Universal modelling and qualitative analysis of an impulsive bioprocess

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\textbf{Abstract}

The work proves that in an impulsive bioprocess the stable oscillation period exists for any microorganisms – i.e., microorganisms of any characteristics of biomass yield and specific growth rate – pointing out the practical and scientific importance of the presented solution. Moreover, universal stability conditions of the impulsive bioprocess are presented. In order to obtain the universality of the solution, a sigmoid function is introduced for description of the biomass yield changes. Further, the universal mathematical model of the impulsive bioprocess is established, tested and discussed. This work shows among others that the impulsive bioprocess extends functionality of a simple continuous bioprocess providing in an easy way to control biomass concentration. The article also introduces a new objective function and then presents and discusses aspects of the impulsive bioprocess multi-criteria optimization. The analytical results presented in the work are validated by numerical simulations.

\section{1. Introduction}

Bioreactor control is an active area of research regarding the continuous microorganism cultivation (Zhao & Skogestad, 1997). Modern control strategies require a mathematical model to check behavior of bioprocess and test it stability. Furthermore they are necessary to optimize bioprocess and obtain maximal profit. According to different reactions and differential control technologies, many dynamic models concerning the culture of microorganism have been established (Beretta & Takeuchi, 1994a, 1994b; Fu, Ma, & Ruan, 2005; Kuang, 1989; Smith, 2003; Sun & Chen, 2007). However, there are a lot of factors affecting the growth and reproduction of the microorganisms in the bioprocesses. For example, for some aerobic microorganisms the dissolved oxygen content in the medium is a key factor to growth. In order to maintain the dissolved oxygen content in an appropriate range it is necessary to monitor and control the dissolved oxygen concentration (DOC) in the bioreactor medium. It is necessary because the low level of DOC decreases biomass yield and specific growth rate (Kasperski, 2008; Kasperski & Miskiewicz, 2008). For given microorganisms the oxygen demand is affected by several factors, e.g., the biomass concentration, the concentration and type of used substrate, the bioprocess conditions. One of the most important ways to maintain the appropriate dissolved oxygen concentration is the control of biomass concentration. For the purpose of continuously culturing microorganisms and decreasing the inhibition effect, it is necessary to keep the biomass concentration lower than a critical level. Many biological phenomena involve thresholds, bursting rhythm models in e.g., medicine, biology, pharmacokinetics and frequency modulated systems, that exhibit impulsive effects. Thus, impulsive differential equations appear as a natural description of the observed evolution phenomena resulting from several real world problems (Lakshmikantham, Bainov, & Simeonov, 1989). Many papers have introduced impulsive differential equations in population dynamics and obtained some interesting results (Meng & Chen, 2008; Sun & Chen, 2008; Tang & Chen, 2003). The research on the chemostat model with impulsive perturbations was studied by Sun and Chen (2007). Tang and Chen (2004) introduced a Lotka–Volterra model with state-dependent impulse and analyzed the existence and stability of the positive period-1 solution. Zeng, Chen, and Sun (2006), Jiang, Lu, and Qian (2007a, 2007b), Guo and Chen (2009a, 2009b) and Tian, Chen, and Kasperski (2010a, Tian, Sun, Chen, and Kasperski (2010) have also studied state-dependent models with impulsive state control.

This paper aims at providing a universal mathematical model of an impulsive bioprocess, i.e., the bioprocess model for any biomass yield, any growth rate and impulsive state feedback control. The sketch map of the apparatus can be seen in Fig. 1. The apparatus includes an optical sensing device which continuously monitors the biomass concentration in the bioreactor medium and two switches...
The proposed mathematical model consists of a set of ordinary differential equations taking into account the biomass growth and the substrate uptake as follows (Chen & Chen, 1993):

\[
\begin{align*}
\frac{dx}{dt} &= \frac{-1}{Y_{x/S}} \mu(S) x \\
\frac{dS}{dt} &= \mu(S)x \\
\dot{x}(0^+) &= x_0, \quad S(0^+) = S_0
\end{align*}
\]  
\tag{1}

where

1. \(x = x(t)\) denotes the biomass concentration and \(S = S(t)\) the substrate concentration in the bioreactor medium at time \(t\), \(x_0\) and \(S_0\) denote the initial biomass concentration and substrate concentration, respectively;
2. \(Y_{x/S}\) is the biomass yield defined as the ratio of the biomass produced to the amount of substrate consumed, and \(Y_{x/S} < 1\) for biological constraints;
3. The function \(\mu(S)\) is the specific growth rate of the microorganisms.

As pointed by Crooke, Wei, and Tanner (1980), the biochemical kinetics expression plays an important role in the intrinsic oscillation mechanisms. Different assumptions for the kinetics models are given in the literature. For example

#1 Monod (Bailey & Ollis, 1994) proposed the Monod-type kinetics in 1942, which is commonly used to model a large variety of biochemical reaction, i.e.

\[
\mu(S) = \frac{\mu_{max} S}{K_S + S};
\]

#2 Han and Levenspiel (1988) proposed an extended Monod kinetics model to consider the existence of a critical inhibitor concentration above which cells cannot grow, i.e.

\[
\mu(S) = \frac{\mu_{max} S}{K_S + S + S_{max}^2/K_i};
\]

#3 Andrews (1968) proposed a kinetics model where the inhibition was modelled as a second-order process in the following form:

\[
\mu(S) = \frac{\mu_{max} S}{K_S + S + S_{max}^2/K_i};
\]

#4 Alba, Shoda, and Nagatani (1968) proposed a kinetics model which assumes that

\[
\mu(S) = \frac{\mu_{max} S}{K_S + S} \exp\left(-\frac{S}{K_i}\right).
\]

Moreover, Crooke et al. (1980) showed that the biomass yield expression plays an important role for the generation of oscillatory behavior in continuous bioreactor models. In reality, growth yields have not shown a constant pattern (Aguilera & Benitez, 1988; Andrews, 1989; Frankenka, Van Verseveld, & Stouthamer, 1988; Tempest & Neijssel, 1984; Tsai & Lee, 1990; Turner, Ramkrishna, & Jansen, 1989), so it is necessary to examine the bioprocess for the real biomass yield.

Not all energy produced in catabolic processes is used for cellular material synthesis, part of it (i.e. so-called maintenance energy) is used for maintaining life functions, for that reason dependence of biomass yield on \(\mu\) is conditioned physiologically. An effect of existence of maintenance energy is biomass yield dependant on growth rate. One of the most important models of quantification of maintenance energy in microorganism growth balance is Pirt’s model (Menkel & Knights, 1995; Nielsens, 1999; Ratledge & Kristiansen, 2001; Rehm & Reed, 1981; Schugler & Bellgardt, 2000). According to this model, for very low substrate concentration the amount of energy obtained from the substrate is not sufficient for maintenance energy. In this case, the energy obtained from the substrate is fully assigned for maintenance energy and biomass yield equals zero. During the increasing of substrate concentration, if the amount of energy assigned for maintenance energy makes a considerable part of the energy produced in the catabolic processes, then it can be assumed an almost linear dependence \(Y_{x/S}\) is on specific growth rate. Further increasing of substrate concentration causes further increasing of specific growth rate. In such conditions biomass yield achieves the maximum value \(Y_{x/S_{max}}\), where \(Y_{x/S_{max}} < 1\) and is practically constant, that is the biomass yield does not depend on the substrate concentration. The described characteristics of cells can be approximated with sigmoid function which has high flexibility in adapting to reality (Fig. 2).
In this work the sigmoid function

\[ Y_{x/S} = \frac{1 - \exp(-bS)}{a + \exp(-bS)} \]  

(see Fig. 2),

which has high flexibility to fit any real biomass yield is used, where \( a = 1/\bar{Y}_{x/S\text{max}} \), \( b \) is the cell sensitivity to the substrate in the optimal growth conditions (optimal temperature, pH, DOC, and other); \( a > 1 \) and \( b > 0 \) are the biological constraints. For the selected known point \((S, Y_{x/S})\), the coefficient \( b \) can be calculated as:

\[ b = \frac{1}{a} \ln \left( \frac{1 + Y_{x/S}}{1 - Y_{x/S}Y_{x/S\text{max}}} \right). \]

Then the model (1) has the following form:

\[
\begin{align*}
\frac{dS}{dt} &= \frac{a + \exp(-bS)}{1 - \exp(-bS)} \mu(S)x \\
\frac{dx}{dt} &= \mu(S)x \\
x(0^+) &= x_0, \quad S(0^+) = S_0
\end{align*}
\]  

(2)

In particular, when substrate concentration \((S)\) is high, \( Y_{x/S} = 1/a = Y_{x/S\text{max}} \), the biomass yield is constant. When the cell sensitivity to the substrate is very high (i.e. \( b > 100 \)), \( Y_{x/S} \) is also practically constant for any substrate concentration different from zero.

According to the design ideas of the bioreactor, the biomass concentration should not exceed a set level. When the biomass concentration in the bioreactor medium reaches the set level \( x_{set} \) (where \( 0 < x_{set} \leq x_{critical} \) and \( x_{critical} \) is the critical level of biomass concentration in the bioreactor medium), then part of the medium containing biomass and substrate is discharged from the bioreactor, and the next portion of medium of a given substrate concentration is inputted impulsively. Therefore, system (2) can be modified as follows by introducing the impulsive state feedback control:

\[
\begin{align*}
\frac{dS}{dt} &= \frac{a + \exp(-bS)}{1 - \exp(-bS)} \mu(S)x, \quad x < x_{set} \\
\frac{dx}{dt} &= \mu(S)x, \quad x = x_{set} \\
\Delta x &= -W_F x, \quad S_{crit} \leq S < S_0 \\
\Delta S &= W_F (S_{set} - S), \\
x(0^+) &= x_0, \quad S(0^+) = S_0
\end{align*}
\]  

(3)

where \( S_F \) is the concentration of the feed substrate which is inputted impulsively, \( 0 < W_F < 1 \) is the part of biomass which is removed from the bioreactor in each biomass oscillation cycle.

3. Existence of the positive periodic solutions of the system (3)

The aim of this section is to use qualitative arguments to derive sufficient conditions for the existence of periodic solutions of the system (3). Before discussing the dynamic behavior of the system (3), we should consider the qualitative characteristics of the system (2). By (2) we have

\[ \frac{dS}{dt} = \frac{1 - \exp(-bS)}{a + \exp(-bS)} = 1 - \frac{a + 1}{a + \exp(-bS)}. \]

Hence we have

\[ x(x_0, S_0, S) = x_0 + S - S_0 + \frac{a + 1}{ab} \ln \left( \frac{a \exp(bS_0) + 1}{a \exp(bS) + 1} \right). \]  

(4)

From the system (3) and Eq. (4) we know that in the process the substrate concentration \( S \) is decreasing and the biomass concentration is increasing. If we do not adopt efficient control strategy, the microorganisms will finally consume the substrate and cause the whole process to terminate. In order to not interrupt the culturing process and gain a stable biomass output, we need to discharge part of the bioreactor medium containing biomass and substrate, and add the medium of a given substrate concentration to the bioreactor when the biomass concentration reaches the set level \( x_{set} \).

Theorem 1. If the set level \( x_{set} \) and the feeding substrate concentration \( S_F \) satisfy the condition \( x_{set} < \Gamma(S_F) \), then there exists a unique period-1 solution (see Definition 1 and Definition 1’ in Appendix A) of the system (3) with \( x_0 - S_0 + ((a + 1)/ab) \ln((a\exp(bS_0) + 1)/(a + 1)) \geq x_{set} \), where \( \Gamma(S_F) = (S_F/\lambda_2) \ln((a + 1)/(a + 1) - \lambda_2) \), \( A = abW_F/S_F \) and \( \lambda_2 = abW_F/S_F/(a + 1) \).

Remark 1. The condition presented in Theorem 1 is only one sufficient condition to guarantee the existence of the period-1 solution for the system (3). For the case of \( g(1) \geq 0 \), i.e. \( x_{set} \geq \Gamma(S_F) \) and \( \lambda > 1 \), where \( \lambda \) is the root of the equation \( u(\lambda) = 0 \), where \( g(u) = abu - Au^1/\ln(\lambda_1) = \frac{1}{\ln(\lambda_1)}[(a + 1)/(a + 1)] + B, \lambda_1 = abW_F/x_{set} \), \( A = abW_F/S_F \) and \( B = \lambda_1 - abW_F/S_F/(a + 1) \), it can be proven that, when \( g(\lambda) < 0 \), the system (3) has two period-1 solutions; when \( g(\lambda) > 0 \), the system (3) has a unique period-1 solution. However, in practical bioprocess, the condition presented in Theorem 1, i.e. \( x_{set} < \Gamma(S_F) \) has more biological sense and is easily carried out, which means that the set level \( x_{set} \) cannot be set too high in practice.

Theorem 2. For any \( x_{set} \) and \( S_F \), there does not exist positive periodic 2 solution (see Definition 1 and Definition 1’ in Appendix A) of the system (3).

Next we will give a complete expression of period of the positive periodic solution. It follows from the first equation of the system (3) that

\[ \frac{dx}{dt} = \exp(-bS) - 1/(a + \exp(-bS))\mu(S)x(S) \]  

(5)

and \( x(S) \) can be determined by the following equation:

\[ x(S) = (1 - W_F)S + \xi_0 + \frac{a + 1}{ab} \ln \left( \frac{a \exp(b\xi_0) + 1}{a \exp(bS) + 1} \right). \]  

(6)

where \( \xi_0 = W_F S_F + (1 - W_F) \ln(u^{*})/b \) and \( u^{*} > 1 \) is the root of Eq. (A4) (see Appendix A).

Then travelling along \( x(S) \) from the point \( P_0(\xi_0, (1 - W_F)x_{set}) \), with \( t = t_0 \) to the point \( P_1(\xi_1, x_{set}) \), with \( t = t_0 \) in the counter-clockwise direction yields the period \( T \).

Theorem 3. The period of the positive period-1 solution can be calculated by the following equation:

\[ T = \int_{\xi_0}^{\xi_1} \frac{\exp(-bS) - 1}{(a + \exp(-bS))\mu(S)x(S)} dS, \]  

(7)
where \( x(S) \) is determined in accordance with Eq. (6), \( x_0 = W_S S + (1 - W_S) \eta \), \( x_1 = \ln(u^r)/b \) and \( u^r > 1 \) is the root of Eq. (A.4) (see Appendix A).

4. Asymptotic behavior the positive period-1 solution

According to the definitions of orbitally asymptotically stable and enjoying the property of asymptotic phase (Bainov & Simeonov, 1993), the following theorem holds.

**Theorem 4.** If the set level \( x_{set} \) and the feeding substrate concentration \( S_F \) satisfy the condition \( x_{set} < \Gamma(S_F) \), where \( \Gamma(S_F) \) is determined in Theorem 1, then the positive period-1 of the system (3) determined in Theorem 1 is orbitally asymptotically stable enjoying the property of asymptotic phase.

**Remark 2.** For the case of \( \bar{u} > 1 \) and \( g(1) > 0 \), i.e. \( x_{set} > \Gamma(S_F) \), when \( g(\bar{u}) < 0 \), one period-1 solution of the system (3) is orbitally asymptotically stable and enjoys the property of asymptotic phase, while the other one is unstable; when \( g(\bar{u}) = 0 \), the stability of the period-1 solution cannot be determined by Bainov and Simeonov’s theorem (see Lemma 1 in Appendix A).

5. Applied instance and simulations

We have analyzed theoretically the feedback control of the universal model of the bioprocess with impulsive substrate dosing and impulsive medium removal. In this section we will take the Andrews kinetics model (Andrews, 1968) as the example of specific growth rate to verify the theoretical results, i.e.

\[
\mu(S) = \frac{\mu_m S}{K_S + S + S^2/K_I},
\]

where \( \mu_m \) is the coefficient of the growth rate, \( K_S \) is the substrate saturation constant, \( K_I \) is the substrate inhibition constant, and \( S \) is the substrate concentration in the medium. \( \mu_m \) is connected to the maximum specific growth rate \( \mu_{\text{max}} \) as follows (Schugel & Bellgardt, 2000):

\[
\mu_m = \mu_{\text{max}}(1 + \sqrt{K_S K_I}).
\]

In addition, with maltose used as the substrate and the microorganisms with \( a = 2 \) (i.e. \( Y_x/S_{\text{max}} = 1/2 = 0.5 \text{g/g} \)), \( b = 5 \), \( \mu_m = 0.71/h \), \( K_S = 3 \text{ g/l} \) and \( K_I = 9 \text{ g/l} \) are used for the demonstration of the system behavior.

5.1. Numerical simulation

We assume in the following that \( W_F = 0.1, S_F = 8 \text{ g/l} \). By computing we have \( \Gamma(S_F) = \Gamma(8) = 2.8 \text{ g/l} \). In addition, we assume the initial substrate concentration \( 4 \text{ g/l} \), i.e. \( S_0 = 4 \text{ g/l} \) and the initial biomass concentration is \( 1.6 \text{ g/l} \). By Eq. (A.3) (see Appendix A) we can calculate that \( \Phi(S_0, x_0) = \Phi(4, 1.6) = 3.5 \text{ g/l} \), therefore the necessary condition for the existence of period-1 solution is \( x_{set} \leq 3.5 \text{ g/l} \). The simulations are carried out by changing one main parameter \( x_{set} \) and fixing all other parameters.

Firstly, we set \( x_{set} = 2.4 \text{ g/l} \). Then by Eq. (A.4) (see Appendix A) we have \( \eta_1 = 3.2 \text{ g/l} \). The time series and phase diagram are shown in Fig. 3. From Fig. 3 we can see that the trajectory \( (S(t), x(t)) \) tends to be periodic. Fig. 4 displays the period-1 solution \( S = \xi(t), x = \eta(t) \) (see Definition 1 and Definition 1 in Appendix A) and the phase diagram in one selected biomass oscillation cycle between 0.25 h and 0.65 h, from which it can be seen that \( T \approx 0.3 \text{ h} \), which is consistent with the computing result according Eq. (7).

Next, we set \( x_{set} = 3.2 \text{ g/l} \). Thus, by Eq. (A.6) (see Appendix A) we can calculate that \( \bar{u} = 1078 \) and \( g(\bar{u}) = g(1078) = -3069 \). According to Remark 1, there exists two period-1 solutions. The change of substrate concentration \( S \), biomass concentration \( x \), specific growth rate \( \mu \), biomass yield \( Y_{x/S} \), biomass productivity (defined as \( P = \mu x \)) and phase diagram are shown in Fig. 5. From Fig. 5 it can be seen that the trajectory \( (S(t), x(t)) \) tends to be periodic.
5.2 Optimization of the bioprocess

In the 3rd section, it is shown that if the set level $x_{set}$ and the feeding substrate concentration $S_F$ satisfy the constraint $x_{set} < \Gamma(S_F)$, then the system (3) has a unique period-1 solution, which is orbitally asymptotically stable enjoying the property of the asymptotic phase. Next, we will discuss aspects of the bioprocess optimization. Let

\[ \Gamma^*(S_F) = \frac{S_F}{\alpha(1 + \sqrt{K_S/(K_S + S_F)})}. \]

5.2.1 The objective function and the constraints

Let $T$ be the period of the biomass oscillation and define $P_{OUT}$ and $S_{OUT}$ as follows:

\[ P_{OUT}(W_f, S_F, x_{set}) = \frac{W_f x(T)}{T}, \quad S_{OUT}(W_f, S_F, x_{set}) = \frac{W_f S(T)}{T}. \]

1. The proposed objective function

\[ F(W_f, S_F, x_{set}) = \text{Criterion 1} + \text{Criterion 2}. \]

where Criterion 1 = $(P_{OUT} / \mu_{m,x_{set}}) \in [0, 1]$—the criterion of biomass productivity; Criterion 2 = $1 - (S_{OUT} / \mu_{m,S_F}) \in [0, 1]$—the criterion of substrate loss.

2. The constraints

(a) $0 < W_f \leq W_{f\text{max}} < 1$

$W_f$—the part of biomass which is removed from the bioreactor in each biomass oscillation cycle; $W_{f\text{max}}$—the maximal part of biomass which is removed from the bioreactor in each biomass oscillation cycle.

(b) $S_{F\text{min}} \leq S_F \leq S_{F\text{critical}}$

$S_F$—the concentration of the dosaged substrate; $S_{F\text{min}}$—the minimal concentration of the dosaged substrate; $S_{F\text{critical}}$—the critical level of the dosaged substrate concentration.
Verification of the Remark 1. The change of substrate concentration \((S)\), biomass concentration \((x)\), and phase diagram for \((S_0, x_0) = (4, 1.6)\), \(S_F = 8\) g/l and \(x_{set} = 3.6\) g/l.

The aim of the optimization is to find the maximum of the objective function (8) under constraints (a)–(c), i.e. the aim of the optimization is simultaneous maximization of the biomass productivity and minimization of the substrate loss.

5.2.2. Determination of the optimal result

As indicated at the beginning of Section 2, in the optimal conditions the biomass yield is practically constant, i.e. \(Y_{x/S} = 1/\alpha = Y_{x/S_{\text{max}}}\). For the period-1 solution \(S = \xi(t)\) and \(x = \eta(t)\) determined in Section 3, we have \(\xi(0^+) = S_F - (1 - W_f) x_{set}/Y_{x/S_{\text{max}}}\), \(\xi(T) = S_F - x_{set}/Y_{x/S_{\text{max}}}\), \(\eta(0^+) = (1 - W_f) x_{set}\) and \(\eta(T) = x_{set}\). Then, according to formula (7) the biomass oscillation period in the steady state is

\[
T = -\frac{1}{\mu m} + \frac{K_S}{S_F} + \frac{S_F}{\mu m S_F} \ln \left( 1 - \frac{W_f x_{set}}{S_F - x_{set}/Y_{x/S_{\text{max}}}} \right) + \frac{W_f x_{set}/Y_{x/S_{\text{max}}}}{S_F - x_{set}/Y_{x/S_{\text{max}}}} - \frac{W_f x_{set}/S_F}{S_F - x_{set}/Y_{x/S_{\text{max}}}}. \tag{9}
\]

Thus the objective function can be formulated as

\[
F(W_f, S_F, x_{set}) = \frac{x_{set} W_f}{\mu m x_{set} T} + \frac{1}{\mu m S_F T} - \frac{S_F - x_{set}/Y_{x/S_{\text{max}}}}{W_f}. \tag{10}
\]

Proposition 1. For given \(S_F\) and \(x_{set} < Y_{x/S_{\text{max}}} S_F\), the impulsive bioproces in a steady state is optimal when \(W_f \to 0\). The maximum is
The dependence of $F_{\text{optimal}}$ on $S_F$ and $Y_{x/S_{\text{max}}}$ are shown in Figs. 8 and 9, respectively.

The dependences of $F_{\text{optimal}}$, Criterion 1 and Criterion 2 on $S_F$ and $Y_{x/S_{\text{max}}}$ are shown in Figs. 10 and 11, respectively.

The dependence of $F_{\text{optimal}}$ on $S_F$ and $Y_{x/S_{\text{max}}}$ simultaneously is shown in Fig. 12.

### 6. Conclusions

In this work, the universal mathematical model of an impulsive bioprocess was established to maintain the biomass concentration in the desired range. Aiming at ensuring the models universality, the flexible sigmoid function was proposed to describe the dependence of the biomass yield on the substrate concentration. Then, the universal stability conditions of the impulsive bioprocess are presented. It was shown that when the stability conditions were fulfilled, the stabilization of a biomass oscillation period would occur in the impulsive bioprocess. Moreover, the stabilization would occur independently on used microorganisms, i.e. for microorganisms with any characteristics of biomass yield and specific growth rate. According to this finding a continuous bioprocess can be changed to the impulsive bioprocess without loss of stability. This work showed that the impulsive bioprocess extends functionality of a simple continuous bioprocess providing in an easy way the control of biomass concentration. In addition, it was shown that during the multi-criteria optimization of the impulsive bioprocess (i.e. simultaneous maximization of the biomass productivity and minimization of the substrate loss), the impulsive bioprocess was striving for a continuous bioprocess (i.e. $W_f \to 0$). Moreover, if the impulsive bioprocess was fully optimized, a continuous bioprocess was obtained. In this case the maximum of the objective function was received (see Eq. (11)), the bioprocess kept open the possibility for the control of the biomass concentration, but lost the possibility of synchronous operation.

### Appendix A

In this appendix, we give the definition of period-1 solution, period-2 solution and Analogue of Poincaré criterion first. Let $(\xi(t), \eta(t))$ be a periodic solution of the system (3) and the closed curve $\Gamma$ be the orbit of the periodic solution $(\xi(t), \eta(t))$.

#### Definition 1 (Bainov & Simeonov, 1993)

$(\xi(t), \eta(t))$ is said to be period-1 solution if in a minimal cycle time, there is one and only one impulse effect. Similarly, $(\xi(t), \eta(t))$ is said to be period-2 solution if in a minimal cycle time, there are two and only two impulse effects.

Definition A.1 adapted to the proposed system in its simple way is as follows.

#### Definition 1

The system (3) has period-1 solution (i.e. $(\xi(t), \eta(t)) = (S(t), x(t))$) if in the biomass oscillation cycle only one impulse effect occurs. Similarly, the system has period-2 solution if in the biomass oscillation cycle exactly two impulse effects occur.

#### Definition 2 (Bainov & Simeonov, 1993)

$\Gamma$ is said to be orbitally stable, if for any $\varepsilon > 0$, there exists $\delta > 0$, with the proviso that every solution $(\xi(t), \eta(t))$ of the system (3) whose distance from $\Gamma$ is less than $\delta$ at $t = t_0$, will remain within a distance less than $\varepsilon$ from $\Gamma$ for all $t \geq t_0$. Such a $\Gamma$ is said to be orbitally asymptotically stable if, in addition, the distance of $(\xi(t), \eta(t))$ from $\Gamma$ tends to zero as $t \to \infty$. Moreover, if there exist positive constants $\alpha$, $\beta$ and a real constant $t_0$ such that $\eta(\xi(t), \eta(t)) \Gamma < \alpha e^{-\beta t}$ for $t > t_0$, then $\Gamma$ is said to be orbitally asymptotically stable and enjoys the property of the asymptotic phase.
Lemma 1 (Bainov & Simeonov, 1993). (Analogue of Poincaré Criterion)
The T-periodic solution \( S = \xi(t), x = \eta(t) \) of the system

\[
\begin{align*}
\frac{dS}{dt} &= P(S, x), \quad \frac{dx}{dt} = R(S, x), \quad \text{if } \phi(S, x) \neq 0 \\
\Delta S &= \alpha(S, x), \quad \Delta x = \beta(S, x), \quad \text{if } \phi(S, x) = 0
\end{align*}
\]  

(A.1)
is orbitally asymptotically stable and enjoying the property of the asymptotic phase if the multiplier \( \mu_2 \) satisfies the condition \( |\mu_2| < 1 \).

Where

\[
\mu_2 = \prod_{k=1}^{q} \Delta_k \exp \left( \int_{0}^{T} \left[ \frac{\partial P}{\partial S}(\xi(t), \eta(t)) + \frac{\partial R}{\partial x}(\xi(t), \eta(t)) \right] dt \right),
\]

\[
\Delta_k = \frac{P_+(\delta t^+_k, \eta^+_k) - P_+(\delta t^-_k, \eta^-_k) - P(-\delta t^-_k, \eta^-_k) + P(-\delta t^+_k, \eta^+_k)}{R(\delta t^-_k, \eta^-_k) + R(\delta t^-_k, \eta^-_k)}\]

is necessary.

By Eq. (4) we have

\[
W_f x_{set} = W_f (\xi_1 - S_f) + \frac{a + 1}{ab} \ln \left( \frac{a \exp(b \xi_0 + 1)}{a \exp(b \xi_1 + 1)} \right).
\]

In view of (A.2) we have

\[
W_f x_{set} = W_f (\xi_1 - S_f) + \frac{a + 1}{ab} \ln \left( \frac{a \exp(b (W_f S_f + (1 - W_f) \xi_1)) + 1}{a \exp(b \xi_1 + 1)} \right)
\]

which can be rewritten as

\[
\exp \left( \frac{a W_f (x_{set} + S_f - \xi_1)}{a + 1} \right) = \frac{a \exp(b (W_f S_f + (1 - W_f) \xi_1) + 1)}{a \exp(b \xi_1 + 1)}.
\]

(A.4)

Let \( u = \exp(b \xi_1) \). Denote \( \lambda_1 = ab W_f x_{set}/(a + 1), \lambda_2 = ab W_f x_{set}/(a + 1). \) Then we have

\[
g(u) = ab - \left( 1 - \frac{W_f}{a + 1} \right) \ln \left( \frac{a \exp(b \xi_0 + 1)}{a \exp(b \xi_1 + 1)} \right),
\]

(A.6)

\[
g''(u) = \left( 1 - \frac{W_f}{a + 1} \right) \frac{W_f}{a + 1} \ln \left( \frac{a \exp(b \xi_0 + 1)}{a \exp(b \xi_1 + 1)} \right) > 0.
\]

(A.7)

Hence \( g'(u) \) is increasing on \( u > 0 \). Since

\[
\lim_{u \to +\infty} g'(u) = -\infty, \quad \lim_{u \to +\infty} g(u) = ab > 0
\]

then there exists \( \hat{u} > 0 \) such that \( g'(\hat{u}) = 0 \).

If \( g(1) < 0 \), i.e.

\[
x_{set} \leq \frac{x_0 - S_0 + (a + 1)/ab}{a \exp(b S_0 + 1)/a + 1} \leq \Phi(S_0, x_0).
\]

(A.3)
is necessary.

For \( t \in [t_0, t_0 + T] \), the solution \( S = \xi(t), x = \eta(t) \) of the system (3) satisfies that

\[
\eta(t) - \eta_0 = \xi(t) - \xi_0 + \frac{a + 1}{ab} \ln \left( \frac{a \exp(b \xi_0 + 1)}{a \exp(b \xi(t) + 1)} \right).
\]

In particular, for \( t = t_0 + T \), we have

\[
\eta(t_0 + T) - \eta_0 = \xi(t_0 + T) - \xi_0 + \frac{a + 1}{ab} \ln \left( \frac{a \exp(b \xi_0 + 1)}{a \exp(b \xi(t_0 + T) + 1)} \right).
\]
Without loss of generality, we can assume that $S_1 > \bar{S}_1$. By the dynamics of the system (3) we have the following two sequences according to $(S_2, x_{set})$ laying on the left or right of $(S_1, x_{set})$.

(a) $\bar{S}_1 < S_1 \leq S_2 \leq S_3 \cdots$ or
(b) $S_1 \geq S_2 \geq S_3 \cdots \geq \bar{S}_1$.

It is known from the sequence (b) that the trajectory tends to the period-1 solution. Since the sequences are monotone, then there does not exist a positive period-2 solution for the system (3). □

The proof of Theorem 4. According to Lemma 1 we calculate the multipliers of the system (3) in variations corresponding to the $T$-periodic solution $(\xi(t), \eta(t))$. Denote $A(\xi_0, \eta_0, B(\xi_1, \eta_1)$, where $\xi_0 = (1 - W_f)x_{set}, \eta_1 = x_{set}$, $\bar{\xi}_0 = W_f S_f + (1 - W_f)\xi_1$. In the system (3), since

$$P(S, x) = a \exp(-b S) \mu(S) x, \quad R(S, x) = \mu(S) x,$$

$$\alpha(S, x) = W_f (S_f - S), \quad \beta(S, x) = -W_f x, \quad \phi(S, x) = x - x_{set},$$

then we have

$$\frac{\partial P}{\partial S} = (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x,$$

$$\frac{\partial R}{\partial S} = a \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x.$$

Therefore

$$\Delta_1 = P_s((\partial P/\partial S) \phi(S, x) - (\partial P/\partial S) \phi(S, x)) + R_s((\partial R/\partial S) \phi(S, x) - (\partial R/\partial S) \phi(S, x)),$$

$$= R_s(1 - W_f) \frac{\mu(\bar{\xi}_0)}{\eta_1} \xi_0,$$

$$= (1 - W_f) \frac{\eta_0 \mu(\bar{\xi}_0)}{\eta_1 \mu(\bar{\xi}_1)},$$

$$\mu_2 = \Delta_1 \exp \left( \int_0^T \frac{\partial P}{\partial S} \delta(t) + \frac{\partial R}{\partial S} \eta(t) \right) dt,$$

$$= \Delta_1 \exp \left( \int_0^T \mu(S) dt + \int_0^T \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right) dt,\right.$$

$$= (1 - W_f) \frac{a + b(\bar{\xi}_0)}{a + b(\bar{\xi}_1)} x - (1 - W_f) \frac{a + b(\bar{\xi}_0)}{a + b(\bar{\xi}_1)} x.$$

Since $\bar{\xi}_0 = W_f S_f + (1 - W_f)\xi_1$, then we have

$$\mu_2 = (1 - W_f) \frac{a + b(\bar{\xi}_0)}{a + b(\bar{\xi}_1)} x - (1 - W_f) \frac{a + b(\bar{\xi}_0)}{a + b(\bar{\xi}_1)} x.$$

By Eq. (A.7) we know that $g'(u)$ is decreasing on $u$. Then for $u^* > U$, we have $g'(u^*) > g'(U) = 0$. Then by Eq. (A.6) we have

$$AB = \left( 1 - \frac{W_f}{a + b} \right) \frac{A(a(\omega W_f/a + 1) - aW_f/a + 1)}{aW_f/a + 1} \mu(\omega W_f/a + 1) > 0.$$

Moreover, we have $g'(u^*) = 0$, i.e.

$$AB = \frac{A(a(\omega W_f/a + 1) - aW_f/a + 1)}{aW_f/a + 1} = 0.$$

By Eq. (9) and Eq. (A.11) we have

$$\frac{\partial G}{\partial W_f} = \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right),\right.$$

$$= \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right) = 1.$$

Therefore, according to Lemma 1 we conclude that the positive period-1 solution is orbitally asymptotically stable and enjoying the property of the asymptotic phase. □

The proof of Proposition 1. Let

$$G(W_f, S_f, x_{set}) = T \frac{W_f}{W_f}.$$

Taking the first partial derivative of $G(W_f, S_f, x_{set})$ with respect to $W_f$, we have

$$\frac{\partial G}{\partial W_f} = \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right),\right.$$

$$= \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right) = 1.$$

Thus, we have $G(0, S_f, x_{set}) = 0$. Since

$$\frac{\partial G}{\partial W_f} = \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right),\right.$$

$$= \frac{W_f}{W_f} \left( (a + b) \exp(-b S) \mu(S) x - a \exp(-b S) \mu(S) x \right) = 1.$$

for $x_{set} \geq T^*(S_f)$, then $G(0, S_f, x_{set}) \geq G(0, S_f, x_{set}) = 0$, which implies that $\partial G/\partial W_f \geq 0$ or $\partial G/\partial W_f \leq 0$. Therefore, the objective function achieves its maximum $F_{optimal}(S_f, x_{set})$ when $W_f \to 0$. On the other hand, since

$$\lim_{W_f \to 0} W_f = \frac{K_f S_f - x_{set} / Y_{x/\max}}{(1 - W_f)^2} \geq 0,$$

for $x_{set} \leq T^*(S_f)$, then $G(0, S_f, x_{set}) = 0$, which implies that $\partial G/\partial W_f \leq 0$ or $\partial G/\partial W_f \leq 0$. Therefore, the objective function achieves its maximum $F_{optimal}(S_f, x_{set})$ when $W_f \to 0$.

References


