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A periodic model for the dynamics of cell volume

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Abstract. We prove the existence and uniqueness of a positive periodic solution for a model describing the dynamics of cell volume flux, introduced by Julio A. Hernández [Bull. Math. Biol. 69 (2007), 1631–1648]. We also show that the periodic solution is a global attractor. Our results confirm the conjectures made in an interesting recent book of P. J. Torres [Atlantis Press, 2015].

1. Introduction. In [He] Julio A. Hernández proposed a general model for describing the dynamics of cell volume related to transport of water and solute across the cell membrane. The interdependence between the mass of solute $x(t)$ and water volume $y(t)$ is governed by the system

$$\begin{aligned} x' &= \alpha(t) - \beta\frac{x}{y}, \\ y' &= -\gamma(t) + \sigma\frac{x}{y} + \frac{\epsilon}{y}. \end{aligned} \tag{1.1}$$

Here $\alpha(t) > 0$ represents the sources of solute, $\gamma(t) > 0$ is related to decrease of the water volume, while the positive constants β, σ and ϵ are biological interaction coefficients. As was shown in [He], this model unifies a number of other solute-solvent flux models, previously considered in the biological literature. This model is also described in detail in a recent book of P. J. Torres [T1]; see also P. J. Torres [T2] and J. D. Benson et al. [BCC]. As explained in [T1], it is natural to assume that $\alpha(t)$ and $\gamma(t)$ are periodic functions, which is related to circadian clocks.

All of the coefficients in (1.1) are assumed to be positive, and we are looking for a positive and periodic solution, with components $x(t)$ and $y(t)$. It is not hard to state a necessary condition for the existence of a periodic

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solution (see (2.10) below). P. J. Torres [T1] proved that the necessary condition is also sufficient. Moreover, he conjectured that the periodic solution is unique and asymptotically stable.

The system (1.1) is of *cooperating type*, also called *monotone system* (see M. W. Hirsch [Hi] and H. L. Smith [S]). We show that this fact allows one to apply the method of monotone iterations, where the trick is in constructing the appropriate supersolutions. We thus obtain an alternative proof of existence of solutions. Moreover, the method of monotone iterations yields the existence of maximal and minimal solutions, from which we conclude the uniqueness. We also show that the periodic solution attracts all other positive solutions, proving the conjectures of P. J. Torres [T1]. The more general model in [T2] is also of cooperating type.

2. The results. Any function $b(t) \in C[0,p]$ may be decomposed as $b(t) = \bar{b} + \tilde{b}(t)$, with $\bar{b} = p^{-1}\int_0^p b(s)\,ds$ and $\int_0^p \tilde{b}(s)\,ds = 0$. The following lemma is proved by a direct integration.

Lemma 2.1. *Consider the equation*

$$y' = b(t)$$

with a continuous p-periodic function $b(t)$. This equation has a p-periodic solution if and only if $\int_0^p b(t)\,dt = 0$.

Lemma 2.2. *Consider the equation*

$$y' + ay = b(t) \tag{2.1}$$

with a positive constant a, and a continuous p-periodic function $b(t)$. The problem (2.1) *has a solution of period p. This solution is unique, and it attracts all other solutions of* (2.1) *as $t \to \infty$. If $b(t)$ is positive, so is the p-periodic solution.*

Proof. The general solution is

$$y(t) = y_0 e^{-at} + e^{-at}\int_0^t e^{as} b(s)\,ds.$$

This solution is p-periodic, provided that $y(p) = y(0) = y_0$, which gives

$$y_0 = \frac{1}{e^{ap}-1}\int_0^p e^{as} b(s)\,ds. \tag{2.2}$$

If $z(t)$ is another solution of (2.1), their difference $w(t) = z(t) - y(t)$ is equal to $w(t) = e^{-at}w(0) \to 0$ as $t \to \infty$, proving that all solutions tend to the periodic solution $y(t)$. In particular, this implies that the periodic solution is unique. ∎

Observe that in case $\bar{b} \neq 0$, the p-periodic solution tends to infinity as $a \to 0$.

LEMMA 2.3. *Let $y(t)$ be the p-periodic solution of* (2.1). *Then*

$$\lim_{a\to 0} ay(t) = \bar{b}.$$

Proof. We have

$$\lim_{a\to 0} a\,y(t) = \lim_{a\to 0} \frac{a}{e^{ap}-1}\int_0^p e^{as} b(s)\,ds = \frac{1}{p}\int_0^p b(s)\,ds = \bar{b}$$

uniformly in t. ∎

Consider a system

$$x'(t) = f(t, x(t), y(t)), \quad y'(t) = g(t, x(t), y(t)), \tag{2.3}$$

where the given differentiable functions $f(t, x, y)$ and $g(t, x, y)$ are assumed to be p-periodic in t for all (x, y). We say that a pair of p-periodic differentiable functions $(a(t), b(t))$ forms a *subsolution pair* if for all t,

$$a'(t) \le f(t, a(t), b(t)), \quad b'(t) \le g(t, a(t), b(t)). \tag{2.4}$$

A *supersolution pair* $(A(t), B(t))$ is defined by reversing the inequalities in (2.4). We say that sub- and supersolution pairs are *ordered* if $a(t) < A(t)$ and $b(t) < B(t)$ for all t.

THEOREM 2.1. *Assume that the problem* (2.3) *has ordered sub- and supersolution pairs $(a(t), b(t))$ and $(A(t), B(t))$. Assume that the system* (2.3) *is of cooperating type, i.e., for all $t \in R$, $x \in (a(t), A(t))$, $y \in (b(t), B(t))$ we have*

$$f_y(t, x, y) \ge 0, \quad g_x(t, x, y) \ge 0. \tag{2.5}$$

Then (2.3) *has a p-periodic solution satisfying $a(t) < x(t) < A(t)$ and $b(t) < x(t) < B(t)$, for all t. Moreover, one can construct two monotone sequences of p-periodic approximations $(x_n(t), y_n(t))$ and $(X_n(t), Y_n(t))$ which converge respectively to the minimal solution $(\underline{x}(t), \underline{y}(t))$ and to the maximal solution $(\overline{x}(t), \overline{y}(t))$. Furthermore, any solution of* (2.3) *with the initial data satisfying $a(0) < x(0) < A(0)$ and $b(0) < y(0) < B(0)$ converges to the product of the strips $(\underline{x}(t), \overline{x}(t)) \times (\underline{y}(t), \overline{y}(t))$.*

Proof. Beginning with $(x_0, y_0) = (a(t), b(t))$, we construct the sequence $(x_n(t), y_n(t))$ by calculating the p-periodic solutions of the equations

$$\begin{aligned} x_n' + Mx_n &= Mx_{n-1} + f(t, x_{n-1}, y_{n-1}), \quad n = 1, 2, \ldots, \\ y_n' + My_n &= My_{n-1} + g(t, x_{n-1}, y_{n-1}), \quad n = 1, 2, \ldots. \end{aligned} \tag{2.6}$$

Here the constant $M > 0$ is chosen so that the functions $Mx + f(t, x, y)$ and $My + g(t, x, y)$ are both increasing in x and y, for $x \in [a(t), A(t)]$, $y \in [b(t), B(t)]$, and all $t \in [0, p]$. Since these intervals are compact, such M

exists. The sequence $(X_n(t), Y_n(t))$ is constructed similarly, beginning with $(X_0, Y_0) = (A(t), B(t))$. A standard argument using Lemma 2.2 shows that (componentwise)

$$(a(t), b(t)) < (x_1, y_1) < \cdots < (x_n, y_n) < \cdots < (X_n, Y_n) < \cdots < (X_1, Y_1) < (A(t), B(t)).$$

It follows that both sequences $\{x_n(t)\}$ and $\{y_n(t)\}$ converge. Define $\underline{x}(t) = \lim_{n\to\infty} x_n(t)$, and $\underline{y}(t) = \lim_{n\to\infty} y_n(t)$. Passing to the limit in the integral version of (2.6), we see that $(\underline{x}(t), \underline{y}(t))$ is a p-periodic solution of (2.3). By a standard argument, this is the minimal solution, i.e., any other p-periodic solution of (2.3) satisfies $\underline{x}(t) \le x(t)$ and $\underline{y}(t) \le y(t)$, for all t.

To show that all solutions are attracted to the interval between the minimal and the maximal solutions, we proceed similarly to E. N. Dancer [D]. We shall show that for any solution $(x(t), y(t))$ of the system (2.3) with the initial data satisfying

$$a(0) < x(0) < A(0), \quad b(0) < y(0) < B(0),$$

we have

$$x_n(t) < x(t) < X_n(t), \quad y_n(t) < y(t) < Y_n(t),$$

for any n, provided that t is sufficiently large. We prove next that $x_n(t) < x(t)$ and $y_n(t) < y(t)$, with the other inequalities being similar.

We claim that $x(t) > a(t)$ and $y(t) > b(t)$, for all t. Letting $w(t) = x(t) - a(t)$ and $z(t) = y(t) - b(t)$, we see from (2.3) and (2.4) that

$$\begin{aligned} w'(t) &\ge p(t)w + q(t)z, \quad w(0) > 0,\\ z'(t) &\ge r(t)w + s(t)z, \quad z(0) > 0, \end{aligned}$$

where $p(t) = \int_0^1 f_x(t, \theta x(t) + (1-\theta)a(t), \theta y(t) + (1-\theta)b(t))\, d\theta$, with similar expressions for $q(t) \ge 0$, $r(t) \ge 0$, and $s(t)$. If we define $\mu(t) = e^{-\int p(t)\, dt}$ and $\nu(t) = e^{-\int s(t)\, dt}$, these inequalities imply that $(\mu(t)w)' \ge \mu(t)q(t)z$ and $(\nu(t)z)' \ge \nu(t)r(t)w$. We see that $\mu(t)w(t)$ and $\nu(t)z(t)$ are positive and increasing functions, and the claim follows.

Define the functions $\xi(t)$ and $\eta(t)$ by integrating the following equations:

$$\begin{aligned} \xi' + M\xi &= Ma(t) + f(t, a(t), b(t)), \quad \xi(0) = a(0),\\ \eta' + M\eta &= Mb(t) + g(t, a(t), b(t)), \quad \eta(0) = b(0), \end{aligned} \tag{2.7}$$

and rewrite (2.3) as

$$\begin{aligned} x'(t) + Mx(t) &= Mx(t) + f(t, x(t), y(t)),\\ y'(t) + My(t) &= My(t) + g(t, x(t), y(t)). \end{aligned} \tag{2.8}$$

By the above claim, the right hand sides in (2.8) are pointwise greater than the ones in (2.7). It follows that for all $t > 0$, $x(t) > \xi(t)$ and $y(t) > \eta(t)$, and moreover $x(t) - \xi(t) > x(0) - a(0)$ and $y(t) - \eta(t) > y(0) - b(0)$. By the definition of (x_1, y_1) and Lemma 2.2, $\xi(t) \to x_1(t)$ and $\eta(t) \to y_1(t)$, as $t \to \infty$. Hence, at some $t_1 > 0$, $x(t_1) > x_1(t_1)$ and $y(t_1) > y_1(t_1)$. We now take t_1 as a new origin, and repeat this argument, showing that $x(t) > x_1(t)$ and $y(t) > y_1(t)$ for all $t > t_1$, and at some $t_2 > t_1$, $x(t_2) > x_2(t_2)$ and $y(t_2) > y_2(t_2)$, and so on. Observe that (x_n, y_n) is a subsolution pair for each n. ■

We now consider the system

$$\begin{aligned} x' &= \alpha(t) - \beta\frac{x}{y}, \\ y' &= -\gamma(t) + \sigma\frac{x}{y} + \frac{\epsilon}{y}. \end{aligned} \tag{2.9}$$

Here $\alpha(t)$ and $\gamma(t)$ are positive p-periodic functions, and β, σ and ϵ are positive constants.

THEOREM 2.2. *The condition*

$$\beta\bar{\gamma} - \sigma\bar{\alpha} > 0 \tag{2.10}$$

is necessary and sufficient for the existence of a positive p-periodic solution of (2.9). *In case* (2.10) *holds, the positive solution is unique, and it attracts all other positive solutions of* (2.9) *as $t \to \infty$.*

Proof. Multiplying the first equation in (2.9) by σ, the second one by β, adding the results and integrating, we get

$$\beta\bar{\gamma} - \sigma\bar{\alpha} = \frac{\epsilon\beta}{p}\int_0^p \frac{1}{y(t)}\,dt > 0, \tag{2.11}$$

proving the necessity of (2.10).

We now apply Theorem 2.1. For a subsolution pair, we consider (p, q), where p and q are two small constants with $\beta p/q < \min_{t\in R}\alpha(t)$. The conditions (2.4) require

$$\begin{aligned} 0 &< \alpha(t) - \beta\frac{p}{q}, \\ 0 &< -\gamma(t) + \sigma\frac{p}{q} + \frac{\epsilon}{q}, \end{aligned}$$

which hold for p and q sufficiently small.

Next we construct a supersolution pair $(A(t), B(t))$. We choose $A(t)$ to be the positive p-periodic solution of

$$A'(t) = \alpha(t) + \theta - \beta\frac{A(t)}{M},$$

with the constants $\theta > 0$ small, and $M > 0$ large to be fixed later. Let $y_0(t)$ be the p-periodic solution of

$$y_0'(t) = -\tilde{\gamma}(t).$$

We set $B(t) = M + y_0(t)$. The conditions (2.4) for supersolutions become

$$A' = \alpha(t) + \theta - \beta\frac{A}{M} > \alpha(t) - \beta\frac{A}{M + y_0},$$
$$B' = -\tilde{\gamma}(t) > -\tilde{\gamma}(t) - \bar{\gamma} + \sigma\frac{A}{M + y_0} + \frac{\epsilon}{M + y_0}.$$

The first of these inequalities simplifies to read

$$\theta > \beta\frac{A}{M} - \beta\frac{A}{M + y_0} = \beta\frac{Ay_0}{M(M + y_0)}. \tag{2.12}$$

The second inequality requires

$$0 > -\bar{\gamma} + \sigma\frac{A}{M} + \sigma\left(\frac{A}{M + y_0} - \frac{A}{M}\right) + \frac{\epsilon}{M + y_0}. \tag{2.13}$$

By Lemma 2.3, $\frac{A}{M} \to \frac{1}{\beta}\bar{\alpha} + \frac{1}{\beta}\theta$ as $M \to \infty$. We now fix $\theta > 0$ so small that

$$0 > -\bar{\gamma} + \sigma\frac{1}{\beta}\bar{\alpha} + \frac{\sigma}{\beta}\theta,$$

and then choosing M sufficiently large, we can satisfy both the inequalities (2.12) and (2.13), and Theorem 2.1 applies, proving the existence.

By (2.11), the y-component of any positive p-periodic solution is equal to that of the maximal solution. But then, from the first equation in (2.9), the first components also coincide, proving the uniqueness.

Observe that with our construction, we can make the supersolutions arbitrarily large, and the subsolutions arbitrarily small. By Theorem 2.1, the unique p-periodic solution is then a global attractor for all positive solutions. ∎

We conclude with a numerical example. We used *Mathematica* to solve the problem (2.9) with $\alpha(t) = 2+\sin(2\pi t)$, $\gamma(t) = 1+\cos^2(2\pi t)$, $\beta = 2$, $\sigma = 1$, $\epsilon = 0.2$, and the initial conditions $x(0) = 1$, $y(0) = 0.4$. Then Theorem 2.1 applies. In Figure 1 one can see quick convergence to the unique periodic

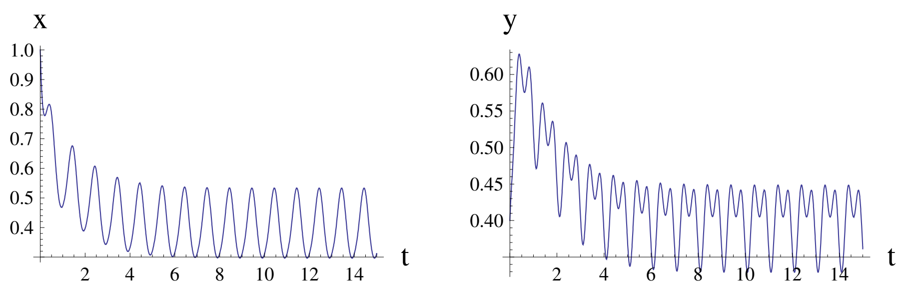

Fig. 1. A positive solution of the problem (2.9) approaching the periodic solution (of period 1)

solution of period 1. We saw similar results for all other initial conditions, and all other systems, that we tried.

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