

Dynamics of the Selkov oscillator

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Abstract

A classical example of a mathematical model for oscillations in a biological system is the Selkov oscillator, which is a simple description of glycolysis. It is a system of two ordinary differential equations which, when expressed in dimensionless variables, depends on two parameters. Surprisingly it appears that no complete rigorous analysis of the dynamics of this model has ever been given. In this paper several properties of the dynamics of solutions of the model are established. With a view to studying unbounded solutions a thorough analysis of the Poincaré compactification of the system is given. It is proved that for any values of the parameters there are solutions which tend to infinity at late times and are eventually monotone. It is shown that when the unique steady state is stable any bounded solution converges to the steady state at late times. When the steady state is unstable it is shown that for given values of the parameters either there is a unique periodic solution to which all bounded solutions other than the steady state converge at late times or there is no periodic solution and all solutions other than the steady state are unbounded. In the latter case each unbounded solution which tends to infinity is eventually monotone and each unbounded solution which does not tend to infinity has the property that each variable takes on arbitrarily large and small values at arbitrarily late times.

1 Introduction

Glycolysis is a part of the process by which living organisms extract energy from sugar. It has been observed that under suitable circumstances the rate at which products of glycolysis accumulate shows oscillations in time although the input rate of sugar to the system is constant. Soon after these experimental observations had been made Higgins [8] used mathematical modelling to obtain a deeper understanding of the process. Later it was observed by Selkov [16] that the model of Higgins did not show sustained oscillations for biologically correct parameter values and he introduced an alternative mathematical model,

which we refer to as the Selkov model. This system of two ordinary differential equations is the subject of what follows. (We comment further on the work of Higgins in the last section of the paper.) It was shown in [16] that the Selkov model exhibits a Hopf bifurcation and thus there exist parameter values for which it has a periodic solution. Results on the uniqueness and stability of periodic solutions of the Selkov model were obtained by d'Onofrio [3].

It turns out that solutions of the Selkov model can be unbounded and thus it becomes relevant to investigate the behaviour of the system near infinity. This can be done by means of a Poincaré compactification. This leads to two new steady states at infinity which are not hyperbolic. It is relatively easy to determine the behaviour of solutions close to one of these steady states, which has a one-dimensional centre manifold, and this was done in [16]. The other steady state is more complicated since the linearization about that point vanishes identically and it was not treated fully in [16]. To do so it is necessary to define some blow-ups of the singularity and this is done in what follows. It is suggested in [16], on the basis of numerical calculations, that for certain parameter values there are unbounded solutions which approach infinity in an oscillatory fashion. Analytically these might be interpreted as solutions which approach a heteroclinic cycle in (a suitable blow-up of) the Poincaré compactification.

Section 2 presents the basic facts about the model. In particular it is shown that the model has a unique steady state for fixed values of the parameters and that there is a Hopf bifurcation. The first Lyapunov coefficient is calculated and shown to be negative. Thus the bifurcation is generic and supercritical and there exist stable periodic solutions for parameter values close to those at the bifurcation. The subject of Section 3 is the Poincaré compactification of the system. In order to obtain a compactification where the dimension of the centre manifold of each steady state is at most one suitable blow-ups are carried out. This allows the qualitative nature of the dynamics near the steady states on the boundary of the compactification to be determined. In addition to this local information it is shown that if there is a heteroclinic cycle in the compactification it is asymptotically stable.

Section 4 goes on to study the global properties of the phase portrait. It is shown that for any values of the parameters there are solutions which are unbounded at late times and eventually monotone. The leading order asymptotics of these solutions is determined. The results of d'Onofrio on the uniqueness and stability of periodic solutions are reviewed and completed. It is proved that when the steady state is stable there exist no periodic solutions and all bounded solutions converge to the steady state at late times. It is also proved that when the steady state is unstable one of two mutually exclusive possibilities occurs. Either exactly one periodic solution exists and all bounded solutions converge to it at late times or no periodic solution exists and all solutions $(x(t), y(t))$ other than the steady state are unbounded. In the latter case for a given unbounded solution either $\lim_{t \rightarrow \infty} x(t) = \infty$ and $\lim_{t \rightarrow \infty} y(t) = 0$ and $x(t)$ and $y(t)$ are eventually monotone or $\limsup_{t \rightarrow \infty} x(t) = \limsup_{t \rightarrow \infty} y(t) = \infty$ and $\liminf_{t \rightarrow \infty} x(t) = \liminf_{t \rightarrow \infty} y(t) = 0$. The final section discusses what remains to be discovered about the Selkov model and how this model relates to other

models of glycolysis in the literature, in particular to a higher-dimensional model considered in [16].

This paper is based in part on the MSc thesis of the first author [1].

2 Basic facts

The system considered in what follows is the system (II) of [16]. It is

$$\frac{dx}{d\tau} = 1 - xy^\gamma, \quad (1)$$

$$\frac{dy}{d\tau} = \alpha y(xy^{\gamma-1} - 1). \quad (2)$$

It is written in dimensionless variables. The quantities x and y represent dimensionless concentrations of ATP and ADP, respectively, while τ is a dimensionless time variable. The aim is to study the future evolution of solutions of these equations for which x and y are positive. The parameter α is a positive real number. The parameter γ is a number greater than one and to avoid technical complications with differentiability properties it will be assumed here to be an integer.

The x -axis is an invariant manifold of the flow of the system (1)-(2) and the vector field is directed towards positive values of x on the y -axis. For each fixed α there is a unique positive steady state and it satisfies $x = y = 1$. Linearizing the system about this point leads to the Jacobi matrix

$$J = \begin{bmatrix} -1 & -\gamma \\ \alpha & \alpha(\gamma-1) \end{bmatrix}. \quad (3)$$

The determinant of J is α which is always positive. Thus the stability of the steady state is determined by the trace of J , which is $\alpha(\gamma-1)-1$. Let $\alpha_0 = \frac{1}{\gamma-1}$. Then for $\alpha < \alpha_0$ the trace of J is negative and the steady state is asymptotically stable while for $\alpha > \alpha_0$ the trace of J is positive and the steady state is a source. The steady state is hyperbolic for all $\alpha \neq \alpha_0$. For $\alpha = \alpha_0$ there is a pair of non-zero imaginary eigenvalues. If we consider the real part of the eigenvalues as a function of α then it passes through zero when $\alpha = \alpha_0$ and its derivative with respect to α at that point is non-zero. Thus a Hopf bifurcation occurs. More information can be obtained by computing the first Lyapunov number σ of the bifurcation and it turns out that it is feasible to do this by hand using the formula given in [15]. The result is $\sigma = -\frac{3\pi(\gamma-1)^{\frac{1}{2}}}{4}(\gamma^2(\gamma-1)+1) < 0$. Thus the Hopf bifurcation is non-degenerate and supercritical. This implies that for α slightly larger than α_0 there exists a unique periodic solution close to the steady state and that this periodic solution is stable and hyperbolic. For $\alpha = \alpha_0$ the steady state is not hyperbolic but it is topologically equivalent to a hyperbolic sink, since this is a property satisfied by all generic Hopf bifurcations.

3 The Poincaré compactification

The aim of this section is to investigate the ways in which the solutions of the Selkov system can tend to infinity at late times. The first step in doing this is to introduce two coordinate transformations, which we refer to as Case 1 and Case 2, respectively. In Case 1 we define $Y = \frac{y}{x}$ and $Z = \frac{1}{x}$. These variables are appropriate for investigating the case where x becomes large. The original variables can be recovered using the relations $x = \frac{1}{Z}$ and $y = \frac{Y}{Z}$. The result of the transformation is the system

$$\frac{dY}{d\tau} = \frac{1}{Z^\gamma}(\alpha Y^\gamma + Y^{\gamma+1} - \alpha Y Z^\gamma - Y Z^{\gamma+1}), \quad (4)$$

$$\frac{dZ}{d\tau} = \frac{1}{Z^{\gamma-1}}(Y^\gamma - Z^{\gamma+1}). \quad (5)$$

We introduce a new time variable t by $\frac{dt}{d\tau} = Z^{-\gamma}$ and obtain the system

$$\frac{dY}{dt} = \alpha Y^\gamma + Y^{\gamma+1} - \alpha Y Z^\gamma - Y Z^{\gamma+1}, \quad (6)$$

$$\frac{dZ}{dt} = Y^\gamma Z - Z^{\gamma+2}. \quad (7)$$

In Case 2 we define $X = \frac{x}{y}$ and $Z = \frac{1}{y}$. These variables are appropriate for investigating the case where y becomes large. The original variables can be recovered using the relations $x = \frac{X}{Z}$ and $y = \frac{1}{Z}$. The result of the transformation is the system

$$\frac{dX}{d\tau} = \frac{1}{Z^\gamma}(Z^{\gamma+1} - X - \alpha X^2 + \alpha X Z^\gamma), \quad (8)$$

$$\frac{dZ}{d\tau} = \frac{1}{Z^{\gamma-1}}(-\alpha X + \alpha Z^\gamma). \quad (9)$$

Introducing a new time variable as in Case 1 gives

$$\frac{dX}{dt} = Z^{\gamma+1} - X - \alpha X^2 + \alpha X Z^\gamma, \quad (10)$$

$$\frac{dZ}{dt} = -\alpha X Z + \alpha Z^{\gamma+1}. \quad (11)$$

Case 2 is easier to analyse than Case 1 and so we begin with that. The system extends smoothly to the boundary where $Z = 0$. This boundary is an invariant manifold for the extended flow and there X is decreasing except when $X = 0$. The origin in the new coordinates is a steady state, which we denote in what follows by P_1 . The linearization of the right hand side of the equations at P_1 has rank one and so there is a one-dimensional centre manifold there. The centre subspace is given by $X = 0$ and the centre manifold is of the form $X = h(Z)$ where h vanishes faster than linearly at the origin. The invariance of the centre manifold under the flow implies that $\dot{X} = h'(Z)\dot{Z}$. Putting this information into the evolution equations gives

$$Z^{\gamma+1} - h(Z) - \alpha(h(Z))^2 + \alpha(h(Z))Z^\gamma = h'(Z)[- \alpha(h(Z))Z + \alpha Z^{\gamma+1}].$$

If we expand this about $Z = 0$ we see that each of the terms other than $Z^{\gamma+1}$ and $h(Z)$ is negligible compared to one of these. It can be concluded that $h(Z) = Z^{\gamma+1} + o(Z^{\gamma+1})$. Substituting this relation into the evolution equation for Z shows that on the centre manifold $\frac{dZ}{dt} = \alpha Z^{\gamma+1} + o(Z^{\gamma+1})$. Hence the flow on the centre manifold is away from the steady state. For $X = 0$ the flow is into the positive region while between the line $Z = 0$ and the centre manifold the flow is topologically equivalent to part of a hyperbolic saddle, as follows from the reduction theorem [14]. In particular, no solution starting in the positive region can tend to the point P_1 at late times.

We now turn to Case 1. The system extends smoothly to the boundaries where $Y = 0$ and $Z = 0$ and these are invariant. The origin is a steady state. Otherwise the variable Z is decreasing when $Y = 0$ and the variable Y is increasing when $Z = 0$. The linearization at the steady state is identically zero and gives no information on the dynamics in a neighbourhood of that point. To go further a blow-up procedure is applied to the steady state. One way of doing this is to pass to polar coordinates. It turns out that a new steady state is produced where the linearization is zero. Introducing polar coordinates a second time then leads to a successful analysis of the dynamics in the case $\gamma = 2$, as was shown in [1]. It seems, however, that for $\gamma > 2$ this method becomes impractical. For this reason we instead use quasihomogeneous directional blow-ups [5]. This allows the analysis to be carried out for general values of γ in a unified way. It is necessary to do one such blow-up for each of the coordinates. They depend on two integers α and β which are determined with the help of a Newton diagram [5]. In the present case $\alpha = \gamma$ and $\beta = \gamma - 1$.

The first blow-up uses the transformation $(Y, Z) \mapsto (\bar{y}, \bar{z})$ with $(Y, Z) = (\bar{y}^\gamma, \bar{y}^{\gamma-1}\bar{z})$. We introduce a new time coordinate by $\frac{ds}{dt} = \frac{1}{\gamma}\bar{y}^{\gamma^2-\gamma}$. Then the system becomes

$$\frac{d\bar{y}}{ds} = \alpha\bar{y} + \bar{y}^{\gamma+1} - \alpha\bar{y}\bar{z}^\gamma - \bar{y}^\gamma\bar{z}^{\gamma+1}, \quad (12)$$

$$\begin{aligned} \frac{d\bar{z}}{ds} = & -\alpha(\gamma-1)\bar{z} - (\gamma-1)\bar{y}^\gamma\bar{z} + \alpha(\gamma-1)\bar{z}^{\gamma+1} \\ & - \bar{y}^{\gamma-1}\bar{z}^{\gamma+2} + \gamma\bar{y}^\gamma\bar{z}. \end{aligned} \quad (13)$$

Evidently the origin of coordinates is a hyperbolic saddle which we denote by P_2 . There is one other steady state P_3 on the boundary where $(\bar{y}, \bar{z}) = (0, 1)$. At P_3 there is a one-dimensional centre manifold, which will now be investigated. Introduce a new variable w by the relation $\bar{z} = 1 + w$. We get the system

$$\begin{aligned} \bar{y}' = & -\alpha\gamma\bar{y}w - \bar{y}^\gamma(1+w)^{\gamma+1} - \alpha\bar{y}[(1+w)^\gamma - 1 - \gamma w] + \bar{y}^{\gamma+1}, \\ w' = & \alpha\gamma(\gamma-1)w - \bar{y}^{\gamma-1} - (\gamma-1)\bar{y}^\gamma(1+w) \\ & + \alpha(\gamma-1)[(1+w)^{\gamma+1} - 1 - (\gamma+1)w] - \bar{y}^{\gamma-1}[(1+w)^{\gamma+2} - 1] \\ & + \gamma\bar{y}^\gamma(1+w). \end{aligned} \quad (14)$$

Important properties of the centre manifold are collected in the following lemma.

Lemma 1 On the centre manifold of P_3 the relations $w = \nu_1\bar{y}^{\gamma-1} + o(\bar{y}^{\gamma-1})$ and $\bar{y}' = -\nu_2\bar{y}^\gamma + o(\bar{y}^\gamma)$ hold with $\nu_1 = \frac{1}{\alpha\gamma(\gamma-1)}$ and $\nu_2 = \frac{\gamma}{\gamma-1}$.

Proof Consider first the case $\gamma \geq 3$. To start with it will be proved that

$$w = O(\bar{y}^{\gamma-1}), \quad w' = O(\bar{y}^\gamma). \quad (15)$$

For $\gamma \geq 3$ the centre subspace is given by $w = 0$. Thus on the centre manifold $w = h(\bar{y}) = O(\bar{y}^2)$ with $h'(\bar{y}) = o(1)$ and hence $\bar{y}' = O(\bar{y}^3)$. Differentiating the equation of the centre manifold gives $w' = h'(\bar{y})y'$ and it follows that $w' = O(\bar{y}^3)$. This completes the proof of (15) if $\gamma = 3$. If $\gamma \geq 4$ we substitute the information obtained so far into the evolution equation for w and obtain the statement that $w = O(\bar{y}^3)$. This implies that $\bar{y}' = O(\bar{y}^4)$ and that $w' = O(\bar{y}^4)$. Thus the proof of (15) is complete if $\gamma = 4$. For a general γ we can repeat the argument just given until (15) is obtained. Substituting the information obtained so far into the evolution equation for w shows that

$$w' = (\gamma - 1) \left\{ \alpha\gamma w - \frac{1}{\gamma-1} \bar{y}^{\gamma-1} + O(\bar{y}^\gamma) \right\}. \quad (16)$$

Combining this with (15) gives the first assertion of Lemma 1. Substituting the information already obtained back into the evolution equation for \bar{y} gives

$$\bar{y}' = -\alpha\gamma\bar{y}w - \bar{y}^\gamma + O(\bar{y}^{\gamma+1}) \quad (17)$$

which implies the second statement.

It remains to treat the case $\gamma = 2$. In that case the centre subspace is of the form $\bar{y} = \mu w$ with $\mu = 2\alpha$. It is convenient to introduce a new coordinate $v = \bar{y} - \mu w$, so that the centre subspace becomes $v = 0$. The centre manifold is of the form $v = h(\bar{y}) = O(\bar{y}^2)$. Thus $w = \frac{1}{\mu}\bar{y} + O(\bar{y}^2)$. This already gives the first assertion of Lemma 1 in the case $\gamma = 2$ since in that case $\nu_1 = \frac{1}{\mu}$. Substituting the equation of the centre manifold into the evolution equation for \bar{y} gives

$$\bar{y}' = -2\alpha\bar{y}w - \bar{y}^2 + O(\bar{y}^3) \quad (18)$$

which implies the second assertion in the case $\gamma = 2$. ■

The second blow-up uses the transformation $(Y, Z) \mapsto (\bar{y}, \bar{z})$ with $(Y, Z) = (\bar{y}\bar{z}^\gamma, \bar{z}^{\gamma-1})$. We introduce a new time coordinate by $\frac{ds}{dt} = \frac{1}{\gamma-1}\bar{z}^{\gamma^2-\gamma}$. Then the system becomes

$$\frac{d\bar{y}}{ds} = -\bar{y}^{\gamma+1}\bar{z}^\gamma + \bar{y}\bar{z}^{\gamma-1} + \alpha(\gamma-1)\bar{y}^\gamma - \alpha(\gamma-1)\bar{y}, \quad (19)$$

$$\frac{d\bar{z}}{ds} = \bar{y}^\gamma\bar{z}^{\gamma+1} - \bar{z}^\gamma. \quad (20)$$

On the boundary $\bar{z} = 0$ there is a steady state with coordinates $(1, 0)$. This is just another coordinate representation of the point P_3 and so it does not need to be analysed further. We denote the steady state at the origin of these coordinates by P_4 . At P_4 the \bar{z} -axis is a centre manifold. Any other centre manifold at that point is of the form $\bar{y} = h(\bar{z})$ where the function h vanishes to all orders for $\bar{z} \rightarrow 0$.

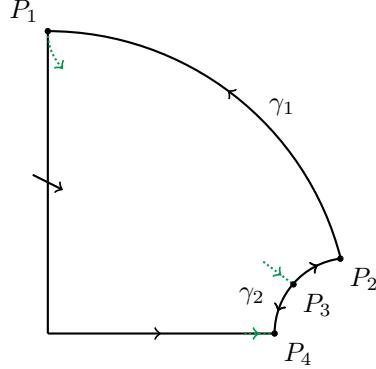


Figure 1: Poincaré compactification.

This analysis can be summarized as follows (cf. Fig. 1).

Lemma 2 There is a smooth mapping ϕ of the closed positive quadrant into itself mapping the axes into themselves with the following properties. The restriction of ϕ to the open quadrant is a diffeomorphism onto its image. This image is a region whose closure is a compact set bounded by intervals $[0, x_0]$ and $[0, y_0]$ on the x - and y -axes and two smooth curves γ_1 and γ_2 . The curve γ_1 joins the point $P_1 = (0, y_0)$ with a point P_2 in the positive quadrant. The curve γ_2 joins the point P_2 with the point $P_4 = (x_0, 0)$. The image of the dynamical system can be rescaled so as to extend smoothly to the closure of the image of ϕ in such a way that P_1 , P_2 and P_4 are steady states and γ_1 , γ_2 and the image of the x -axis are invariant manifolds. There is precisely one further steady state P_3 on the boundary of the image of ϕ and it belongs to the interior of γ_2 .

The notation in Lemma 2 has been chosen to fit with that in the preceding analysis. Using that analysis we obtain the following picture of the flow of the compactified system. Within the closure of the image of ϕ the points P_1 , P_2 and P_3 are saddles while P_4 is a sink. The flow on γ_1 is towards P_1 . The flow on γ_2 is away from P_3 , i.e. towards P_2 and P_4 . The flow on the horizontal axis is towards P_4 . The centre manifold of P_1 enters the image of ϕ and the flow on it is away from P_1 . The flow on the centre manifold of P_3 is towards P_3 . It is conceivable that the centre manifold of P_1 might approach P_3 , in which case it would coincide with the centre manifold of P_3 . In that case we say that there is an unbounded heteroclinic cycle. Note that a solution remains bounded towards the future on any finite time interval. For it is obvious that x remains bounded on such an interval and that y remains bounded follows by considering the Poincaré compactification.

It will now be shown that if a heteroclinic cycle at infinity exists it is asymptotically stable. This is based on a study of the passage of a solution close to the steady states belonging to the cycle. In fact it will be shown that this can be reduced to the study of the corresponding passages for some simplified dynamical systems, which will be examined first. The next lemma concerns the

case of a hyperbolic steady state.

Lemma 3 Consider the dynamical system $\dot{x} = -ax$, $\dot{y} = by$ for positive constants a and b . The solution which starts at the point $(1, y_0)$ reaches the line $y = 1$ at the point $(x_1, 1)$ with $x_1 = (y_0)^{\frac{a}{b}}$.

Proof The dynamical system can be solved explicitly. Substituting the initial and final conditions into the solution gives an expression for the time T required for the solution to go from the first to the second point. Substituting the expression for T back into the solution gives the final result. ■

Treating a non-hyperbolic steady state requires the following more complicated statement.

Lemma 4 Consider the dynamical system

$$\dot{x} = -ax(1 + \epsilon r_1(y, \epsilon)), \quad (21)$$

$$\dot{y} = by^k(1 + \epsilon r_2(y, \epsilon)), \quad (22)$$

where $a > 0$, $b > 0$, $k \geq 2$ and r_1, r_2 are bounded. Suppose that the solution which starts at the point $(1, y_0)$ reaches the line $y = 1$ at the point $(x_1, 1)$. For any fixed $\eta > 0$ and ϵ and y_0 sufficiently small the inequalities $x_1 \leq \exp(-[(1 - \eta)a/(b(k - 1))]y_0^{1-k})$ and $y_0 \leq C(-\log x_1)^{\frac{1}{1-k}}$ hold for a constant C .

Proof Suppose that the solution crosses the lines $x = 1$ and $y = 1$ for $t = 0$ and $t = T$, respectively. Given $\delta > 0$ there exists $\epsilon_0 > 0$ such that $\epsilon \leq \epsilon_0$ implies $|\epsilon r_1| \leq \delta$ and $|\epsilon r_2| \leq \delta$. It follows that $x_1 \leq e^{-a(1-\delta)T}$ and $y_0^{1-k} \leq 1 - b(1 - k)(1 + \delta)T$. Hence $T \geq \frac{1}{b(k-1)(1+\delta)}(y_0^{1-k} - 1)$ and if y_0 is small enough $x_1 \leq \exp\{-\frac{a(1-\delta)}{b(k-1)(1+\delta)^2}y_0^{1-k}\}$. For δ small enough $\frac{1-\delta}{(1+\delta)^2} \geq 1 - \eta$ and we get the desired inequality for x_1 . On the other hand $x_1 \geq e^{-a(1+\delta)T}$ and $y_0^{1-k} \geq 1 - b(1 - k)(1 - \delta)T$. Hence $T \leq \frac{1}{b(k-1)(1-\delta)}(y_0^{1-k} - 1)$ and $x_1 \geq \exp\{-\frac{a(1+\delta)}{b(k-1)(1-\delta)^2}y_0^{1-k}\}$. Hence $y_0 \leq C(-\log x_1)^{\frac{1}{1-k}}$.

The reduction of the case of more general dynamical systems to these explicit cases is a consequence of the following Lemma.

Lemma 5 (i) Consider a two-dimensional dynamical system which has a steady state at a point (x_*, y_*) which is a hyperbolic saddle, the eigenvalues of whose linearization at that point are $-a$ and b , where a and b are positive. Let (x'_0, y'_0) and (x'_1, y'_1) be points on the stable and unstable manifolds of (x_*, y_*) which are sufficiently close to (x_*, y_*) . Fix curves β_1 and β_2 through (x'_0, y'_0) and (x'_1, y'_1) which are transverse to the stable and unstable manifolds respectively. Let (x_0, y_0) be a point on β_1 sufficiently close to, but not equal to, (x'_0, y'_0) . By the Grobman-Hartman theorem this solution intersects β_2 and let (x_1, y_1) be the first such point it reaches. Let s_1 and s_2 be any smooth coordinates on β_1 and β_2 which vanish on the corresponding invariant manifolds and increase in the direction of the points (x_0, y_0) and (x_1, y_1) . Then for s_1 sufficiently small the inequality $s_2 \leq C(s_1)^{\frac{a}{b}}$ holds for a positive constant C .

(ii) Consider a two-dimensional dynamical system which has a steady state at a point (x_*, y_*) whose centre and stable manifolds have dimension one. Suppose that the non-zero eigenvalue is equal to $-a$, the flow on the centre manifold is away from (x_*, y_*) and the leading term in the evolution equation along the

centre manifold is bs^k for a coordinate s on that manifold. Define points, curves and coordinates on the curves as in part (i) except that the unstable manifold is replaced by the centre manifold and the Grobman-Hartman theorem by the reduction theorem. Then for any $\eta > 0$ the inequalities $s_2 \leq C \exp(-[(1 - \eta)a/b(k - 1)]s_1^{1-k})$ and $s_1 \leq C(-\log s_2)^{\frac{1}{1-k}}$ hold for s_1 sufficiently small and a positive constant C .

Proof (i) It follows from Sternberg's theorem [17] that there is a smooth diffeomorphism which transforms the situation described to the model situation in Lemma 3 and this implies the desired statement. Note in particular that a suitable scaling of the coordinates ensures that after the transformations the distance between the steady state and the points where the transverse sections cross the axis is one. Sternberg's theorem requires the hypothesis that there are no resonances. In the given case a resonance would mean an equation of the form $b = -na$ or $a = -nb$ for a positive integer n , which is clearly impossible. (ii) In this case we must replace Sternberg's theorem by Takens' theorem [18], allowing us to reduce the original system to the model system by a diffeomorphism of arbitrarily high finite differentiability. When there is only one non-zero eigenvalue the condition that there are no resonances is trivially fulfilled. In this case scaling the coordinate y allows ϵ to be made arbitrarily small.

Lemma 6 When for a given value of the parameter α in the Selkov system a heteroclinic cycle at infinity exists this cycle is stable.

Proof Consider curves β_i with the following properties. Let β_1 be a curve transverse to the unstable manifold of P_2 and sufficiently close to P_2 . Similarly let β_2 be transverse to the stable manifold of P_1 and close to P_1 , β_3 transverse to the centre manifold of P_1 and close to P_1 , β_4 transverse to the centre manifold of P_3 and close to P_3 , β_5 transverse to the unstable manifold of P_3 and close to P_3 and β_6 transverse to the stable manifold of P_2 and close to P_2 . For each i let s_i be a coordinate on β_i which is zero on the relevant invariant manifold and increases towards the interior of the image of ϕ . Each solution which crosses β_1 for a sufficiently small positive value of s_1 crosses each β_i at some parameter value $s_i = f_{i-1}(s_{i-1})$. It then crosses β_1 again at some value $s_1 = f_6(s_6)$. The aim is to obtain an estimate for the composition f of the f_i which shows that the iterates of f tend to zero. The simplest mappings to estimate are f_1 , f_3 and f_5 . These maps are smooth at zero and so by Taylor's theorem there is a constant C so that $f_1(s_1) \leq Cs_1$, $f_3(s_3) \leq Cs_3$ and $f_5(s_5) \leq Cs_5$. It is also relatively easy to estimate f_6 since P_2 is hyperbolic. Using part (i) of Lemma 5 we get the estimate $s_1 \leq Cs_6^{\gamma-1}$. The mapping f_2 can be estimated using part (ii) of Lemma 5 with the result that $s_3 \leq Ce^{-cs_2^{-\gamma}}$ for a constant c . A similar estimate holds for s_4 . To estimate f_4 we use the second conclusion of Lemma 4. This gives $s_5 \leq C(-\log s_4)^{-\frac{1}{\gamma-1}}$. Composing $f_4 \circ f_3 \circ f_2$ and simplifying leads to an estimate of the form $s_5 \leq Cs_2^{\gamma-1}$. Putting all these estimates together gives an inequality of the form $f(s_1) \leq Cs_1^\gamma$. Hence if s_1 is small the distance to the cycle is reduced by a fixed factor with each return and the cycle is stable.

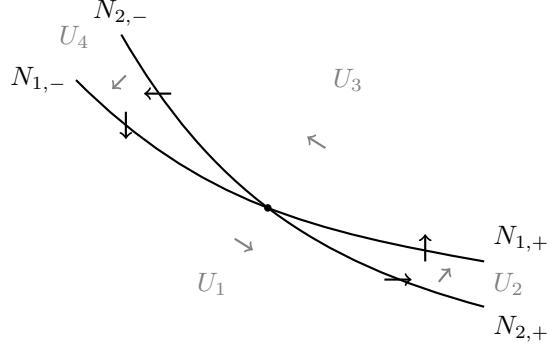


Figure 2: Nullclines.

4 The global phase portrait

To understand the global phase portrait of the Selkov system it is helpful to consider the nullclines N_1 and N_2 which are given by the equations $xy^\gamma = 1$ and $xy^{\gamma-1} = 1$, respectively. The relevant geometry is illustrated in Figure 2. The complement U of $N_1 \cap N_2$ has four connected components which can be distinguished by the signs of the right hand sides of the evolution equations. We denote them by U_1 , U_2 , U_3 and U_4 for the combinations of signs $(+, -)$, $(+, +)$, $(-, +)$ and $(-, -)$ respectively. The set $N_1 \setminus N_2$ has two connected components $N_{1,+}$ and $N_{1,-}$ which are distinguished by the sign of $x - 1$. Similarly $N_2 \setminus N_1$ two connected components $N_{2,+}$ and $N_{2,-}$. A solution which starts at a point of U_1 for $t = t_0$ must either stay in U_1 for $t \geq t_0$ or it must reach a point of $N_{2,+}$ after a finite time, after which it immediately enters U_2 . If it stays in U_1 then either it is bounded and then it converges to $(1, 1)$ for $t \rightarrow \infty$ or it is unbounded and in the latter case $\lim_{t \rightarrow \infty} x(t) = \infty$ and $\lim_{t \rightarrow \infty} y(t) = 0$. A solution which starts in U_2 for $t = t_0$ must reach a point of $N_{1,+}$ after a finite time, after which it immediately enters U_3 . If a solution which starts in U_3 for $t = t_0$ were unbounded while remaining in U_3 then it would approach P_1 in the Poincaré compactification for $t \rightarrow \infty$ and this has already been ruled out in the last section. Thus it must either converge to $(1, 1)$ as $t \rightarrow \infty$ or reach $N_{2,-}$ after a finite time, after which it immediately enters U_4 . A solution which starts in U_4 for $t = t_0$ must reach a point of $N_{1,-}$ after a finite time, after which it immediately enters U_1 . Putting all this information together we get the following result

Lemma 7 Each solution of the Selkov system has one of the following behaviours in the future.

- (i) it converges to $(1, 1)$ for $t \rightarrow \infty$ while staying in U_1 or U_3
- (ii) $\lim_{t \rightarrow \infty} x(t) = \infty$ and $\lim_{t \rightarrow \infty} y(t) = 0$
- (iii) it cycles indefinitely between the regions U_i .

A similar analysis can be done in the past time direction. Note that it is not possible that a solution is always in U_3 before a certain time because no solution

can approach the curve γ_2 in the Poincaré compactification towards the past. Thus we have the following result

Lemma 8 Each solution of the Selkov system has one of the following behaviours in the past.

- (i) it converges to $(1, 1)$ for $t \rightarrow -\infty$ while staying in U_1 or U_3
- (ii) it starts on the y -axis
- (iii) $\lim_{t \rightarrow -\infty} x(t) = 0$ and $\lim_{t \rightarrow -\infty} y(t) = \infty$
- (iv) it cycles indefinitely between the regions U_i .

If a solution cycles indefinitely in the future then it passes through points of the form $(1, y)$ with $y < 1$ at an infinite increasing sequence of times t_i . Let $y_i = y(t_i)$. It follows from Poincaré-Bendixson theory that the sequence y_i is monotone. If the sequence is constant then the solution is periodic. Otherwise the sequence is strictly monotone. If it is monotone decreasing then it must tend to some $y_{-,*} > 0$. That this number is strictly positive follows from the fact that in the Poincaré compactification all solutions which start with $x = 1$ and y sufficiently small converge to P_4 for $t \rightarrow \infty$. Poincaré-Bendixson theory further shows that either $(1, y_{-,*})$ lies on a periodic solution or on a heteroclinic cycle at infinity. If the sequence y_n is monotone increasing then $y_{-,*}$ lies on a periodic solution. This discussion tells us that to classify the asymptotic behaviour of all solutions of the Selkov system for given values of γ and α it suffices to know how many periodic solutions there are, whether there is a heteroclinic cycle at infinity and what the stability properties of the periodic solutions and the heteroclinic cycle are. Note that every periodic solution must contain a point of the form $(1, y)$ with $y < 1$.

For any values of the parameters in the Selkov system there are unbounded solutions where x gets large and y gets small at late times and which have an asymptotic behaviour which can be determined. This is the content of the following theorem. These are exactly the solutions which belong to Case (ii) in Lemma 7.

Theorem 1 There exists a positive number $\epsilon > 0$ such that any solution of the Selkov system with initial data $x(0) = x_0$ and $y(0) = y_0$ which satisfies $x_0 > \epsilon^{-1}$ and $x_0 y_0^\gamma < \epsilon$ has the late-time asymptotics

$$x(\tau) = \tau(1 + o(1)), \quad (23)$$

$$y(\tau) = y_1 e^{-\alpha\tau}(1 + o(1)). \quad (24)$$

for a constant y_1 . There exists a solution, unique up to time translation, which has the asymptotic behaviour

$$x(\tau) = \tau(1 + o(1)), \quad (25)$$

$$y(\tau) = \tau^{-\frac{1}{\gamma-1}}(1 + o(1)). \quad (26)$$

Proof Any solution which starts close to the point P_4 converges to that point as $t \rightarrow \infty$. Using this information in the evolution equations for \bar{y} and \bar{z} allows them to be integrated in leading order. First we have

$$\frac{d\bar{z}}{ds} = -\bar{z}^\gamma(1 + o(1)) \quad (27)$$

and hence

$$\bar{z}(s) = [(\gamma - 1)s]^{-\frac{1}{\gamma-1}}(1 + o(1)). \quad (28)$$

Putting this information back into the evolution equation allows the error term $o(1)$ to be improved to $O(s^{-\frac{1}{\gamma-1}})$. The relation

$$\frac{d\bar{y}}{ds} = \bar{y}(-(\gamma - 1)\alpha + o(1)) \quad (29)$$

shows that \bar{y} decays exponentially as $t \rightarrow \infty$. Using this fact and substituting the improved version of (28) into the evolution equation for \bar{y} gives

$$\frac{d\bar{y}}{ds} = \bar{y} \left[-(\gamma - 1)\alpha + \frac{1}{\gamma - 1}s^{-1} + q(s) \right] \quad (30)$$

where the function q is integrable on intervals of the form $[s_0, \infty)$. Integrating this last relation gives

$$\bar{y}(s) = As^{\frac{1}{\gamma-1}}e^{-\alpha(\gamma-1)s}(1 + o(1)) \quad (31)$$

for a constant A . It follows from the estimates obtained up to now that the image of each such solution is tangent to the \bar{z} -axis at P_4 and is therefore a centre manifold at P_4 . It remains to transform these formulae from the variables (\bar{y}, \bar{z}, s) to the variables (x, y, τ) . Note that $\frac{ds}{dt} = \frac{1}{\gamma-1}Z^\gamma$ and $\frac{d\tau}{dt} = Z^\gamma$. The coordinate s is only defined up to an additive constant and if this constant is chosen appropriately it follows that $\tau = (\gamma - 1)s$. Using the expressions (27) and (29) and the definitions of the coordinate transformations gives the first part of the theorem. The solution mentioned in the second part of the theorem is a solution on the centre manifold of P_3 . Integrating the equation for \bar{y} in Lemma 1 gives $\bar{y}(s) = (\nu_2(\gamma - 1)s)^{-\frac{1}{\gamma-1}}(1 + o(1)) = (\gamma s)^{-\frac{1}{\gamma-1}}(1 + o(1))$. Putting this into the equation for w given there leads to $w(s) = \nu_1(\gamma s)^{-1}(1 + o(1))$. Now $\frac{ds}{dt} = \gamma^{-1}(\gamma s)^{-\gamma}(1 + o(1))$. On the other hand $\frac{d\tau}{dt} = Z^\gamma = (\gamma s)^{-\gamma}(1 + o(1))$. Thus we can choose s so that $\tau = \gamma s$. Using the definitions of the coordinate transformation gives the second part of the theorem. ■

To obtain more information about periodic solutions it is helpful to do the following changes of variables. Introduce a time variable by $\frac{dt}{d\tau} = y^\gamma$ and define $v = \frac{dy}{dt}$. Let $f(y) = 1 - \alpha(\gamma - 1)y^{-\gamma}$ and $g(y) = \alpha(y - 1)y^{-\gamma}$. Denote by F the primitive of f which vanishes for $y = 1$. Introduce variables by $\tilde{x} = y - 1$ and $\tilde{y} = -v - F(y)$. Dropping the tildes gives the system

$$\dot{x} = -y - F(x), \quad (32)$$

$$\dot{y} = g(x). \quad (33)$$

We are interested in solutions of this for which $x > -1$ and where there is no restriction on y . It will be shown that under suitable circumstances the system (32)-(33) defined on a region of the form $(x_0, \infty) \times \mathbb{R}$ has at most one periodic solution and that if such a solution exists it is asymptotically stable.

This implies a corresponding result for the Selkov system. Next we discuss some auxiliary results used in the proof of these statements.

Theorem 2 Suppose that the system (32)-(33) satisfies the following conditions:

- (i) $xg(x) > 0$ when $x \neq 0$ and $g'(0) > 0$
- (ii) $F(0) = 0$ and $f(0) < 0$ where $f(x) = F'(x)$
- (iii) There exists a real number α such that the function $f_1(x) = f(x) + \alpha g(x)$ has zeroes $x_1 < 0$ and $x_2 > 0$ with $f_1(x) \leq 0$ for $x_1 < x < x_2$ and there exists x_* with $f_1(x_*) > 0$ and $(x_*, 0)$ in the interior of L_1 .
- (iv) All the limit cycles are contained in the interval $x_3 \leq x \leq x_4$, where $x_3 < x_1 < 0 < x_2 < x_4$ and the function f_1/g does not decrease for $x_3 \leq x \leq x_1$ and $x_2 \leq x \leq x_4$.
- (v) all the limit cycles contain the interval $x_1 \leq x \leq x_2$ on the x -axis.

Then the system has at most one limit cycle and if one exists it is stable.

This theorem is closely related to a result stated in Kuang and Freedman [13], which is in turn related to a result of Cherkas and Zhilevich [2]. The differences between Theorem 2 and Theorem 3.1 in [13], apart from the different notation, are as follows. For simplicity the function $\phi(y)$ in [13] has been set to y and the constant β has been set to zero. The condition (4) of the theorem of [13] has been replaced by the condition (4)'. The condition $g'(0) > 0$ has been added since without it the proof in [13] is incomplete. The conditions that x_1 and x_2 are simple zeroes have been replaced by the assumption concerning the existence of the point x_* . This is because we could not see how to prove that Theorem 3.2 of [13] follows from Theorem 3.1, a claim made without proof in the paper.

Proof of Theorem 2 We give only an outline of the proof. More details can be found in [13] and [1]. The unique steady state of the system is at the origin. It follows from the condition $f(0) < 0$ that this steady state is unstable. The proof of the theorem is by contradiction and we assume that there exist two limit cycles L_1 and L_2 . It is necessarily the case that the steady state is in the interior of the Jordan curves defined by the solutions and that one of them is in the interior of the other. Suppose that L_1 is in the interior of L_2 . To examine the stability of the solutions the Poincaré stability criterion [15] will be used. It involves the quantity obtained by integrating the divergence of the vector field defining the dynamical system over the solution. We call this the Poincaré quantity. Let A and A_1 be the points on L_1 and L_2 with $x = x_2$ and $y > 0$ and let D and D_1 be the points with $x = x_2$ and $y < 0$. Let E and E_1 be the points on L_2 with the same y coordinates as A and D . Integrate the differential form $(f_1/g)dy$ over the boundary of the region R_1 bounded by the line segments AE and DE_1 and the parts of L_1 and L_2 joining A with D and E with E_1 . This results in the sum of two integrals along the curved parts of the boundary. On the other hand, by Stokes' theorem this integral is equal to the integral of a non-negative quantity over R_1 . Thus we get an inequality relating the integrals of f_1 along certain parts of L_1 and L_2 . We can do a similar construction starting from $x = x_1$ with points B, B_1, C, C_1, K, K_1 corresponding to A, A_1, D, D_1, E, E_1 . Next we replace $(f_1/g)dy$ in this construction by $f_1/(y + F(x))dx$ and integrate over regions with corners C, D, C_1, D_1 and A, B, A_1, B_1 . Putting these computations together shows that the integral of f_1 over L_2 is equal to its integral over L_1 .

plus contributions from the parts of L_2 joining E with A_1 , B_1 with K , K_1 with C_1 and D_1 with E_1 . In fact these extra contributions are non-negative. This is because f_1 is non-negative on the relevant intervals. Moreover it is positive on the interval $[x_*, x_4]$, due to the monotonicity of f_1/g . It follows that the integral of f_1 over L_2 is strictly greater than its integral over L_1 . It can be shown that the integrals of g over L_1 and L_2 are zero so that the integral of f over L_2 is strictly greater than its integral over L_1 . The divergence of the vector field defining the system is equal to $-f$ and so the Poincaré quantity for L_2 is less than that for L_1 . Since $g'(0) > 0$ the steady state is a hyperbolic source. Hence there must be an innermost periodic solution and there must be a solution starting near the steady state and converging to this periodic solution for $t \rightarrow \infty$. As a consequence it is a limit cycle and we choose it as L_1 . It follows that L_1 is stable from the inside and that the Poincaré quantity is non-positive and hence the integral of $-f$ over L_1 also non-positive. Hence the Poincaré quantity for L_2 must be negative. If L_1 were stable on the outside we could choose L_2 to be the closest limit cycle outside it. L_2 would have to be unstable on the inside, a contradiction. Thus L_1 is semistable (stable on one side and unstable on the other). It can be shown by perturbing the system using the method of rotated vector fields [6] that if this were the case there would be a system where the above contradiction is obtained. It follows that no second limit cycle can exist and if one limit cycle does exist it is stable. ■

This theorem can be used to prove another where the opaque condition involving the function f_1 is removed from the hypotheses. It is a modification of a theorem of Zhang [19].

Theorem 3 Suppose that the system (32)-(33) satisfies the conditions (i) and (ii) of Theorem 2 and that all limit cycles are contained in the interval $a < x < b$ where $a < 0 < b$ and $f(x)/g(x)$ is non-decreasing when x increases in $a < x < 0$ and $0 < x < b$. Then the conclusion of Theorem 2 holds.

Proof The condition that f_1/g is non-decreasing is equivalent to the condition that f/g is non-decreasing. The requirement on the region where this function is non-decreasing in the hypotheses of Theorem 3 implies that in the hypotheses of Theorem 2. We need to show that α can be chosen so that f_1 has zeroes with the properties required in condition (iii) of Theorem 2. Following [19] let \tilde{x} be the smallest value of x attained at a point of L_1 and define $\alpha = -\frac{f(\tilde{x})}{g(\tilde{x})}$. Then $f_1(\tilde{x})$ is zero by construction and \tilde{x} is a zero of f_1 with $\tilde{x} < 0$. Let x_1 be the largest value of x for which $f_1(x) = 0$ for $\tilde{x} \leq x \leq x_1$. Since $f_1(0) < 0$ we can conclude that $x_1 < 0$. We will now show that f_1 has a second zero $x_2 > x_1$ which is in the interior of L_1 . If this were not the case then L_1 would lie completely in the region where f_1 is non-positive, as will now be shown. For $\frac{f_1(x_1)}{g(x_1)} = 0$ and we have assumed that $\frac{d}{dx} \left(\frac{f_1(x)}{g(x)} \right)$ is non-negative on the interval $[x_1, 0]$. Thus $\frac{f_1(x)}{g(x)} \geq 0$ and $f_1(x) \leq 0$ on that interval. At the origin $\frac{f_1(x)}{g(x)} < 0$ and so in fact $\frac{f_1(x)}{g(x)}$ is negative on an interval beginning at x_1 and extending beyond $x = 0$. This establishes the claim concerning L_1 . It can be concluded that the integral of f_1 over L_1 is negative. For under the given assumptions f_1 is non-positive

everywhere on L_1 and negative at some point of L_1 . The Poincaré criterion then implies that L_1 is unstable in the interior. This contradicts the fact that there are solutions starting near the steady state which converge to L_1 . Thus in reality f_1 has a zero $x_2 > 0$ in the interior of L_1 . In fact f_1 must become positive for some $x_* > 0$ with $(x_*, 0)$ in the interior of L_1 since otherwise the contradiction would still occur. Choosing x_2 to be the smallest $x > 0$ for which f_1 is negative on $(0, x_2)$ ensures that the hypotheses of Theorem 3 are satisfied.

■

Theorem 3 can be used to obtain a result about the Selkov system following d'Onofrio.

Theorem 4 [3] If the steady state in the Selkov model is unstable for a given value of α then there is at most one limit cycle and if one exists it is asymptotically stable.

In his proof of this theorem d'Onofrio cites the Theorem of Kuang and Freedman. However the theorem he formulates (Proposition 1 of his paper) is not equivalent to the corresponding result stated by Kuang and Freedman (Theorem 3.2 of their paper). In [13] the assumptions include the condition that $\phi(y) + F(x)$ is defined for all $x \in (-\infty, \infty)$. In the case $\phi(y) = y$ of interest here this means that F would have to be defined on the whole real line. This condition is not assumed in d'Onofrio's Proposition 1 and indeed it does not hold in the situation of the application to the Selkov model. It is this apparent gap which motivates our discussion of Theorem 2 and Theorem 3 above. That discussion shows that the extra assumption is not necessary. When this has been clarified a calculation done by d'Onofrio showing the monotonicity of f/g in the case of the Selkov model suffices to show that Theorem 4 follows from Theorem 3.

Theorem 4 can be used to obtain information about the long-time behaviour of solutions in the case that the steady state is unstable. Using Poincaré-Bendixson theory it follows that the ω -limit set in the Poincaré compactification of any solution which cycles indefinitely in the future (case (iii) of Lemma 7) is either the unique periodic solution or the heteroclinic cycle at infinity. We know as a result of Lemma 6 and Theorem 4 that both the periodic solution and the heteroclinic cycle are stable whenever they exist. If both existed then by continuity there would have to be a periodic solution between them and this would contradict Theorem 4. Thus we obtain the following result

Theorem 5 In the case $\alpha > \alpha_0$ exactly one of the following three situations occurs.

- (i) The centre manifolds of P_1 and P_3 coincide so that there is a heteroclinic cycle at infinity. Any solution which starts below this centre manifold converges to P_4 as $t \rightarrow \infty$ while any solution other than the steady state which starts above this manifold converges to the heteroclinic cycle at infinity as $t \rightarrow \infty$.
- (ii) The centre manifolds of P_1 and P_3 do not coincide. There exists a unique periodic solution. Any solution which starts below the centre manifold of P_3 converges to P_4 as $t \rightarrow \infty$ while any solution other than the steady state which starts above this manifold converges to the periodic solution as $t \rightarrow \infty$.
- (iii) The centre manifolds of P_1 and P_3 do not coincide. Any solution other

than the steady state which does not lie on the centre manifold of P_3 converges to P_4 as $t \rightarrow \infty$.

We next turn to the case $\alpha \leq \alpha_0$. For this case d'Onofrio proved a result (Proposition 5.3 of his paper) as an application of a Theorem of Hwang and Tsai [9]. It was shown in [1] that one of the conditions in his result is satisfied automatically for $\alpha \leq \alpha_0$, thus showing that the result can be generalized. We do so in Theorem 7 below. The following theorem is closely related to Theorem 2.1 of [9].

Theorem 6 Suppose that in the system (32)-(33) defined on the region $(r_1, r_2) \times \mathbb{R}$ the following conditions hold:

- (i) there exists $\lambda \in (r_1, r_2)$ such that $g'(\lambda) > 0$ and $(x - \lambda)g(x) > 0$ for all $x \in (r_1, r_2) \setminus \{\lambda\}$.
- (ii) there exist constants $a, b \in \mathbb{R}$ such that the function $f(x) + ag(x) + bg(x)F(x)$ is non-negative on (r_1, r_2) and not identically zero.

Then the system has no periodic solutions.

The relation of this statement to that of Theorem 2.1 of [9] is that y has been replaced by $-y$, the function ϕ has been taken to be equal to one and the function $\pi(y)$ equal to y . Under these circumstances conditions (A1), (A2) and (A4) of the theorem of [9] are satisfied automatically and the remaining conditions reduce to (i) and (ii) above. In the case of the Selkov system the interval can be chosen to be $(-1, \infty)$ and condition (i) is satisfied by $\lambda = 0$. Thus it only remains to consider the condition (ii) and in fact it suffices to choose $b = 0$.

Substituting the values of f and g in the case of the Selkov system into the positivity condition in (ii) gives

$$(x+1)^\gamma + a\alpha(x+1) + \alpha(1-\gamma-a) \geq 0. \quad (34)$$

Let $\beta = \alpha(\gamma-1)$, so that the stability condition is $\beta \leq 1$. Choose $a = -\gamma(\gamma-1)$. Then

$$\begin{aligned} & (x+1)^\gamma + a\alpha(x+1) + \alpha(1-\gamma-a) \\ &= (x+1)^\gamma - \alpha\gamma(\gamma-1)(x+1) + \alpha(\gamma-1)^2 \end{aligned} \quad (35)$$

$$= (x+1)^\gamma - \beta\gamma(x+1) + \beta(\gamma-1). \quad (36)$$

The last function has a global minimum in $(0, \infty)$. This occurs at the point $x+1 = \beta^{\frac{1}{\gamma-1}}$. Substituting this back into the function shows that the minimum is $(\gamma-1)\beta(1 - \beta^{\frac{1}{\gamma-1}}) \geq 0$. Thus this choice of a has the desired property and Theorem 6 can be applied to the Selkov system.

Theorem 7 If the positive steady state of the Selkov system is stable then there are no periodic orbits and every solution either tends to the positive steady state or tends to P_3 or P_4 at late times.

Proof The first statement follows from Theorem 6. There cannot be a heteroclinic cycle at infinity since the fact that both the cycle and the steady state are stable would mean that there would have to be a periodic solution between them. The only remaining possibilities for the ω -limit set of a solution are those listed in the theorem.

5 Further remarks

The main question which has been left open by the analysis in this paper is whether there are parameter values for which there are solutions of the Selkov model which exhibit unbounded oscillations. This is the question, whether case (i) in Theorem 5 ever occurs. To prove this it would suffice to show that there is a value of α for which cases (ii) and (iii) of Theorem 5 are ruled out. To rule out case (ii) for a given value of α it would be enough to show that the system admits a Lyapunov function or a Dulac function.

The model (1)-(2) which we have studied in this paper was originally derived by Selkov from a five-dimensional model, the system (4) in [16], by a singular limiting process. This limit will now be considered. The variables s_1 , s_2 , x_1 , x_2 and e in the larger model are the concentrations of the substrate ATP, the product ADP, the activated enzyme, the complex between the activated enzyme and the substrate and the inactive enzyme, respectively. With some assumptions about the nature of these reactions and assuming mass action kinetics the following system of equations is obtained.

$$\frac{ds_1}{dt} = v_1 - k_1 s_1 x_1 + k_{-1} x_2, \quad (37)$$

$$\frac{ds_2}{dt} = k_2 x_2 - \gamma k_3 s_2^\gamma e + \gamma k_{-3} x_1 - k s_2, \quad (38)$$

$$\frac{dx_1}{dt} = -k_1 s_1 x_1 + (k_{-1} + k_2) x_2 + k_3 s_2^\gamma e - k_{-3} x_1, \quad (39)$$

$$\frac{dx_2}{dt} = k_1 s_1 x_1 - (k_{-1} + k_2) x_2, \quad (40)$$

$$\frac{de}{dt} = -k_3 s_2^\gamma e + k_{-3} x_1. \quad (41)$$

Note that $e_0 = e + x_1 + x_2$ is a conserved quantity (total amount of enzyme) and this can be used to eliminate e from the first four evolution equations and discard the evolution equation for e . This reduces the system to four equations.

Next dimensionless variables are introduced by defining $\sigma_1 = \frac{k_1 s_1}{k_{-1} + k_2} s_1$, $\sigma_2 = \left(\frac{k_3}{k_{-3}}\right)^{\frac{1}{\gamma}} s_2$, $u_1 = \frac{x_1}{e_0}$, $u_2 = \frac{x_2}{e_0}$, $\theta = \frac{e_0 k_1 k_2}{k_{-1} + k_2} t$. This leads to the system

$$\frac{d\sigma_1}{d\theta} = \nu - \frac{k_2 + k_{-1}}{k_2} u_1 \sigma_1 + \frac{k_{-1}}{k_2} u_2, \quad (42)$$

$$\frac{d\sigma_2}{d\theta} = \eta \left(u_2 - \gamma \frac{k_{-3}}{k_2} \sigma_2^\gamma (1 - u_1 - u_2) + \gamma \frac{k_{-3}}{k_2} u_1 - \chi \sigma_2 \right), \quad (43)$$

$$\epsilon \frac{du_1}{d\theta} = u_2 - \sigma_1 u_1 + \frac{k_{-3}}{k_2 + k_{-1}} (\sigma_2^\gamma (1 - u_1 - u_2) - u_1), \quad (44)$$

$$\epsilon \frac{du_2}{d\theta} = \sigma_1 u_1 - u_2. \quad (45)$$

Explicit expressions for the parameters ϵ , ν , η and χ can be found in [1] or [10]. Formally setting $\epsilon = 0$ in the equations (44) and (45) gives $u_2 = \sigma_1 u_1$ and

$u_1 = \frac{\sigma_2^\gamma}{1 + \sigma_2^\gamma + \sigma_1 \sigma_2^\gamma}$ and substituting these relations into the evolution equations for σ_1 and σ_2 gives

$$\frac{d\sigma_1}{d\theta} = \nu - \left(\frac{\sigma_1 \sigma_2^\gamma}{1 + \sigma_2^\gamma + \sigma_1 \sigma_2^\gamma} \right), \quad (46)$$

$$\frac{d\sigma_2}{d\theta} = \eta \left(\frac{\sigma_1 \sigma_2^\gamma}{1 + \sigma_2^\gamma + \sigma_1 \sigma_2^\gamma} - \chi \sigma_2 \right). \quad (47)$$

It can be shown that solutions of this system of two equations can be approximated by solutions of the four-dimensional system (42)-(45) using geometric singular perturbation theory [12]. To do this we need to examine the transverse eigenvalues. This means computing the matrix of partial derivatives of the right hand sides of the evolution equations for u_1 and u_2 with respect to the variables u_1 and u_2 and evaluating the result for $\epsilon = 0$. A computation shows (for details see [1]) that this matrix has determinant $\frac{k_{-3}}{k_2+k_{-1}}(\sigma_1 \sigma_2^\gamma + \sigma_2^\gamma + 1) > 0$ and trace $-\sigma_1 - \frac{k_{-3}}{k_2+k_{-1}}(\sigma_2^\gamma + 1) - 1 < 0$. Hence both eigenvalues have negative real parts and the limit is well-behaved.

Selkov claims that starting from the assumptions of Higgins and supposing on biological grounds that certain quantities are small leads to system (46)-(47) with $\gamma = 1$. This system has the unfortunate property that it does not admit periodic solutions. This can be proved using the fact that $\frac{1+\sigma_2^\gamma+\sigma_1\sigma_2^\gamma}{\sigma_1\sigma_2}$ is a Dulac function.

Consider now the additional rescaling $x = \frac{\nu^{\gamma-1}}{\chi^\gamma} \sigma_1$, $y = \frac{\chi}{\nu} \sigma_2$ and $\tau = \left(\frac{\nu}{\chi}\right)^\gamma \theta$.

In the equations for $\frac{dx}{d\tau}$ and $\frac{dy}{d\tau}$ with parameters ν , χ and η we can replace η by $\alpha = \frac{\eta \chi^{\gamma+1}}{\nu^\gamma}$. Then the limit $\nu \rightarrow 0$ is regular. In this limit we obtain the system (1)-(2) studied in this paper. This means that when the Selkov system has a periodic solution (which is then known to be hyperbolic and stable) the system (46)-(47) will also have a periodic solution for certain values of the parameters which is hyperbolic and stable. These are parameters for which χ is of order one, ν is small and η is small. Geometric singular perturbation theory then allows us to conclude that the system (42)-(45) possesses a periodic solution which is hyperbolic and stable for ϵ small.

Note that there is an alternative mathematical model of glycolysis due to Goldbeter and Lefever [7] which appears to explain some of the experimental observations better than that of Selkov. For a discussion of this issue we refer to [10]. The model of [7] exhibits intricate dynamical behaviour which has been investigated using advanced methods of geometric singular perturbation theory in [11]. The Goldbeter-Lefever model was also studied mathematically in [4].

Acknowledgement We thank Hussein Obeid for drawing our attention to the possible relevance of quasihomogeneous directional blow-ups for this problem.

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