Global Dynamics of a Piecewise Smooth System for Brain Lactate Metabolism

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GLOBAL DYNAMICS OF A PIECEWISE SMOOTH SYSTEM FOR BRAIN LACTATE METABOLISM

J.-P. FRANÇOISE[1] , HONGJUN JI[1], DONGMEI XIAO[2], JIANG YU[2]

Abstract. In this article, we study a piecewise smooth dynamical system inspired by a previous reduced system modeling compartimentalized brain metabolism. The piecewise system allows the introduction of an autoregulation induced by a feedback of the extra-cellular or capillary Lactate concentrations on the Capillary Blood Flow. New dynamical phenomena are uncovered and we discuss existence and nature of two equilibrium points, attractive segment, boundary equilibrium and periodic orbits depending of the Capillary Blood Flow.

1. Introduction

The nonlinear system of ODEs defined as follows:

$$\begin{aligned} \frac{dx}{dt} &= J - T\left(\frac{x}{k+x} - \frac{y}{k'+y}\right) \qquad T,\ k,\ k',\ J > 0, \\ \frac{dy}{dt} &= F(L-y) + T\left(\frac{x}{k+x} - \frac{y}{k'+y}\right) \qquad F,\ L > 0, \end{aligned} \tag{1.1}$$

where $(x, y) \in \mathbb{R}^2_+$ was first proposed and studied as a model for coupled energy metabolism between Neuron-Astrocyte and Capillary by [Costalat, Françoise, Guillevin, Lahutte-Auboin] (see [4, 10, 11, 12]). In this context, $x = x(t)$ and $y = y(t)$ correspond to the Lactate concentrations in an interstitial (i.e. extra-cellular) domain and in a Capillary domain, respectively. Furthermore, the nonlinear term $T(\frac{x}{k+x} - \frac{y}{k'+y})$ stands for a co-transport through the Brain-Blood Boundary (see [9]). The forcing term J represents the Lactate flux in the intracellular domain. Furthermore the input F stands for the Capillary Blood Flow through capillaries from arterial to venous, and L represents arterial Lactate. In these previous articles, different time scales were considered on the evolution of the two variables and the asymptotics of fast-slow dynamical systems was used (see also a more recent reference [6]). Here, our results are independent of this scaling. Recently, in [13, 7], a PDE's system obtained by adding diffusion of Lactate was introduced. The authors proved existence and uniqueness of nonnegative solutions and obtained linear stability results. In system (1.1) the forcing term J and input terms F are assumed frozen.

In [12], the physiological domain was discussed in terms of bounds on the Lactate concentrations x and y. It is natural to push further this study with the introduction of a kind of autoregulation of the system induced by a feedback (for instance of Astrocytes on the Capillary) of the two concentrations (x or y) on the Capillary Blood Flow F. This is discussed in this article where the autoregulation is represented by a piecewise variation of

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F such as

$$F(x,y)=\begin{cases}F^{+} & when \quad (x,y)\in\Omega^{+}\\ F^{-} & when \quad (x,y)\in\Omega^{-}\end{cases}$$

We suppose that F^+ and F^- are different positive real numbers and $\Omega^+\cup\Omega^-=\mathbb{R}^2_+$, $\Omega^+\cap\Omega^-=\varnothing$. We further denote the system $\mathcal{V}_F$:

$$\begin{aligned}\frac{dx}{dt}&=J-T(\frac{x}{k+x}-\frac{y}{k'+y}),\\ \frac{dy}{dt}&=F(x,y)(L-y)+T(\frac{x}{k+x}-\frac{y}{k'+y}).\end{aligned}\tag{1.2}$$

If $\Omega^+=\mathbb{R}^2_+$ and $\Omega^-=\varnothing$ (i.e $F=F^+$ everywhere), we denote system (1.2) as $\mathcal{V}_{F^+}$. If $\Omega^-=\mathbb{R}^2_+$ and $\Omega^+=\varnothing$ (i.e $F=F^-$ everywhere), we denote system (1.2) as $\mathcal{V}_{F^-}$. System $\mathcal{V}_{F^+}$ and system $\mathcal{V}_{F^-}$ are the two special cases of system (1.2) and they have same topological properties of trajectories as system (1.2). From a modeling point of view, the relevance of considering a piecewise constant function is a first step/approximation to analyze more general inputs considered in experimental protocols (Hu and Wilson [8]).

The article is organized as follows: we discuss two different choices of domains in (3.1) and (4.1). In section 2, we give some general properties of system (1.1) which are common to systems $\mathcal{V}_{F^\pm}$. In sections 3 and 4, we show our main theorems from a point of view of dynamics. Usual terminology adopted in the field of Piecewise Smooth Dynamical Systems (PWS) are used here (including Pseudo Equilibrium, Sliding Section, Sawing Section, Boundary Equilibrium). See for instance the textbook [3].

2. Qualitative analysis of system (1.1)

In this section, we study dynamics of system (1.1) in $\mathbb{R}^2_+$ for a given constant F [12, 4, 5]. In particular, we investigate the existence of some orbits of systems $\mathcal{V}_{F^\pm}$ in $\mathbb{R}^2_+$ for given two constants F^+ and F^-, respectively. This will help us to study global dynamics of the piecewise system (1.2) in $\mathbb{R}^2_+$.

Proposition 1. *System (1.1) is cooperative in $\mathbb{R}^2_+$ and all solutions of system (1.1) are positive if the initial points are in the interior of the first quadrant $\mathbb{R}^2_+$.*

Proof. Let

$$\begin{aligned}f_1&:=J-T(\tfrac{x}{k+x}-\tfrac{y}{k'+y}),\\ f_2&:=F(L-y)+T(\tfrac{x}{k+x}-\tfrac{y}{k'+y}).\end{aligned}$$

Then the Jacobian matrix A of the vector field of system (1.1) is

$$A=\begin{pmatrix}-\frac{Tk}{(x+k)^2} & \frac{Tk'}{(y+k')^2}\\ \frac{Tk}{(x+k)^2} & -F-\frac{Tk'}{(y+k')^2}\end{pmatrix}.$$

The off-diagonal entries of matrix A are nonnegative. Such a matrix is called a Metzler matrix. A vector field such that its Jacobian matrix is a Metzler matrix is said to be cooperative (see [16]). Note that system $\mathcal{V}_F$ is defined in $\mathbb{R}^2_+$ and satisfies the following condition: $\forall(x,y)\in bd(\mathbb{R}^2_+)$: $f_1(0,y)\geq 0$ and $f_2(x,0)\geq 0$. Hence system $\mathcal{V}_F$ is positive. □

Lemma 1. *System (1.1) has at most an equilibrium point in $\mathbb{R}^2_+$ denoted $s^0(x^0,y^0)$ if and only if $T>J[1+\frac{1}{k'}(L+\frac{J}{F})]$, where $x^0=k(\frac{J}{T}+\frac{y^0}{k'+y^0})/(1-(\frac{J}{T}+\frac{y^0}{k'+y^0}))$ and $y^0=L+\frac{J}{F}$. And the unique equilibrium $s^0(x^0,y^0)$ of system (1.1) is a global asymptotically stable node in $\mathbb{R}^2_+$ if $T>J[1+\frac{1}{k'}(L+\frac{J}{F})]$, otherwise, all orbits of system (1.1) are positively unbounded in $\mathbb{R}^2_+$.*

Proof. The existence of equilibrium points of system (1.1) in $\mathbb{R}^2_+$ is given by nonnegative solutions of $f_1 = 0$ and $f_2 = 0$. An elementary computation yields that equations $f_1 = 0$ and $f_2 = 0$ have at most one solution (x^0, y^0), and both $x^0 > 0$ and $y^0 > 0$ if and only if $T > J[1 + \frac{1}{k'}(L + \frac{J}{F})]$, where

$$x^0 = \frac{k(\frac{J}{T} + \frac{y^0}{k'+y^0})}{1 - (\frac{J}{T} + \frac{y^0}{k'+y^0})},\ y^0 = L + \frac{J}{F}.$$

Consider the Jacobian matrix of system (1.1) at equilibrium point $s^0(x^0, y^0)$, denoted by

$$A_{|s^0} = \begin{pmatrix} -\dfrac{Tk}{(x^0+k)^2} & \dfrac{Tk'}{(y^0+k')^2} \\ \dfrac{Tk}{(x^0+k)^2} & -F - \dfrac{Tk'}{(y^0+k')^2} \end{pmatrix}.$$

It is easy to check that the matrix $A_{|s^0}$ has two real distinct eigenvalues λ_1 and λ_2 which satisfy

$$\begin{aligned} &\lambda_1 + \lambda_2 = -\tfrac{Tk}{(x^0+k)^2} - F - \tfrac{Tk'}{(y^0+k')^2} < 0, \\ &\lambda_1\lambda_2 = \tfrac{FTk}{(x^0+k)^2} > 0, \\ &\delta = [F + \tfrac{Tk}{(x^0+k)^2} + \tfrac{Tk'}{(y^0+k')^2}]^2 - 4F\tfrac{Tk}{(x^0+k)^2} > 0. \end{aligned}$$

Hence, the unique equilibrium point $s^0(x^0, y^0)$ of system (1.1) is a locally stable node.

Note that the divergence of system (1.1) is

$$-\frac{Tk}{(x+k)^2} - F - \frac{Tk'}{(y+k')^2} < 0, \quad \forall (x,y) \in \mathbb{R}^2_+.$$

By Bendixson's criterion, we know that system (1.1) has no limit cycle in $\mathbb{R}^2_+$ for any positive parameters F.

To prove that the unique equilibrium point $s^0(x^0, y^0)$ of system (1.1) is globally stable in $\mathbb{R}^2_+$, we only need to prove that all solutions of system (1.1) are bounded in $\mathbb{R}^2_+$.

Given a sufficiently large positive number M,$M > x^0$, we construct a trapezoidal area Ω_M (see Fig.1(b)) surrounded by four line segments:

$$\begin{aligned} &\ell_1 = \{(x,y) | x = 0, 0 \le y \le M + y^0\}, \\ &\ell_2 = \{(x,y) | x = M, 0 \le y \le y^0\}, \\ &\ell_3 = \{(x,y) | 0 \le x \le M, y = 0\}, \\ &\ell_4 = \{(x,y) | 0 \le x \le M, y = -(x - M) + y^0\}. \end{aligned}$$

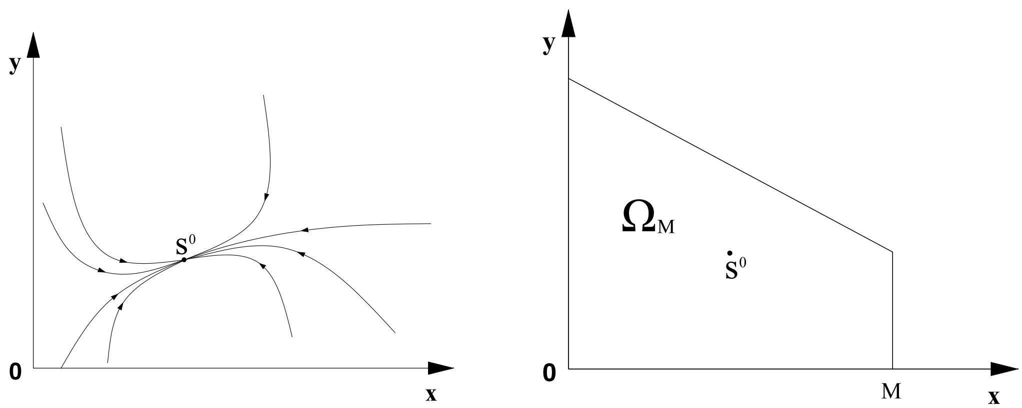
Clearly, the restriction of the vector field (1.1) on the boundary of Ω_M is $\frac{d(\ell_1)}{dt}|_{(1.1)} > 0$, $\frac{d(\ell_3)}{dt}|_{(1.1)} > 0$, furthermore,

$$\begin{aligned} \frac{d(\ell_2)}{dt}|_{(1.1)} &= J - T(\frac{M}{k+M} - \frac{y}{k'+y}) \le J - T(\frac{M}{k+M} - \frac{y^0}{k'+y^0}) < 0, \\ \frac{d(\ell_4)}{dt}|_{(1.1)} &= F(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}) + \left(J - T(\frac{x}{k+x} - \frac{y}{k'+y})\right) \\ &= J + F(L-y) \le J + F(L - y^0) = 0. \end{aligned}$$

Thus, Ω_M is a positively invariant subset of the system (1.1) in $\mathbb{R}^2_+$, and all solutions of system (1.1) in $\mathbb{R}^2_+$ enter the convex set Ω_M as t tends to $+\infty$ as system (1.1) has a unique equilibrium point in $\mathbb{R}^2_+$.

On the other hand, if system (1.1) has no equilibrium points in $\mathbb{R}^2_+$, then all solutions of system (1.1) are unbounded as t tends to $+\infty$ since the direction of vector field of system (1.1) on the positive x-axis (y-axis) is from down (left, resp.) to up (right, resp.) and system (1.1) has no closed orbits in $\mathbb{R}^2_+$.

Below, Fig.1(a) is a preliminary sketch of orbits of system (1.1) when $s^0 \in \mathbb{R}^2_+$.



(a) Orbits of system (1.1) when $s^0 \in \mathbb{R}^2_+$ (b) The convex set Ω_M

FIGURE 1

$\square$

Lemma 2. *When the system (1.1) has a unique equilibrium point $s^0 \in \mathbb{R}^2_+$, there exist two characteristic directions at s^0, denoted v_1 and v_2, where*

$$\begin{aligned} v_1 &= \left(\tfrac{1}{2a}(F+b-a) - \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right), \\ v_2 &= \left(\tfrac{1}{2a}(F+b-a) + \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right), \end{aligned} \tag{2.1}$$

with $a = \frac{Tk}{(x^0+k)^2}$ and $b = \frac{Tk'}{(y^0+k')^2}$. In addition, all the orbits tend to s^0 along characteristic direction v_2 except two orbits along characteristic direction v_1.

Proof. Define

$$A_{|s^0} = \begin{pmatrix} -\dfrac{Tk}{(x^0+k)^2} & \dfrac{Tk'}{(y^0+k')^2} \\ \dfrac{Tk}{(x^0+k)^2} & -F-\dfrac{Tk'}{(y^0+k')^2} \end{pmatrix} := \begin{pmatrix} -a & b \\ a & -F-b \end{pmatrix},$$

where $a = \frac{Tk}{(x^0+k)^2}$ and $b = \frac{Tk'}{(y^0+k')^2}$. Hence

$$\lambda_1 = -\frac{1}{2}(a+b+F) - \frac{1}{2}\sqrt{(a+b+F)^2-4aF},$$

$$\lambda_2 = -\frac{1}{2}(a+b+F) + \frac{1}{2}\sqrt{(a+b+F)^2-4aF},$$

and

$$\begin{aligned} v_1 &= \left(\tfrac{1}{2a}(F+b-a) - \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right), \\ v_2 &= \left(\tfrac{1}{2a}(F+b-a) + \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right). \end{aligned}$$

Clearly, we have:

$$\frac{1}{2a}(F+b-a)-\frac{1}{2a}\sqrt{(F+b-a)^2+4ab}<0,$$
$$\frac{1}{2a}(F+b-a)+\frac{1}{2a}\sqrt{(F+b-a)^2+4ab}>0.$$

Furthermore, $|\lambda_1|>|\lambda_2|$, this implies that v_2 is the strong characteristic direction. As s^0 is a globally asymptotically stable after Lemma 1, then we can conclude that all the orbits tends to s^0 along characteristic direction v_2 except two orbits along characteristic direction v_1. □

In the following we consider two systems $\mathcal{V}_{F^+}$ and $\mathcal{V}_{F^-}$. From Lemma 1, we know that system $\mathcal{V}_{F^+}$ (or system $\mathcal{V}_{F^-}$) has a unique equilibrium at $s^+(x^+,y^+)$ ($s^-(x^-,y^-)$, resp.) in $\mathbb{R}^2_+$ if $T>J[1+\frac{1}{k'}(L+\frac{J}{F^+})]$ ($T>J[1+\frac{1}{k'}(L+\frac{J}{F^-})]$, resp.), where

$$x^{\pm}=\frac{k(\frac{J}{T}+\frac{y^{\pm}}{k'+y^{\pm}})}{1-(\frac{J}{T}+\frac{y^{\pm}}{k'+y^{\pm}})},\qquad y^{\pm}=L+\frac{J}{F^{\pm}}. \tag{2.2}$$

We consider the following problem of the initial value

$$\begin{aligned}\frac{dx}{dt}&=J-T(\frac{x}{k+x}-\frac{y}{k'+y}),\\ \frac{dy}{dt}&=F^+(L-y)+T(\frac{x}{k+x}-\frac{y}{k'+y}),\\ x(0)&=x^-,y(0)=y^-.\end{aligned} \tag{2.3}$$

Then there exists a unique orbit $\varphi^+(t;s^-)$ of system (2.3) passing through the point s^-. If $T>J[1+\frac{1}{k'}(L+\frac{J}{F^+})]$, then

$$\lim_{t\to+\infty}\varphi^+(t;s^-)=s^+$$

by Lemma 1. Similarly, we can consider the problem of system $\mathcal{V}_{F^-}$ with the initial values $x(0)=x^+,y(0)=y^+$, which has a unique orbit $\varphi^-(t;s^+)$ passing through the point s^+. If $T>J[1+\frac{1}{k'}(L+\frac{J}{F^-})]$, then

$$\lim_{t\to+\infty}\varphi^-(t;s^+)=s^-.$$

The following proposition gives the tangential direction of the orbit $\varphi^+(t;s^-)$ ($\varphi^-(t;s^+)$) at the point s^- (s^+, resp.), which is important to qualitative analysis of system (1.2).

Proposition 2. *(i) The tangential direction of orbit $\varphi^+(t;s^-)$ at the point s^- is $d_1=(0,\frac{J(F^--F^+)}{F^-})$, which is vertical.*
(ii) The tangential direction of orbit $\varphi^-(t;s^+)$ at the point s^+ is $d_2=(0,\frac{J(F^+-F^-)}{F^-})$, which is vertical.

Proof. We substitute s^- into system $\mathcal{V}_{F^+}$ and obtain

$$\begin{aligned}\frac{dx}{dt}&=J-T(\frac{x^-}{k+x^-}-\frac{y^-}{k'+y^-}),\\ \frac{dy}{dt}&=F^+(L-y^-)+T(\frac{x^-}{k+x^-}-\frac{y^-}{k'+y^-}).\end{aligned}$$

Notice that $T(\frac{x^-}{k+x^-} - \frac{y^-}{k'+y^-}) = J$ and $y^- = L + \frac{J}{F^-}$ by the expression of s^-. An elementary computation yields that

$$\begin{aligned}\frac{dx}{dt} &= 0,\\ \frac{dy}{dt} &= \frac{J(F^- - F^+)}{F^-}.\end{aligned}$$

This leads to the conclusion (i). Using the similar arguments, we can obtain the conclusion (ii). □

From Lemma 1 and the expressions (2.2), we can obtain the relative position of points s^+ and s^- in R^2_+.

In the following, we only discuss the cases where the orbits are bounded in $\mathbb{R}^2$. Therefore, the conditions $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^{\pm}})]$ always hold in the next two sections.

3. Global dynamics of system (1.2) when F depends on the Lactate concentration of Capillary domain

In this section we consider that the piecewise input function $F(x, y)$ depends only on y, the concentration inside the Capillary domain , and F follows:

$$F(x,y) = \begin{cases} F^+ & y < h \\ F^- & y \geq h \end{cases} \tag{3.1}$$

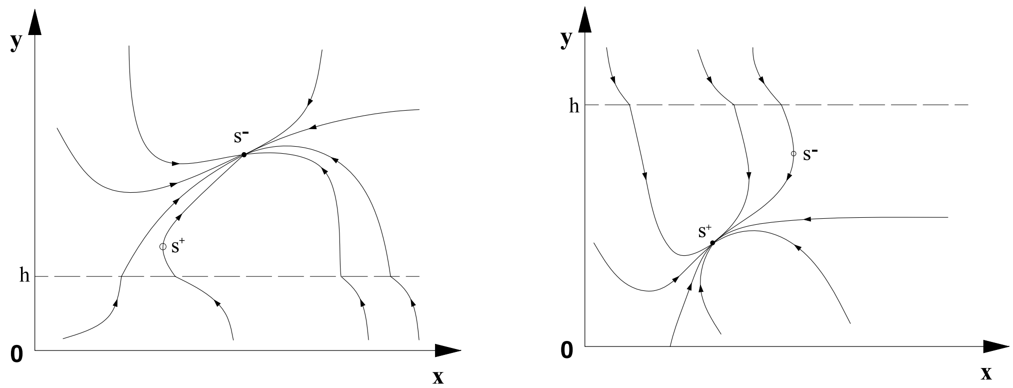
Here h is a positive threshold and the Capillary blood flow F changes between F^+ and F^-. So $\Omega^+ = \mathbb{R}_+ \times [0, h)$ and $\Omega^- = \mathbb{R}_+ \times [h, +\infty)$. We call $\overline{\Omega^+} \cap \overline{\Omega^-} = \{(x, y)|x \geq 0, y = h\}$ the **separator line**.

Theorem 1. *Suppose $F^+ > F^-$ ($F^- > F^+$, respectively) and $F(x, y)$ follows (3.1), then the piecewise system (1.2) displays one equilibrium point in $\mathbb{R}^2_+$ if $h \leqslant L + \frac{J}{F^+}$ or $h > L + \frac{J}{F^-}$.*

(i) *When $h \leqslant L + \frac{J}{F^+}$ ($h \leqslant L + \frac{J}{F^-}$, respectively), s^- (s^+, respectively) is the unique globally stable equilibrium point of the piecewise system (1.2).*
(ii) *When $h > L + \frac{J}{F^-}$ ($h > L + \frac{J}{F^+}$, respectively), s^+ (s^-, respectively) is the unique globally stable equilibrium point of the piecewise system (1.2).*

Proof. For $h \leqslant L + \frac{J}{F^+}$, we know that the orbits of the piecewise system in Ω^+ tend to the equilibrium points s^+ but s^+ is in Ω^-. On the other hand, the orbits in Ω^- tend to the point s^-. Therefore, all orbits in $\mathbb{R}^2_+$ tend to s^-. Combining Proposition 2 and Lemma 4, we draw a rough phase portrait where the piecewise system has one equilibrium point for $F^+ > F^-$ and $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^{\pm}})]$. Fig.2(a) is the case when $h \leqslant L + \frac{J}{F^+}$ and Fig.2(b) is the case when $h > L + \frac{J}{F^-}$.

For the case when $h > L + \frac{J}{F^+}$, using the the same arguments for statement (ii), we finish the proof.



(a) The case when $h \leqslant L + \frac{J}{F^+}$ and $F^+ > F^-$ (b) The case when $h > L + \frac{J}{F^-}$ and $F^+ > F^-$

FIGURE 2. Piecewise system (1.2) has one globally asymptotically stable equilibrium point in $\mathbb{R}^2_+$

$\square$

Lemma 3. *For system $\mathcal{V}_{F^\pm}$, there exists a unique tangent point $c^\pm$ with the separator line $y = h$, denoted by $c^\pm = (\frac{k\beta^\pm}{1-\beta^\pm}, h)$, where $\beta^\pm = \frac{h}{k'+h} - \frac{F^\pm(L-h)}{T}$. In addition, if $h \in (h_1^\pm, h_2^\pm)$, where $h_1^\pm = -\frac{1}{2}(k' - L - \frac{T}{F^\pm}) + \frac{1}{2}\sqrt{(k' - L - \frac{T}{F^\pm})^2 + 4Lk'}$ and $h_2^\pm = -\frac{1}{2}(k' - L) + \frac{1}{2}\sqrt{(k' - L)^2 + 4(Lk' + \frac{Tk'}{F^\pm})}$, then $c^\pm \in \mathbb{R}^2_+$.*

Proof. Compute

$$F^+(L-h) + T(\frac{x}{k+x} - \frac{h}{k'+h}) = 0, \tag{3.2}$$

we obtain

$$x = \frac{k(\frac{F^+(L-h)}{T} + \frac{h}{k'+h})}{1 - (\frac{F^+(L-h)}{T} + \frac{h}{k'+h})} := \frac{k\beta^+}{1-\beta^+},$$

which is the abscissa of tangent point with separator line $y = h$ for subsystem with $F = F^+$. The abscissa of the tangent point c^+ is positive if and only if $0 < \beta^+ < 1$. That requires

$$0 < \frac{h}{k'+h} + \frac{F^+(L-h)}{T} < 1,$$

which is equivalent to:

$$\begin{cases} h^2 + (k' - L - \frac{T}{F^+})h - Lk' < 0, \\ h^2 + (k' - L)h - Lk' - \frac{Tk'}{F^+} > 0. \end{cases}$$

A straightforward calculation further shows that

$$\eta_1^+ < h < \eta_2^+,$$

where $\eta_1^+ = \min\{h_1^+, h_2^+\}$ and $\eta_2^+ = \max\{h_1^+, h_2^+\}$ with

$$h_1^+ = \frac{1}{2}(k' - L - \frac{T}{F^+}) + \frac{1}{2}\sqrt{(k' - L - \frac{T}{F^+})^2 + 4Lk'},$$

and

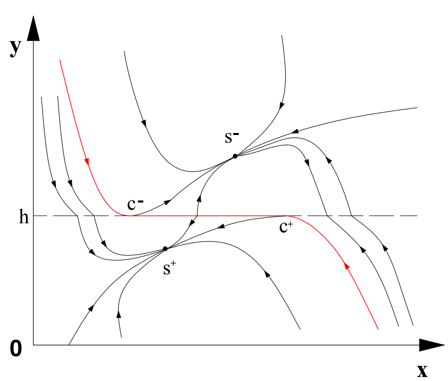
$$h_2^+ = -\frac{1}{2}(k' - L) + \frac{1}{2}\sqrt{(k' - L)^2 + 4(Lk' + \frac{Tk'}{F^+})}.$$

Hence, for $h \in (\eta_1^+, \eta_2^+)$, then $c^+ \in \mathbb{R}_+^2$. Similar calculus for system $\mathcal{V}_{F^-}$, we can find η_1^- and η_2^-. □

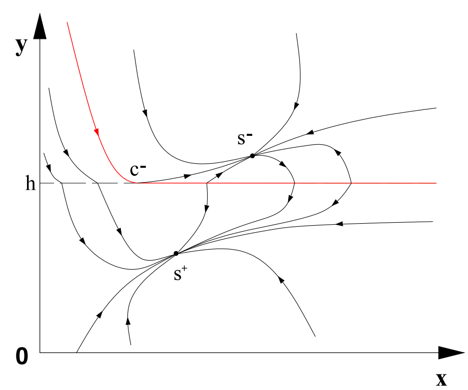
Theorem 2. *Suppose $F^+ > F^-$ and $F(x,y)$ follows (3.1), Assume that $L + \frac{J}{F^+} < h \leqslant L + \frac{J}{F^-}$, then the piecewise system (1.2) displays two equilibrium points s^+ and s^- in $\mathbb{R}_+^2$. In addition, there exist two non intersecting invariant domains $\mathcal{A}^+$ and $\mathcal{A}^-$ which are separated by a boundary curve in $\mathbb{R}_+^2$; all the orbits of system (1.2) in $\mathcal{A}^+$ ($\mathcal{A}^-$ respectively) tend to s^+ (s^- respectively). In other words, $\mathcal{A}^+$ ($\mathcal{A}^-$ respectively) is the basin of attraction of the attracting node s^+ (s^- respectively).*

Proof. By lemma 1 and 2, under the conditions $F^+ > F^-$ and $L + \frac{J}{F^+} < h \leqslant L + \frac{J}{F^-}$, there exist two equilibrium points s^+ and s^- in $\mathbb{R}_+^2$ such that $s^+ \ll s^-$. By lemma 3, there is a tangent point $c^- \in \mathbb{R}_+^2$ if $y^+ = L + \frac{J}{F^+} < h \leqslant h_2^+$ see Fig.3(a) and the tangent point $c^+ \notin \mathbb{R}_+^2$ if $h_2^+ < h \leqslant y^- = L + \frac{J}{F^-}$ see Fig.3(b). In Fig.3, $\mathcal{A}^-$ is the region above the boundary curve in $\mathbb{R}_+^2$ and $\mathcal{A}^+$ is the region under the boundary curve in $\mathbb{R}_+^2$. It is clear that $s^+ \in \mathcal{A}^+$ and $s^- \in \mathcal{A}^-$.

Furthermore, s^+ and s^- are both stable node in each domain by lemma 1. Hence, $\mathcal{A}^+$ and $\mathcal{A}^-$ are the two invariant regions. Finally, if $y^+ < h \leqslant h_2^+$, c^- and c^+ are on the boundary line and c^- is on the left side of c^+. If $h_2^+ < h \leqslant y^-$, then c^- is on the boundary line and c^+ does not exist. So there are two types of boundary curve as showed in Fig.3. In case $y^+ < h \leqslant h_2^+$, the boundary is a union of a segment of the tangent solution to c^-, the segment $c^- < x < c^+$ on the line $y = h$, and a segment of the tangent solution to c^+. In case $h_2^+ < h \leqslant y^-$, the boundary is a union of a segment of the tangent solution to c^- and of the semi-line $c^- < x < +\infty$ on the line $y = h$.



(a) The case $y^+ < h \leqslant h_2^+$



(b) The case $h_2^+ < h \leqslant y^-$

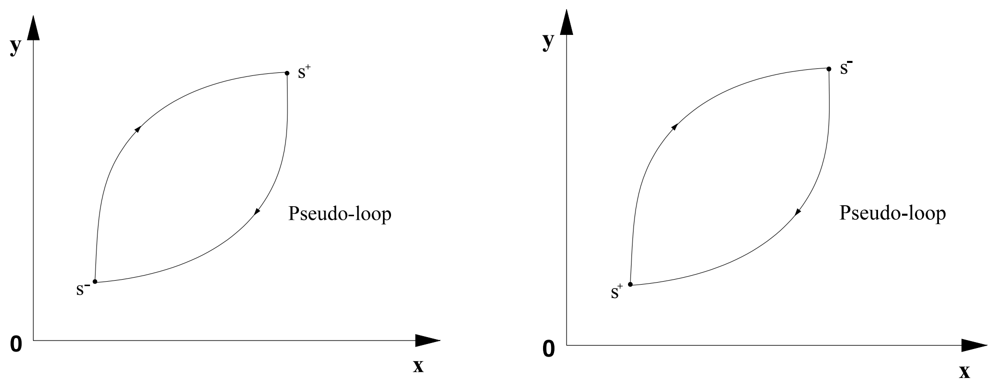
FIGURE 3. Basins of attraction separated by the boundary curve

□

Lemma 4. (i) *If $F^+ > F^- > 0$ and $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^-})]$, then $0 \ll s^+ \ll s^-$, i.e. $0 < x^+ < x^-$ and $0 < y^+ < y^-$.*

(ii) *If* $F^- > F^+ > 0$ *and* $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^+})]$*, then* $0 \ll s^- \ll s^+$*, i.e.* $0 < x^- < x^+$ *and* $0 < y^- < y^+$*.*

In xy-plane we draw the orbits $\varphi^+(t; s^-)$ and $\varphi^-(t; s^+)$ depending on Lemma 2. There would be a loop which links the points s^+ and s^- by $\varphi^\pm$, that we call **pseudo-loop** since it is not an orbit of system $\mathcal{V}_F$ for any constant F. However, this pseudo-loop play an important role on qualitative analysis of system (1.2). There exist two types of pseudo-loop according to the relative values of F^- and F^+ as shown below in Fig.4.



(a) Pseudo loop when $F^- > F^+$

(b) Pseudo loop when $F^+ > F^-$

FIGURE 4

Theorem 3. *Suppose* $F^- > F^+$ *and* $F(x, y)$ *follows* (3.1)*, and assume furthermore that* $L + \frac{J}{F^-} < h \leq L + \frac{J}{F^+}$*, then the piecewise system* (1.2) *displays a sliding section on line* $y = h$*, which is a attracting set. In this case,* s^+ *and* s^- *are pseudo equilibrium points and the system has no periodic orbits in* $\mathbb{R}^2_+$*.*

Proof. First, noticing from Lemma 4 that s^+, s^- are located at the different side of the separator line $y = h$ for $L + \frac{J}{F^-} < h \leq L + \frac{J}{F^+}$, we claim that the pseudo-loop transversally intersect $y = h$. Otherwise, $\varphi^+(t; s^-)$ or $\varphi^-(t; s^+)$ has to be double tangent to $y = h$, which is a contradiction with Lemma 3. Hence, the tangent points $c^\pm$ of the vector fields $\mathcal{V}_{F^\pm}$ on $y = h$ are outside of the pseudo-loop. Moreover, c^+ is at the left side of $\varphi^+(t; s^-)$, while c^- is at the right side of $\varphi^-(t; s^+)$. In fact, observing the stable node $s^+ = (x^+, y^+)$, we can deduce from (2.1) that $\dot{y}|_{s^+} = 0$ and there is a unique point c^+ near s^+ on $y = h = y^+ - \epsilon$, where ϵ is a small positive number, such that $\dot{y}|_{c^+} = 0$. Obviously, c^+ is at the left side of $\varphi^+(t; s^-)$. Then we get a tangent-point curve of c^+ for $L + \frac{J}{F^-} < h \leq L + \frac{J}{F^+}$, which does not intersect $\varphi^+(t; s^-)$. Similarly, it can be checked for c^-.

Next, by a simple qualitative analysis, we obtain that there is a sliding section $[c^+, c^-]$ on $y = h$, which is an attractor set of the piecewise system (1.2).

Finally, if there is a piecewise periodic orbit of (1.2), then it has to go around the section $[c^+, c^-]$ and the pseudo-loop, but it is impossible because $\varphi^-(t; s^+)$ tends to a infinity singular point as $t \to -\infty$. See following Fig.5:

$\square$

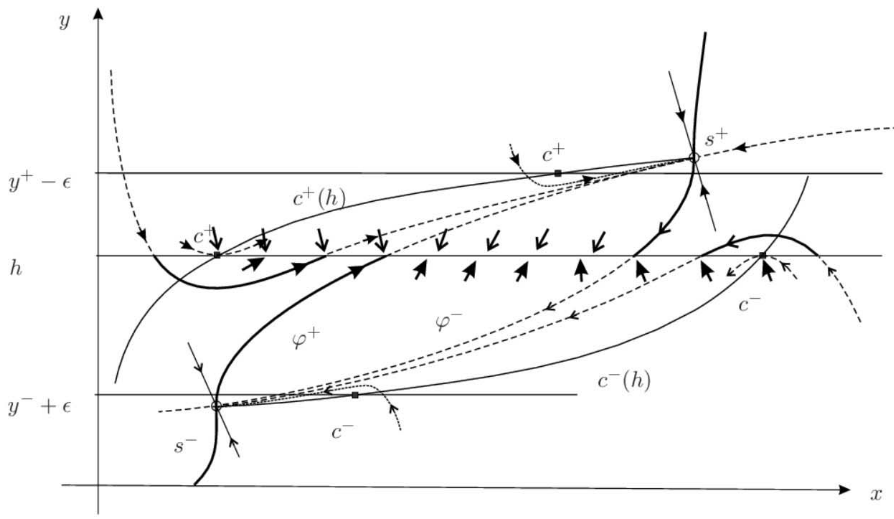


FIGURE 5. Piecewise system (1.2) has non equilibrium point but an attracting set in $\mathbb{R}^2_+$ with $F^- > F^+$

4. Global dynamics of system (1.2) when F depends on the Lactate concentration of the interstitial domain

We consider in this section the case where the input function $F(x, y)$ depends only on the concentration of the interstitial domain x. Here h is a real positive value and F follows

$$F(x,y) = \begin{cases} F^+ & x < h \\ F^- & x \geqslant h \end{cases} \tag{4.1}$$

Here $\Omega^+ = [0, h) \times \mathbb{R}_+$ and $\Omega^- = [h, +\infty) \times \mathbb{R}_+$. So $\{(x, y)|x = h, y \geq 0\}$ is the separator line in this section.

Theorem 4. *Suppose $F^+ > F^-$ ($F^- > F^+$, respectively) and $F(x, y)$ follows (4.1), then the piecewise system (1.2) has one equilibrium point in $\mathbb{R}^2_+$ if $h \leqslant x^+$ or $h > x^-$. In addition,*

(i) *When $h \leqslant x^+$ ($h \leqslant x^-$, respectively), s^- (s^+, respectively) is the unique globally stable equilibrium point of the piecewise system (1.2).*

(ii) *When $h > x^-$ ($h > x^+$, respectively), s^+ (s^-, respectively) is the unique globally stable equilibrium point of the piecewise system (1.2).*

In both cases, the equilibrium point is an attractive node.

Proof. The proof follows the lines of the proof of Theorem 1. □

Lemma 5. *System $\mathcal{V}_{F^\pm}$ displays a same unique tangent point $c = (h, \frac{k'\alpha}{1-\alpha})$ with the separator line $x = h$ for $h > 0$, where $\alpha = \frac{h}{k+h} - \frac{J}{T}$. In addition, if $h \in (\max\{\eta, 0\}, +\infty)$ with $\eta = \frac{Jk}{J-T}$, then $c \in \mathbb{R}^2_+$.*

Proof. The equation

$$J - T(\frac{h}{k+h} - \frac{y}{k'+y}) = 0,$$

yields

$$y = \frac{k'(\frac{h}{k+h} - \frac{J}{T})}{1 - (\frac{h}{k+h} - \frac{J}{T})},$$

which is the ordinate of tangent point c with separator line $x = h$ of both systems $\mathcal{V}_{F^{\pm}}$. The condition $0 < \alpha < 1$, which is equivalent to:

$$0 < \frac{h}{k+h} - \frac{J}{T} < 1,$$

and is necessary and sufficient to the ordinate of the tangent point be positive. A straightforward calculation shows that

$$\eta < h < +\infty,$$

where

$$\eta = \frac{Jk}{J-T}.$$

And we have also $h > 0$. So we can conclude that for $h \in (\max\{h_3, 0\}, +\infty)$, then $c \in \mathbb{R}^2_+$. □

Theorem 5. *Suppose $F^+ > F^-$ and $F(x,y)$ follows (4.1), then the piecewise system (1.2) displays two equilibrium points s^+ and s^- in $\mathbb{R}^2_+$ if $x^+ < h \leqslant x^-$.*
In addition, there exist two non intersecting invariant domains $\mathcal{A}^+$ and $\mathcal{A}^-$ which are separated by a boundary curve in $\mathbb{R}^2_+$; all the orbits of system (1.2) in $\mathcal{A}^+$ ($\mathcal{A}^-$, respectively) tend to s^+ (s^-, respectively). In other words, the invariant domains $\mathcal{A}^+$ and $\mathcal{A}^-$ are the basins of attraction of, respectively, the attracting nodes s^+ and s^-.

Proof. By lemma 4, since $F^+ > F^-$, we have $s^+ \ll s^-$. Under the conditions $x^+ < h \leqslant x^-$ and $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^{\pm}})]$, the equilibrium points s^+ and s^- are located at the different side of the separator line $x = h$. By Lemma 5, there exists a unique tangent point c for both the right and left subsystem, which is a point located at the boundary curve (the S-shaped curve in Fig.6). In Fig.6, $\mathcal{A}^-$ is the region above the boundary curve in $\mathbb{R}^2_+$ and $\mathcal{A}^+$ is the region under the boundary curve in $\mathbb{R}^2_+$. Hence, $\mathcal{A}^+$ and $\mathcal{A}^-$ are two basins of attraction separated by the boundary curve. □

Theorem 6. *Suppose $F^- > F^+$ and $F(x,y)$ is the piecewise function given by (4.1), then*

(i) *the piecewise system (1.2) has no equilibrium in $\mathbb{R}^2_+$ for $x^- < h < x^+$, and a unique boundary equilibrium c on $x = h$.*
(ii) *The segments $(x = h) \setminus c$ are sawing sections. Inside the pseudo-loop, there exists a ω-limit set given either by the boundary equilibrium point c or by an attractive limit cycle.*

Proof. First, under the conditions $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^{\pm}})]$, $F^- > F^+$ and $x^- < h \leq x^+$, we know that there are two pseudo-equilibria s^+ and s^- which are located at the different side of the separator line $x = h$ and $s^- \ll s^+$. We claim that the pseudo-loop transversally intersect $x = h$. Otherwise, $\varphi^+(t; s^-)$ or $\varphi^-(t; s^+)$ would be double tangent to $x = h$, which is a contradiction with Lemma 5. Furthermore, the unique tangent point c of the vector fields $\mathcal{V}_{F^{\pm}}$ on $x = h$ is inside the pseudo-loop. In fact, observing the stable node $s^+ = (x^+, y^+)$, we can deduce from the characteristic directions (2.1) that $\dot{x}|_{s^+} = 0$ and there is a unique point $(x, c(x))$ near s^+ on $x = x^+ - \epsilon$, where ϵ is a small positive number,

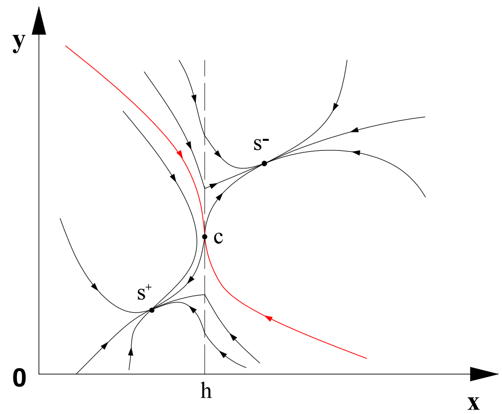


FIGURE 6. $F(x, y)$ is a piecewise function follows (4.1) with $F^+ > F^-$

such that $\dot{x}|_{(x,c(x))} = 0$. Obviously, $c(x)$ is below the curve $\varphi^+(t; s^-)$. Similarly, there is a unique point $(x, c(x))$ near s^- on $x = x^- + \epsilon$, $0 < \epsilon \ll 1$, such that $\dot{x}|_{(x,c(x))} = 0$. Clearly, $(x, c(x))$ is above the curve $\varphi^-(t; s^+)$, see Fig.7. Then we get a tangent-point curve $(x, c(x))$ for $x^- < x \leq x^+$, which can not intersect the pseudo-loop. Hence $c = (h, c(h))$ is a unique boundary equilibrium.

Second, noticing that c is the unique tangent point of the vector fields $\mathcal{V}_{F^\pm}$ on $x = h$, it follows that $\mathcal{V}_{F^+}|_{x=h}$ and $\mathcal{V}_{F^-}|_{x=h}$ have the same component of x-axis. So $\{x = h\} \setminus c$ are sawing sections. Noticing the nodes s^+ and s^-, we can construct a Poincaré map on $x = h$ inside the pseudo-loop. Specially, the orbit starting from intersecting point p_0 of $x = h$ and φ^- has to go through point q_0 on $x = h$ following the vector field V_{F^-}, then it arrives at p_1 on $x = h$ following the vector field V_{F^+}, as shown in Fig.7. By a simple qualitative analysis, we obtain a series of points $p_n, n \in \mathbb{N}$, which is increasing on $x = h$ and upper bounded. Hence there is a limit point p^* of p_n. If $p^* = c$, then c is a stable boundary focus. If $p^* \neq c$, then there is a stable limit cycle around c.

Finally, it follows from Lemma 1 that the pseudo-nodes s^+ and s^- are globally stable, which implies that any orbit of (1.2) shall go through the separating line $x = h$, then tend to c or a limit cycle as $t \to \infty$.

□

4.1. **An example of numerical simulation.** Here we give an example of numerical simulations in the case $F^- > F^+$ and $F(x, y)$ is the piecewise function which follows (4.1) (see Fig.9). We take $F^+ = 1$, $F^- = 10$, $T = 10$, $J = F = L = k = k' = \epsilon = 1$ and $h = 2$; hence the separator line is $x = 2$ and also the condition $T > J[1 + \frac{1}{k'}(L + \frac{J}{F^\pm})]$ is satisfied. In Fig.9(a) we draw one orbit which begins with the initial point $s^- = (1.658, 1.1)$ and in Fig.9(b) we draw two orbits which begin with the two different intersection points between the pseudo-loop and the separator line $x = 2$

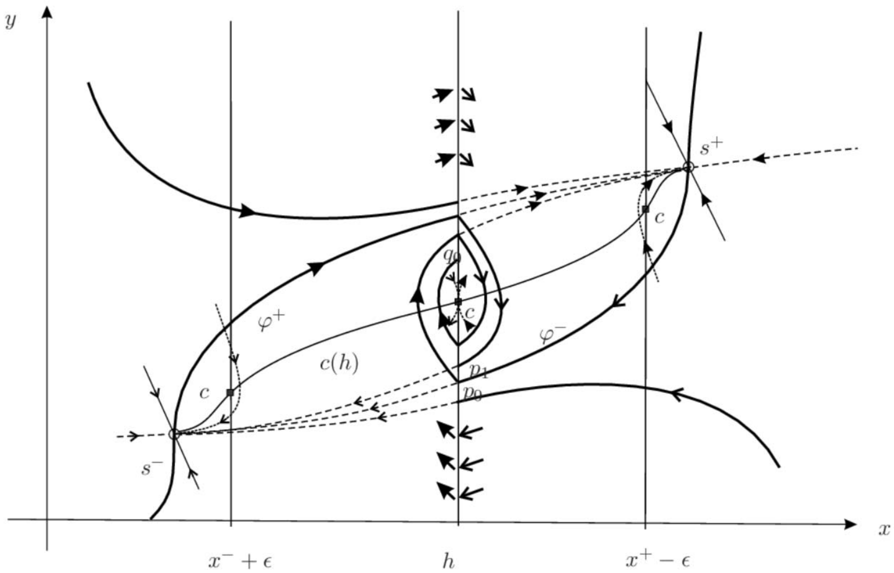


FIGURE 7. The piecewise system (1.2) displays a Poincaré mapping associated to the sawing section $\{x = h\} \setminus h$ surrounding the unique boundary equilibrium point c inside the pseudo-loop.

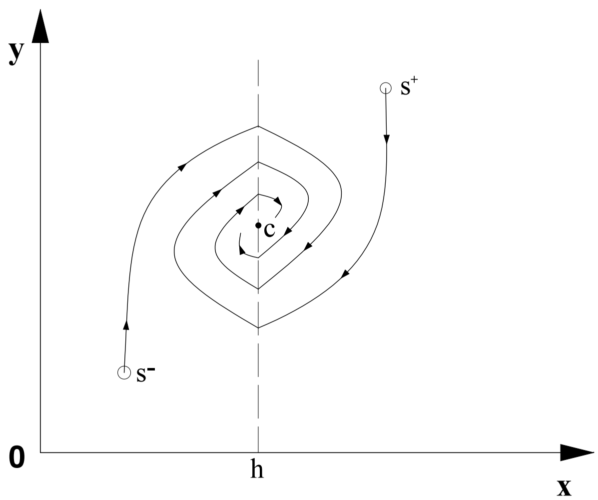
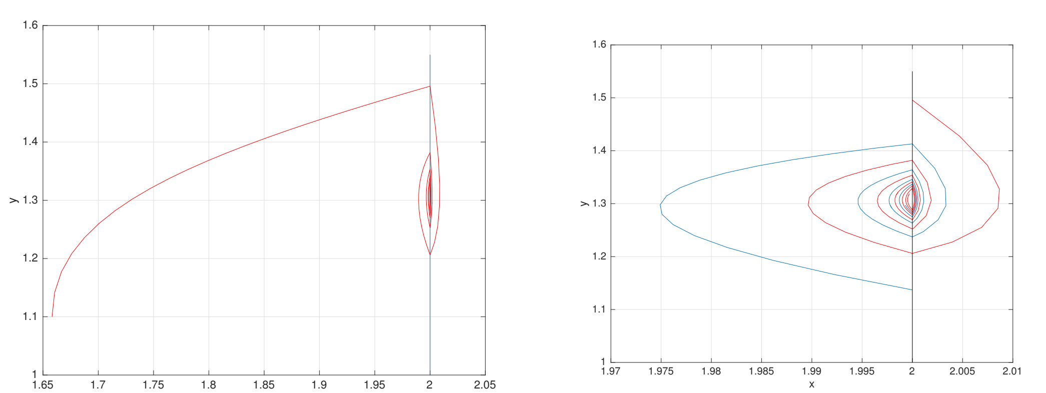


FIGURE 8. Two orbits connecting the pseudo equilibrium points s^+ and s^- with the boundary equilibrium



(a) One orbit with initial point s^- (b) Two orbits with two different initial points

FIGURE 9. Numerical simulation of orbits for $F^- > F^+$ and $F(x, y)$ follows (4.1)

5. Conclusions

In this article, we have introduced an autoregulation in the Neuron-Astrocyte-Capillary system preceedingly studied as a mathematical reduction of a compartimentalized Brain Lactate kinetics Model (cf. [1, 2, 4, 10, 12, 11]). This autoregulation looks natural and can be thought as a feedback process induced by the Astrocytes to the Capillary when the extra-cellular (or the Capillary) Lactate concentration is beyond the viability limits (cf [12, 10]).

The mathematical tool which looks the most adapted for this context is the qualitative analysis of Piecewise Smooth Dynamical Systems (PWS).

Our study uncovered several new phenomenon which where not present in the ODE model.

Within the conditions of Theorem 2 and 5 the PWS displays a bistability with two attracting nodes. The two basins of attraction are separated by a boundary that we can explicitely determine.

With the conditions of Theorem 3, there exists an attracting set which is a sliding section.

With the conditions of Theorem 6, the system displays a pseudo-loop. Inside this pseudo-loop, there is a Poincaré map associated to a sawing section. The qualitative analysis allows to show the existence of a boundary equilibrium. There are two possibilities for the ω-limit set of the orbits inside the pseudo-loop: either a limit cycle or the boundary equilibrium which is then an attractive focus.

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