given by $X_i = a_i$ $\forall i \in \{1, \dots, n\}$ for certain constants $a_i \in (0, 1)$. Note that 0 and 1 are not included, as mentioned in Theorem 5.24. To see why this means that the growth rates should be equal now, we write the convergence in terms of the microbial fractions:

$$\frac{x_i}{x_\iota} = \frac{\frac{X_i}{Z}}{\frac{X_\iota}{Z}} = \frac{X_i}{X_\iota} \to \frac{a_i}{a_\iota} \quad \text{as } t \to \infty,$$

for all $i \in \{1, \dots, n\}$ and $\iota = (i \mod n) + 1$, with every fraction being a finite non-zero number. Because it is an equilibrium point the derivatives $\dot{X}_i \to 0$, from which can be deduced that derivative of the microbial fraction $\dot{\left(\frac{x_i}{x_\iota}\right)} = \dot{\left(\frac{X_i}{X_\iota}\right)} \to 0$. Hence for $t \to \infty$ and every $i \in \{1, \dots, n\}$:

$$(Q_i - Q_\iota)\frac{a_i}{a_\iota} = (Q_i - Q_\iota)\frac{x_i}{x_\iota} = \frac{Q_i x_i x_\iota - x_i Q_\iota x_\iota}{x_\iota^2} = \frac{\dot{x}_i x_\iota - x_i \dot{x}_\iota}{x_\iota^2} = \dot{\left(\frac{x_i}{x_\iota}\right)} \to 0,$$

thus $Q_i - Q_\iota \to 0$ for every $i \in \{1, \dots, n\}$ and $\iota = (i \mod n) + 1$ as $t \to \infty$. ■

Finally, as we showed that the growth rate should converge to the same rate using the transformed system, we can consider the original system again and make a final statement about the value of the growth rates and the values of the relative fractions when $t \to \infty$.

THEOREM 5.27 *Consider the system of differential equations* (5.2) *with yield parameters such that* $R > 1$. *Denote* $k = \arg\min_{1 \le i \le n} V_i$. *Then the growth rates converge to the smallest maximum growth rate* $Q_i \to V_k$ *for all* $i \in \{1, \dots, n\}$ *for* $t \to \infty$.

Moreover, for all $i \in \{1, \dots, n\} \setminus k$ *and* $\iota := (i \mod n) + 1$, *the ratios of the microbe concentrations converge as follows:*

$$\frac{x_i}{x_\iota} \to \frac{G_{\iota\iota}}{H_{\iota i}}.$$

Proof: First note that because $R > 1$, we know by Theorem 5.7 that the sum of nutrient concentrations $\sum_{1\leq i\leq n} m_i$ grows to infinity for $t \to \infty$. Every Q_i is a monotone increasing function with respective upper bound V_i, with V_k of $Q_k(m_\kappa)$ for $\kappa := (k \mod n) + 1$ being the smallest maximum growth rate.

Theorem 5.26 states that every biologically meaningful trajectory with positive initial concentrations on the sphere converges to an equilibrium point where all growth rates are equal; for all $1 \leq i \leq n$ we have $Q_i \to Q^*$ form some growth rate Q^*. Since $\sum m_i \to \infty$, at least one m_i should grow to infinity. Suppose some nutrient concentration other than m_κ grows to infinity, say m_ι for some $\iota \neq \kappa$. Then the growth rate $Q_i(m_\iota) \to V_i > V_k \geq Q_\kappa$, implying that $Q_i \not\to Q_k$; contradiction. So m_κ is the only possible nutrient concentration that grows to infinity, in which case $Q_k \to V_k$, hence $Q_i \to V_k$ for all $1 \leq i \leq n$.

For the second implication, suppose $Q_i \to V_k$ for all $1 \leq i \leq n$. Then $m_\kappa \to \infty$ and $m_\iota \to m_\iota^*$ for positive constants m_ι^* for all $\iota \neq \kappa$. Since we can write the nutrient concentration in terms of the initial conditions and microbe concentrations, the following equations should be satisfied for all $1 \leq i \leq n$ such that $i \neq k$ (hence $\iota \neq \kappa$):

$$m_\iota^* = G_{\iota\iota} x_\iota - H_{\iota i} x_i + C_\iota.$$

Write this in terms of the ratio of microbial concentrations:

$$\frac{x_i}{x_\iota} = \frac{G_{\iota\iota}}{H_{\iota i}} + \frac{C_\iota - m_\iota^*}{H_{\iota i} x_\iota} \xrightarrow{t\to\infty} \frac{G_{\iota\iota}}{H_{\iota i}}.$$

■

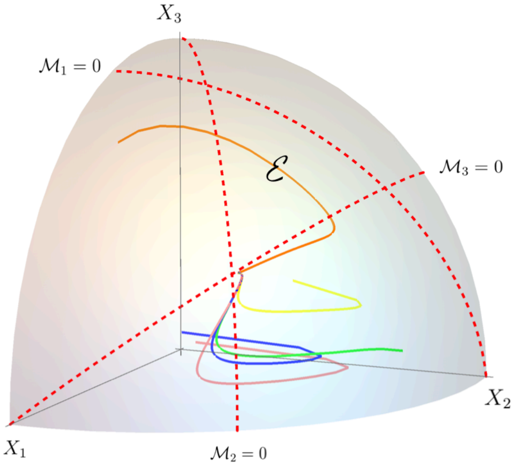

FIGURE 5.4 For the four-dimensional Poincaré system, the trajectories are shown for only X_1, X_2, X_3. This results in trajectories inside the unit ball converging towards the surface.

One can consider again a four-dimensional system (of which the equator was visualized in Figure 5.2 and 5.3) and visualize the trajectories by only plotting X_1, X_2 and X_3; this results in trajectories in the interior of the three-dimensional ball, moving towards boundary (which corresponds to the equator of the four-dimensional sphere). One can see that trajectories indeed converge to a unique equilibrium point where two functions $\mathcal{M}_i, \mathcal{M}_j$ equal zero.

COROLLARY 5.28 *For system* (5.2) *with* $R > 1$, *the nutrient concentration that is consumed by the species with the smallest growth rate is the only one that grows to infinity when* $t \to \infty$.

5.5 Discussion on the generalization

We showed that there is a yield parameter condition that ensures unbounded growth for all species in a microbial community with a cyclic cross-feeding topology. A simplification of the $2n$-dimensional to a n-dimensional system can be obtained by writing the nutrient concentrations in terms of the microbe concentrations and certain constants C_i for all $i \in \{1, \ldots, n\}$. For any fixed value of C_i the values $(x_1, \ldots, x_n)$ give the values $(m_1, \ldots, m_2)$; the collection of points for which is satisfied that these nutrient concentrations are positive, is called the biologically meaningful region. The original idea of the Poincaré sphere was really to analyze the points on the equator with linear stability analysis. However, we observed that the important functions $\mathcal{M}_i$ are elegantly described in this transformation, so that we held on to this transformation.

After the transformation of the flows onto the Poincaré sphere, the trajectories inside the biologically meaningful region on the sphere move towards $Z = 0$ since unbounded growth of the microbes $x_i \to \infty$ corresponds to $Z \to 0$ as $t \to \infty$. One could show that all trajectories eventually end up in some equilibrium point(s) for strictly positive values $X_1, \ldots, X_n$, implying convergence of the growth rates to the same rate. It could then be shown that there is a unique equilibrium point to which all trajectories converge, as all other equilibrium points would give a contradiction to the converging growth rates. Note that this proof does not depend on the parameter values other than that they are biologically relevant and satisfy the condition for unbounded growth $R > 1$; whether C_i is positive or negative does not change a thing in the proof.

Note that this is now only proved for systems with a *cyclic* cross-feeding topology. Nevertheless, this way of proving the long-term behaviour for systems with unbounded growth should also be possible for alternative systems. In the next chapter, a different cross-feeding topology will be considered to see which of the foregoing theorems do and which do not hold in those systems.

6

Non-cyclic cross-feeding system

In this chapter we consider cross-feeding topologies different from the cyclic topology that was discussed in the previous chapter. In a microbial community with three species one can think of different possibilities of how the microbes interact with each other, as will be shown in this chapter. It is interesting to analyze what the long-term behaviour for the growth rates are for two species that grow on the production of a third species for different systems. In the context of the more popular predator-prey model coexistence means that neither the predator nor the prey would become extinct. However, as this model does not consider death or dilution the definition of coexistence of two species in this setting is as follows:

DEFINITION 6.1 Two species are said to coexist if the species grow on growth-limiting nutrient(s) being produced by a third species with which they are both cross-feeding, such that there is unbounded growth and the concentrations stay in the same order of magnitude. Thus, two species do not coexist if the species grow such that eventually one microbe concentration is negligible compared to the other.

6.1 Characteristics for the alternative systems

From the general scheme of Figure 6.1 several cross-feeding communities can be created; different combinations of the produced and consumed nutrients of the species give different systems with varying analytic difficulties. The general equation of modeling the growth of the species is always

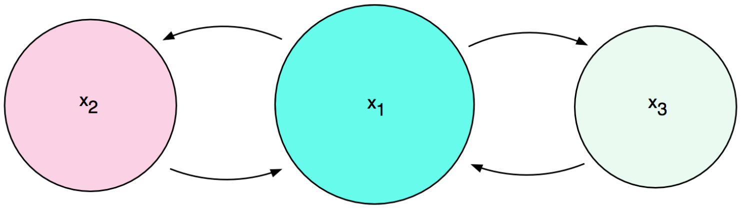

FIGURE 6.1 General schematic figure of the alternative systems discussed in this chapter. One can obtain different systems by considering different combinations of nutrients produced by the species.

the same, i.e., every species' growth is modeled by:

$$\dot{x}_i = Q_i x_i. \tag{6.1}$$

The growth rates of the species, Q_i, vary in the following system because not only it depends per system which nutrient (concentration) their argument is, but also the explicit expressions for the nutrient concentrations are different per system. This can cause completely different behaviour than what we have seen in Chapter 5. Nevertheless, on can follow the exact same procedure as in Section 5.2.2. That is, write the nutrient concentrations in terms of the microbe concentrations and substitute these in the growth rates so that the remaining system is three equations of the form of equation (6.1). Then, multiply every equation by all the denominators of the growth rates and change the time scale in such way so that we can write for every equation:

$$\begin{cases}\dot{x}_i = p_i(x_1, x_2, x_3)x_i \quad \text{for all } 1 \leq i \leq 3,\end{cases}$$

where p_i is a multiplication of the nominator of the growth rate Q_i and the denominators of the growth rates Q_j for all $j \neq i$. In the first two systems that follow p_i are also polynomials of degree 3 (degree 4 in the last system) which agrees exactly with system (5.4), so that the Poincaré transformation is in its general form identical to (5.6):

$$\begin{cases}\dot{X}_i = X_i P_i + X_i(-\sum_i X_i^2 P_i) \quad \text{for all } 1 \leq i \leq 3,\\ \dot{Z} = -Z\sum_i X_i^2 P_i,\end{cases} \tag{6.2}$$

with P_i cubic polynomials (in the last system in this chapter they are quartic). The exact terms of P_i are slightly different and will be discussed for each system. Since the Poincaré sphere is four-dimensional in this chapter it is convenient to denote the variables by X, Y, U, in stead of X_1, X_2, X_3.

Because of this similar form we are able to use many of the ideas of Chapter 5 even though the exact terms of P_i and $\mathcal{M}_j$ are different in the systems. Using the same notation as in the previous chapter the following statements are satisfied for all of the alternative systems, but will not be proved:

CLAIM 6.2 *The following statements are true.*

- *The biologically meaningful region $\mathcal{B}$ is an invariant region (cf. Theorem 5.20).*
- *Unbounded growth means that trajectories in $\mathcal{B}$ converge to $Z = 0$ for $t \to \infty$ (cf. Proposition 5.23.*
- *On $\mathcal{E}$ we have that $V_2V_3P_1 = V_1V_3P_2 = V_1V_2P_3$ (cf. Proposition 5.19);*
- *In the interior of $\mathcal{E}$ we have that $\mathcal{M}_j > 0\,\forall j$, hence $P_i > 0$ for all $i \in \{1, 2, 3\}$ (cf. Proposi-*

tion 5.17 and Corollary 5.18);

- *The equilibrium points on $\mathcal{E}$ lie on the boundary $\partial\mathcal{E}$ (cf. Theorem 5.24);*
- *In the case of unbounded growth, for $t \to \infty$ we have $\mathcal{M}_j \to 0$ is equivalent to $m_j < \infty$ (easy proof left for the reader);*

In particular the last statement will be useful for proving the long-term behaviour of trajectories in this chapter. The reason for not stating the set from which j can be chosen, is because the number of functions differs per system.

Again, only biologically meaningful parameter values are considered, hence special cases where certain parameters are equal can be ignored. By the symmetry of the system we can assume without loss of generality that $V_2 > V_3$. The magnitude of V_1 will be an important factor and each of the following cases should be considered:

1) $V_1 > V_2 > V_3$;
2) $V_2 > V_1 > V_3$;
3) $V_2 > V_3 > V_3$.

Finally, since it is a four-dimensional system we can visualize the trajectories as we did in the previous chapter: by only plotting X, Y, U, the trajectories can be shown inside the unit ball that move towards the surface, which is in fact the equator of the four-dimensional sphere. However, these are just for additional understanding purpose; the proofs are in an abstract setting and done without observations of the sphere, so that the proving technique is not limited to only visualizable systems (in the same sense as the previous chapter). It will only be proven whether the growth rates converge and to which rates, the corollaries regarding the relative microbe fractions are left out in this chapter. The same notation of the regions and notion of the boundary and interior of these regions as in Chapter 5 are used.

6.2 Competitive cross-feeding topology

If species 2 and 3 consume the same nutrient essential limited nutrient, then they are competing for the same nutrient and thus have the following cross-feeding topology.

THEOREM 6.3 *We say that the microbial community has a competitive cross-feeding topology if there are (at least) two species consuming the same essential nutrient.*

An example of such a three-species system can be found in the article of Baltzis et al. [5], although in the environment of a chemostat. Suppose that two species both consume the essential nutrient produced by the third species and both produce the same essential nutrient consumed by the third species. The expressions for the derivatives of the two nutrient concentrations are then as follows:

$$\begin{cases} \dot{m}_1 &= G_{11}Q_1(m_2)x_1 - H_{12}Q_2(m_1)x_2 - H_{13}Q_3(m_1)x_3, \\ \dot{m}_2 &= G_{22}Q_2(m_1)x_2 + G_{23}Q_3(m_1)x_3 - H_{21}Q_1(m_2)x_1. \end{cases} \tag{6.3}$$

For simplicity, species 2 and 3 are called the *competing* species, as they consume the product of species 1. Since species 1 is connecting the other two species, we denote this species as the *common* species.

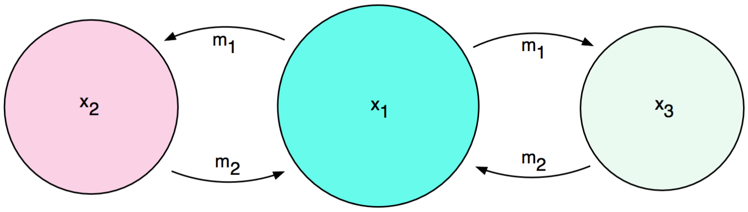

FIGURE 6.2 Cross-feeding scheme where two species consume and produce the same nutrient, corresponding to the expressions (6.3).

6.2.1 Nutrient dynamics

The analysis for this system should again start with the behaviour of the nutrients. It is not difficult to show that also here the nutrient concentrations either all converge to zero, or none does (just like Proposition 5.6).

The ratio that the yield parameters should satisfy for unbounded growth (similar to Theorem 5.7) is this time less straight-forward. Since there is only two equations for five independent variables, the sum of the nutrients can at most be written in terms of two species concentrations. That is, one can eventually write (for example in x_1 and x_2):

$$G_{23}\dot{m}_1 + H_{13}\dot{m}_2 = (G_{23}G_{11} - H_{13}H_{21})Q_1(m_2)x_1 + (H_{13}G_{22} - G_{23}H_{12})Q_2(m_1)x_2.$$

From this relation it is less obvious to conclude what the parameters should satisfy to obtain a positive derivative on the left-hand side. One could set all the yield parameters such that on the right-hand side both terms are positive, but this could be too strict. This needs further investigation, which shall not be done in this thesis. However, for now suppose that

$$R := \min\{\frac{G_{23}G_{11}}{H_{13}H_{21}}, \frac{H_{13}G_{22}}{G_{23}H_{12}}\} > 1.$$

Then unbounded growth is ensured.

For the *possibility* of convergence of all growth rates to the same rate when there is unbounded growth, one should consider how Q_2 and Q_3 are defined. Since these functions both depend on

m_1, they can only be equal if their graphs intersect (since $V_2 > V_3$). The following proposition is easily obtained by setting equal $Q_2(m_1) = Q_3(m_1)$ and solving for m_1.

PROPOSITION 6.4 *A positive intersection for $Q_2(m_1) = Q_3(m_1)$ exists if the parameters satisfy the following condition:*

$$\frac{V_2 K_{31} - V_3 K_{21}}{V_3 - V_2} > 0.$$

This is in fact the positive value for m_1 that gives $Q_2 = Q_3$. However, the growth rate Q_1 can only converge to the other two growth rates if V_1 is exactly the value of Q_2 and Q_3 at their intersection. This is because for unbounded growth the sum of nutrients should go to infinity, but m_1 certainly cannot grow to infinity if $Q_2 = Q_3$ should be satisfied; hence m_2 should grow to infinity, thus $Q_1 \to V_1$. However, having exactly $V_1 = Q_2 = Q_3$ at the intersection is in the biological sense not relevant. Therefore we may assume that the parameters are such that even if they satisfy Proposition 6.4 then the intersection is not equal to V_1, so the following claim is true:

CLAIM 6.5 *For system* (6.3) *with unbounded growth, convergence of all growth rates to the same non-zero rate is not possible.*

6.2.2 Biologically meaningful region

As described in the introductory section, one can rewrite the system in the same way as done in Chapter 5 to obtain the Poincare system (6.2). The differences between the system lie in the functions P_i and $\mathcal{M}_j$, where in particular the latter has a major influence in the long-term behaviour of the growth rates as we will see. The functions P_i are given as follows:

$$\begin{aligned} P_1 &= V_1 \mathcal{M}_2 (\mathcal{M}_1 + K_{21} Z)(\mathcal{M}_1 + K_{31} Z), \\ P_2 &= V_2 \mathcal{M}_2 (\mathcal{M}_2 + K_{12} Z)(\mathcal{M}_1 + K_{31} Z), \\ P_3 &= V_3 \mathcal{M}_1 (\mathcal{M}_2 + K_{12} Z)(\mathcal{M}_1 + K_{21} Z). \end{aligned}$$

One can see that indeed on $Z = 0$ these functions are again equal up to a multiplication of the maximum growth rate (cf. Proposition 5.19), which is the most important results for these functions. The functions $\mathcal{M}_1$ and $\mathcal{M}_2$ are explicitly given by:

$$\begin{aligned} \mathcal{M}_1 &= G_{11} X - H_{12} Y - H_{13} U + C_1 Z, \\ \mathcal{M}_2 &= G_{22} Y + G_{23} U - H_{21} X + C_2 Z. \end{aligned}$$

The exact forms of these functions have a big influence on the long-term behaviour of the system since these functions, from these functions the biologically meaningful region is defined and characteristics of the functions P_i are derived. In particular, consider $\mathcal{E}$: by definition of $\mathcal{M}_1$ and $\mathcal{M}_2$

this region is given by X, Y, U that satisfy both:

$$G_{11}X - H_{12}Y - H_{13}U \geq 0, \quad G_{22}Y + G_{23}U - H_{21}X \geq 0. \tag{6.4}$$

From this description of the region and using that on $Z = 0$ it is not possible that $X = Y = U = 0$, one can obtain that on $\mathcal{E}$ we have that $X > 0$ (from the first inequality) and that $Y > 0$ or $U > 0$ (from the second inequality). Since $\mathcal{E}$ is now not contained in the interior of the positive equator, the boundary $\partial\mathcal{E}$ does not consist solely of points where $\mathcal{M}_i = 0$ is satisfied for some $1 \leq i \leq n$. Furthermore, from these two inequalities the following inequality can be derived:

$$\frac{G_{11}X - H_{12}Y}{H_{13}} \geq U \geq \frac{H_{21}X - G_{22}Y}{G_{23}},$$

hence, X and Y should be such that:

$$(G_{11}G_{23} - H_{13}H_{21})X + (H_{13}G_{22} - H_{12}G_{23})Y \geq 0.$$

Since both terms with the yield parameters are positive by our assumption of $R > 1$ this condition is satisfied. From the results of the preceding two subsections, the previously stated list for characteristics of the system (Claim 6.2 can be extended with the following statements.

CLAIM 6.6 *The following statements are true.*

- *$\mathcal{E}$ exists and coincides with the subset of $\mathcal{B}$ on $Z = 0$.*
- *In the case of unbounded growth trajectories in the interior of the biologically meaningful region converge towards $\mathcal{E}$;*
- *On $\mathcal{E}$ we have that $X > 0$ and that $Y > 0$ or $U > 0$;*
- *Equilibrium points on $\mathcal{E}$ lie on the boundary $\partial\mathcal{E}$, but not necessarily the whole boundary is an equilibrium (compare to the previous chapter where the whole set $\partial\mathcal{E}$ is an equilibrium);*
- *Moreover, equilibrium points on $\partial\mathcal{E}$ can only be given by points where $\mathcal{M}_j = 0$ for some j.*

6.2.3 Convergence to the equator

For the three cases of the maximum growth rates the resulting behaviour on $\mathcal{E}$ is different. These cases are discussed and the general behaviour in the biologically meaningful region will be derived.

Recall that $\mathcal{E}$ is the biologically meaningful region $\mathcal{B}$ on $Z = 0$, hence the region towards which the trajectories converge as $t \to \infty$ in the case of unbounded growth (Proposition 5.23). Dynamics and equilibria on $\mathcal{E}$ give information about the actual long-term behaviour of the trajectories in the interior of the biologically meaningful region. The statement for dynamics on $\mathcal{E}$ which can also still be used for this system is Proposition 5.25: the variable corresponding to the growth rate with the smallest maximum growth rate always decreases on the interior of $\mathcal{E}$ and its steady states do not lie in the interior. Since $\mathcal{E}$ is invariant and compact this variable decreases towards the boundary. The three cases of V_1 compared to $V_2 > V_3$ are now considered, which will eventually prove the statement:

CLAIM 6.7 *Coexistence is never possible in the microbial community defined by* (6.3)*, as in the long term one species will always have a lower growth rate than the other two species.*

Trajectories converging towards $\mathcal{E}$ can either move directly towards the boundary or towards the interior of $\mathcal{E}$. Since in this system *not* the whole boundary $\partial\mathcal{E}$ is an equilibrium, dynamics on the boundary should also be considered. It will be shown that trajectories end up in an equilibrium point in any case. From this fact, it can be shown to what growth rates they should converge.

THEOREM 6.8 *Suppose there is unbounded growth and $V_1 > V_2 > V_3$. Then $Q_1, Q_2 \to V_2$ and $Q_3 < V_2$ for $t \to \infty$.*

Proof: Consider trajectories that move towards the boundary $\partial\mathcal{E}$. Then they either converge to equilibrium points given by $\mathcal{M}_i = 0$ for some $i \in \{1, 2\}$, or to the boundary where either $U = 0$ or $Y = 0$ ($X = 0$ does not lie in $\mathcal{E}$). However, in the case of $U = 0$, one can write by the properties of P_i on $Z = 0$:

$$X^2 P_1 + Y^2 P_2 = X^2 \frac{V_1}{V_2} P_2 + Y^2 P_2 > (X^2 + Y^2) P_2 = P_2.$$

Since all P_i are positive in $\mathcal{E}$, the inequality gives that $\dot{Y}$ is negative on $U = 0$ in $\mathcal{E}$. As mentioned, the point where both $Y = U = 0$ does not lie in $\mathcal{E}$. Thus on $U = 0$ in $\mathcal{E}$ trajectories decrease in Y to some steady state where $Y > 0$, which is where $\mathcal{M}_1 = 0$ or $\mathcal{M}_2 = 0$, hence again an equilibrium point. The same is true for the boundary on $Y = 0$ resulting in a convergence towards some $U > 0$. Thus trajectories converging towards the boundary always end up in an equilibrium point where $\mathcal{M}_1 = 0$ or $\mathcal{M}_2 = 0$.

Now consider trajectories moving towards the interior of $\mathcal{E}$. Since V_3 is the smallest *on* the interior of $\mathcal{E}$ the variable U decrease towards the boundary $\partial\mathcal{E}$ (compare to Proposition 5.25), which decreases either towards $U = 0$ (steady state for U) or to some point $U > 0$ where $\mathcal{M}_1 = 0$ or $\mathcal{M}_2 = 0$ (equilibrium). We already showed that on $U = 0$, Y decreases to some steady state on $Y > 0$ where $\mathcal{M}_1 = 0$ or $\mathcal{M}_2 = 0$. Hence trajectories converging towards the interior of $\mathcal{E}$ will eventually adopt these dynamics and thus converge towards an equilibrium point.

The previous two paragraphs show that trajectories in $\mathcal{E}$ always end up in equilibrium points, where they are at least of one of the following forms:

$$(X > 0, Y > 0, U > 0),\ (X > 0, Y = 0, U > 0),\ (X > 0, Y > 0, U = 0). \tag{6.5}$$

We will show which of these types of equilibria are actually not possible by contradiction. The first type of equilibrium point is already not possible, as this would mean that all growth rates converge to the the same non-zero growth rate, which was stated not to be possible by Claim (6.7).

On the other hand, suppose trajectories converge to an equilibrium point of the form $Y = 0$ and $U > 0$. This means that the growth rates Q_1 and Q_3 should converge to each other, while the growth rate Q_2 (corresponding to Y) should be smaller than Q_1 for $t \to \infty$. Since $m_1 + m_2 \to \infty$ and $V_1 > V_3$, this convergence only happens if $m_1 \to \infty$ and $m_2 \to m_2^*$ for some $m_2^* \in \mathbb{R}$ such that $Q_1, Q_3 \to V_3$ as $t \to \infty$. But then also $Q_2(m_1) \to V_2 > V_3$, which contradicts the fact that $Q_2 < Q_1$.

Hence the only possible equilibria are of the form $(X > 0, Y > 0, U = 0)$. So the trajectories on $\mathcal{E}$ converge to an equilibrium point on $\mathcal{E}$ for some positive X and Y, giving that $Q_1 - Q_2 \to 0$. Then again by the fact that the sum of the nutrient blows up and $V_1 > V_2$, this can only occur if $m_1 \to \infty$ and $m_2 \to m_2^*$ so that $Q_1, Q_2 \to V_2$. ■

THEOREM 6.9 *Suppose there is unbounded growth and $V_2 > V_1 > V_3$. Then $Q_1, Q_2 \to V_1$ and $Q_3 < V_1$ for $t \to \infty$.*

Proof: Same proof as above, with the only difference that $Q_1 - Q_2 \to 0$ can now only occur if $m_1 \to m_1^*$ and $m_2 \to \infty$ so that $Q_1, Q_2 \to V_1$. ■

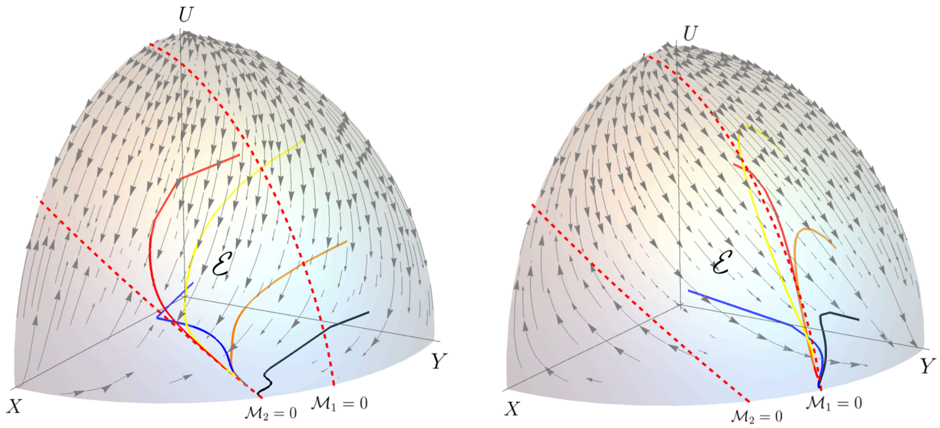

FIGURE 6.3 The left figure shows the stream plot on the equator and some trajectories that come from inside the ball, when $V_1 > V_2 > V_3$; the right figure shows the case $V_2 > V_3 > V_1$. The figures are made for relatively small time t to improve the accuracy of the shown trajectories, at the expense of the long-term behaviour, since it converges slowly towards the equilibrium point when it is near $\mathcal{M}_i = 0$ for some i.

The third possibility of the order of the growth rates shows the least obvious result of the convergence of the growth rates. First introduce the following lemma which can be easily obtained by solving the equations $Q_2(m_1) = V_1$ and $Q_3(m_1) = V_1$ for m_1, hence the proof is omitted.

LEMMA 6.10 *The growth rate Q_2 or Q_3 which needs the smallest concentration m_1 to equal V_1, that is, $\min\{m_1^{Q_2}, m_1^{Q_3}\}$ for $m_1^{Q_2} := Q_2^{-1}(V_1)$ and $m_1^{Q_3} := Q_3^{-1}(V_1)$, can be obtained from the parameter values:*

$$m_1^{Q_2} < m_1^{Q_3} \iff \frac{K_{21}}{V_2 - V_1} < \frac{K_{31}}{V_3 - V_1},$$

and similar for strictly greater signs.

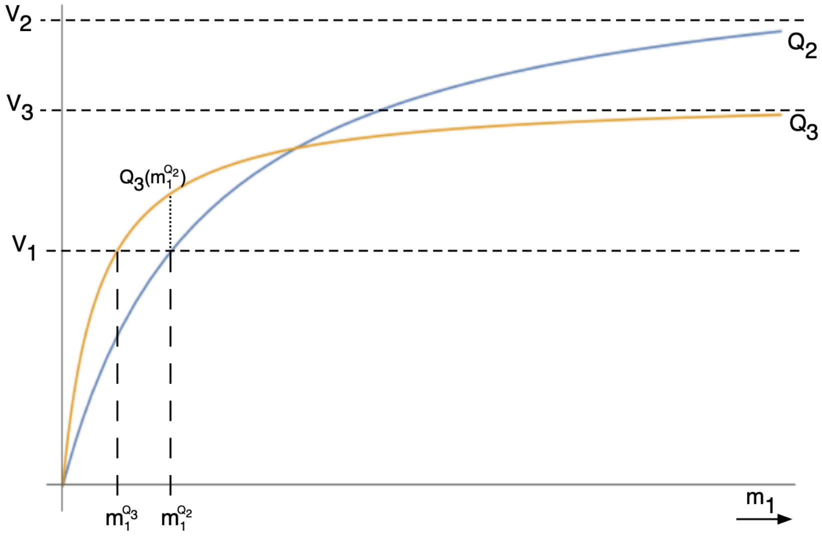

FIGURE 6.4 Growth curves Q_2 and Q_3 both depend on m_1 and V_1 smallest maximum growth rate. If $\min\{m_1^{Q_2}, m_1^{Q_3}\} = m_1^{Q_2}$, then $Q_3(m_1^{Q_2}) > Q_2(m_1^{Q_2}) = V_1$.

THEOREM 6.11 *Suppose there is unbounded growth and* $V_2 > V_3 > V_1$. *The growth rate that corresponds to the minimum* $\min\{m_1^{Q_2}, m_1^{Q_3}\}$ *will in fact converge together with* Q_1 *to* V_1 *for* $t \to \infty$, *while the other converges to some rate smaller than* V_1.

Proof: Since V_1 is the smallest X decreases in $\mathcal{E}$ towards the boundary $\partial\mathcal{E}$. In the previous subsection was mentioned that $X = 0$ is not contained in $\mathcal{E}$, hence the variable X decreases towards the point where $X > 0$ is such that $\mathcal{M}_1 = 0$ or $\mathcal{M}_2 = 0$. Since either give that $\dot{U} = 0$ and $\dot{Y} = 0$, the trajectories on $Z = 0$ should end up in an equilibrium point. Hence all trajectories in the interior of biologically meaningful region, will eventually converge to some equilibrium point with again one of the given forms as in (6.5).

It is not possible that the trajectories on $Z > 0$ converge to an equilibrium point where $Y > 0$ and $U > 0$; this would imply that all growth rates converge to the same rate, which was shown not to be possible. Hence equilibrium points to which trajectories converge have either $Y = 0$ or $U = 0$ (see Claim 6.6). To know which of the two variables goes down to zero, we should consider their corresponding growth rate curves. Suppose without loss of generality that $\min\{m_1^{Q_2}, m_1^{Q_3}\} = m_1^{Q_3}$ (as in Figure 6.4). By contradiction, we will show that $U \neq 0$.

Suppose the trajectories converge to an equilibrium where $U = 0$ and $Y > 0$. This means that the corresponding growth rates of X and Y converge to each other and are bigger than the corresponding growth rate of U; $Q_1, Q_2 \to Q^* > Q_3$. As we have that V_1 is the smallest growth rate and that the sum of nutrients $m_1 + m_2$ grows to infinity, this convergence can only happen if $m_2 \to \infty$ and $m_1 \to m_1^{Q_2}$ for $t \to \infty$. However, because of the assumption that $m_1^{Q_3} < m_1^{Q_2}$, then $Q_3(m_1^{Q_2}) > Q_2(m_1^{Q_2}) = V_1$, contradicting the fact that the growth rates Q_1, Q_2 converge to some rate which is bigger than Q_3. Hence the trajectories converge to the equilibrium point where $U > 0$ and $Y = 0$, in which case $m_2 \to \infty$ and $m_1 \to m_1^{Q_3}$ so that $Q_1, Q_3 \to V_1$ and $Q_2(m_1^{Q_3}) < V_1$. ■

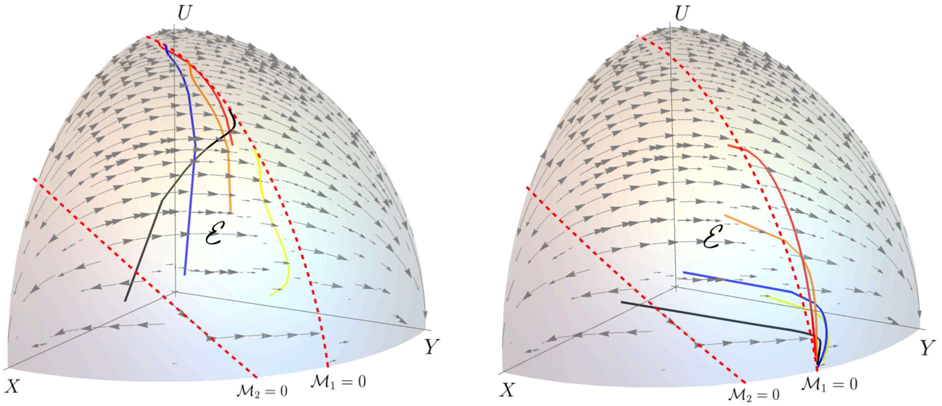

FIGURE 6.5 The two figures show what happens to the stream plot on the equator and thus the trajectories converging toward $\mathcal{E}$ when the argument for $Q_2(m_1) = V_1$ is smaller than the argument of $Q_3(m_1) = V_1$, opposed to the other way round (r).

REMARK (1) *For all of the three cases of the maximum growth rates one can again obtain from the definitions of $\mathcal{M}_1$ or $\mathcal{M}_2$ where the relative fractions of the microbe concentrations converge to, as one of both converges to zero for $t \to \infty$ and one variable (Y or U) converges to zero. This gives an expression for the two non-zero variables, so that for each case a unique point can be obtained which is the unique equilibrium point to which all trajectories converge.*

REMARK (2) *As a final remark on the condition for unbounded growth, notice that for example in the very last case shown in Figure 6.5(r) the line $\mathcal{M}_1 = 0$ is to the right of $\mathcal{M}_2 = 0$ as long as $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. This is indeed implied by the condition $R > 1$, but seems to be a sufficient condition on its own for unbounded growth. However, this observation can only be done after knowing where the trajectories converge to, as this condition is different for the other case shown in Figure 6.5(l).*

6.3 Non-competitive cross-feeding

Suppose that the two competing species both consume a different essential nutrient produced species 1, but both still produce the same essential nutrient consumed by species 1. In this case, species 2 and 3 are in fact not competing since they are consuming different products of the common species.

$$\begin{cases} \dot{m}_1 &= G_{11}Q_1(m_2)x_1 - H_{12}Q_2(m_1)x_2, \\ \dot{m}_2 &= G_{22}Q_2(m_1)x_2 + G_{23}Q_3(m_3)x_3 - H_{21}Q_1(m_2)x_1, \\ \dot{m}_3 &= G_{31}Q_1(m_2)x_1 - H_{33}Q_3(m_3)x_3. \end{cases} \tag{6.6}$$

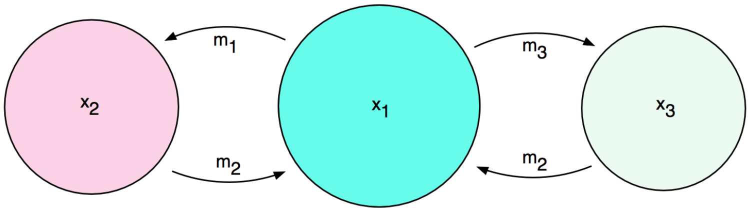

FIGURE 6.6 Cross-feeding scheme where two species produce the same nutrient, but consume different nutrients produced by the third species.

6.3.1 Nutrient dynamics

Once again, Proposition 5.6 stating that a nutrient depletes if and only if all nutrients deplete is true. Hence, we should be able to find a threshold R for the parameters so that there is unbounded growth. One can eliminate x_2 and x_3 from the equations (6.6) to obtain the relation:

$$G_{22}H_{33}\dot{m}_1 + H_{12}H_{33}\dot{m}_2 + H_{12}G_{23}\dot{m}_3 = (G_{11}G_{22}H_{33} + G_{31}G_{23}H_{12} - H_{12}H_{21}H_{33})Q_1x_1.$$

Hence, for this system, there is unbounded growth if and only if

$$R := \frac{G_{11}G_{22}H_{33} + G_{31}G_{23}H_{12}}{H_{12}H_{21}H_{33}} > 1.$$

In this system there are three nutrients for the three different growth rates and therefore it could again be possible that all growth rates converge to the same rate (contrary to the previous system).

6.3.2 Biologically meaningful region

Again, if we follow the same procedure that is done in the introductory section of this chapter we end up with the Poincaré transformed system (6.2), where P_i are cubic polynomials with a similar form (that satisfy Proposition 5.19 again) and where $\mathcal{M}_i$ are defined as:

$$\begin{aligned}
\mathcal{M}_1 &= G_{11}X - H_{12}Y + C_1Z, \\
\mathcal{M}_2 &= G_{22}Y + G_{23}U - H_{21}X + C_2Z, \\
\mathcal{M}_3 &= G_{31}X - H_{33}U + C_3Z.
\end{aligned}$$

We saw in the previous system that we only need to consider these functions, as they define the biologically meaningful region. Setting these functions $\mathcal{M}_i$ on $Z = 0$ greater or equal to zero one can obtain the following inequality, which should be satisfied in the region $\mathcal{E}$:

$$\frac{G_{22}G_{11}}{H_{12}}X + \frac{G_{23}G_{31}}{H_{33}}X > G_{22}Y + G_{23}U > H_{21}X,$$

which again writes to the condition $R := \frac{G_{22}G_{11}H_{32}+G_{23}G_{31}H_{12}}{H_{12}H_{21}H_{33}} > 1$. With the same observations as for the preceding system we can state that the exact same statements as in Claim 6.6 are true.

6.3.3 Convergence to the equator

Since the proof for convergence towards an equilibrium point on the boundary $\partial\mathcal{E}$ is going to be similar as the ones that were done for system (6.3) in the previous section, these are omitted in this section. The main idea is again that trajectories move towards $\mathcal{E}$ in the case of unbounded growth. All trajectories move towards an equilibrium (on the boundary $\partial\mathcal{E}$), either directly or via the dynamics on $\mathcal{E}$. In any case, analogue to the result of the equilibrium points in the previous system (6.5), so we state the following without proof:

CLAIM 6.12 *Trajectories in $\mathcal{B}$ converge to some equilibrium point on $\partial\mathcal{E}$. These equilibria are points where $X > 0$ and where $Y > 0$ or $U > 0$.*

In this case however, we will see that it is less obvious which of the type of equilibrium is the only possible one to which trajectories converge; an additional condition for the yield ratio influences the growth rate behaviour.

THEOREM 6.13 *Suppose trajectories converge to some equilibrium on $\partial\mathcal{E}$ and suppose that $V_1 > V_2 > V_3$. If the yield parameters satisfy the condition*

$$\frac{G_{11}G_{22}}{H_{21}H_{12}} > 1,$$

then $Q_1, Q_2 \to V_2$ and $Q_3 \to V_3$.

On the other hand, if the inequality has a strictly smaller sign, then $Q_1, Q_2, Q_3 \to V_3$.

Proof: From the previous claim, the possible equilibrium points to which trajectories could converge, are points of the following forms:

1) $(X > 0, Y > 0, U > 0)$,

2) $(X > 0, Y = 0, U > 0)$,

3) $(X > 0, Y > 0, U = 0)$.

Equilibria of the first kind correspond with convergence of all growth rates to the same rate, whereas the other two correspond with convergence of two growth rates to a rate bigger than the third growth rate. We will show for each type of equilibrium points if and when trajectories can converge to them.

1) $(X > 0, Y > 0, U > 0)$.
   Trajectories converging to this type of equilibrium, eventually show equal growth rates, and since $V_1 > V_2 > V_3$, this can only be satisfied if at least $m_1 < \infty$ and $m_2 < \infty$ (thus in

which case $m_3 \to \infty$) for $t \to \infty$. This is equivalent to $\mathcal{M}_1 \to 0$ and $\mathcal{M}_2 \to 0$ for $t \to \infty$ (see Claim 6.2), and expressed as follows:

$$G_{11}X - H_{12}Y \to 0, \quad G_{22}Y + G_{23}U - H_{21}X \to 0.$$

Hence, for $t \to \infty$, the two convergences give that in the limit $\frac{G_{22}Y+G_{23}U}{H_{21}} = \frac{H_{12}}{G_{11}}Y$, which is rewritten as $G_{23}U = (\frac{H_{12}H_{21}}{G_{11}} - G_{22})Y$. Obviously, this can only be satisfied if $\frac{H_{12}H_{21}}{G_{11}} - G_{22} > 0$, that is, $\frac{G_{11}G_{22}}{H_{12}H_{21}} < 1$.

2) $(X > 0, Y = 0, U > 0)$.
These equilibria correspond to $Q_1, Q_3 \to V_3$ and $Q_2 < V_3$, implied by the fact that in this case again $m_1 < \infty$ and $m_2 < \infty$ for $t \to \infty$ (hence $m_3 \to \infty$). Then for $t \to \infty$:

$$G_{11}X - H_{12}Y \to 0, \quad G_{22}Y + G_{23}U - H_{21}X \to 0.$$

However, since now $Y \to 0$ in the limit, the first equation implies that also $X \to 0$. That is not possible as $X > 0$ in $\mathcal{E}$. So these equilibria cannot be stable.

3) $(X > 0, Y > 0, U = 0)$.
In the limit $t \to \infty$, for the growth rate Q_1 to be smaller or equal to V_2 we should have $\mathcal{M}_2 = 0$, hence

$$G_{22}Y + G_{23}U - H_{21}X \to 0.$$

Since the equilibrium lies in $U = 0$, in the limit $G_{22}Y = H_{21}X$. On the other hand, on $\mathcal{E}$ we have that $\mathcal{M}_1 \geq 0$ which means that $G_{11}X \geq H_{12}Y$. Combining the two inequalities one obtains

$$\frac{G_{22}}{H_{21}}Y = X \geq \frac{H_{12}}{G_{11}}Y.$$

One can see that the inequality is strict for $\mathcal{M}_1 > 0$, whereas it is an equality for $\mathcal{M}_1 = 0$. Moreover, this inequality can only be satisfied if $\frac{G_{11}G_{22}}{H_{12}H_{21}} \geq 1$. If we omit the special case of equal to 1, hence $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$, then $\mathcal{M}_1 = 0$ would violate the inequality, thus $\mathcal{M}_1 \not\to 0$ for $t \to \infty$. Moreover, in this case $Q_2 \to V_2$ thus also $Q_1 \to V_2$. Also, considering the expression for $\mathcal{M}_3$ one can see that this cannot equal zero, as this would imply that $X = 0$. Hence $m_3 \to \infty$, thus $Q_3 \to V_3$.

■

Figures 6.7 shows the stream plot on the equator and several trajectories for the two different cases of the additional condition of the yield ratio. From the figures we see what happens for the two cases of this additional condition. In the same way we can state this again for $V_2 > V_1 > V_3$ with the same condition and an identical proof, which is therefore omitted. We see that the condition for the maximum growth rates that should actually be considered is whether $\min_{\{} V_1, V_2, V_3\} = V_1$ or not.

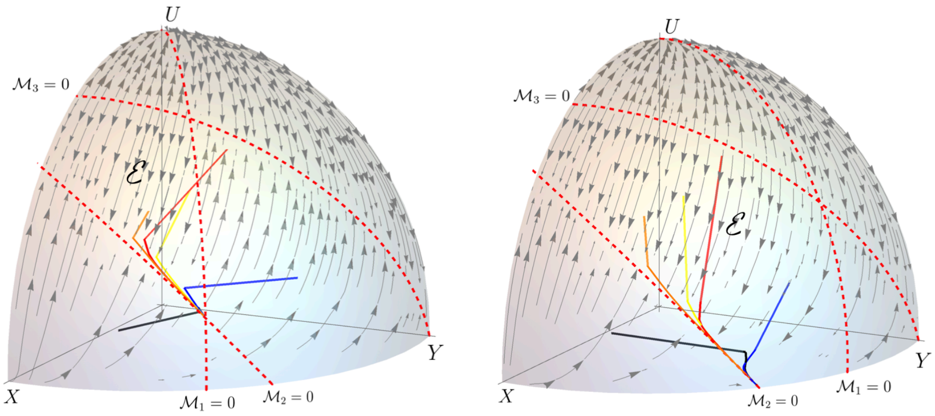

FIGURE 6.7 For the system with $V_1 > V_2 > V_3$, the left figure shows the stream plot on the equator and several trajectories when $\frac{G_{11}G_{22}}{H_{12}H_{21}} < 1$, in which case trajectories converge to the intersection of $\mathcal{M}_1 = 0$ and $\mathcal{M}_2 = 0$. The right figure show these when $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$, where trajectories converge to $U = 0$.

THEOREM 6.14 *Suppose trajectories converge to some equilibrium on $\partial\mathcal{E}$ and suppose that $V_2 > V_1 > V_3$. If the yield parameters satisfy the condition*

$$\frac{G_{11}G_{22}}{H_{21}H_{12}} > 1,$$

then $Q_1, Q_2 \to V_1$ and $Q_3 \to V_3$.

On the other hand, if the inequality has a strictly smaller sign, then $Q_1, Q_2, Q_3 \to V_3$.

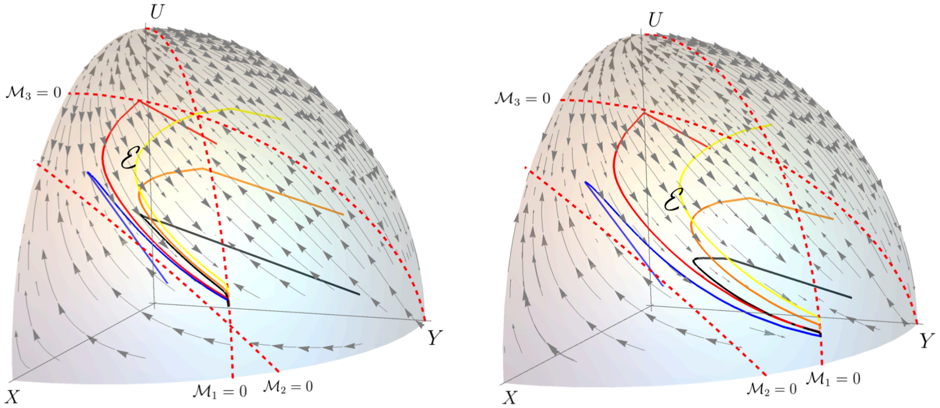

FIGURE 6.8 For the system with $V_2 > V_1 > V_3$, the left figure shows the case when $\frac{G_{11}G_{22}}{H_{12}H_{21}} < 1$, whereas the right figure shows the case when $\frac{G_{11}G_{22}}{H_{12}H_{21}} > 1$. Due to the computational inaccuracy only a small time span is considered; as time t increases, the trajectories move further down to the intersection or $U = 0$ respectively.

THEOREM 6.15 *Suppose trajectories converge to some equilibrium on $\partial\mathcal{E}$ and suppose that $V_2 > V_3 > V_1$. Then $Q_1, Q_2, Q_3 \to V_1$.*

Proof: Again, we will consider for the different candidate types of equilibria and prove that two types cannot be stable in this case. Suppose trajectories converge to an equilibrium point of the type $(X > 0, Y = 0, U > 0)$. This corresponds to $Q_1 - Q_3 \to 0$, and Q_2 smaller than these two, which can only be satisfied if $m_1 < \infty$ and $m_3 < \infty$, hence $m_2 \to \infty$. This translates to $\mathcal{M}_1 \to 0, \mathcal{M}_2 \not\to 0, \mathcal{M}_3 \to 0$. However, the first convergence implies by definition that $G_{11}X - H_{12}Y \to 0$. Since $Y = 0$ in the equilibrium, also X should go to zero, which contradicts that $X > 0$.

A similar contradiction arises when the equilibrium $(X > 0, Y > 0, U = 0)$ is considered. Hence the only type of equilibria which can be stable are of the form $(X > 0, Y > 0, U > 0)$, in which case all growth rates $Q_1, Q_2, Q_3 \to V_1$, since $m_1 < \infty, m_3 < \infty$, hence $m_2 \to \infty$. ■

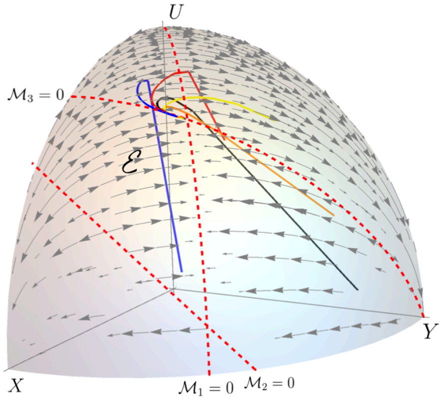

FIGURE 6.9 In the system where V_1 is the smallest growth rate all the trajectories converge to some equilibrium point where $Q_1 = Q_2 = Q_3 = V_1$.

REMARK *The exact values to which the relative fractions converge (the unique equilibrium point) can be obtained again by considering the solving the system of equations given by $\mathcal{M}_i = 0$, for all the $\mathcal{M}_i$ that converge to zero in each case.*

6.4 Double-nutrient limited growth

When a microbial species consumes two scarce essential nutrients both concentration levels should influence the growth rate. One would however still expect that the consumption rate and production rate are proportional to the growth rate; the ratio between much an amount of substrate resulting into an amount of increased size is still given by the yield coefficient. If the common species consumes two different nutrients produced by the competing species we can model the nutrients as follows:

$$\begin{cases} \dot{m}_1 = G_{11}Q_1(m_2, m_3)x_1 - H_{12}Q_2(m_1)x_2 - H_{13}Q_3(m_1)x_3, \\ \dot{m}_2 = G_{22}Q_2(m_1)x_2 - H_{21}Q_1(m_2, m_3)x_1, \\ \dot{m}_3 = G_{33}Q_3(m_1)x_3 - H_{31}Q_1(m_2, m_3)x_1, \end{cases} \tag{6.7}$$

Note that Q_1 depends on two nutrients now. When there is a scarcity two essential nutrients for growth, there can be argued how the growth rate Q_i is defined. The original Monod growth rate

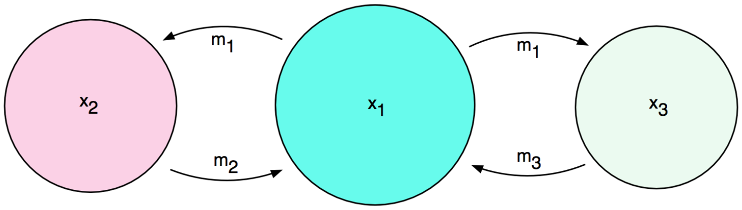

FIGURE 6.10 Cross-feeding scheme where two species consume the same nutrient but produce different nutrients.

curve is defined for an environment where only one nutrient is of low concentration. Two possible extensions of this curve for a multiple-substrate depending growth rate is presented in the article of Bader [13]:

$$Q_i(\mathbf{m}) = V_i \prod_{j=1}^{M} \frac{m_j}{K_{ij} + m_j}, \tag{6.8}$$

$$Q_i(\mathbf{m}) = V_i \min_{1 \le j \le M} \frac{m_j}{K_{ij} + m_j}, \tag{6.9}$$

in which the growth rate of a species is modeled for M possibly restricting nutrients. The interactive model (6.8) defines a growth function where all essential nutrient concentrations always contribute to the growth, in contrast to the non-interactive model (6.9) where the essential nutrient concentration that gives the lowest growth rate is the sole influence. The physiological state of an organism depends upon the availability of *all* nutrients, so it is unlikely that the growth would be independent of each other. When the degree of interaction between certain subsystems (influencing the growth) may be rather small, a non-interactive type of model may accurately describe the growth rate of the organism. Otherwise, the interactive model should describe the growth rate in a better way. Since this model is also computationally and theoretically more easily implemented, it will define the multi-substrate growth rate in this chapter.

6.4.1 Nutrient dynamics are not trivial

Numerical simulations show that this system does not only depend on the yield parameters to show unbounded growth, but it is also sensitive for different values of the maximum growth rate V_i, parameters K_{ik} and initial conditions. How does this system differ from the cyclic system and which theorems do not apply? The very first proposition introduced, with its generalization given by Proposition 5.6, is already not true for this system.

PROPOSITION 6.16 *In system* (6.7) *we have for* $1 \le i \le n$*:* $\exists i\, m_i \to 0 \iff \forall i\, Q_i \to 0$. *However,* $\exists i\, m_i \to 0$ *does not necessarily imply that* $\forall i\, m_i \to 0$.

Proof: Suppose that $m_1 \to 0$. Then by definition also $Q_2(m_1) \to 0$ and $Q_3(m_1) \to 0$. One can rewrite $\dot{x}_2 = Q_2 x_2$ to $\frac{\dot{x}_2}{x_2} = Q_2$, where the left-hand side is in fact $\frac{\mathrm{d}}{\mathrm{d}t} \ln x_2$. Since $Q_2 \to 0$, this derivative converges to zero, hence $\ln x_2$ converges to some constant which implies that x_2 converges to a certain constant; hence $Q_2 x_2 \to 0$. Similarly, also $Q_3 x_3 \to 0$. So for t large enough $m_1 \to 0$ implies that we can express $\dot{m}_2 = -H_{21} Q_1(m_2, m_3) x_1$ and $\dot{m}_3 = -H_{31} Q_1(m_2, m_3) x_1$. So these nutrient concentrations keep decreasing until $m_2 = 0$ or $m_3 = 0$ in which case $Q_1 = 0$; not necessarily both have to be zero.A similar proof can be given if we suppose $m_2 \to 0$ or $m_3 \to 0$. ■

The fact that depletion of one nutrient does not imply depletion of every nutrient seems only a small difference with respect to the preceding systems. However, it has big consequences for other theorems that were stated for these systems. First of all, the ratio $R > 1$ now does not give a sufficient condition about the blowup of the nutrient concentrations, but only a necessary:

THEOREM 6.17 *Let the system of ODEs be given by* (6.7). *The sum of nutrients may diverge, if*

$$R := \frac{G_{11} G_{22} G_{33}}{G_{33} H_{12} H_{21} + G_{22} H_{13} H_{31}} > 1.$$

Proof: Consider again only the nutrient dynamics appropriately, so that the derivatives can be expressed in terms of the growth of one species:

$$G_{22} G_{33} \dot{m}_1 + G_{33} H_{12} \dot{m}_2 + G_{22} H_{13} \dot{m}_3 = (G_{11} G_{22} G_{33} - G_{33} H_{21} H_{21} - G_{22} H_{31} H_{13}) Q_1 x_1. \quad (6.10)$$

The right-hand side is positive if $G_{11} G_{22} G_{33} - G_{33} H_{12} H_{21} - G_{22} H_{31} H_{13} > 0$, that is, if $R := \frac{G_{11} G_{22} G_{33}}{G_{33} H_{21} H_{21} + G_{22} H_{13} H_{31}} > 1$. However, the total sum being positive in this system does not exclude that none of the nutrients converge to zero, as Proposition 6.16 is less strict. This could mean that even though one nutrient would deplete the sum can still satisfy condition (6.10), as not all nutrients then have to deplete. This implies that also in the case of $R > 1$ it is possible that $Q_1 \to 0$, so that even in this case the sum of nutrients does not grow to infinity. ■

6.4.2 Possible growth rate convergence

The presence of unbounded growth seems to depend on more conditions than just the yield ratio R. *If* there is unbounded growth it seems probable that the growth rates again do converge to each other, considering the previous systems. But in this case the parameters should at least satisfy the condition given in the following statement:

PROPOSITION 6.18 *A necessary condition for the parameters that should be satisfied for the possibility to have convergence to the same non-zero growth rate, is the following:*

$$0 < \frac{V_2 K_{31} - V_3 K_{21}}{K_{31} - K_{21}} \leq V_1.$$

Proof: If all growth rates should converge to the same non-zero rate, then in particular also $Q_2 - Q_3 \to 0$; hence there should at least exist a positive intersection of Q_2 and Q_3 as they both depend on m_1 (see Figure 6.11). Set $Q_2(m_1) = Q_3(m_1)$ and derive for the non-trivial intersection $m_1^* = \frac{V_2K_{31} - V_3K_{21}}{V_3 - V_2}$. Then $Q_2(m_1^*) = \frac{V_2K_{31} - V_3K_{21}}{K_{31} - K_{21}} := V^*$. This is the value for Q_2 and Q_3 at their intersection. Since also Q_1 should converge to the other two growth rates, this intersection must lie below V_1 and must obviously be positive. ■

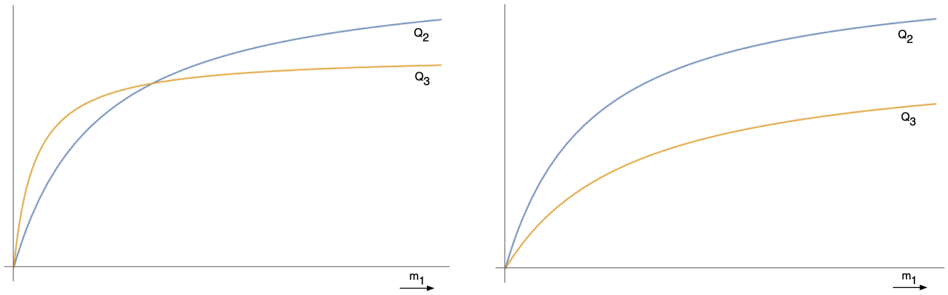

FIGURE 6.11 Two figures of possible growth rate curves Q_2 and Q_3 for $V_2 > V_3$. For the possibility of all growth rates converging to the same rate, the parameter values should be such that these curves intersect (left).

Note that this is actually a similar statement as Proposition 6.4. However, the difference is now that this intersection does not have to equal V_1 if for the growth rates to converge to the same non-zero rate; since Q_1 now depends on two nutrient concentrations (instead of one), one may grow to infinity while the other could attain any value, in particular the value such that Q_1 is equal to the value of Q_2 and Q_3 at their intersection. It is also not clear in that case which of the concentrations should converge. Hence we are at a dead end now with the proving technique that we have been using so far for the other systems. Additional information needs to be found to know for which initial conditions or parameter conditions the microbes concentrations will grow infinitely large. As I have not been able to find certain patterns, this thesis ends with this unsolved problem that is interesting for further research on this topic.

Finding sufficient conditions (for parameters and initial values) for which the species have unbounded growth in this system is beyond the scope of this thesis. If we know more about the conditions for the presence of unbounded growth, then the same analysis could be done to gain more insight about the long-term behaviour of the trajectories.

7

Conclusion

Different models of a cross-feeding microbial community were studied. The fundamentals of these models were introduced and derived in Chapter 2, which were mainly based on the works of Monod. A two-species cross-feeding community was modeled by a four-dimensional system of differential equations, which could be rewritten to a two-dimensional system of differential equations with a constraint that the initial conditions satisfy a certain equation.

Chapter 3 gave insights into the behaviour of the system by transforming the system to a system defined on $[0,1]^2$ and giving the phase portraits for different parameter values. This showed that the fraction $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ had an influence on the long-term behaviour and that one nutrient concentration m_i at the equilibrium points on $v = 1$ (the critical points at infinity in the original system) was in fact undefined. This observation shows that these equilibrium points are not quite normal.

In the search of more information about the long-term behaviour the mathematical analysis in Chapter 4 was done by compactifying the space using the Poincaré transformation. The initial approach of classifying all equilibria on the first octant of the sphere with linear stability analysis showed difficulties since the non-trivial equilibrium points on the equator turned out to be non-hyperbolic, which confirms the idea that these equilibrium points give some difficulty. By observing the lines $P_1 = 0$ and $P_2 = 0$ and the nullclines around the non-hyperbolic equilibria, one could eventually show to which equilibrium all trajectories in the first octant converge to. However, this only proved the unbounded growth and convergence for certain parameter conditions since the analysis was too laborious. We did see in both chapters that the yield ratio $\frac{G_{11}G_{22}}{H_{12}H_{21}}$ was important for the long-term behaviour.

A more general approach of analyzing the behaviour was done by first considering the condition that actually ensures unbounded growth (for positive initial conditions). This condition is where the proofs of Chapter 5 and Chapter 6 rely on. In the most cases, it was relatively easily obtained that the sum of nutrient concentrations blows up as time t approaches infinity and none of the nutrients deplete; then the microbe concentrations also grow to infinity. Subsequently, the Poincaré transformation turned out to be useful to prove behaviour on infinity; the points at infinity are mapped onto the equator of the sphere, on which steady states, equilibria and the behaviour of trajectories can be considered. One could prove that on the equator, all trajectories at least converge to some equilibrium on the equator. Subsequently could be proved that for every system a unique equilibrium exists to which all trajectories in the biologically meaningful region converge. The latter was not explicitly done for the systems in Chapter 6 but is a corollary of the results which is similar to the statement of Theorem 5.27. This way we could prove to which values the growth rates converge and we could give the microbial concentrations relative to each other in the long-term.

For the last system in Chapter 6, it could not be proved whether there would be unbounded growth for certain parameter conditions. This example gave the insight that the long-term behaviour of not every system of cross-feeding microbes can be deduced from the techniques presented, whence the last section follows.

7.1 Future work

The systems in which some species consumes two scarce essential nutrients could be interesting for further research, such as the last system that was introduced. This system showed behaviour that can not be explained by the techniques previously used; even when the parameter values are such that the ratio $R > 1$, it can still occur that the growth rates converge to zero. I have not been able to find any pattern in numerical simulations which might give a clue. However, it might be possible that the long-term behaviour cannot be predicted at all.

One could also consider other underlying assumptions of the system. For example, Andrews describes in his article [14] a growth rate curve where the nutrient limits the growth at low concentration, but is inhibitory for a micro-organism when a high concentration is present in the environment. This could be interesting, since in our model (at least) one nutrient concentration increases to infinity when time t approaches ∞; if this nutrient is indeed inhibitory for the corresponding microbe species, it changes the long-term behaviour drastically.

Research also shows that bacterial competition is not restricted to a passive consumption process; microorganisms have evolved strategies to acquire their resources. These strategies can make a significant change to the competitive behaviour, which could result in outcomes that are different than those which are predicted by resource availability alone. A well-known strategy is the production of an inhibitory substrate for the competing species, but there are also more complex strategies which require cooperation between species. In the article of Hibbing et al. [15] several strategies are presented, albeit non-mathematically. One can imagine that incorporating active strategies could be mathematically very challenging.

Popular Summary

Microbial growth is defined as the division of a microbe into two identical daughter cells, which means that their growth is exponential. If x_0 denotes the initial concentration of a species, then the total concentration at time t is given by $x(t) = x_0 e^{\mu t}$, where μ is defined as the growth rate. Subsequently, the rate of change of the microbe concentration is defined as $\frac{\mathrm{d}x(t)}{\mathrm{d}t} = \frac{\mathrm{d}x_0 e^{\mu t}}{\mathrm{d}t} = x_0 e^{\mu t}\mu = x(t)\mu$. The growth rate does not have to be constant; in this thesis, the concentration of an essential nutrient is scarce in the environment. If we denote this essential nutrient by m, the nutrient-controlled growth rate is then some function denoted by $Q(m)$. The simplest example of the type of models we consider is shown in the following figure.

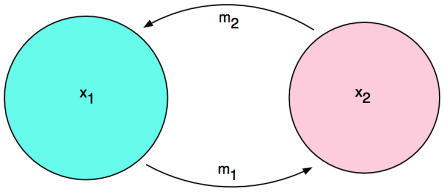

FIGURE P.1 The concentration of microbe species 1 is denoted by x_1 and of species 2 by x_2. The concentration in the environment of the nutrient produced by species 1 (and consumed by species 2) is denoted by m_1. Similarly, m_2 denotes the concentration produced by species 2.

This figure can be mathematically expressed in terms of a system of ordinary equations, where the nutrient concentrations m_1 and m_2 in the environment fluctuate due to the production and consumption of these nutrients by the microbes.

$$\begin{cases} \dot{x}_1 = Q_1(m_2)x_1, \\ \dot{x}_2 = Q_2(m_1)x_2, \\ \dot{m}_1 = G_{11}Q_1(m_2)x_1 - H_{12}Q_2(m_1)x_2, \\ \dot{m}_2 = G_{22}Q_2(m_1)x_2 - H_{21}Q_1(m_2)x_1, \end{cases}$$

The equations for $\dot{m}_1$ and $\dot{m}_2$ arise from the proportionality of the growth rates with the production and consumption rates, with their proportions given by the constants G_{11}, G_{22} (w.r.t production) and H_{12}, H_{21} (w.r.t. consumption).

The microbe concentrations increase as long as there is a positive concentration of the essential nutrient in the environment; we consider this as the only factor in the environment that affects the growth rate. This means that the other essential nutrients are always in excess, thus the microbe concentrations could in fact grow infinitely large as time t approaches ∞. This is called *unbounded growth* and will be our focus in this thesis. Critical points of these systems lie at infinity, hence we want to make the system compact in order to study these points. The Poincaré transformation projects the (x_1, x_2) onto the unit sphere in such a way that infinity is mapped to the equator of the sphere. The non-negative values $x_1, x_2 \geq 0$ are mapped to the first octant of the sphere ($X, Y, Z \geq 0$), hence only this part of the sphere has to be analyzed.

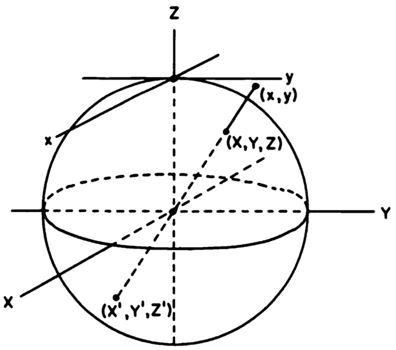

FIGURE P.2 Projection of the (x, y)-plane onto the surface of the unit sphere in the (X, Y, Z)-space.

We want to show what happens to the long-term behaviour of the trajectories on the sphere, since convergence towards an equilibrium point on the equator might imply that the growth rates converge to the same rate. We will not stick with a two-species systems, but also consider higher-dimensional system in which a higher-dimensional sphere will be considered. For the two-species system that was introduced, one can visualize in the case of unbounded growth some trajectories converging towards an equilibrium point on the equator for certain parameter values.

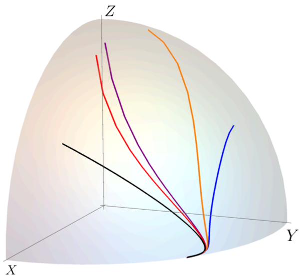

FIGURE P.3 Trajectories on the surface of the sphere converge to an equilibrium point on the equator.

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