DISCRETE AND CONTINUOUS
DYNAMICAL SYSTEMS–SERIES B
Volume **7**, Number **4**, June **2007**

Website: http://AIMsciences.org
pp. **779–792**

CIRCULAR AND ELLIPTIC ORBITS IN A FEEDBACK-MEDIATED CHEMOSTAT

Willard S. Keeran
Department of Mathematics, University of Florida, Gainesville, FL 32611-8105

Patrick De Leenheer
Department of Mathematics, University of Florida, Gainesville, FL 32611-8105

Sergei S. Pilyugin[1]
Department of Mathematics, University of Florida, Gainesville, FL 32611-8105

(Communicated by Hal Smith)

Abstract. A chemostat with two organisms competing for a single growth-limiting nutrient controlled by feedback-mediated dilution rate is analyzed. A specific feedback function is constructed which yields circular and elliptical periodic orbits for the limiting system. A theorem on the stabilization of periodic orbits in conservative systems is developed and for a given elliptical orbit, the result is used to modify the chemostat so that the chosen orbit is asymptotically stable. Finally, the feedback function is modified so that finitely many nested periodic orbits of alternating stability exist.

1. Introduction.

The chemostat has been used for over fifty years to gain experimental insight into and theoretical analysis of the fundamental mechanisms of microbial interactions [16, 20]. Central to the understanding of these basic ecosystems is the topic of coexistence of microorganisms. For a simple chemostat with a constant dilution rate and a single growth-limiting nutrient supplied at a fixed concentration, the principle of competitive exclusion states that at most one organism can survive [10]. Researchers have modified the simple chemostat by various means including the addition of multiple substrates [3, 15], periodically varying substrate concentrations and dilution rates [4, 9, 18, 19, 23], variable yields [1, 2, 11, 12, 17, 21], unstirred chemostats [20], and most recently by feedback-mediated dilution rates [5, 6, 7, 8, 13, 22]. The result of these modifications are models in which coexistence has been analytically proved or indicated using numerical techniques. Many of these models demonstrate coexistence by producing periodic orbits the shape of which can only be approximated by computer simulation or by perturbation methods.

In this report, we present a method for constructing the chemostats with periodic orbits of prescribed shapes. The original motivation for designing orbits of specific shape by means of feedback stems from a problem encountered in our previous work [7, 13] where we studied a feedback-controlled chemostat with three species. We first showed that it was possible to have a stable limit cycle when only two of the

2000 *Mathematics Subject Classification.* 92D25, 92D37, 92D45.
Key words and phrases. Chemostat, periodic coexistence, feedback-mediated control, conservative system.

[1]The corresponding author.

competitors are present. This limit cycle is part of the boundary dynamics of the three-species system, and we showed next that one can bifurcate this limit cycle into the interior of the state space, thus establishing oscillatory coexistence of all three species [7]. Determining the stability of the resulting periodic solution was rather difficult, mainly due to the fact that the exact location of the bifurcating two-species limit cycle was unknown. In [13], we partially addressed this problem by analyzing a codimension two bifurcation resulting from the interaction of the planar Hopf bifurcation in the two-species subsystem and the transcritical bifurcation of limit cycles in the full three-species system. As a result, we were able to obtain a stability criterion for the bifurcating three-dimensional limit cycles. Due to the local nature of the bifurcation, this stability criterion was limited to the periodic orbits of small amplitude. This raised the question of whether it is possible to design specifically shaped periodic solutions by means of feedback, and subsequently extend the stability criterion of the three-dimensional limit cycles to the cycles of large amplitude. This question led to the research in the present paper.

Here, we investigate the theoretical possibilities provided by the state-dependent feedback approach which is perhaps most natural in the lab setting. For instance, a chemostat with a flow cytometer can be used to measure the concentrations of the species. In an experiment, different species can be labeled with GFPs (Green Fluorescence Proteins) that have distinct fluorescence properties, thus allowing to measure individual concentrations of all species. The measurements of individual concentrations can be processed in real time by a computer that recalculates the dilution rate or, equivalently, the rate of the pump -the device that is being actuated- which supplies the reactor with fresh medium. An alternative approach is based on the feedback-mediated resource concentration and it will not be considered here. Specifically, we assume that the the resource concentration in the feed remains constant.

The present paper analyses a chemostat with two organisms, a single growth limiting nutrient, constant yield, and a feedback-mediated dilution rate. In particular, we demonstrate that for growth functions which intersect transversally at an intermediate substrate concentration and are not necessarily monotone, it is possible to design a dilution rate which yields a circular periodic orbit. In addition, we show that there exists a region containing the circular orbit such that any point in this region is either an equilibrium or lies on an elliptical periodic orbit. Next, a general result on the stabilization of level sets of conservative systems is established and this result is used to modify the dilution rate so that the circular orbit or a particular elliptical orbit is made locally asymptotically stable. A final modification to the dilution rate is made and an accompanying theorem proved which verifies the existence of a finite number of nested elliptical orbits of alternating stability.

2. The model of the feedback-mediated chemostat.

We begin with a set of equations which represent the chemostat described in the introduction and which have been rescaled so that the feed concentration and yield coefficients are all equal to one:

$$\begin{aligned}\dot{S} &= (1-S)D(x,y) - xf(S) - yg(S),\\ \dot{x} &= x(f(S) - D(x,y)),\\ \dot{y} &= y(g(S) - D(x,y)),\end{aligned} \tag{1}$$

where S is the concentration of growth limiting nutrient; x and y are the concentrations of the organisms; $D(x,y)$ is the dilution rate which is a function of x and

y; and $f(S)$ and $g(S)$ are the growth functions for organisms x and y respectively and both functions are at least C^2. We assume that the state variables x, y, and S are all greater than or equal to zero. We also assume that the growth functions are equal to zero when the substrate concentration is zero, and are equal at some intermediate substrate concentration $\bar{S} \in (0,1)$. Finally, we assume that the growth functions satisfy the inequality $(f(S) - g(S))(S - \bar{S}) > 0$ for $S \in (0,1),\ S \neq \bar{S}$. [2] In order to reduce the number of equations representing the system, we define a new variable $z = 1 - S - x - y$ and using (1) and the time dependence of x and y obtain the equation $\dot{z} = -D(x(t), y(t))z$. The solutions of this equation are given by $z(t) = z(0)e^{-\int_0^t D(x(s),y(s))\,ds}$ and they clearly converge to zero as long as $\int_0^{+\infty} D(x(t), y(t))\,dt = +\infty$. In particular, this will happen if $D(x(t), y(t)) > 0$ is bounded away from zero. The set $\{z = 0\}$ is an exponentially attracting invariant set for system (1). In what follows, we restrict the analysis to the dynamics on this set. As a result, we substitute $S = 1 - x - y$ into (1), and obtain the so-called limiting system

$$\begin{aligned} \dot{x} &= x(f(1 - x - y) - D(x, y)), \\ \dot{y} &= y(g(1 - x - y) - D(x, y)), \end{aligned} \tag{2}$$

where $D(x, y)$ is strictly positive. Since $1 - S = x + y \geq 0$, the state space for this system is the triangular region in the xy plane with vertices $(0,0), (1,0)$, and $(0,1)$. The intersection of this triangle with the line $1 - \bar{S} = x + y$ provides a segment upon which all nontrivial equilibria (if they exist) occur. In the subsequent sections, we will present several different constructions for the feedback function $D(x, y)$ that produce both stable and unstable periodic solutions of (2). Here, we present a formal justification that the stability of such periodic solutions under the dynamics of the full system (1) remains the same. Suppose that $(x(t), y(t))$ is a periodic solution of (2) of period $T > 0$ with Floquet multipliers $\mu_1 = 1$ and $\mu_2 \neq 1$. Then $(x(t), y(t), 0)$ is a T-periodic solution of the system

$$\begin{aligned} \dot{x} &= x(f(1 - x - y - z) - D(x, y)), \\ \dot{y} &= y(g(1 - x - y - z) - D(x, y)), \\ \dot{z} &= -D(x, y)z, \end{aligned} \tag{3}$$

which is equivalent to (1). The variational system of (3) along $(x(t), y(t), 0)$ is given by

$$\dot{\phi} = \begin{pmatrix} M(t) & \begin{matrix} -x(t)f'(1 - x(t) - y(t)) \\ -y(t)g'(1 - x(t) - y(t)) \end{matrix} \\ 0 \quad 0 & -D(x(t), y(t)) \end{pmatrix} \phi,\ \ \phi(0) = I_3,$$

where $M(t)$ is the 2×2 matrix of the variational system of (2) along $(x(t), y(t))$. Consequently, the Floquet multipliers of $(x(t), y(t), 0)$ are $\mu_1 = 1$, $\mu_2 \neq 1$, and $\mu_3 = \exp\left(-\int_0^T D(x(t), y(t))\,dt\right) < 1$. In both cases, the stability of the corresponding periodic solution is determined by μ_2.

3. **A dilution rate for circular and elliptic orbits.** The main focus of this paper is the construction of dilution rates which control the shape, number, and stability of periodic orbits for the given chemostat system. The following theorem establishes the basic results for orbits of prescribed shape.

[2] Importantly, we do not assume that the growth functions f and g are monotonically increasing.

Theorem 1. *Let f, g be C^n ($n \geq 2$) smooth and suppose that there exists $\bar{S} \in (0,1)$ such that $f(\bar{S}) = g(\bar{S})$, $f'(\bar{S}) \neq g'(\bar{S})$, and $f(S) \neq g(S)$ for all $S \in (0,1]\backslash\{\bar{S}\}$. Then there exists a non-empty elliptic domain $\Omega \subset \{(x,y): \ 0 < x, y < x+y < 1\}$ and a C^{n-1} smooth function $D : \Omega \to (0,\infty)$ such that*

- *The domain Ω is invariant under the flow of system (2) with $D = D(x,y)$;*
- *System (2) with $D = D(x,y)$ is conservative in Ω;*
- *The point $(\frac{1-\bar{S}}{2}, \frac{1-\bar{S}}{2}) \in \Omega$ is the only equilibrium of (2) in Ω, any other point of Ω belongs to an elliptic periodic orbit. One of the elliptic orbits is a circle.*

The proof proceeds in several stages. First, we construct a smooth dilution rate which produces a circular periodic orbit. Second, we show that all orbits interior to the circle are elliptic periodic orbits and that the only equilibrium occurs at $\left(\frac{1-\bar{S}}{2}, \frac{1-\bar{S}}{2}\right)$. The region Ω is then defined and the properties of the orbits in Ω are shown to be identical to those of the orbits in the interior of the circle. Once these properties are established, the invariance of Ω and the conservative nature of system (2) on Ω follow naturally.

Proof of Theorem 1. We begin by introducing a new coordinate system defined by $z = x+y, w = x-y$. In the new variables, the system (2) becomes

$$\begin{array}{rcl} \dot{z} & = & zF(z) + wG(z) - zD(z,w), \\ \dot{w} & = & zG(z) + wF(z) - wD(z,w), \end{array} \tag{4}$$

where

$$F(z) = \frac{f(1-z)+g(1-z)}{2}, \ G(z) = \frac{f(1-z)-g(1-z)}{2}.$$

The triangular state space in the new coordinates is formed by the intersection of the lines $w = z, w = -z$, and $z = 1$ and the segment containing possible nontrivial equilibria is on the line $z = 1 - \bar{S} = \lambda$.

3.1. **Construction of $D(z,w)$.** We assume the existence of a circular periodic orbit given algebraically by $(w-w_0)^2 + (z-z_0)^2 = r^2$ and determine the necessary dilution rate. Differentiating both sides of this equation with respect to time yields

$$(w-w_0)\dot{w} + (z-z_0)\dot{z} = 0,$$

and substituting from the transformed system provides

$$(w-w_0)(zG(z)+wF(z)-wD(z,w))+(z-z_0)(zF(z)+wG(z)-zD(z,w)) = 0. \tag{5}$$

For any T-periodic solution $(z(t), w(t))$ of (4) in the region $z > 0, \ -z < w < z$, we can define $\alpha(t) = w(t)/z(t) \in (-1,1)$ so that

$$\dot{\alpha} = (1-\alpha^2)G(z).$$

Integrating over the period, we obtain

$$0 = \int_0^T \frac{\dot{\alpha}(t)}{1-\alpha^2(t)}\, dt = \int_0^T G(z(t))\, dt.$$

Therefore, any nontrivial periodic orbit of (4) must contain points where $G(z) < 0$ and $G(z) > 0$. For instance, if the periodic orbit is a circle, it must intersect the line $z = \lambda$ at two distinct points. To find these points we substitute $z = \lambda$ and $w = w^*$ into (5) and obtain

$$(f(1-\lambda) - D(\lambda, w^*))(\lambda(\lambda - z_0) + w^*(w^* - w_0)) = 0.$$

If w^* is such that $f(1-\lambda)-D(\lambda,w^*)=0$, then $g(1-\lambda)-D(\lambda,w^*)=0$ and there is an equilibrium at the intersection of the circle and the line $z=\lambda$ so that the orbit is no longer periodic. Hence we must have

$$\begin{aligned}\lambda(\lambda-z_0)+w^*(w^*-w_0) &= 0,\\ f(1-\lambda)-D(\lambda,w^*) &\neq 0.\end{aligned}$$

Solving for w^*, we find $w^*=\frac{w_0\pm\sqrt{w_0^2-4\lambda(\lambda-z_0)}}{2}$. Substituting (λ,w^*) into the equation for the circle and rearranging gives

$$\left(\frac{-w_0\pm\sqrt{w_0^2-4\lambda(\lambda-z_0)}}{2}\right)^2=r^2-(\lambda-z_0)^2=\text{Const}.$$

This equation is consistent if and only if $w_0=0$ or $\sqrt{w_0^2-4\lambda(\lambda-z_0)}=0$. If the radical is equal to zero, this implies that the line $z=\lambda$ intersects the circle at only one point which is a contradiction; thus $w_0=0$ and $w^*=\frac{\pm\sqrt{-4\lambda(\lambda-z_0)}}{2}$. The fact that $w_0=0$ immediately leads to several constraints on the circular orbit. First, since w^* is real and λ is real and positive, this implies $z_0>\lambda$ or that the center of the circle, $(z_0,0)$, lies to the right of the line $z=\lambda$. Using this fact and considering that the circle must intersect the line $z=\lambda$ twice while not intersecting the line $z=1$ implies $\lambda<z_0<\frac{1}{2}(1+\lambda)$. In addition, there are several constraints on the radius of the circle. Since the circle may not intersect the line $z=1$, this implies $r<1-z_0$; since the circle may not intersect the line $z=0$, this implies $r<z_0$. The fact that the circle may not intersect the lines $w=\pm z$ provides the restriction: $r<\frac{\sqrt{2}z_0}{2}$. Returning to equation (5), we substitute $w_0=0$ and solve for $D(z,w)$ to obtain for all (z,w) on the circle

$$D(z,w)=\frac{(z-z_0)(zF(z)+wG(z))+w(zG(z)+wF(z))}{r^2-z_0^2+z_0z}$$

or by defining the formal expression

$$\tilde{G}(z)=\frac{(2z-z_0)}{r^2+z_0(z-z_0)}\,G(z),$$

the equation for D becomes

$$D(z,w)=F(z)+w\tilde{G}(z). \tag{6}$$

Substituting the dilution rate (6) into (4), we obtain the system

$$\begin{aligned}\dot{z} &= w(G(z)-z\tilde{G}(z)),\\ \dot{w} &= zG(z)+w^2\tilde{G}(z),\end{aligned} \tag{7}$$

For the function $D(z,w)$ to be a feasible dilution rate for the chemostat model, it must be smooth, strictly positive, and not produce any equilibria on the circle.

3.2. **Feasibility and smoothness of** $D(z,w)$**.** In determining the smoothness of the dilution rate $D(z,w)$, we note that $F(z)$ and $G(z)$ are as smooth as the growth functions $f(S)$ and $g(S)$ which by assumption are C^n. Examining the denominator of the expression $\tilde{G}(z)$ we find that a first degree zero exists at the point $z^*=\frac{z_0^2-r^2}{z_0}$. For the dilution rate to remain smooth, the function $G(z)$ must also have at least a first degree zero at z^*. By assumption, the growth functions intersect only at one point in $(0,1]$, so that the only zero of $G(z)$ occurs at $z=\lambda$. Thus a criterion for smoothness is that $z^* = \lambda$ which implies $r = \sqrt{z_0(z_0 - \lambda)}$. The value of $\tilde{G}(\lambda)$ is then determined from l'Hospital's rule,

$$\tilde{G}(z) = \begin{cases} \frac{(2z-z_0)}{r^2+z_0(z-z_0)}\, G(z), \ z \neq \lambda, \\ \frac{(2\lambda-z_0)}{z_0}\, G'(\lambda), \ z = \lambda. \end{cases}$$

By the definitions of $\tilde{G}(z),\ G(z),\ F(z)$, and (6), the function $D(z,w)$ is C^{n-1}. To ensure that the dilution rate D remains positive on the circle, we begin by fixing an h with $0 < h < \min(\lambda, 1-\lambda)$ and such that $[z_0 - r, z_0 + r] \subset [\lambda - h, \lambda + h]$; by continuity of F and $\tilde{G}$, there exist positive constants m_1 and m_2 such that $F(z) \geq m_1$ and $|\tilde{G}(z)| \leq m_2$ for $z \in [\lambda - h, \lambda + h]$. Using the definition of D given by (6) and the fact that $|w| \leq r$ on the circle, we establish the following inequality

$$D(z,w) = F(z) + w\tilde{G}(z) \geq m_1 - rm_2.$$

Thus by choosing $0 < r < \min\big(h, \frac{m_1}{m_2}\big)$ the dilution rate will remain positive for all points on the circular orbit. Finally, we must ensure that our choice of the dilution rate does not produce equilibria on the invariant circle. It was previously noted that equilibria can only occur on the line $z = \lambda$ so that the only candidate points on the circle would be $(\lambda, w^*) = (\lambda, \frac{\pm\sqrt{-4\lambda(\lambda - z_0)}}{2})$. These points are equilibria if and only if $D(\lambda, w^*) = f(1-\lambda) = g(1-\lambda)$ which implies that $w^*\tilde{G}(\lambda) = 0$. In particular, if $w^* \neq 0$, then $\tilde{G}(\lambda) = 0$. Hence, our choice of D produces no equilibria on the circle if and only $G'(\lambda) \neq 0$ (equivalently, $f'(1-\lambda) \neq g'(1-\lambda)$). Summarizing the results, we find that the dilution rate defined by (6) will produce a circular periodic orbit provided that the following constraints are satisfied:

1. the circle is centered at $(z_0, 0)$, and $\lambda < z_0 < \frac{1}{2}(1+\lambda)$;
2. the radius of the circle is $r = \sqrt{z_0(z_0-\lambda)}$, and $r < \min\big(1 - z_0, \frac{\sqrt{2}z_0}{2}, \frac{m_1}{m_2}, h\big)$;
3. $f'(\bar{S}) \neq g'(\bar{S})$.

Note that the second condition can always be satisfied by choosing z_0 sufficiently close to λ. It is important to note that the dilution rate $D(z,w)$ was constructed on a circle and that its sign and continuity are yet undetermined at other points of the state space. However, the special form (6) and the above arguments imply that the function $D(z,w)$ is both smooth and positive at all points interior to the circular periodic orbit. Beyond the circle, the sign of the function may change since the inequality $|w| \leq r$ no longer holds. The region in the state space where the function D is positive depends on the particular growth functions involved. If the dilution rate becomes negative in some domain, it must be modified via a continuous, positive extension. It can be shown that there exists a Lipschitz extension of $D(z,w)$ into the entire state space but the global dynamics of the extended system is outside the scope of this paper. The domain Ω can now be defined as the disk $(z-z_0)^2 + w^2 \leq r^2$. Since the boundary of Ω is a periodic orbit, the set Ω is invariant under the flow of (7). In what follows, we will show that the invariant domain Ω can be further extended to include a larger elliptical region.

3.3. **System (7) is conservative in Ω.** Having established the existence of a circular periodic orbit, we will now show that all orbits in the interior of the circle are elliptical. Since the vector field of (7) has a special symmetry with respect to the z axis ($\dot{z}$ is an odd function of w and $\dot{w}$ is an even function of w), it is clear that all interior orbits are closed. To prove that these orbits are ellipses, we begin by rewriting system (7) in the form

$$\begin{aligned}\dot z &= \tfrac{G(z)}{r^2+z_0(z-z_0)}(r^2 - z_0^2 + 2zz_0 - 2z^2)w,\\ \dot w &= \tfrac{G(z)}{r^2+z_0(z-z_0)}(z(r^2 - z_0^2) + z_0 z^2 + w^2(z_0 - 2z)).\end{aligned}$$

From the condition $(f(S)-g(S))(S-\bar S) > 0$ for $S \in (0,1)$, $S \neq \bar S$ stated in Section 2, we have that $f'(\bar S) - g'(\bar S) \geq 0$. In addition, we require that $f'(\bar S) \neq g'(\bar S)$. Hence, we have that $G'(\lambda) < 0$ and the the expression $\frac{G(z)}{r^2+z_0(z-z_0)} = \frac{G(z)}{z_0(z-\lambda)}$ is strictly negative in Ω. As a result, the phase portrait of the above system is identical (by reversing the direction of the flow) to that of the system

$$\begin{aligned}\dot z &= (r^2 - z_0^2 + 2zz_0 - 2z^2)w,\\ \dot w &= z(r^2 - z_0^2) + z_0 z^2 + w^2(z_0 - 2z).\end{aligned} \tag{8}$$

We observe that the new system (8) retains the same symmetry with respect to the z-axis. Hence all elliptical orbits (if any) must be symmetric about the z-axis. With this in mind, we seek elliptical orbits of the form

$$\frac{(z-\hat z)^2}{a^2} + \frac{w^2}{b^2} = 1. \tag{9}$$

Taking the derivative of this equation with respect to time and substituting the equations for $\dot z$ and $\dot w$ from (8) yields

$$\frac{w(z-\hat z)}{a^2}(r^2 - z_0^2 + 2zz_0 - 2z^2) + \frac{w}{b^2}(z(r^2 - z_0^2) + z^2 z_0 + w^2(z_0 - 2z)) = 0.$$

By performing the substitution $w^2 = b^2(1 - \frac{(z-\hat z)^2}{a^2})$ and rearranging the above equation as a polynomial in z we obtain

$$P_3 z^3 + P_2 z^2 + P_1 z + P_0 = 0,$$

where

$$\begin{aligned}P_3 &= 0,\\ P_2 &= \tfrac{b^2}{a^2}(z_0 - 2\hat z) + z_0,\\ P_1 &= \tfrac{b^2}{a^2}(r^2 - z_0^2 + 2\hat z^2 - 2a^2) + r^2 - z_0^2,\\ P_0 &= \tfrac{b^2}{a^2}(-\hat z r^2 + \hat z z_0^2 + a^2 z_0 - \hat z^2 z_0).\end{aligned}$$

In order for the ellipse to be invariant, all the coefficients in the above expression must be zero. Setting P_2 and P_0 equal to zero, we obtain the constraints

$$1 + \frac{a^2}{b^2} - 2\frac{\hat z}{z_0} = 0,\ \ \hat z(z_0^2 - r^2) = z_0(\hat z^2 - a^2).$$

We also note that $P_2 = P_0 = 0$ implies that $P_1 = 0$, so that the constraint $P_1 = 0$ is redundant. From these equations we obtain the expressions for both semi-axes of the ellipse

$$a^2 = \hat z(\hat z - \lambda),\ \ b^2 = \frac{z_0 \hat z(\hat z - \lambda)}{2\hat z - z_0},$$

where both a and b are functions of $\hat z$. These functions impose additional constraints on $\hat z$, namely that $\hat z > \lambda$ and $\hat z > z_0/2$. In addition, if $\hat z \to \lambda^+$, then both functions approach zero while a and b approach r as $\hat z \to z_0^-$. This implies that each point in the interior of the circle lies on one such ellipse with the point $(\lambda, 0)$ being the only equilibrium in this region. We can use the constructed $D(z,w)$ on the exterior of the circle as long as the function remains positive and we define this region of the state space as Ω (alternatively if we desire a closed set, we can define Ω to be the set of all points in and on the largest elliptical orbit in the state space). By an extension of the above arguments, it is evident that any orbit lying entirely in Ω will be elliptical (with the circle being a "symmetric" ellipse). □

Fig. 1 presents a numerical example illustrating the conservative flow of (1) for an appropriate choice of $D(z, w)$. The details are given in the figure legend.

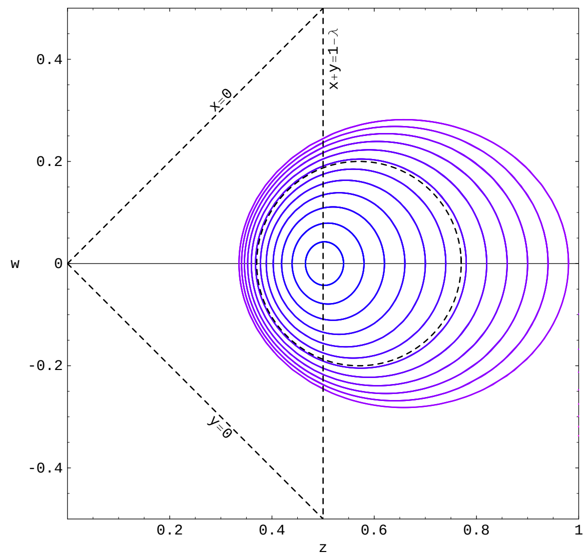

FIGURE 1. A family of nested elliptical orbits in the region Ω. The feedback control $D(z, w)$ was constructed following the steps of the proof of Thm. 1. The growth functions are $f(s) = \frac{2s}{s+1/2}$ and $g(s) = \frac{3s}{s+1}$ respectively. Their graphs intersect at the common value $\lambda = 1/2$. Representative elliptical orbits are shown in purple (solid). The circular orbit (dashed) has parameters $r = 0.2$ and $z_0 = \frac{5+\sqrt{41}}{20} \approx 0.57$. The numerical integration was performed using Mathematica.

4. **Stabilizing elliptical orbits.** We now wish to modify the dilution rate so that the circular orbit (or any elliptical orbit in Ω) is asymptotically stable. We begin by developing a technique for the stabilization of invariant level sets of conservative systems. Consider a system

$$\dot{x} = f(x), \tag{10}$$

where $x \in U$, an open set of R^n, and f is smooth. We assume that the system (10) is conservative, that is, there exists a smooth function $V : U \to R$ such that $\nabla V \neq 0$ almost everywhere in U, and $\langle \nabla V, f \rangle = 0$, for all $x \in U$ (such V is also referred to as the first integral). In particular, we have that $\dot{V} = 0$ along solutions of (10), and V is a conserved quantity. We will impose two additional assumptions on V:

1. V is bounded below. Without loss of generality we therefore assume $V \geq 0$ in U (by simply adding a constant to V if it takes negative values).
2. V is proper, i.e. $V^{-1}([0, K]) := \{x \in U | V(x) \in [0, K]\}$ is a compact set in U for

all $K \geq 0$.
These assumptions imply that all forward solutions of (10) are bounded and hence defined for all $t \geq 0$. Consider the following controlled version of system (10):

$$\begin{array}{rcl} \dot{x} & = & f(x) + ug(x), \\ y & = & V(x), \end{array} \tag{11}$$

where $y \in R^+$ and $g : U \to R^n$ is a smooth vector field which satisfies the weak transversality condition: $\langle g(x), \nabla V(x) \rangle \geq 0$ in U and $\langle g(x), \nabla V(x) \rangle > 0$ almost everywhere in U. Now we pick an arbitrary level set $V_C := \{x \in U | V(x) = C\}$ of V, where $C > 0$. We wish to find a feedback control $u(y)$ which transforms the level set V_C into an attractor. Note that the proposed feedback control $u(y)$ only uses the information given by the current value of the function V, and not by the entire state x. We prove the following Theorem.

Theorem 2. *Suppose that $u : R^+ \to R$ is such that*

$$u(y)(C - y) > 0, \ \forall y \neq C. \tag{12}$$

Let $B = \{x \in U | \langle g(x), \nabla V(x) \rangle = 0\}$, and suppose that

1. *The largest invariant subset in $V_C \bigcup B$ is $V_C \bigcup B_\omega$ for some compact set B_ω such that $V_C \bigcap B_\omega = \emptyset$.*
2. *For all $x \in U \backslash B_\omega$, $\omega(x) \bigcap B_\omega = \emptyset$.*

Then for any $x \in U \backslash B_\omega$, $\omega(x) \subset V_C$.

Proof of Theorem 2. Define $W : U \to R^+$ as $W := (V - C)^2$ and calculate $\dot{W}$ along a forward solution of (11):

$$\dot{W} = -2u(y)(C - y)\langle g, \nabla V \rangle \ \ \leq \ 0.$$

Since W is positive semi-definite in U and proper, all forward solutions of (11) are bounded, and LaSalle's invariance principle [14] implies that for any $x \in U$ the omega limit set $\omega(x)$ is contained in the largest invariant set contained in the set $V_C \bigcup B$. Thus by our first assumption, $\omega(x) \subset V_C \bigcup B_\omega$. If $x \in U \backslash B_\omega$, then by our second assumption, $\omega(x) \bigcap B_\omega = \emptyset$, and thus $\omega(x) \subset V_C$. □

We wish to use Theorem 2 and modify the dilution rate so that a given elliptical orbit of (4) is locally asymptotically stable. We begin by designating the set of all orbits in Ω by $\mathbf{E}$ and defining the elements, $E(a, b, \hat{z})$, in this set as

$$E(a, b, \hat{z}) = \{(z, w) \in \Omega | \frac{(z - \hat{z})^2}{a^2} + \frac{w^2}{b^2} = 1\}.$$

The desired result is summarized below.

Theorem 3. *Given the system (4) with the dilution rate (6), any ellipse $E(a, b, \hat{z}) \in$ $\mathbf{E}$ can be made globally asymptotically stable by defining a new dilution rate*

$$D(z, w) = F(z) + w\tilde{G}(z) - \alpha\left(z\frac{\partial V}{\partial z}(z, w) + w\frac{\partial V}{\partial w}(z, w)\right)(C - V(z, w)), \tag{13}$$

where

$$V(z, w) = (z - \hat{z}(z, w))^2 + \left(\frac{a(z, w)}{b(z, w)}\right)^2 w^2,$$

$$\hat{z}(z, w) = \frac{z_0(w^2 - z^2)}{2w^2 - z_0(2z - \lambda)},$$

$a(z,w) = a(\hat{z})$ and $b(z,w) = b(\hat{z})$ are as previously defined, $\alpha \in R^+$ is sufficiently small, and $C = a^2(\hat{z})$.

Proof of Theorem 3. We consider (4) to be the system referenced in the Theorem 2 and seek an appropriate function $V(z,w)$. Any point (z,w) in Ω belongs to an elliptical orbit of the form (9). Since a and b were previously shown to be functions of $\hat{z}$, these relations can be used to express $\hat{z}$ as a function of (z,w). Specifically, we substitute the expressions

$$a^2 = \hat{z}(\hat{z}-\lambda),\ b^2 = \frac{z_0\hat{z}(\hat{z}-\lambda)}{2\hat{z}-z_0},$$

into (9), and solve for $\hat{z}$ to obtain

$$\hat{z}(z,w) = \frac{z_0(w^2-z^2)}{2w^2-z_0(2z-\lambda)}.$$

This equation demonstrates that both $a = a(\hat{z})$ and $b = b(\hat{z})$ can be treated as functions of the state variables. Motivated by the result of Theorem 2, we define the function

$$V(z,w) = (z-\hat{z}(z,w))^2 + \left(\frac{a(z,w)}{b(z,w)}\right)^2 w^2.$$

For a given point $(z,w) \in \Omega$, the constant $C = a^2(\hat{z})$ can be chosen to define a level curve, V_C, which is the elliptical orbit $E(a,b,\hat{z})$ and it follows that on this ellipse $\nabla V(z,w)\cdot(\dot{z},\dot{w})^T = 0$ so that $E(a,b,\hat{z})$ remains invariant under the new system. We also calculate

$$\frac{\partial V}{\partial z} = \frac{2z_0(w^2(-2z+z_0)+zz_0(z-\lambda))\big(2w^2(z_0-\lambda)-z_0(2z^2-2z\lambda+\lambda^2)\big)}{(2w^2+z_0(\lambda-2z))^3}, \quad (14)$$

$$\frac{\partial V}{\partial w} = \frac{2wz_0(2z(z-z_0)+z_0\lambda)\big(2w^2(z_0-\lambda)-z_0(2z^2-2z\lambda+\lambda^2)\big)}{(2w^2+z_0(\lambda-2z))^3}, \quad (15)$$

and conclude that $\nabla V(z,w) \neq (0,0)$ almost everywhere in Ω. In addition, we have that $V(z,w) \geq 0$ for $(z,w) \in \Omega$, and $V(z,w)$ is proper. For the second function associated with Theorem 2 we choose

$$g(z,w) = \begin{pmatrix} z \\ w \end{pmatrix}\left(z\frac{\partial V}{\partial z}(z,w) + w\frac{\partial V}{\partial w}(z,w)\right)$$

and it is clear that

$$\langle g, \nabla V\rangle = \left(z\frac{\partial V}{\partial z}(z,w) + w\frac{\partial V}{\partial w}(z,w)\right)^2 \geq 0$$

for all $x \in U$. To determine the set B where $\langle g, \nabla V\rangle = 0$, we set

$$z\frac{\partial V}{\partial z}(z,w) + w\frac{\partial V}{\partial w}(z,w) = 0.$$

Substituting the expressions (14) and (15) for $\frac{\partial V}{\partial z}$ and $\frac{\partial V}{\partial w}$ respectively and simplifying, we find that

$$z\frac{\partial V}{\partial z}(z,w) + w\frac{\partial V}{\partial w}(z,w) =$$
$$\frac{2(w^2-z^2)z_0^2(z-\lambda)\big(-2w^2(z_0-\lambda)+z_0(2z^2-2z\lambda+\lambda^2)\big)}{(2w^2+z_0(\lambda-2z))^3}. \quad (16)$$

Expression (16) equals zero if one of the following holds: either $w = \pm z$, or $z = \lambda$, or

$$-2w^2(z_0 - \lambda) + z_0(2z^2 - 2z\lambda + \lambda^2) = 0. \tag{17}$$

Solving the above equation for w^2, we obtain

$$w^2 = \frac{z_0(z^2 + (z-\lambda)^2)}{2(z_0 - \lambda)}.$$

Using condition 2 on page 6, namely that $\sqrt{z_0(z_0-\lambda)} < z_0/\sqrt{2}$, we replace (17) with the inequality

$$w^2 > z^2 + (z-\lambda)^2 \geq z^2,$$

and conclude that (17) defines a curve that lies outside of the sector $-z \leq w \leq z$. Since the domain Ω is contained in the interior of the sector $-z \leq w \leq z$, it does not intersect the boundary of this sector $w = \pm z$ and it does not intersect the curve defined by equation (17). We conclude that the set B consists of all points in Ω where $z = \lambda$. Substituting $z = \lambda$ into (6), we find that $\dot{z} = -w\lambda\tilde{G}(\lambda)$. Therefore, the largest invariant set B_ω in B is the equilibrium $(\lambda, 0)$, which is clearly disjoint with any nontrivial ellipse $E(a, b, \hat{z})$. To apply the result of Theorem 2, we need to verify that B_ω does not contain limit points of any forward solution starting outside of B_ω. We will do so by showing that B_ω is asymptotically stable in reverse time. We observe that when time is reversed, the function $V(z, w)$ becomes a Lyapunov function inside the ellipse $E(a, b, \hat{z})$ which serves as a neighborhood of B_ω where $\dot{V} \leq 0$. Since B_ω is the only invariant set in $B = \{(z, w) \in \text{Int } E(a, b, \hat{z}) | \dot{V} = 0\}$, we apply the LaSalle's invariance principle and conclude that any solution starting inside $E(a, b, \hat{z})$ converges to B_ω in reverse time. Therefore, B_ω cannot contain limit points of any forward solution starting outside of B_ω. Now we apply the result of Theorem 2 and conclude that all forward solutions in Ω except the equilibrium B_ω have their ω-limit sets in $V_C = E(a, b, \hat{z})$. Finally, we remark that $\alpha > 0$ must be sufficiently small so that the expression (13) defines a positive dilution rate in Ω. □

5. **Nested orbits of alternating stability.** As a final result, we design a dilution rate which produces a finite number of elliptical orbits with alternating stability. The number and selection of ellipses in Ω to be stabilized is determined by the appropriate modification of (6). The following theorem formalizes our assertion.

Theorem 4. *Suppose that $\lambda < \hat{z}_1 < \hat{z}_2 < \cdots < \hat{z}_k$ and consider the corresponding ellipses $E_i = E(a_i, b_i, \hat{z}_i) \in \mathbf{E}$ for i = 1,2,...,k. Let $\alpha > 0$ and define a new dilution rate for system (4) by*

$$D(z, w) = F(z) + w\tilde{G}(z) + H(z, w)$$

where

$$H(z, w) = \alpha(z - \lambda)\prod_{i=1}^{k}\left(\frac{(z-\hat{z}_i)^2}{a_i^2} + \frac{w^2}{b_i^2} - 1\right). \tag{18}$$

Then the ellipses $\{E_1, ..., E_k\}$ are the only periodic orbits in Ω. Moreover, the stability of the ellipses alternates with E_k (the largest) being stable. If $k = 0$, then all orbits in Ω converge to $(z_0, 0)$.

Proof of Theorem 4. Since the function $H(z, w)$ is zero at all points contained on the ellipses E_i, these ellipses remain periodic orbits. Consider a new ellipse $E_0(a_0, b_0, \hat{z}_0)$ which is a member of $\mathbf{E}$ but which is not an element of the set $\{E_1, ..., E_k\}$ and define a new function by

$$V(z, w) = \frac{(z - \hat{z}_0)^2}{a_0^2} + \frac{w^2}{b_0^2} - 1.$$

Differentiating $V(z, w)$ with respect to t we find

$$\dot{V} = \nabla V \cdot (\dot{z}, \dot{w})^T = -\big(z\frac{\partial V}{\partial z} + w\frac{\partial V}{\partial z}\big)H,$$

that is,

$$\dot{V}(z, w) = -2\alpha(z - \lambda)\Big(\frac{z(z - \hat{z}_0)}{a_0^2} + \frac{w^2}{b_0^2}\Big)\prod_{i=1}^{k}\Big(\frac{(z - z_i)^2}{a_i^2} + \frac{w^2}{b_i^2} - 1\Big).$$

For all $(z, w) \in E_0(a_0, b_0, \hat{z}_0)$, we have

$$\begin{aligned}\frac{z(z - \hat{z}_0)}{a_0^2} + \frac{w^2}{b_0^2} &= \frac{(z - \hat{z}_0)^2}{a_0^2} + \frac{w^2}{b_0^2} + \frac{\hat{z}_0(z - \hat{z}_0)}{a_0^2}\\ &= 1 + \frac{\hat{z}_0(z - \hat{z}_0)}{a_0^2} = 1 + \frac{\hat{z}_0(z - \hat{z}_0)}{\hat{z}_0(\hat{z}_0 - \lambda)} = \frac{z - \lambda}{\hat{z}_0 - \lambda},\end{aligned}$$

where we used the fact that $a_0^2 = \hat{z}_0(\hat{z}_0 - \lambda)$. Consequently,

$$\dot{V}(z, w) = -2\alpha\frac{(z - \lambda)^2}{\hat{z}_0 - \lambda}\prod_{i=1}^{k}\Big(\frac{(z - z_i)^2}{a_i^2} + \frac{w^2}{b_i^2} - 1\Big). \tag{19}$$

In expression (19), each term of the form

$$\frac{(z - z_i)^2}{a_i^2} + \frac{w^2}{b_i^2} - 1$$

is positive (negative) for $(z, w) \in E_0$ if and only if $E_i \subset E_0$ ($E_0 \subset E_i$). Therefore, with the exception of two points $(\lambda, \pm w)$ on E_0 where $\dot{V}(z, w) = 0$, the sign of $\dot{V}(z, w)$ is negative (positive) if an even (odd) number of ellipses E_i lie outside of E_0. If $\dot{V}(z, w)$ is negative, then (19) implies that all orbits traverse E_0 from the exterior to the interior while the opposite is true for positive valued $\dot{V}(z, w)$; since the sign of $\dot{V}(z, w)$ is constant for all E_0 between E_i and E_{i+1}, the alternating stabilities of these ellipses is established. The largest ellipse E_k is always stable. If $k = 0$, then $\dot{V}(z, w) = -2\alpha\frac{(z-\lambda)^2}{\hat{z}_0-\lambda} < 0$ for any $E_0 \in \mathbf{E}$ (again, excluding the points with $z = \lambda$) and thus the equilibrium point $(z_0, 0)$ is globally attracting in Ω. □

Fig. 2 presents a numerical example illustrating the flow of (1) where $D(z, w)$ is chosen to stabilize two elliptical orbits. The details are given in the figure legend.

6. **Conclusions.** In this paper we have demonstrated that for a feedback-mediated chemostat with two organisms and growth functions which intersect transversally at some intermediate substrate concentration, it is possible to design a dilution rate which yields circular and elliptical periodic orbits. We remark that our analysis does not require the growth functions to be monotonically increasing. By modifying the dilution rate it is also possible to select any one of the elliptical orbits and make it asymptotically stable. Finally, it is possible to design $D(z, w)$ such that there exists a finite number of elliptical orbits of alternating stability. The ability

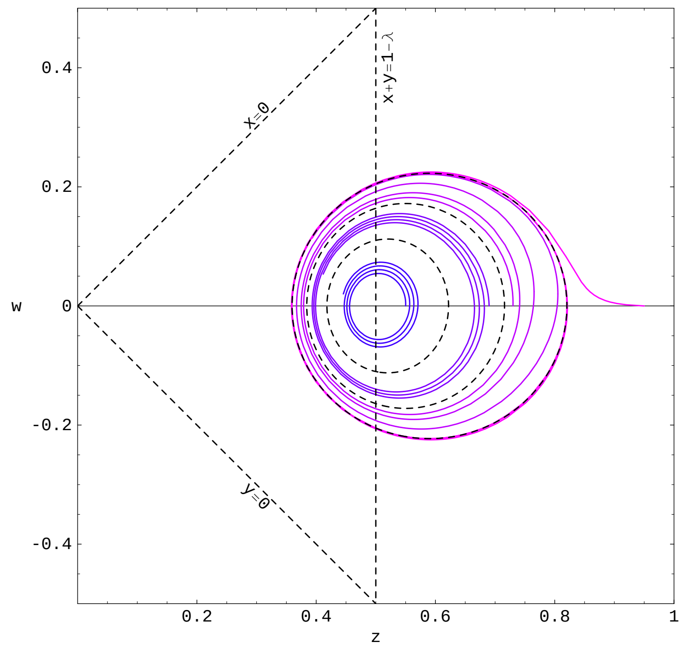

FIGURE 2. A numerical example illustrating the result of Thm. 4. The growth functions are the same as in Fig. 1. The initial feedback control $D(z, w)$ was modified by adding a function $H(z, w)$ of the form (18) with $\alpha = 0.01$, $k = 3$, $\hat{z}_1 = 0.52$, $\hat{z}_2 = 0.55$, and $\hat{z}_3 = 0.59$. The corresponding invariant ellipses are shown by dashed curves. The largest and the smallest ellipses are stable while the intermediate ellipse is unstable. Representative orbits starting at $(z, 0)$ with $z \in \{0.55,\ 0.69,\ 0.73,\ 0.95\}$ are shown in purple (solid). The numerical integration was performed using Mathematica.

to design orbits of known shapes is a new addition to the chemostat literature and presents many interesting questions. The present development assumes an instantaneous and continuous knowledge of organism concentrations as well as the ability to instantaneously change dilution rates. Modern techniques for fluorescently labeling microorganisms and advances in hardware have significantly decreased the "lag-time" present in laboratory experiment, however, some delay should always be expected in a laboratory experiment. The question of how this delay would affect such a system would be quite difficult to answer analytically and can perhaps only be answered at the present time using numerical simulations for particular systems [22]. In addition, the possibilities of designing orbits of arbitrary shape for two organisms or of designing orbits of specific shape for chemostats with three or more organisms appear to be challenging problems.

Acknowledgements. This work is a part of the doctoral thesis of W.S.K. Research of P.D.L. is partially supported by NSF grant DMS-0614651. Research of W.S.K. and S.S.P. is partially supported by NSF grant DMS-0517954. We are grateful to the anonymous reviewers for their valuable comments and suggestions.

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Received August 2006; revised January 2007.

E-mail address: wkeeran@math.ufl.edu
E-mail address: deleenhe@math.ufl.edu
E-mail address: pilyugin@math.ufl.edu