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A SIZE-STRUCTURED MODEL FOR THE NUTRIENT-DRIVEN SELF-CYCLING FERMENTATION PROCESS

R.J. Smith[1] and G.S.K. Wolkowicz[2]

[1]Department of Applied Mathematics
University of Western Ontario, London, Ontario N6A 5B7
E-mail: rsmith43@uwo.ca
[2]Department of Mathematics and Statistics
McMaster University, Hamilton, Ontario L8S 4K1
E-mail: wolkowic@mcmaster.ca

Abstract. Self-cycling fermentation is a computer-aided process used for culturing microorganisms. Applications include sewage treatment and toxic waste cleanup. We consider a model of self-cycling fermentation with nutrient level as the triggering factor. The model is formulated in terms of impulsive ordinary and partial differential equations and refined to include the size of the microorganisms. A threshold is determined in terms of biologically relevant parameters that show that size specific parameters can affect the outcome. The model predicts that either the system fails and the population of microorganisms essentially washes out or, more favourably, the fermentor cycles indefinitely, with one impulse per period, maintaining a positive, though oscillatory, number of cells. However, in any case, the average length and surface area always equilibrate.

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AMS (MOS) subject classification: 34K45, 34K60, 92D25, 92D40, 62P12

1 Introduction

Nutrient driven self-cycling fermentation can be described as follows. A culture of microorganisms is introduced into a tank in which it is assumed there is a single growth limiting nutrient. The cells process the nutrient in order to grow and reproduce. It is assumed that the tank is well-stirred, so that cells and nutrient are distributed uniformly throughout the tank. A probe inserted in the tank measures the nutrient level and relays the information to a computer. When the nutrient level reaches a predetermined tolerance, the computer initiates an emptying and refilling process. A set fraction of the volume of the tank is removed and replaced by an equal volume of fresh medium. Once the fresh medium has been added to the tank, the cells are allowed to process the nutrient until the tolerance is reached once more. The same fraction of the contents is again removed and then replaced with an equal volume of fresh medium. This process is allowed to continue. The process is considered successful if it reaches the threshold within a reasonable (finite) time, indefinitely.

The instant at which the threshold is reached and the emptying and refilling process initiates is referred to as the time of impulsive effect, the impulse time, the harvesting time, or the moment of impulse. Usually, the time taken to empty and refill the tank is negligible compared to the time between impulsive effects. For this reason, we assume that it can be ignored and model the system using impulsive differential equations.

As the process evolves, it seems possible that even though we are regularly removing a fraction of the contents of the tank, some cells may avoid removal and instead grow relatively large. It is interesting to consider what effect this would have on the process. In order to do this, we refine the impulsive differential equations model introduced in Smith [6] to include population density, length, and surface area as well as the number of cells. We follow one of the approaches of Cushing [3], who studied size structure in the chemostat.

The paper is organized as follows. In section 2, we describe some preliminary results for the nutrient-driven self-cycling fermentation process, ignoring size structure. In section 3 we refine the model to include size structure. The model takes the form of an impulsive differential equation for the resource coupled with a hyperbolic partial differential equation for the size density function of the population with appropriate initial and boundary conditions. In section 4, we reduce the model to a system of four ordinary differential equations with impulsive effect. We prove that two of the variables always converge to zero, and then consider the resulting two dimensional model that results when these two variables are eliminated. We are then able to apply the results for the non-structured model of self-cycling fermentation. However, now the model predictions are based on criteria that include parameters related to size. In section 5, we consider the average surface area and average length of the population of microorganisms. We illustrate our results will numerical simulations in section 6, and we conclude with a discussion in section 7.

2 Preliminary results

First we consider a model that describes the nutrient-driven self-cycling fermentation process. This model was developed in Smith [6] and is an adaptation of a model described by Wincure, Cooper, and Rey [5]. In this model no account is taken of individual variations in size.

Let t_k denote the time at which the kth moment of impulse occurs, i.e., when the nutrient reaches the specified threshold, $\bar{s}$. In accordance with the theory of impulsive differential equations (see Bainov and Simeonov [1], [2]), we define

$$\Delta y \equiv y^+ - y^- \equiv y_k^+ - y_k^- \equiv y(t_k^+) - y(t_k^-) \equiv \lim_{t \to t_k^+} y(t) - \lim_{t \to t_k^-} y(t).$$

Consider the impulsive system

$$\begin{array}{rcllcl} \frac{ds}{dt} & = & -\frac{1}{Y} f(s) x & s & \neq & \bar{s} \\ \frac{dx}{dt} & = & -\bar{d}x + f(s)x & s & \neq & \bar{s} \\ \Delta s & = & -r\bar{s} + rs^i & s & = & \bar{s} \\ \Delta x & = & -rx(t_k^-) & s & = & \bar{s} \end{array} \tag{2.1}$$

$$s(0) > \bar{s},\ x(0) \geq 0.$$

Here, s denotes the concentration of waste (nutrient) in the fermentation tank, assumed to be toxic to the environment, x the biomass of the population of microorganisms that consume the nutrient, Y the cell yield constant, $\bar{d}$ the species specific death rate, $\bar{s}$ the tolerance of the waste in the environment, consistent with standards set by an environmental protection agency, s^i the concentration of the pollutant in the environment added to the tank at the beginning of each new cycle, and r the emptying/refilling fraction. It is assumed that $\bar{d} \geq 0,\quad Y > 0,\quad s^i > \bar{s} > 0$, and $0 < r < 1$.

The response function is denoted f and satisfies

$$\begin{array}{rl} \text{i.} & f : \mathbb{R} \to \mathbb{R}, \\ \text{ii.} & f \text{ is continuously differentiable,} \\ \text{iii.} & f(0) = 0, \\ \text{iv.} & f'(s) > 0, \quad \text{if } s > 0. \end{array} \tag{2.2}$$

Define

$$s_{\text{int}} \equiv Y \int_{\bar{s}}^{(1-r)\bar{s}+rs^i} \left(1 - \frac{\bar{d}}{f(s)}\right) ds.$$

The following theorem is a special case of a result proved in Smith [6].

Theorem 1 *Consider system (2.1). If $s_{\text{int}} > 0$, then there exists a positive periodic orbit with exactly one impulse per period. This nontrivial periodic orbit attracts all solutions with initial conditions satisfying $s(0) \geq (1-r)\bar{s} + rs^i$ and $x(0) > 0$. The periodic orbit cycles, between $((1-r)\bar{s} + rs^i, \frac{1-r}{r} s_{\text{int}})$ and $(\bar{s}, \frac{1}{r} s_{\text{int}})$. If $s_{\text{int}} < 0$, then there are at most a finite number of impulses and* $\lim_{t\to\infty} x(t) = 0$. *If* $s_{\text{int}} = 0$, *then* $\liminf_{t\to\infty} x(t) = 0$.

Thus, the outcome depends on the sign of s_{int}. See Smith [6] for a discussion on how to adjust s_{int}.

3 Development of the size-structured model

Following the approach in Cushing [3], let $\rho(t,l)$ be the density of individuals of length l at time t, assume that all individuals are the same length, l_b at birth, and $l_b \leq l$. Let $g(s)$ denote the uptake rate per unit surface area. Assume also that g satisfies the conditions in (2.2). Thus, in the case when $s \neq \bar{s}$, the rate of uptake of nutrient, summing over all individuals of all sizes, is given by,

$$\frac{ds}{dt} \quad = \quad -g(s(t)) \int_{l_b}^{\infty} l^2 \rho(t,l)dl, \quad s \neq \bar{s}. \tag{3.1}$$

The number of individuals with length $a \leq l \leq b$, at time t, is given by $\int_a^b \rho(t,l)dl$. Suppose a fraction κ of energy derived from ingested nutrient is used for growth, and $1-\kappa$ is used for reproduction. Energy required for maintenance is neglected. Let ϖ be the conversion factor relating nutrient to biomass and ω be the conversion factor relating nutrient units to weight of offspring.

Under these assumptions, one can derive the following model describing how ρ changes with time, just as is done in Smith and Waltman [4] in the setting of the chemostat,

$$\frac{\partial \rho}{\partial t} + \frac{\kappa}{3\varpi} g(s(t)) \frac{\partial \rho}{\partial l} \quad = \quad -\bar{d}\rho, \quad l > l_b, \quad t > 0, \quad t \neq t_k. \tag{3.2}$$

As in the model of the chemostat, it is necessary to specify the appropriate initial conditions (distribution),

$$s(0) \quad = \quad s_0 > \bar{s}, \tag{3.3}$$
$$\rho(0,l) \quad = \quad \rho^0(l), \quad l \geq l_b, \tag{3.4}$$

and boundary conditions describing how offspring of length l_b are added to the population,

$$\rho(t,l_b) \quad = \quad \frac{3\varpi(1-\kappa)}{\kappa\omega l_b^3} \int_{l_b}^{\infty} l^2 \rho(t,l)dl, \quad t \neq t_k. \tag{3.5}$$

At times t_k, when $s = \bar{s}$, a fraction r of the contents of the (well-stirred) tank is replaced by an equal volume of fresh medium. Therefore, there is a discontinuity in the concentration of nutrient, described by,

$$\Delta s \quad = \quad -r\bar{s} + rs^i, \quad t = t_k, \tag{3.6}$$

and a discontinuity in the size distribution ρ,

$$\Delta \rho \quad = \quad -r\rho(t_k^-, l), \quad t = t_k, \quad \text{for each} \quad l > l_b. \tag{3.7}$$

This is basically equivalent to starting over with new initial conditions (distribution).

When $t = t_k$, the boundary condition becomes,

$$\rho(t_k^+, l_b) = \frac{3\varpi(1-\kappa)}{\kappa\omega l_b^3} \int_{l_b}^{\infty} l^2(1-r)\rho(t_k^-, l)dl. \tag{3.8}$$

Thus the size structured model is described by the impulsive ordinary and partial differential equations with the appropriate initial and boundary conditions (3.1) – (3.8).

4 Reduction of the model to a two dimensional system of impulsive differential equations

The total surface area of the population at time t, $A(t)$, the total length of the population at time t, $L(t)$ and the total number of individuals at time t, $P(t)$ up to a scaling factor, are given by

$$\begin{aligned} A(t) &= \frac{1}{l_b^2} \int_{l_b}^{\infty} \rho(t,l) l^2 dl, \\ L(t) &= \frac{1}{l_b} \int_{l_b}^{\infty} \rho(t,l) l dl, \\ P(t) &= \int_{l_b}^{\infty} \rho(t,l) dl. \end{aligned}$$

At each moment of impulse, i.e. when $s = \bar{s}$,

$$\begin{aligned} \Delta A(t_k) &= \frac{1}{l_b^2} \int_{l_b}^{\infty} \rho(t_k^+, l) l^2 dl - \frac{1}{l_b^2} \int_{l_b}^{\infty} \rho(t_k^-, l) l^2 dl \\ &= \frac{1}{l_b^2} \int_{l_b}^{\infty} \Delta\rho(t_k, l) l^2 dl \\ &= -\frac{r}{l_b^2} \int_{l_b}^{\infty} \rho(t_k^-, l) l^2 dl \\ &= -rA(t_k^-). \end{aligned}$$

Similarly $\Delta L(t_k) = -rL(t_k^-)$ and $\Delta P(t_k) = -rP(t_k^-)$.

Using the same argument given in Smith and Waltman [4], the model can be reduced to the following system of ordinary differential equations with impulsive effect.

$$\begin{array}{rcll} s' & = & -g(s)l_b^2 A & s \neq \bar{s} \\ A' & = & -\bar{d}A + \dfrac{1-\kappa}{\omega l_b} g(s)A + \dfrac{2\kappa}{3 l_b \varpi} g(s)L & s \neq \bar{s} \\ L' & = & -\bar{d}L + \dfrac{1-\kappa}{\omega l_b} g(s)A + \dfrac{\kappa}{3 l_b \varpi} g(s)P & s \neq \bar{s} \\ P' & = & -\bar{d}P + \dfrac{1-\kappa}{\omega l_b} g(s)A & s \neq \bar{s} \\ \Delta s & = & -r\bar{s} + rs^i & s = \bar{s} \\ \Delta A & = & -rA(t_k^-) & s = \bar{s} \\ \Delta L & = & -rL(t_k^-) & s = \bar{s} \\ \Delta P & = & -rP(t_k^-) & s = \bar{s} \end{array} \tag{4.1}$$

$$s(0) > \bar{s},\ A(0) \geq 0,\ L(0) \geq 0,\ P(0) \geq 0,$$

where $g(s)$ and parameters $\bar{d}$, r, $\bar{s}$ and s^i are as in model (2.1) and l_b, κ, ω and ϖ are positive (and defined in section 3).

If we let

$$\vec{p} = \begin{pmatrix} A \\ L \\ P \end{pmatrix} \qquad \text{and} \qquad H = \begin{pmatrix} \frac{1-\kappa}{\omega} & \frac{1-\kappa}{\omega} & \frac{1-\kappa}{\omega} \\ \frac{2\kappa}{3\varphi} & 0 & 0 \\ 0 & \frac{\kappa}{3\varphi} & 0 \end{pmatrix},$$

then the impulsive system is

$$\begin{array}{rcll} s' & = & -g(s)l_b^2 A & s \neq \bar{s} \\ \vec{p}\,' & = & -\bar{d}\vec{p} + \dfrac{g(s)}{l_b} H^t \vec{p} & s \neq \bar{s} \\ \Delta s & = & -r\bar{s} + rs^i & s = \bar{s} \\ \Delta \vec{p} & = & -r\vec{p}(t_k^-) & s = \bar{s}. \end{array}$$

If we make the change of variable $\vec{q} = T^t \vec{p}$, where T is a nonsingular matrix, then

$$\begin{array}{rcll} \vec{q} & = & -\bar{d}\vec{q} + \dfrac{g(s)}{l_b} \left(T^{-1}HT\right)^t \vec{q} & s \neq \bar{s} \\ \Delta \vec{q} & = & -r\vec{q}(t_k^-) & s = \bar{s}. \end{array} \tag{4.2}$$

Using Lemma 1 (page 845) of Cushing [3], H has a positive eigenvalue $\bar{\mu}$. From Lemma 9.3.1 (page 216) of Smith and Waltman [4], H has a corresponding eigenvector $\vec{v} = \left(\frac{9}{2}\left(\frac{\bar{\mu}\varphi}{\kappa}\right)^2, \frac{3\bar{\mu}\varphi}{\kappa}, 1\right)^T$, where $\bar{\mu} = \bar{\mu}(\kappa, \omega, \varphi)$.

The characteristic polynomial of H is

$$\lambda^3 - \frac{1-\kappa}{\omega}\lambda^2 - \frac{2}{3}\frac{(1-\kappa)\kappa}{\omega\varphi}\lambda - \frac{2}{9}\frac{1-\kappa}{\omega}\left(\frac{\kappa}{\varphi}\right)^2 = 0. \tag{4.3}$$

Corresponding to the eigenvalue $\bar{\mu}$, H^t also has a positive eigenvector $\vec{w}$, that satisfies $\vec{w} \cdot \vec{v} = 1$ and has first component

$$w_1 = \frac{2\bar{\mu}\left(\frac{\kappa}{\varphi}\right)^2}{9\bar{\mu}^3 + 6\left(\frac{(1-\kappa)\kappa}{\omega\varphi}\right)\bar{\mu} + 4\frac{1-\kappa}{\omega}\left(\frac{\kappa}{\varphi}\right)^2}.$$

The remaining eigenvalues of H are $\gamma \pm i\nu$, where $\gamma < 0$ and $\nu > 0$. There is a nonsingular matrix T such that

$$T^{-1}HT = \begin{pmatrix} \bar{\mu} & 0 & 0 \\ 0 & \gamma & \nu \\ 0 & -\nu & \gamma \end{pmatrix}.$$

The first column of T is the eigenvector $\vec{v}$ and the first row of T^{-1} is $\vec{w}^t$. $\bar{\mu}$ is the *physiological efficiency coefficient* of the population, reflecting both reproductive and growth efficiency.

In the new variables, we have $\vec{q} = (x, y, z)^t$, where $x = \vec{v} \cdot \vec{p} = \frac{9}{2}\left(\frac{\bar{\mu}\varphi}{\kappa}\right)^2 A + \frac{3\bar{\mu}\varphi}{\kappa} L + P > 0$ is a weighted average of A, L and P that serves as a measure of population size. Note that $A = \vec{c} \cdot \vec{q} = w_1 x + c_2 y + c_3 z$, where $c = (w_1, c_2, c_3)^t$ is the first column of T^{-1}, containing the first component $w_1 > 0$ of the positive eigenvector $\vec{w}$. Consequently, from (4.2), the impulsive differential equations are

$$\begin{array}{rcl} s' & = & -g(s) l_b^2 \left(w_1 x + c_2 y + c_3 z\right) \\ x' & = & -\bar{d} x + \frac{\bar{\mu}}{l_b} g(s) x \\ y' & = & -\bar{d} y + \frac{g(s)}{l_b} (\gamma y - \nu z) \\ z' & = & -\bar{d} z + \frac{g(s)}{l_b} (\nu y + \gamma z) \\ \Delta s & = & -r\bar{s} + r s^i \\ \Delta x & = & -r x(t_k^-) \\ \Delta y & = & -r y(t_k^-) \\ \Delta z & = & -r z(t_k^-) \end{array} \qquad \begin{array}{rcl} s & \neq & \bar{s} \\ s & \neq & \bar{s} \\ s & \neq & \bar{s} \\ s & \neq & \bar{s} \\ s & = & \bar{s} \\ s & = & \bar{s} \\ s & = & \bar{s} \\ s & = & \bar{s} \end{array} \tag{4.4}$$

$$s(0) > \bar{s}, \;\; x(0) \geq 0, \;\; y(0) \geq 0, \;\; z(0) \geq 0,$$

where the function $g(s)$ and the parameters l_b, $\bar{d}$, r, $\bar{s}$ and s^i are as described in model (4.1), the parameters w_1, $\bar{\mu}$ and ν are positive, γ is negative and c_1 and c_2 are arbitrary.

Proposition 1 *Consider model (4.4). Let* $u = y + iz$. *Then* $u(t) \to 0$ *as* $t \to \infty$.

Proof. For $s \neq \bar{s}$, we have

$$\begin{aligned}
\frac{d|u|^2}{dt} &= 2yy' + 2zz' \\
&= 2y\left[-\bar{d}y + \frac{\gamma}{l_b}g(s)y - \frac{\nu}{l_b}g(s)z\right] + 2z\left[-\bar{d}z + \frac{\nu}{l_b}g(s)y + \frac{\gamma}{l_b}g(s)z\right] \\
&= 2\left[-\bar{d} + \frac{\gamma}{l_b}g(s(t))\right](y^2+z^2) \\
&= 2\left[-\bar{d} + \frac{\gamma}{l_b}g(s(t))\right]|u|^2 \\
&\leq -2\bar{d}|u|^2 \qquad (4.5)
\end{aligned}$$

since $\gamma < 0$.

Either (4.5) holds for all t sufficiently large, or there exists a sequence $\{t_k\}_{k=1}^{\infty}$ with $t_k \to \infty$ as $k \to \infty$ such that $s(t_k^-) = \bar{s}$. In the first case, $|u|^2 \to 0$ as $t \to \infty$. Otherwise

$$\frac{d|u|^2}{dt} \leq -2\bar{d}|u|^2, \qquad t \neq t_k.$$

Since $\Delta y(t_k) = y(t_k^+) - y(t_k^-) = -ry(t_k^-)$, it follows that $y(t_k^+) + y(t_k^-) = (2-r)y(t_k^-)$. Thus $y^2(t_k^+) - y^2(t_k^-) = -r(2-r)y^2(t_k^-)$. Similarly $z^2(t_k^+) - z^2(t_k^-) = -r(2-r)z^2(t_k^-)$. Hence

$$\Delta|u|^2(t_k) = \left(y^2(t_k^+) + z^2(t_k^+)\right) - \left(y^2(t_k^-) + z^2(t_k^-)\right) = -r(2-r)|u|^2(t_k^-).$$

With (4.5), we obtain the impulsive differential inequality

$$\begin{aligned}
\frac{d}{dt}|u|^2 &\leq -2\bar{d}|u|^2 \qquad & t &\neq t_k \\
\Delta|u|^2 &= -r(2-r)|u|^2 \qquad & t &= t_k.
\end{aligned}$$

We thus have

$$\begin{aligned}
|u|^2(t) &\leq |u|^2(t_k^+)e^{-2\bar{d}(t-t_k)} \qquad & t_k < t < t_{k+1} \\
|u|^2(t_{k+1}^-) &\leq |u|^2(t_k^+)e^{-2\bar{d}(t_{k+1}-t_k)}
\end{aligned}$$

Now, $|u|^2(t_k^+) - |u|^2(t_k^-) = -r(2-r)|u|^2(t_k^-)$, so $|u|^2(t_k^+) = (1-r)^2|u|^2(t_k^-)$. Thus, for $t_k < t < t_{k+1}$,

$$\begin{aligned}
|u|^2(t) &\leq (1-r)^2|u|^2(t_k^-)e^{-2\bar{d}(t-t_k)} \\
&\leq (1-r)^2\left[(1-r)^2|u|^2(t_{k-1}^-)e^{-2\bar{d}(t_k-t_{k-1})}\right]e^{-2\bar{d}(t-t_k)} \\
&= (1-r)^4|u|^2(t_{k-1}^-)e^{-2\bar{d}(t-t_{k-1})} \\
&\vdots \\
&\leq (1-r)^{2k}|u|^2(t_1^-)e^{-2\bar{d}(t-t_1)} \\
&\leq (1-r)^{2k}|u|^2(0^+)e^{-2\bar{d}(t-t_0)}.
\end{aligned}$$

Now, $0 < r < 1$. Therefore, as $t \to \infty$, $k \to \infty$, $\lim_{t\to\infty} |u|^2(t) = 0$.

$\square$

By Proposition 1, it follows immediately that in model (4.4) we have $\lim_{t\to\infty} y(t) = \lim_{t\to\infty} z(t) = 0$. Therefore, the omega limit set of (4.4) is contained in the set $\{(s, x, y, z) \in \mathbb{R}^4_+ : s \geq \bar{s}, y = z = 0\}$.

Next, we study the dynamics of (4.4) with initial conditions restricted to this set, giving the autonomous impulsive system

$$\begin{array}{rcl} s' &=& -g(s) l_b^2 w_1 x \\ x' &=& -\bar{d}x + \bar{\mu} l_b^{-1} g(s) x \\ \Delta s &=& -r\bar{s} + r s^i \\ \Delta x &=& -r x(t_k^-) \end{array} \qquad \begin{array}{rcl} s &\neq& \bar{s} \\ s &\neq& \bar{s} \\ s &=& \bar{s} \\ s &=& \bar{s}. \end{array} \tag{4.6}$$

$$s(0) > \bar{s}, \; x(0) \geq 0.$$

Define

$$s_{\text{intsize}} \equiv \int_{\bar{s}}^{(1-r)\bar{s}+rs^i} \left(\frac{\bar{\mu}}{l_b^3 w_1} - \frac{\bar{d}}{g(s) l_b^2 w_1} \right) ds.$$

In the notation of Theorem 1,

$$\begin{array}{rcl} s_{\text{int}} &=& s_{\text{intsize}} \\ f(s) &=& \dfrac{\bar{\mu} g(s)}{l_b}, \\ Y &=& \dfrac{\bar{\mu}}{l_b^3 w_1}. \end{array}$$

By Theorem 1, if $s_{\text{intsize}} > 0$, then there exists a periodic orbit with one impulse per period, and solutions with $s(0) \geq (1-r)\bar{s} + rs^i$ and $x(0) > 0$ approach this periodic orbit as $t \to \infty$. The periodic orbit cycles between $((1-r)\bar{s} + rs^i, \frac{1-r}{r} s_{\text{intsize}})$ and $(\bar{s}, \frac{1}{r} s_{\text{intsize}})$. If $s_{\text{intsize}} < 0$, then $x(t) \to 0$ as $t \to \infty$. If $s_{\text{intsize}} = 0$, then $\liminf_{t\to\infty} x(t) = 0$.

Thus, in order to control the fermentor, one needs to understand how to manipulate s_{intsize}. Define

$$\begin{array}{rcl} l_{b_0} &\equiv& \dfrac{\bar{\mu} r (s^i - \bar{s})}{\bar{d} \int_{\bar{s}}^{(1-r)\bar{s}+rs^i} [g(s)]^{-1} ds}, \\ \bar{\mu}_0 &\equiv& \dfrac{\bar{d} l_b \int_{\bar{s}}^{(1-r)\bar{s}+rs^i} [g(s)]^{-1} ds}{r(s^i - \bar{s})}. \end{array}$$

It follows that if $l_b < l_{b_0}$ or equivalently if $\bar{\mu} > \bar{\mu}_0$, then $s_{\text{intsize}} > 0$. That is, if the size at birth is sufficiently small, or the physiological efficiency coefficient is sufficiently large, then the population of microorganisms will survive in the self-cycling fermentation process. Otherwise, $s_{\text{intsize}} \leq 0$, and so the population will be eliminated.

5 Average Cell Size

Consider model (4.1). Let $\bar{A}(t) = \frac{A(t)}{P(t)}$ and $\bar{L}(t) = \frac{L(t)}{P(t)}$ denote the average surface area and the average length of the population at time t.

Either A, L, and P are continuous for all sufficiently large t, or there exists a sequence $\{t_k\}_{k=1}^{\infty}$ with $t_k \to \infty$ as $k \to \infty$ such that $s(t_k^-) = \bar{s}$.

When $t = t_k$, $\Delta\bar{A}(t_k) = \frac{A(t_k^+)}{P(t_k^+)} - \frac{A(t_k^-)}{P(t_k^-)}$. From model (4.1), it follows that $A(t_k^+) = (1-r)A(t_k^-)$, $P(t_k^+) = (1-r)P(t_k^-)$ and $L(t_k^+) = (1-r)L(t_k^-)$. Therefore, $\Delta\bar{A}(t_k) = 0$. Similarly $\Delta\bar{L}(t_k) = 0$.

Differentiating $\bar{A}$ and $\bar{L}$ and using (4.1), it follows that

$$\begin{aligned}
\frac{d\bar{A}}{dt} &= l_b^{-1} g(s(t)) \left[\frac{1-\kappa}{\omega}\bar{A} + \frac{2\kappa}{3\varpi}\bar{L} - \frac{1-\kappa}{\omega}\bar{A}^2\right] && t \neq t_k \\
\frac{d\bar{L}}{dt} &= l_b^{-1} g(s(t)) \left[\frac{1-\kappa}{\omega}\bar{A} + \frac{\kappa}{3\varpi} - \frac{1-\kappa}{\omega}\bar{A}\bar{L}\right] && t \neq t_k \\
\Delta\bar{A} &= 0 && t = t_k \\
\Delta\bar{L} &= 0 && t = t_k.
\end{aligned} \tag{5.1}$$

Thus, there is no discontinuity, and $\bar{A}$ and $\bar{L}$ satisfy the first two equations for all $t > 0$. This seems reasonable, since the tank is well-stirred and the harvesting is applied uniformly.

Define

$$\tau \equiv \frac{1-\kappa}{\omega l_b}\int_0^t g(s(r))dr, \qquad k \geq 1,$$

with the understanding that τ is evaluated piecewise over the values t_k.

Equations (5.1) can thus be transformed into the system of ordinary differential equations (without jump discontinuities)

$$\begin{aligned}
\frac{d\bar{A}}{d\tau} &= \bar{A} + \frac{2\kappa}{3\varpi(1-\kappa)}\bar{L} - \bar{A}^2 \\
\frac{d\bar{L}}{d\tau} &= \bar{A} + \frac{\kappa}{3\varpi(1-\kappa)} - \bar{A}\bar{L}
\end{aligned} \tag{5.2}$$

$$\bar{A}(0) > 0, \ \bar{L}(0) > 0.$$

The following theorem is an immediate consequence of results in Smith and Waltman [4] (Chapter 9).

Theorem 2 *For any solution of (4.1) with* $A(0), L(0), P(0) > 0$,

$$\lim_{t\to\infty}\left(\bar{A}(t), \bar{L}(t)\right) = \left(\frac{\bar{\mu}\omega}{1-\kappa}, 1 + \frac{\kappa}{3\bar{\mu}\varpi}\right).$$

Furthermore, the standard deviation, given by $\sigma(t) = l_b\left[\bar{A}(t) - \bar{L}^2(t)\right]^{1/2}$ *satisfies* $\lim_{t\to\infty}\sigma(t) = \frac{l_b\kappa}{3\bar{\mu}\varpi}$.

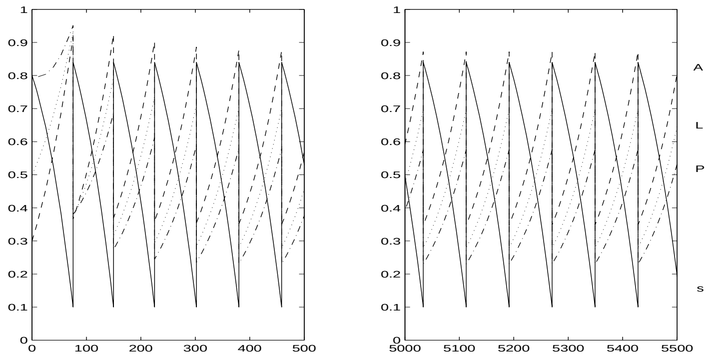

Figure 1: The dynamics of the nutrient concentration, surface area, length and total population for model (4.1). The surface area, length and population approach a periodic orbit.

6 Numerical Simulations

Numerical simulations were run on model (4.1), using a Michaelis-Menten uptake function, $g(s) = \frac{ms}{K+s}$. In this case

$$\begin{aligned} l_{b_0} &= \frac{\bar{\mu} m r(s^i - \bar{s})}{\bar{d}} \left[K \ln\left(\frac{(1-r)\bar{s} + r s^i}{\bar{s}} \right) + r(s^i - \bar{s}) \right]^{-1} \\ \bar{\mu}_0 &= \frac{\bar{d} l_b}{m r(s^i - \bar{s})} \left[K \ln\left(\frac{(1-r)\bar{s} + r s^i}{\bar{s}} \right) + r(s^i - \bar{s}) \right]. \end{aligned}$$

Simulations were carried out in MATLAB using ODE45 with the appropriate events option to calculate the moment of impulsive effect. We set $s^i = 1.333$, $\bar{s} = 0.1$, $m = 0.0167$, $K = 0.007$, $\bar{d} = 0.005$, $r = 0.6$, $l_b = 1$, $\omega = 0.822$, $\kappa = 0.45$ and $\varpi = 0.7$. This produced corresponding values of $w_1 = 0.6409$ and $\bar{\mu} = 1.6123$. The calculated value of s_{intsize} was 3.598, $\bar{\mu}_0$ was 0.377 and l_{b_0} was 3.314. Note that $\bar{\mu} > \bar{\mu}_0$ and $l_b < l_{b_0}$. The initial conditions used were $s(0) = 0.8$, $A(0) = 0.3$, $L(0) = 0.5$, $P(0) = 0.8$. See Figure 1.

Figure 2 was obtained by dividing the curves $A(t)$ and $L(t)$ in Figure 1 by $P(t)$ and thus shows the corresponding average surface area and average length. These exhibited no discontinuities and the curves equilibrated, as predicted.

7 Discussion

The size of individuals is an important factor in controlling the outcome of the self-cycling fermentation process. The approach of Cushing [3], who included

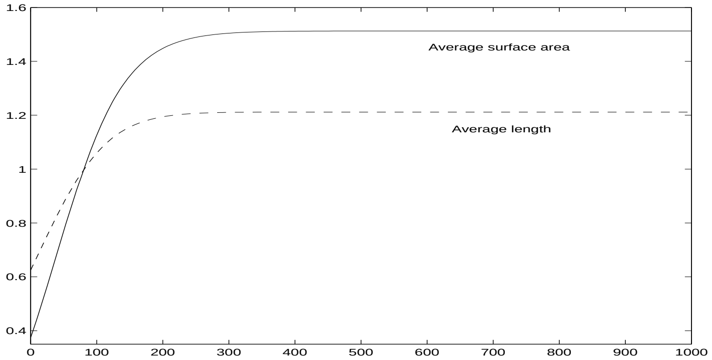

Figure 2: The dynamics of the average surface area of the population and the average length of the population for model (4.1), demonstrating equilibrating values and no discontinuities.

size in his model of the chemostat, was modified to produce a size-structured model for self-cycling fermentation.

Our model resulted in a system of impulsive ordinary and partial differential equations. It was possible to reduce this model to one in which we could apply the results for the nonstructured model of self-cycling fermentation. Thus, we determined a threshold s_{intsize} that depends on the uptake function $g(s)$ and biologically relevant parameters r, $\bar{s}$, s^i as in the unstructured model (see Smith [6]), as well as the size of the microorganisms at birth and the physiological efficiency coefficient. If $s_{\text{intsize}} > 0$ then there exists a positive periodic orbit with one impulse per cycle and solutions with initial conditions satisfying $s(0) > (1-r)\bar{s} + rs^i$ and $x(0) > 0$ approach the periodic orbit. The fermentor will cycle indefinitely, periodically releasing batches of the tank into the environment, with only a small level of waste product remaining.

If $s_{\text{intsize}} < 0$ then the cycle time increases. The cleanup process eventually runs down and the population of microorganisms washes out. If $s_{\text{intsize}} = 0$, then the cycle time increases without bound and the population essentially washes out.

If the size at birth is small enough, or the physiological efficiency coefficient is large enough, then s_{intsize} will be positive and hence the population will survive in the form of an impulsive periodic orbit. This mirrors a result in Cushing [3]. He showed that survival in the chemostat depended on the parameters in a similar fashion. However, in that case, the survival is in terms of a globally asymptotically stable fixed point in the interior, instead of a periodic orbit. On the other hand, we showed that the average length and surface area of the microorganisms always equilibrates and that the standard deviation approaches a constant value. Thus, as for the chemostat, if some cells in the self-cycling fermentation process grow unnaturally large, they still form a negligible fraction of the overall population.

As in the original model of Cushing, the most serious deficiency of this model is the description of the reproduction process. However, the analysis of a model that treats cell division more realistically and at the same time treats growth and consumption as discussed here would be very difficult.

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