

Growth Dynamics of Algal-bacterial Cocultures: A Control Engineering Perspective

Mohammad Abbadi¹ and Sarah Spurgeon²

Abstract—Despite internal complexity, algae and bacteria have coexisted since the early stages of evolution. This co-evolution follows relatively simple laws that can be clearly expressed using mathematical models. This paper performs a quantitative analysis, motivated from the perspective of control theory, of a classical model from the literature. The model has been developed using data from an in vivo experimental two-species system where the bacterium *Mesorhizobium loti* supplies the vitamin B_{12} required for growth to the freshwater green alga *Lobomonas rostrata* and where the action of the B_{12} riboswitch is known to be a determinant of system behaviour. Analysis of the model both before and after the add-back of nutrients is carried out. A focus is exploring the robustness of the system. The paper first describes a simple model of algal-bacterial growth and analysis is undertaken. The effect of system parameters and control mechanisms is quantified. Motivated by the inherent switching action within the biology, a sliding mode interpretation of the control mechanisms is hypothesized based on knowledge of the maximum carrying capacities for each growth. The results of a range of experiments reported in the literature are used to validate the assertions.

I. INTRODUCTION

The co-evolution between algae and bacteria has revolutionized life on earth. Several studies have shown that algae and bacteria synergistically affect each other's physiology and metabolism. Amin et al. [1] studied the interaction and signalling between a cosmopolitan phytoplankton and associated bacteria and they proved the linkage in growth between the two populations. A study performed by Croft et al. [2] investigated how algae acquire vitamin B_{12} through a symbiotic relationship with bacteria. It is important to understand these interactions from an evolutionary and ecological standpoint. Bacterial and algal growth have the same growth phases and both contain parameters that affect mutual growth. Many studies have shown that algal and bacterial growth are coupled. Rhee et al. [3] showed that the growth of *Scenedesmus* algae increases exponentially, hitting a saturation level of 40×10^6 when growing alone without *Pseudomonas* bacteria. When *Pseudomonas* bacteria is added, the steady-state population of algae reduces to 15×10^6 . This is because the population of the bacteria is determined by the number of bacteria required to reach half the maximum carrying capacity. Haines et. al [4] experimentally measured the algal growth with and without bacteria. The algal growth without bacteria was 5×10^4 and the algal growth increased to 10^6 with bacteria added. The most important parameters

regulating algal and bacterial growth are nutrient quantity and quality, light, pH, turbulence, salinity and temperature [5].

The interaction between bacteria and algae is complex [6]. For growth, bacteria require nutrient supply and organic matter which are produced by plants and algae. In comparison, the stoichiometry of plants and algae is more flexible [7]. Algae take up nutrients such as phosphorus and nitrogen from water, thus growing in open water, and capture their energy from sunlight. To maintain energy and carbon, dissolved organic carbon (DOC) is essential for bacteria and are provided by algae. In exchange, over 50% of microalgae are dependent on a vitamin synthesized by bacteria only for growth – an exogenous source of cobalamin [8]. Systems models are required to associate the inputs' effects on these complex biological systems, as well as capture the factors that affect the final products' quality. A recent survey paper [10] has emphasized the importance of developing such models which can contribute to understanding eco systems as varied as oceans to lichens as well as processes in biotechnology. The interaction between algae and bacteria is often considered as contamination during commercialization but some recent studies have shown that bacteria not only enhance algal growth but also help in flocculation, both essential processes underpinning algal biotechnology.

Algal [11], bacterial [12] and coculture algal-bacterial growth mathematical models in the literature include Kazamia et. al.'s [8] model describing the *L. rostrata* / *M. Loti* cocultures behaviour, with that of the B_{12} riboswitch being described as a determinant of system behaviours. Riboswitches are naturally occurring RNA-based regulatory components with two functional domains. First, they sense essential cofactors, amino acids and nucleotides. Then, they regulate the expression level of proteins in the corresponding metabolic pathways. Because different regulatory activities are associated with each pathway, the increase of ligand concentrations either lead to an increase (ON behaviour) or a decrease (OFF behaviour) of gene expression. This is dependent on the conformation that contains the formed aptamer [13]. As the vitamin B_{12} riboswitch changes between ON and OFF behaviours, the output will be stabilized, thus influencing the vitamin B_{12} concentration. Therefore, in this case, depending on the switching mechanisms, the supply of bacteria for algal growth will be determined. This reliance on switching mechanisms motivates the work presented in this paper which begins to consider the control process from the point of view of discontinuous control.

Sliding mode control is a particular type of variable structure system [14]. A sliding mode control is typically

^{1,2} Mohammad Abbadi and Sarah Spurgeon are from the Department of Electronic & Electrical Engineering, University College London, Gower St, Bloomsbury, London WC1E 6BT, United Kingdom
uceemdo@ucl.ac.uk, s.spurgeon@ucl.ac.uk

composed of feedback control laws and a decision rule. The decision rule, termed the switching function, has as its input some measure of the current system performance and determines the particular feedback controller, which should be used at that time. In sliding mode control, the control is designed to drive and then constrain the system to lie within a neighbourhood of the switching function. The design thus comprises two steps; the first determines the switching function by solving the so-called existence problem and the second prescribes a control which makes the switching function attractive by solving the reachability problem. A great advantage of the paradigm is that the dynamic behaviour of the system is directly tailored by the choice of switching function. In addition, the closed-loop response becomes insensitive to a particular class of system uncertainty called matched uncertainty. The novelty of this paper is the use of the Variable Structure Control (VSC) paradigm to explain the robustness of the system.

The organisation of the paper is as follows: first, a preliminary analysis for the model of the algal and bacterial growth before and after the add-back of nutrients is conducted. Next, the analytical analysis of a sliding mode control perspective is presented.

II. MODEL OF ALGAL AND BACTERIAL GROWTH

A. Before the add-back of nutrients

This section will consider the algal and the bacterial growth equations before the add-back of nutrients such as vitamin B_{12} and carbon, which is the first step towards analysis of the feedback control mechanisms inherent in the biology. The model of Kazamia et. al [8] is considered which describes the behaviour of the *L. rostrata*/ *M. loti* co-cultures. A model containing a minimal set of terms, which will elucidate the main processes is described as:

$$\dot{a} = \alpha a \left[1 - a \left(\frac{K_a b}{b_c + b} \right)^{-1} \right], \quad (1)$$

$$\dot{b} = \beta b \left[1 - b \left(\frac{K_b a}{a_c + a} \right)^{-1} \right]. \quad (2)$$

where a and b denote the *L. rostrata* algal population and *M. loti* bacterial population, respectively. The biological meaning of the parameters in (1) - (2) are shown in Table I.

The values in Table I were taken from the literature where possible [8], with the remainder being established to achieve a satisfactory qualitative fit to experimental data [16]. From (1) and (2), it is seen that the algal growth is affected by K_a and $\frac{b}{b_c + b}$. The bacterial growth is affected by K_b and $\frac{a}{a_c + a}$. The switches present in the system are $\frac{b}{b_c + b}$ and $\frac{a}{a_c + a}$. In biological terminology, the switch represents a positive or a negative feedback depending on the system conditions. If the switch corresponds to increasing the value of the output, it is denoted as positive feedback with:

$$\frac{X(t)}{\delta + X(t)} \quad (3)$$

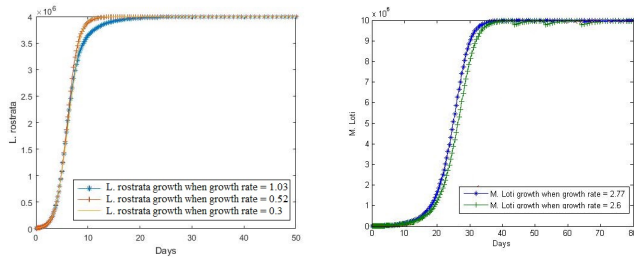
TABLE I: Parameters in the mathematical model (1) - (2)

Symbol	Biological Meaning	Value
α	Growth rate of <i>L. rostrata</i>	$1.5 \log 2 \text{ days}^{-1}$
K_a	Maximum number of algae that the bacteria can support	$4 \times 10^6 \text{ ml}^{-1}$
b_c	Number of bacteria required to reach half K_a	10^4 ml^{-1}
δ_a	Fractional decrease in carbon production by algae when vitamin B_{12} is provided externally	0.4
K_v	Maximum number of algae when vitamin B_{12} is provided externally	$4 \times 10^6 \text{ ml}^{-1}$
β	Growth rate of <i>M. loti</i>	$4 \log 2 \text{ days}^{-1}$
K_b	Maximum number of bacteria that the algae can support	10^7 ml^{-1}
a_c	Number of algae required to reach half K_b	$5 \times 10^3 \text{ ml}^{-1}$
δ_b	Fractional decrease in vitamin B_{12} production by bacteria when carbon is provided externally	0.9
K_c	Maximum number of bacteria if carbon is provided externally	$2 \times 10^8 \text{ ml}^{-1}$

where δ is a constant value. This switch will increase the value of the output and it will enforce a steady state value depending on the value of δ and $X(t)$. The corresponding negative feedback is given by :

$$\frac{\delta}{X(t) + \delta} \quad (4)$$

where δ is a constant value. By increasing the value of $X(t)$, the output of the switch will go to zero, and this switch decreases the value of the desired output. In the algal and bacterial growth equations, $X(t)$ may be the value of b and a and the corresponding value of δ is b_c and a_c respectively. Robustness is the ability of the closed loop system to be insensitive to component variations and/or disturbances. It is one of the most useful properties of feedback and it is helpful to understand robustness properties of systems. From (1) and (2), the system is affected by two different types of parameters. These may be characterised by those parameters that are included in the control and those that are not. The parameters that determine the control are K_b , K_a , a_c and b_c and the parameters that impact on the remaining dynamics are α and β , the algal and bacterial growth rate respectively. The algal growth rate has been determined experimentally in many studies and in different algae. Fundamental experimental conditions frequently differ in the work reported across the literature. To enable comparison, work that has applied conditions corresponding to a temperature of 25 °C and light intensity of 2500 Lux is considered here. Harris et. al [17] experimentally found the *L. rostrata* growth rate to be 1.03 divisions per day and under the same conditions, Fogg et. al [18] found the growth rate of Xanthophyceae *Monodus subterraneus* and Bacillariophyceae *Asterionella japonica* to be 0.3 and 0.52 respectively. As the variation in the algal growth rate appears in the same channel as the switched control, the effect of such changes on the dynamics can be expected to be small by appealing to well known robustness properties of switched control systems in



(a) The growth curve of *L. rostrata* when varying α (b) The growth curve of *M. loti* when varying β

Fig. 1: The algal and bacterial growth curve when varying α and β where $a(0) = 10^6$ and $b(0) = 10^6$.

engineering [19]. This is verified in Fig. 1a where *L. rostrata* has the same growth when $\alpha = 0.3$ and $\alpha = 0.52$. The bacterial growth rate has been determined experimentally in many studies and in different bacteria. Mason [20] made a comparison of the maximal growth rates of various bacteria under optimal conditions showing that the bacterial growth rate of *Streptococcus Liquefaciens* to be equal to 1.54 and the bacterial growth rate of *Escherichia communior* to be equal to 2.6. Harris et. al [17] experimentally found the *M. loti* growth rate to be 2.7726 divisions per day. The effect of the bacterial growth rate is shown to be small in Fig. 1b as expected.

B. Following the add-back of nutrients

This section will consider the algal and bacterial growth equations including the add-back of nutrients. The nutrients that have been used in this paper are vitamin B_{12} and carbon. The mathematical model that describes the algal and bacterial growth after the add-back of nutrients is assumed as follows [8]:

$$\dot{a} = \alpha a \left[1 - a \left(\frac{K_a b (1 - \hat{H}(K_c) \delta_b)}{b_c + b} + K_v \right)^{-1} \right], \quad (5)$$

$$\dot{b} = \beta b \left[1 - b \left(\frac{K_b a (1 - \hat{H}(K_v) \delta_a)}{a_c + a} + K_c \right)^{-1} \right]. \quad (6)$$

The values and the biological meanings of K_v , K_c , δ_a and δ_b are shown in Table I and \hat{H} is the Heaviside step function:

$$\hat{H}(x) = \begin{cases} 0 & x \leq 0 \\ 1 & x > 0 \end{cases} \quad (7)$$

Previous work in the literature [16] has considered these values to be constant. Models are available [8] relating the concentration of vitamin B_{12} with bacterial growth, so changing the concentration of vitamin B_{12} will change the value of K_v . Kazamia et al. [16] experimentally showed that the interactions between vitamin B_{12} -dependent algae and heterotrophic bacteria exhibit regulation. The experiments prove that by increasing the amount of vitamin B_{12} , the overall growth will increase. Moreover, Cole [21] experimentally validated the impact of adding vitamin B_{12} to *Thalassiosira pseudonana* algal growth. The *Thalassiosira pseudonana* algal growth before adding vitamin B_{12} was 9×10^3 and

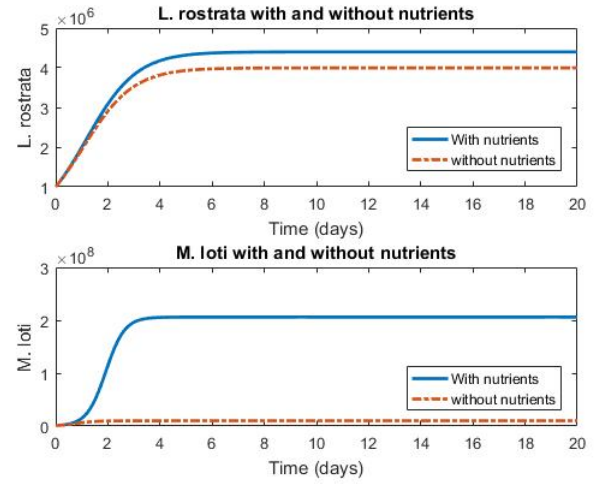


Fig. 2: Algal and bacterial growth before and after the add-back of nutrients where $a(0) = 10^6$ and $b(0) = 10^6$.

after adding vitamin B_{12} became 2×10^6 . Fig. 2 shows a comparison of both algal and bacterial growth before and after the add-back of nutrients, using the parameter values in Table I and the system model (5) and (6).

III. A SLIDING MODE CONTROL PERSPECTIVE

In this section, the algal and bacterial growth will be studied from the perspective of sliding mode control both before and after the add back of nutrients. This paradigm is used to explain the robustness of the system.

A. Analysis with no add back of nutrients

The simulation results shown in Fig. 1a-1b indicate that the system may exhibit a natural sliding mode. Consider the corresponding candidate switching functions for the algal and bacterial growth before the add back of nutrients:

$$S_1 = a - K_a \quad (9)$$

$$S_2 = b - K_b \quad (10)$$

where S_1 is the sliding surface for the algal growth and S_2 is the sliding surface for the bacterial growth. It is clear that surfaces S_1 and S_2 will become zero when the values of a and b are equal to the values of K_a and K_b , respectively, and thus reach the carrying capacity.

When in the sliding mode, it follows that $S_1 = 0$ and $S_2 = 0$ and, if the sliding mode is to be maintained, the following must also hold: $\dot{S}_1 = 0$ and $\dot{S}_2 = 0$. The system dynamics in the sliding mode satisfy the following:

$$\dot{S}_1 = \dot{a} = \alpha a \left[1 - \frac{a}{U_1^{eq}} \right] = 0, \quad (11)$$

$$\dot{S}_2 = \dot{b} = \beta b \left[1 - \frac{b}{U_2^{eq}} \right] = 0. \quad (12)$$

where U_1^{eq} and U_2^{eq} represent the corresponding equivalent control signals required to maintain sliding. Note that these are not the control signals applied to the system but represent,

on average, the control action experienced by the plant. Solving for U_1^{eq} and U_2^{eq} from (11) and (12) yields

$$\begin{aligned} U_1^{eq} &= a \\ U_2^{eq} &= b \end{aligned} \quad (13)$$

To ensure a sliding mode is attained, the so-called reaching condition [19] must be satisfied, which is given by

$$S \dot{S} < 0 \quad (14)$$

where S is the switching function. Application of the reachability condition (14) shows that the sliding surfaces are reached if:

$$R_1 = S_1(\alpha a \left[1 - \frac{a}{U_1}\right]) < 0 \quad (15)$$

$$R_2 = S_2(\beta b \left[1 - \frac{b}{U_2}\right]) < 0. \quad (16)$$

where R_1 is the reachability condition corresponding to the algal sliding surface, R_2 is the reachability condition for the bacterial sliding surface, $U_1 = \left(\frac{K_a b}{b_c + b}\right)$ and $U_2 = \left(\frac{K_b a}{a_c + a}\right)$ are the applied control signals.

Consider first S_1 in (9). As a is a population, it will be positive and, given the set-point, is the carrying capacity of the population. It follows that $a \leq K_a$ and thus S_1 is negative. As α is a positive parameter, the reachability condition (15) is satisfied if the following holds:

$$1 - \frac{a}{U_1} > 0 \quad (17)$$

whereby $U_1 > a$ if the system is to satisfy the reachability condition and attain a sliding mode. As previously defined, the applied control signal is given by $U_1 = \left(\frac{K_a b}{b_c + b}\right)$ and for the sliding condition to be attained, it follows that

$$\frac{K_a b}{b_c + b} > a \quad (18)$$

Performing the same computation for the reachability condition in (16) yields:

$$\frac{K_b a}{a_c + a} > b \quad (19)$$

If the conditions (18) and (19) are satisfied, and a sliding mode is exhibited, then the system will be insensitive to parameter variations. Simulations have been performed with different values of the algal and bacterial growth rate α and β to test this hypothesis and the results are shown in Fig. 3.

Fig. 3A shows the algal sliding surface S_1 from equation (9) when varying the algal growth rate α between $\log 2$ and $10 \log 2$. It is seen that a sliding mode is exhibited and as previously asserted the dynamics of the sliding mode is insensitive to variations in the the algal growth rate. The same test is carried out for the bacterial sliding surface S_2 in (10) and the results are shown in Fig. 3B. Here the bacterial growth rate β is varied between $\log 2$ and $15 \log 2$. Fig. 3C and Fig. 3D show the sliding surfaces (9), (10) when varying b_c between 5×10^3 and 10^8 and a_c between 5×10^3 and 10^9 respectively. Both figures show that varying a_c and b_c affect the ability of the system to attain a sliding mode.

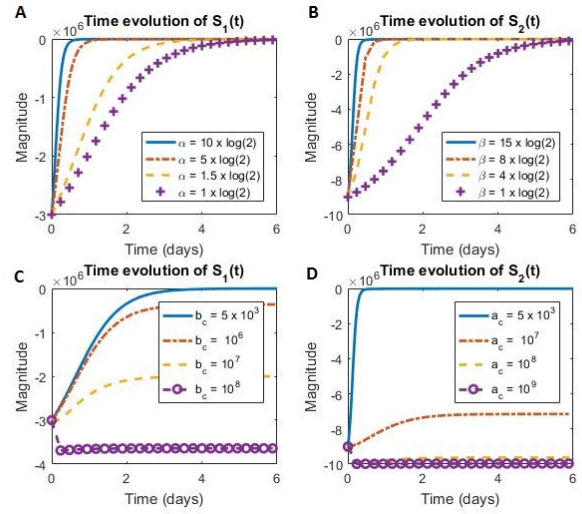


Fig. 3: Time evolution of the sliding surface S_1 (9) and S_2 (10) when varying the parameters α , β , b_c , a_c

Equation (18) shows that the reachability condition R_1 in (15) depends on the value of b_c and the value of b_c that breaks the reachability condition is as follows:

$$b_c > b \left(\frac{K_a}{a} - 1 \right) \quad (20)$$

Once the sliding condition ceases to hold, the system becomes sensitive to all parameter variations. Performing the same computation for the bacterial reachability condition R_2 in (16) shows that the reachability condition is broken when:

$$a_c > a \left(\frac{K_b}{b} - 1 \right) \quad (21)$$

Simulations have been performed with different values of b_c to find the exact value of b_c that breaks the reachability condition (15). The results in Fig. 4 show that the value that breaks the reachability condition is $b_c = 3 \times 10^6$.

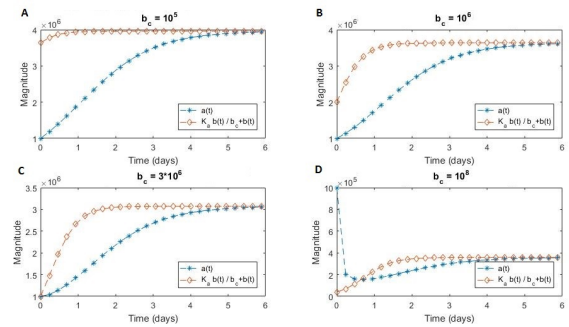


Fig. 4: Time evolution of the elements of (18) when varying b_c between 10^5 and 10^8 to determine the value of b_c that breaks sliding

Fig. 4 shows the time evolution of the condition (18) when varying b_c between 10^5 and 10^8 . It is clear from Fig. 4C that when $b_c = 3 \times 10^6$, the value of $a(t)$ will become bigger than $\frac{K_a b(t)}{b_c + b(t)}$ which means the sliding mode will no longer be

exhibited. Fig. 4D shows the simulation when $b_c = 10^8$; this demonstrates that $\frac{K_a b(t)}{b_c + b(t)}$ is bigger than $a(t)$. The simulation results in Fig. 4 tie in with the analytical results presented in equation (20) using the parameter values provided in Table I. Corresponding results for the condition in (19) with the sliding surface (10) are obtained by varying a_c between 10^5 and 10^8 . In Fig. 5 it is seen that $a_c = 9 \times 10^6$ will break the condition (19). This is also supported by the analytical results presented in (21) using the parameter values provided in Table I.

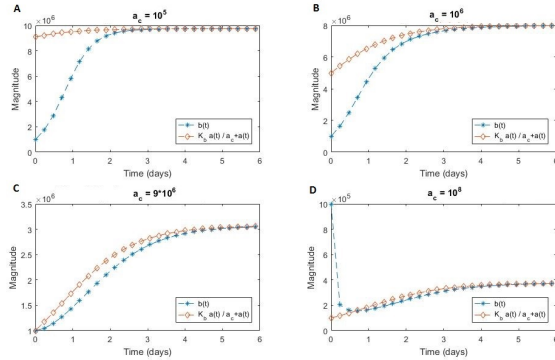


Fig. 5: Time evolution of the elements of (19) when varying a_c between 10^5 and 10^8 to determine the value of a_c that breaks sliding.

B. Analysis with add back of nutrients

Consider the following switching functions for the algal and bacterial growth after the add back of nutrients:

$$S_3 = a - (K_a(1 - \hat{H}(K_c)\delta_b) + K_v) \quad (22)$$

$$S_4 = b - (K_b(1 - \hat{H}(K_c)\delta_a) + K_c) \quad (23)$$

Note that add back of nutrients effectively modifies the carrying capacity. The surfaces S_3 (22) and S_4 (23) will become zero when the values of a and b are equal to the new carrying capacities. When in the sliding mode, it follows that $S_3 = 0$ and $S_4 = 0$ and, if the sliding mode is to be maintained, $\dot{S}_3 = 0$ and $\dot{S}_4 = 0$. From (22) and (23), a and b are the only variables that vary with time if K_v and K_c are assumed constant. This yields $\dot{S}_3 = \dot{a}$ and $\dot{S}_4 = \dot{b}$. Going back to (5) and (6), and denoting $U_3 = \frac{K_a b(1 - \hat{H}(K_c)\delta_b)}{b_c + b}$, $U_4 = \frac{K_b a(1 - \hat{H}(K_v)\delta_a)}{a_c + a}$ so that they are considered to be control signals within the closed loop system (5) - (6), the system dynamics in the sliding mode satisfies the following:

$$\dot{S}_3 = \dot{a} = \alpha a \left[1 - \frac{a}{U_3^{eq}} \right] \quad (24)$$

$$\dot{S}_4 = \dot{b} = \beta b \left[1 - \frac{b}{U_4^{eq}} \right]. \quad (25)$$

where U_3^{eq} and U_4^{eq} represents the corresponding equivalent control signals required to maintain sliding. Solving for U_3^{eq} and U_4^{eq} from equations (24) and (25) yields

$$\begin{aligned} U_3^{eq} &= a \\ U_4^{eq} &= b \end{aligned} \quad (26)$$

Note that the value of \dot{S}_3 and \dot{S}_4 will be different if the amount of vitamin B_{12} and carbon varies with time as the derivative of S_3 and S_4 will involve the derivative of K_v and K_c . Application of the reachability condition (14) shows that the sliding surfaces after the add back of nutrients are reached if:

$$R_3 = S_3(\alpha a \left[1 - \frac{a}{U_3} \right]) < 0 \quad (27)$$

$$R_4 = S_4(\beta b \left[1 - \frac{b}{U_4} \right]) < 0. \quad (28)$$

Consider first (27). As a is a population, it will be positive and, given the set-point is the maximum number of cells following the add back of nutrients, it follows that $a < (K_a(1 - \hat{H}(K_c)\delta_b) + K_v)$ and thus S_3 in (27) is negative. As α is a positive parameter, the reachability condition (27) is satisfied if the following holds:

$$1 - \frac{a}{U_3} > 0 \quad (29)$$

so that $U_3 > a$ if the system is to satisfy the reachability condition and attain a sliding mode. As previously defined, the applied control signal is given by $U_3 = \left(\frac{K_a b(1 - \hat{H}(K_c)\delta_b)}{b_c + b} + K_v \right)$ and it follows that

$$\frac{K_a b(1 - \hat{H}(K_c)\delta_b)}{b_c + b} + K_v > a \quad (30)$$

for the sliding condition to be attained. Performing the same computation for the reachability condition in (28) yields:

$$\frac{K_b a(1 - \hat{H}(K_v)\delta_a)}{a_c + a} + K_c > b \quad (31)$$

If a sliding mode is reached, the dynamic behaviour will be independent of variations in the algal and bacterial growth rate α and β . Equations (30) and (31) show that reachability after the add back of nutrients is affected by more parameters than in the case before the add back (18),(19). Note that when $K_v = K_c = \delta_a = \delta_b = 0$, the reachability conditions before and after the add back of nutrients will be the same, as expected.

First consider (30). The parameters that affect reachability are δ_b and K_v . Note that the value of δ_b is between 0 and 1 [8]. The values of b_c that break the reachability condition R_3 satisfy:

$$b_c > b \left(\frac{K_a(1 - \delta_b)}{a - K_v} - 1 \right) \quad (32)$$

The system then becomes sensitive to all parameter variations. Performing the same computation for the bacterial reachability condition R_4 (28) yields that the values of a_c that break the reachability condition satisfy:

$$a_c > a \left(\frac{K_b(1 - \delta_a)}{b - K_c} - 1 \right) \quad (33)$$

The value of K_v that breaks R_3 is as follows

$$K_v < a - \left(\frac{K_a b(1 - \delta_b)}{b_c + b} \right) \quad (34)$$

Performing the same computation for the bacterial reachability condition (31) show that the values of a_c that break the reachability condition satisfy:

$$K_c < b - \left(\frac{K_b a (1 - \delta_a)}{a_c + a} \right) \quad (35)$$

Performing the same analysis on (30), $K_v = 0.604 \times 10^6$ is the value where the sliding condition fails. The results of the simulations are shown in Fig. 6. These results tie in with the analytical results presented in (34) using the same parameter values provided in Table I.

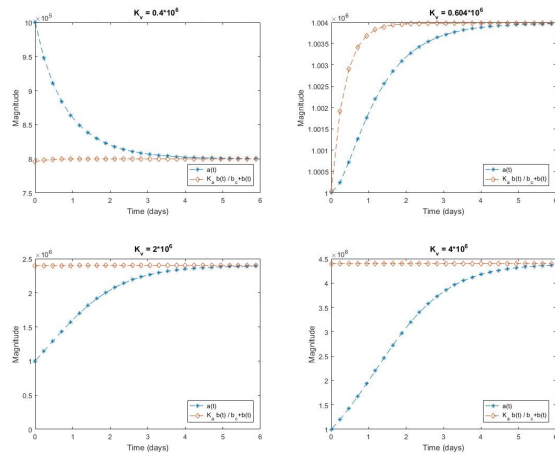


Fig. 6: Time evolution of the elements of condition (30) when varying K_v between 0.4×10^6 and 4×10^6 to determine the conditions where sliding fails

IV. CONCLUSIONS

In this paper, mathematical models for growth of *L. rostrata* algae and *M. loti* bacteria have been studied both before and after the add back of nutrients. The specific nutrients studied are vitamin B_{12} and carbon. The physical limitations on the parameters have been identified and simulations show how the growth saturates. Sliding mode analysis has been carried out to quantify explicitly the action of the control mechanisms and the system robustness.

Models of the vitamin B_{12} riboswitch at a cellular level are currently under development and the longer term objective of this work is to establish a dynamic model linking the action of the riboswitch at the cellular level to the cell population level. This will be the subject of future study.

ACKNOWLEDGEMENT

The support of Professor Martin Warren (University of Kent, UK) and Professor Alison Smith (University of Cambridge, UK) and their teams by providing experimental data for this work is gratefully acknowledged.

REFERENCES

- [1] S. A. Amin, L. R. Hmelo, T. H. M. van, B. P. Durham, L. T. Carlson, K. R. Heal, R. L. Morales, C. T. Berthiaume, M. S. Parker, B. Dju-naedi, A. E. Ingalls, M. R. Parsek, M. A. Moran, and E. V. Armbrust, "Interaction and signalling between a cosmopolitan phytoplankton and associated bacteria.," *Nature*, 2015, doi: 10.1038/nature14488
- [2] M. T. Croft, A. D. Lawrence, E. Raux-Deery, M. J. Warren, and A. G. Smith, "Algae acquire vitamin B_{12} through a symbiotic relationship with bacteria," *Nature*, 2005, doi: 10.1038/nature04056
- [3] G.-Y. Rhee, "Competition between an alga and an aquatic bacterium for phosphate," *ASLO*, 1972, doi: 10.4319/lo.1972.17.4.0505
- [4] K. C. Haines and R. R. L. Guillard, "growth of vitamin B_{12} -requiring marine diatoms in mixed laboratory cultures with vitamin B_{12} -producing marine bacteria," *Journal of Phycology*, 1974.
- [5] Patrick Lavens and Patrick Sorgeloos "Manual on the Production and Use of Live Food for Aquaculture," *FAO Fisheries Technical Paper*, 1996.
- [6] Y. K. Hao Wang, H. L. Smith and J. J. Elser, "Dynamics of stoichiometric bacteria-algae interactions in the epilimnion," *SIAM Journal on Applied Mathematics*, vol. 68, 2007, doi: 10.1137/060665919
- [7] A. A. Julius, . Halasz, M. S. Sakar, H. Rubin, V. Kumar and G. J. Pappas, "Stochastic Modeling and Control of Biological Systems: The Lactose Regulation System of *Escherichia Coli*," *IEEE Transactions on Automatic Control*, vol. 53, pp. 51-65, 2008. doi: 10.1109/TAC.2007.911346
- [8] M. Grant, E. Kazamia, P. Cicuta, and A. G. Smith, "Direct exchange of vitamin B_{12} is demonstrated by modelling the growth dynamics of algalbacterial cocultures," *The ISME Journal*, pp. 1418–1427, 2014, doi: 10.1038/ismej.2014.9
- [9] J.B. Cotner, E.K. Hall, J.T. Scott and M. Heldal, (2010). "Freshwater Bacteria are Stoichiometrically Flexible with a Nutrient Composition Similar to Seston", *Frontiers in Microbiology*, vol. 1, doi: 10.3389/fmicb.2010.00132
- [10] R. Ramanan, B. Kim, D. Cho, H. Oh and H. Kim, "Algaebacteria interactions: Evolution, ecology and emerging applications", *Biotechnology Advances*, Volume 34, Issue 1, Pages 14-29, 2016. doi: 10.1016/j.biotechadv.2015.12.003
- [11] C. X. Zhang J, Shi J, "A mathematical model of algae growth in a pelagic-benthic coupled shallow aquatic ecosystem.," *National Center for Biotechnology Information Search database*, 2017,
- [12] M.H. Zwietering, I. Jongenburger, F.M. Rombouts and K. van t Riet, "Modeling of the Bacterial Growth Curve. Applied and Environmental Microbiology", *Appl Environ Microbiology* 56(6), 1875-1881, 1990.
- [13] N. J. Baird, N. Kulshina and A. R. Ferr D' Amar, "Riboswitch function: flipping the switch or tuning the dimmer?," *RNA Biology*, 7:3, 328-332, 2010.
- [14] B. Bandyopadhyay, S. Janardhanan, S. K. Spurgeon, *Advances in Sliding Mode Control: concept, theory and implementation*. Springer International Publishing, 2013.
- [15] V. I. Utkin, "Sliding mode control design principles and applications to electric drives," *IEEE Transactions On Industrial Electronics*, Vol. 40, NO. 1, 1993.
- [16] E. Kazamia, H. Czesnick, T. T. V. Nguyen, M. T. Croft, E. Sherwood, S. Sasso, S. J. Hodson, M. J. Warren, and A. G. Smith, "Mutualistic interactions between vitamin B_{12} -dependent algae and heterotrophic bacteria exhibit regulation," *Environmental Microbiology*, 2012,
- [17] E. Harris, "Chlamydomonas as a model organism," *Annual Review of Plant Physiology and Plant Molecular Biology*, 2001.
- [18] "Algal Cultures and Growth Equations," *Developments in Water Science*, Vol. 2, 1975, Pages 174-198
- [19] S. K. Spurgeon. A. J. N. Anelone, "Modelling and Simulation of the Dynamics of the Antigen-Specific T Cell Response Using Variable Structure Control Theory," *PLOS ONE*, 2016.
- [20] M. M. Mason, "A comparison of the maximal growth rates of various bacteria under optimal conditions," 1934.
- [21] J. J. Cole, "Interactions between bacteria and algae in aquatic ecosystems," 1982.