HAL
open science

Cooperative dynamic systems applied in biology

Hongjun Ji

To cite this version:

Hongjun Ji. Cooperative dynamic systems applied in biology. Dynamical Systems [math.DS]. Sorbonne Université, 2018. English. NNT : 2018SORUS514 . tel-03001246

HAL Id: tel-03001246

https://theses.hal.science/tel-03001246

Submitted on 12 Nov 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Sorbonne Université
Paris 6

Laboratoire Jacques-Louis Lions
UMR 7598

Thèse de Doctorat

de Sorbonne Université

pour l'obtention du grade de

Docteur de Sorbonne Université

Spécialité : Mathématiques Appliquées

par

Hongjun JI

sous la direction de

Jean-Pierre FRANÇOISE

Systèmes dynamiques coopératifs Appliqués en biologie

Présnetée et soutenue publiquement le 11 octobre 2018
devant un jury composé de :

M.	Jean-Pierre FRANÇOISE	Directeur de Thèse
M.	Armengol GASULL	Rapporteur
M.	Jean-Luc GOUZÉ	Rapporteur
M.	Alain HARAUX	Examinateur

École Doctorale de Sciences Mathématiques
de Paris Centre ED 386

Faculté de Mathématiques
UFR 929

Remerciements

Je tiens tout d'abord à remercier mon directeur de thèse Jean-Pierre Françoise, de m'avoir proposé des sujets d'étude passionnants et de m'avoir encadré durant mon séjour au Laboratoire Jacques-Louis Lions. Il a su me communiquer son goût pour les mathématiques appliquées à la biologie en me faisant profiter de son expérience et de ses contacts, aussi bien mathématiciens que biologistes. J'ai beaucoup apprécié la liberté qu'il m'a laissée dans le choix des sujets à aborder, tout en étant toujours disponible pour répondre à mes questions et m'apporter son aide précieuse.

Je remercie également Benoît Perthame pour toute son aide sur mes études à l'UPMC (depuis le master 1), ainsi que pour ses conseils pour mon financement et sa proposition de progamme d'échange à Shanghai Jiao Tong University (SJTU).

J'adresse mes sincères remerciements à Martin Strugarek, avec qui j'ai eu grand plaisir à discuter de mes sujets de recherche. Les méthodes auxquelles il m'a introduit m'ont grandement aidé et il a toujours répondu à mes questions très précisément.

C'est un honneur pour moi que Armengol Gasull et Jean-Luc Gouzé aient accepté de rapporter ma thèse. Merci à Alain Haraux qui a accepté de faire partie du jury.

Je remercie Dongmei Xiao et Jiang Yu, professeurs à SJTU de m'avoir accueilli et encadré pendant ma visite à Shanghai.

Merci aux doctorants du bureau 16-26 324, Ethem,Idriss, Ana et David, pour la fraîcheur que vous avez su apporter au bureau. Je ne peux bien évidemment pas manquer de remercier les membres permanents du LJLL avec qui j'ai eu la chance d'interagir. Enfin, merci à vous toutes et tous, membres Chinois du LJLL, Chaoyu Quan, Heling Gong, Shijie Dong, Yangyang Cao qui sont devenus des amis.

Pour finir, je ne peux que remercier du fond du coeur ma famille (mes parents,

mon épouse, mon fils et mes proches) pour m'avoir constamment soutenu pendant toutes ces années d'études en France.

Contents

1 Introduction générale 9

2 Principaux résultats 12

3 General introduction 19

4 Main results 22

1 Notations and Background 29

1.1 Notations 29

1.2 Background of biological Model 41

2 Application for model of Brain Lactate Metabolism in high dimension 47

2.1 Introduction 47

2.2 Extension to N neuron compartments and A astrocyte compartments 49

2.3 Asymptotic stability of the stationary point, cooperative dynamics and boundedness 53

2.4 Remarks and Perspectives 57

3 Application for model of Brain Lactate Metabolism with piecewise system 59

3.1 Introduction 59

3.2 Qualitative analysis of system (3.1.1) 61

3.3 Global dynamics of system (3.1.2) when F depends on the lactate concentration of Capillary domain 67

3.4 Global dynamics of system (3.1.2) when F depends on the lactate concentration of the interstitial domain 71

3.5 Conclusions 78

4 Sharp seasonal threshold property for cooperative population dynamics with concave nonlinearities 81

4.1 Introduction 81

4.2 Context and motivation 84

4.3 Results 86

4.4 Proofs 89

4.5 Discussion and extensions 101

Bibliography 114

List of Symbols

$\mathbb{R}$	The field of real numbers
$\mathbb{R}_+$	The set of nonnegative real numbers
$\mathbb{R}^n$	The space of column vectors of size n of real numbers
$\mathbb{R}^n_+$	The positive orthant of $\mathbb{R}^n$, given by $\{x \in \mathbb{R}^n : x \geq 0\}$
$\mathbb{C}$	The field of complex numbers
$\mathrm{Re}(c)$	The real part of the complex number c
$\mathrm{Im}(c)$	The imaginary part of the complex number c
x_i	The ith entry of the vector $x \in \mathbb{R}^n$, for $i \in \{1, \cdots, n\}$
$\mathcal{M}_n(\mathbb{R})$	The space of $n \times n$ matrices of real numbers
a_{ij}	The (i, j) entry of the matrix A
A^T	The transpose of the matrix A
A^{-1}	The inverse of the matrix A
$\lvert A \rvert$	The determinant of the matrix A
$\lVert A \rVert$	Any p-norm of the matrix A
I	The identity matrix of proper dimensions
0	The zero matrix of proper dimensions
$\sigma(A)$	The set of all eigenvalues (spectrum) of the matrix A
$\rho(A)$	The spectral radius of the matrix A
$\mu(A)$	The spectral abscissa of the matrix A
$A \gg B$	$a_{ij} > b_{ij}$, for all $i, j \in \{1, \cdots, n\}$
$A > B$	$a_{ij} \geq b_{ij}$, for all $i, j \in \{1, \cdots, n\}$ and $A \neq B$
$A \geq B$	$a_{ij} \geq b_{ij}$, for all $i, j \in \{1, \cdots, n\}$
$\mathcal{L}(X, Y)$	the space of linear applications from X to Y
$\mathcal{L}(X)$	the space of linear applications from X to X

Introduction en Français

1 Introduction générale

Ce travail de thèse est constitué de nouvelles applications de la théorie des systèmes dynamiques coopératifs à l'étude de modèles en Biologie. Les systèmes dynamiques monotones (qui comprennent les systèmes coopératifs et compétitifs) ont étés naturellement introduits par des modèles, en particulier dans les dynamiques de populations (Lotka-Volterra, Kolmogoroff)[89, 62, 61, 92, 70]. Dès les années 1920-30, les mathématiciens commencent à construire les approches théoriques (M. Muller 1927 [75], E. Kamke 1932 [49], J. Kingman 1961 [52]). Mais c'est avec l'école des systèmes dynamiques de Berkeley et les travaux de Hirsch (ensembles limites, convergence presque partout, stabilité structurelle, closing lemma) [36, 38, 40, 39, 41, 42] et Smale (exemple de dynamique compétitive avec n'importe quel type d'attracteur) [78, 79] qu'ils connaissent un développement spectaculaire. Il faut y ajouter des références aux travaux de Hiroshi Matano [66, 67] et de Hal L. Smith [43, 81, 82, 83] qui étendent aux systèmes dynamiques sur les espaces de Banach et établissent des théorèmes de type Perron-Frobenius. Le livre de Josef Hofbauer et Karl Sigmund est aussi une référence importante du sujet qui fait le lien entre la théorie des Jeux et les dynamiques de populations ou dynamiques de l'évolution [44]. En France, il y a eu des contributions dans les applications aux modèles en Biologie (travaux de Jean-Luc Gouzé, L. Mailleret et V. Lemesle [31, 32, 33, 63, 34, 57, 64, 65, 77]).

Deux domaines d'application sont concernés par cette thèse. Le premier s'inscrit dans une série de travaux initiés par les physiologistes Agnès Aubert et Robert Costalat, Luc Pellerin et Pierre Magistretti concernant la dynamique des lactates en lien avec le métabolisme énergétique cérébral [4, 5]. Le deuxième concerne l'étude de modèles de population d'insectes avec un effet marquant de seuil saisonnier en relation avec des travaux développés à l'UPMC par Benoît Perthame et Martin Strugarek.

1.1 Dynamiques des Lactates

Un premier modèle réduit d'une dynamique compartimentalisée couplant l'hémodynamique et le métabolisme énergétique cérébral (cf.[4]) fût introduit par [5]. Il

s'agit d'une dynamique à deux variables x, décrivant la concentration en lactate extracellulaire et y représentant la concentration en lactate capillaire avec un mécanisme de cotransport à travers la barrière hemato-encéphalique. Le modèle permet de reproduire avec une exactitude remarquable des données expérimentales obtenues par Hu et Wilson [46]. Dans la thèse de Marion Lahutte et la série de travaux qui l'a accompagnée [54, 56, 18], on a complétement caractérisé la nature du point stationnaire du système et montré analytiquement par des méthode d'asymptotique des systèmes lents-rapides l'existence d'une déplétion initiale du lactate en présence d'une stimulation. On a aussi établit l'existence d'un domaine de viabilité. Dans deux autres articles, on a proposé l'étude d'une extension naturelle de ce modèle comprenant deux compartiments intracellulaires distincts, un représentant un neurone et l'autre un astrocyte en plus du compartiment extracellulaire (aussi appelé interstitiel) et du compartiment capillaire. Dans ces articles, on avait pas encore réussi à déterminer la nature du point stationnaire mais on avait démontré son unicité.

Dans cette thèse, on a commencé par observer que ce système (et même une extension de ce système à N neurones et A astrocytes) est un système coopératif. On a pu alors appliquer les techniques dévelopées par Hal L. Smith et démontrer (en toutes dimensions) que l'unique point stationnaire est asymptotiquement stable. On a pu même obtenir des estimations sur le bassin d'attraction. Il faut bien remarquer que dans cette direction de travail, nous n'avons plus besoin de considérer l'asymptotique des systèmes lent-rapide. Ces résultats consistuent le chapitre 2 du document. Ils ont fait l'objet d'un premier article, en collaboration avec Jean-Pierre Françoise accepté dans Discrete and Continuous Dynamical Systems.

Dans la suite, nous avons considéré une variante du système réduit de dimension 2 dans laquelle on considère une dynamique différentiable par morceaux qui présente un saut lorsque la variable x ou la variable y dépasse un certain seuil. Ce type de systèmes dynamiques à saut est très étudié dans les applications. Une référence générale pour ce sujet est par exemple le livre [9]. Ce sujet est aussi très bien développé dans le groupe de systèmes dynamiques de l'Université de Shanghai Jiao Tong (SJTU). Cet article a été fait en collaboration avec Dongmei Xiao, Jiang Yu et Jean-Pierre Françoise. Cette modélisation permet d'introduire une autorégulation induite par un rétro-contrôle des concentrations en lactactes extracellulaire (interstitiel) et capillaire sur le flot sanguin capillaire. On découvre de nouveaux phénomènes dynamiques. On discute en particulier la présence de régimes avec deux points stationnaires (bistabilité), d'un segment attractif, de point stationnaire à la frontière de discontinuité et d'un pseudo-loop. Ces résultats forment l'ensemble du chapitre 3. Ils ont donné lieu à un article accepté dans QTDS (Qualitative Theory of Dynamical Systems) en 2018.

A. Gasull et J. Torregrosa sont beaucoup contribué à l'analyse qualitative des systèmes plans dynamiques linéaire par morceaux dans [11, 68, 15, 12, 29]. M. Desroches a aussi contribué à l'étude des solutions canards dans les systèmes dynamiques linéaire par morceaux dans [19, 25, 24, 21, 20].

1.2 Dynamiques avec un effet marquant de seuil saisonnier

Dans le dernier chapitre, on considère, en contraste avec les chapitres précédents, un système dynamique forcé (ou autrement dit non-autonome):

$$\dot{x} = f(t, x), x \in \mathbb{R}^n, t \in \mathbb{R}.$$

Ce système dynamique modélise une population dont l'environnement varie périodiquement dans le temps. En particulier il y a au cours de l'année, deux saisons différentes. Une est "favorable" et l'autre est "défavorable". Dans sa dépendance en x, le système dynamique est supposé monotone avec des non-linéarités concaves. Nous considérons la question suivante. Supposons que la période T est fixée. A quelle condition existe-t-il une durée critique "maximale" pour la saison défavorable? Par durée critique "maximale", nous entendons un seuil tel que si la durée de la saison défavorable excède ce seuil, les populations ne peuvent pas survivre et elles tendent à l'extinction. Tandis que si la durée de la saison défavorable est inférieure à ce seuil, les solutions du système dynamique tendent vers une unique solution stable et positive. S'il existe un tel seuil, nous dirons que le système possède la propriété SSTP (Sharp Seasonal Threshold Property). Nous démontrons l'existence de conditions suffisantes pour qu'un système ait la propriété SSTP.

On suppose que $F(t, x)$ est monotone et concave (en x). De tels systèmes ont des propriétés de contraction bien connues lorsque F est continue [37, 52, 80, 48]. On étend ces résultats aux cas des dynamiques continues par morceaux. Cette extension est motivée par les applications. On suppose que $F(t, 0) \equiv 0$. Le problème de l'existence d'un seuil maximal se réduit à l' étude de la valeur propre de module maximal de la linéarisation de $F(t, x)$ à $x = 0$. Cette valeur propre est égale au rayon spectral de l'application de Poincaré que l'on calcule ici pour un système continu par morceaux. L'importance de la valeur propre de Perron-Frobenius pour quantifier les effets de saisonalité a été reconnue au moins dans trois champs d'application des mathématiques pour la biologie: les rythmes circadiens, les moissons en agro-écologie et l'épidémiologie [7, 6, 14, 16, 30, 85, 88, 91].

En dimension 1, Dongmei Xiao a démontré la propriété SSTP pour l'équation logistique avec moissons, où les deux saisons distinctes correspondent aux moissons (saison "défavorable") et aux périodes de jachères-semailles (saison "favorable"). Nos résultats étendent en partie les résultats de Dongmei Xiao à une dimension quelconque pour des systèmes monotones et concaves [85, 88].

Nous appliquons notre théorème à l'exemple d'une dynamique de population d'insectes (moustiques) avec un stade juvénile exposé à une compétition quadratique et un stade adulte. Cette dynamique est sujette à un forçage périodique saisonnier. En particulier, dans les pays tempérés, les moustiques sont très rares en hiver et connaissent une croissance explosive après les premiers épisodes pluvieux de la saison

chaude.

Le chapitre 4 a fait l'objet d'un article de Hongjun Ji et Martin Strugarek publié au Bulletin des Sciences Mathématiques 147 (2018) 58–82 [47].

2 Principaux résultats

2.1 Modèle du métabolisme du lactate du cerveau en haut dimension

Au chapitre 2, nous nous conçentrons sur un système coopératif non linéaire de dimension $d = N + A + 2$, qui est un système de modélisation de la concentration cinétique du lactate cérébral, avec N compartiments neurones, A compartiments astrocytaires, un compartiment interstitiel et un compartiment capillaire. Considérons aussi ce système dynamique avec les termes de forçage $J_i > 0, i = 0, 1, \ldots, N + A$, et le terme d'entrée $F > 0$ et tous les paramètres $C, C_n, D_a, E_a > 0$ avec $n \in \{1, \ldots, N\}$, $a \in \{1, \ldots, A\}$:

$$
\begin{aligned}
\frac{dx}{dt} &= J_0 + \sum_{n=1}^{N} C_n\left(\frac{u_n}{k_n + u_n} - \frac{x}{k + x}\right) + \sum_{a=1}^{A} D_a\left(\frac{v_a}{k_{N+a} + v_a} - \frac{x}{k + x}\right) \\
&\quad - C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right), \\
\frac{du_1}{dt} &= J_1 - C_1\left(\frac{u_1}{kn_1 + u_1} - \frac{x}{k + x}\right), \\
&\vdots \\
\frac{du_N}{dt} &= J_N - C_N\left(\frac{u_N}{kn_N + u_N} - \frac{x}{k + x}\right), \\
\frac{dv_1}{dt} &= J_{N+1} - D_1\left(\frac{v_1}{ka_1 + v_1} - \frac{x}{k + x}\right) - E_1\left(\frac{v_1}{ka_1 + v_1} - \frac{y}{k' + y}\right), \\
&\vdots \\
\frac{dv_A}{dt} &= J_{N+A} - D_A\left(\frac{v_A}{ka_A + v_A} - \frac{x}{k + x}\right) - E_A\left(\frac{v_A}{ka_A + v_A} - \frac{y}{k' + y}\right), \\
\frac{dy}{dt} &= F(L - y) + C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right) + \sum_{a=1}^{A} E_a\left(\frac{v_a}{ka_a + v_a} - \frac{y}{k' + y}\right).
\end{aligned}
\tag{2.1}
$$

Pour $N = A = 1$, ce système coïncide avec le système de dimension 4 considéré dans [54, 55]. Il peut être considéré comme un modèle de cinétique du lactate cérébral avec des co-transports (intracellulaire-extracellulaire) à travers N membranes de neurones et (intracellulaire-extracellulaire) à travers les membranes des astrocytes et croisement direct (intracellulaire-capillaire) d'astrocyte à capillaire. La

variable x représente la concentration extracellulaire. Les variables $u_n, n = 1, \ldots, N$ représentent la concentration intracellulaire à l'intérieur des neurones. Les variables $v_a, a = 1, \ldots, A$ représentent la concentration intracellulaire dans les astrocytes. La variable y représente la concentration dans le capillaire. Par commodité, nous désignons par W l'ensemble des variables $W = (x, u_n, v_a, y) \in \mathbb{R}^d, d = N + A + 2$.

Pour notre système (2.1), nous avons trois résultats principaux:

Theorem 2.1 *Le système* (2.1) *admet un point stationnaire unique noté* s^*.

Theorem 2.2 *Le point stationnaire du système* (2.1) *est asymptotiquement stable.*

Theorem 2.3 *Si le point stationnaire* $s^* \in int(\mathbb{R}^d_+)$, *alors le système* (2.1) *n'a pas de solution périodique dans* $\mathbb{R}^d_+$.

Nous discutons aussi des conditions de la positivité du point stationnaire de notre système dans ce chapitre. Supposons que les conditions de positivité pour l'unique point stationnaire sont satisfaites. Alors dans ce cas, le bassin d'attraction du point fixe fournit un ensemble positivement invariant d'intérieur non vide des solutions qui sont bornées et positives. Nous donnons un calcul explicite pour le cas $d = 4$. Voir plus de détails dans chapitre 2.

2.2 Modèle du métabolisme du lactate du cerveau avec système continu par morceaux

Dans le chapitre 3, nous étudions une dynamique différentiable par morceaux qui est inspirée par le système compartimental du métabolisme cérébral du chapitre 2. Le système continu par morceaux permet l'introduction d'une autorégulation induite par un retour des concentrations de lactate extracellulaire ou capillaire sur le flux sanguin capillaire.

Dans [56], le domaine physiologique a été discuté en termes de limites sur les concentrations de lactate x et y. Il est naturel de pousser plus loin cette étude avec l'introduction d'une autorégulation du système par les deux concentrations (x ou y) sur le flux sanguin capillaire F. Ceci est discuté dans ce chapitre où l'autorégulation sur F est représentée par une variation continue par morceaux telle que

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

Nous supposons que F^+ et F^- sont des nombres réels positifs distincts et $\Omega^+ \cup \Omega^- = \mathbb{R}^2_+$, $\Omega^+ \cap \Omega^- = \varnothing$. Nous notons le système $\mathcal{V}_F$:

$$\begin{aligned} \frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \\ \frac{dy}{dt} &= F(x,y)(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}). \end{aligned} \tag{2.2}$$

Pour ce système continu par morceaux (2.2), nous donnons ici quelques théorèmes concernant des nouveaux phénomènes dynamiques.

Theorem 2.4 *Supposons que $F^+ > F^-$ et $F(x,y)$ suit* (3.3.1)*, supposons que $L+\frac{J}{F^+} < h \leq L+\frac{J}{F^-}$, alors le système continu par morceaux* (2.2) *admet deux points d'équilibre s^+ et s^- dans $\mathbb{R}^2_+$. De plus, il existe deux domaines invariants disjoints $\mathcal{A}^+$ et $\mathcal{A}^-$ qui sont séparés par une courbe de frontière dans $\mathbb{R}^2_+$; toutes les orbites du système* (3.1.2) *dans $\mathcal{A}^+$ (resp. $\mathcal{A}^-$) tendent à s^+ (resp. s^-). En d'autres termes, $\mathcal{A}^+$ (resp. $\mathcal{A}^-$) est le bassin d'attraction du nœud d'attraction s^+ (resp. s^-).*

Theorem 2.5 *Supposons que $F^- > F^+$ et $F(x,y)$ suit* (3.3.1)*, et supposons en outre que $L+\frac{J}{F^-} < h \leq L+\frac{J}{F^+}$, alors le système continu par morceaux* (2.2) *admet une section glissante sur la ligne $y = h$, qui est un ensemble attractant. Dans ce cas, s^+ et s^- sont des points de pseudo-équilibre et le système n'a pas d'orbites périodiques dans $\mathbb{R}^2_+$.*

Theorem 2.6 *Supposons que $F^+ > F^-$ et $F(x,y)$ suit* (3.4.1)*, alors le système continu par morceaux* (2.2) *admet deux points d'équilibre s^+ et s^- dans $\mathbb{R}^2_+$ si $x^+ < h \leqslant x^-$.*
De plus, il existe deux domaines invariants disjoints $\mathcal{A}^+$ et $\mathcal{A}^-$ qui sont séparés par une courbe limite dans $\mathbb{R}^2_+$; toutes les orbites du système (2.2) *dans $\mathcal{A}^+$ (resp. $\mathcal{A}^-$) tendent à s^+ (resp. s^-). En d'autres termes, le domaine invariant $\mathcal{A}^+$ (resp. $\mathcal{A}^-$) est le bassin d'attraction du nœud d'attraction s^+ (resp. s^-).*

Theorem 2.7 *Supposons que $F^- > F^+$ et $F(x,y)$ est la fonction continue par morceaux donnée par* (3.4.1)*, alors*

(i) le système continu par morceaux (2.2) *n'a aucun equilibre dans $\mathbb{R}^2_+$ pour $x^- < h < x^+$, et un unique frontière point d'équilibre c sur $x = h$.*

(ii) les segments $(x = h) \setminus c$ sont des sections de sciage. A l'intérieur du pseudo-loop, il existe un ensemble de ω-limite qui est donné soit par le point d'équilibre limite c, soit par un cycle limite attractif.

Dans ce chapitre, nous avons introduit une autorégulation dans le système Neuron-Astrocyte-Capillary qui est précédemment étudié comme une réduction mathématique d'un modèle de cinétique du lactate du cerveau compartimenté. Cette autorégulation

semble naturelle et peut être considérée comme un processus de rétroaction induit par les astrocytes vers le capillaire lorsque la concentration extra-cellulaire (ou capillaire) du lactate est au-delà des limites de viabilité.

L'outil mathématique qui semble le plus adapté à ce contexte est l'analyse qualitative des systèmes dynamiques continus par morceaux(PWS).

Notre étude a mis au jour plusieurs nouveaux phénomènes qui n'étaient pas présents dans le modèle EDO.

Avec les conditions de Théorème 4.4 et 4.6, le PWS admet une bistabilité avec deux nœuds d'attraction. Les deux bassins d'attraction sont séparés par une courbe de frontière que nous pouvons déterminer explicitement.

Avec les conditions de Théorèm 4.5, il existe un ensemble attractant qui est une section glissante.

Avec les conditions de Théorèm 4.7, le système affiche un pseudo-loop. A l'intérieur de ce pseudo-loop, il y a une application de Poincaré associée à une section de sciage. L'analyse qualitative permet de montrer l'existence d'un frontière point d'équilibre. Il y a deux possibilités pour l'ensemble ω-limite des orbites à l'intérieur du pseudo-loop: soit un cycle limite ou soit un frontière point d'équilibre qui est alors asymptotiquement stable.

2.3 Propriété de seuil saisonnier pour les systèmes dynamiques monotones avec des non-linéarités concaves

Le chapitre 4 est une contribution théorique à l'étude de dynamiques saisonnières.

Nous étudions les systèmes dynamiques différentiels issus des équations différentielles positives non linéaires périodiques de la forme

$$\frac{dx}{dt} = F(t, x), \tag{2.3}$$

où F est monotone et concave (en x). Ces systèmes présentent des propriétés de contraction bien connues lorsque F est continu (voir [46], [80], [48]). Nous étendons dans le théorème 4.3.1 ces propriétés à des non-linéarités qui ne sont continues que par morceaux en temps. Cette extension est motivée par l'étude des systèmes saisonniers typiques dans la dynamique des populations.

Nous notons $\theta \in [0, 1]$ la proportion de l'année passée en saison défavorable. Ensuite, nous disons que le temps t appartient à une saison défavorable (ou favorable) si $nT \leq t < (n + \theta)T$ (resp. Si $(n + \theta)T \leq t < (n + 1)T$) pour certains $n \in \mathbb{Z}_+$. En d'autres termes, nous étudions les solutions pour:

$$\frac{dX}{dt} = G(\pi_\theta(t), X), \quad \pi_\theta(t) = \begin{cases} \pi^U \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [0, \theta), \\ \pi^F \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [\theta, 1), \end{cases} \tag{2.4}$$

pour certains $G : \mathcal{P} \times \mathbb{R}^N \to \mathbb{R}^N$, avec $\pi^U, \pi^F \in \mathcal{P}$ où $\mathcal{P}$ est l'espace des paramètres. Nous sommes à la recherche de conditions garantissant qu'une propriété de seuil saisonnier forte est vérifiée, c'est-à-dire:

$$\exists \theta_* \in [0,1] \text{ tel que } \begin{cases} \text{si } \theta < \theta_*, \exists\, !\, q : \mathbb{R}_+ \to \mathbb{R}^N, T\text{-périodique}, q \gg 0 \text{ et} \\ \forall X_0 \in \mathbb{R}^N_+ \backslash \{0\}, X \text{ tend vers } q, \\ \text{si } \theta > \theta_*, \forall X_0 \in \mathbb{R}^N_+,\ X \text{ tend ves } 0. \end{cases} \tag{SSTP}$$

Sur le plan écologique, la durée respective des saisons sèches et humides est cruciale pour la durabilité de la population de diverses espèces. La propriété (SSTP) signifie que si la saison défavorable est plus longue que $\theta_* T$ alors la population s'effondre et si elle est plus courte alors les densités de population auront tendance à être périodiques.

Dans un premier temps, nous généralisons un résultat de Smith [80] sur les non-linéarités concaves et coopératives à un système qui est continu (en temps) par morceaux.

Theorem 2.8 *Soit $F : \mathbb{R}_t \times \mathbb{R}^N_x \to \mathbb{R}^N$ T-périodique et continu par morceaux en t et telle que pour tout $t \in \mathbb{R}_+$, $F(t, \cdot) \in \mathcal{C}^1(\mathbb{R}^N, \mathbb{R}^N)$. Supposons que F vérifie les hypothèses* (P), (M), (C) *et* (I), *de sorte que le système différentiel associé* (4.1.1) *soit positif, monotone et concave avec linéarisation en* 0 *irréductible. Soit $\lambda \in \mathbb{R}$ le multiplicateur de Floquet de module maximal de* (4.1.3).

Si $\lambda \leq 1$ alors toute solution non-négative de (4.1.1) *converge vers* 0. *Autrement,*

(i) soit chaque solution non-négative de (4.1.1) *vérifie* $\lim_{t\to\infty} x(t) = \infty$,

(ii) soit (4.1.1) *possède une unique T-périodique solution (non nulle) $q(t)$.*

Dans le cas (ii), $q \gg 0$ et $\lim_{t\to\infty}(x(t) - q(t)) = 0$ pour chaque solution non-négative de (4.1.1).

Deuxièmement, nous donnons des conditions assez générales pour les systèmes en toute dimension d'espace $N \in \mathbb{Z}_{>0}$ pour satisfaire SSTP voir Théorème 4.3.2.

Finalement, nous présentons dans le Théorème 4.3.3 une application au système (4.1.2) de dimension 2, pour lequel nous pouvons montrer la propriété de seuil (SSTP) pour une large gamme de paramètres. Nous entendons par là que la durée relative des deux saisons est un paramètre critique: si elle est supérieure à ce seuil, la population disparaît, et si elle est inférieure, alors la dynamique converge vers un profil périodique unique.

2.4 Perspectives de développements de ce travail

- Il semble naturel de considérer le système de dimension 4 plutôt que le système de dimension 2 parce qu'il distingue les neurones des astrocytes. Maintenant que nous savons qu'il est coopératif et qu'il possède un unique point stationnaire stable, nous pouvons testé les conditions pour l'existence de la navette du Lactate découverte par L. Pellerin et P. Magistretti [5]. Le lecteur pourra aussi se reporter au livre "l'homme glial" récemment publié par Y. Agid et P. Magistretti [2] pour comprendre l'importance du couplage neurone-astrocyte pour le métabolisme cérébral.

- Le modèle à deux variables a connu récemment un dévelopement important dans le domaine des systèmes d' EDP de réaction-diffusion [73, 35, 72, 71]. Il est possible que le résultat de coopérativité obtenu dans le chapitre 3 puisse donner un nouvel éclairage sur le système perturbé par une faible diffusion considéré dans ces travaux. Une perspective intéressante serait d'étudier une perturbation par une faible diffusion du système de dimension 4.

- On peut remarquer que l'article de Dongmei Xiao [88] étudie aussi la récolte maximale par rapport à une notion de développement durable. Il serait intéressant d'approfondir cet aspect avec les outils que nous avons introduits pour dimension quelconque de chapitre 4.

- Le résultat de SSTP peut être mis en perspective avec des problèmes de contrôle associés aux techniques de lutte anti-vectorielle modélisées (notamment par l'étude des propriétés du cycle limite périodique), et son extension à d'autres types de non-linéarités doit être étudiée (par exemple, alternance saisonnière de dynamiques bistable et monostable d'extinction).

Introduction in English

3 General introduction

This thesis work consists of new applications of the theory of cooperative dynamical systems to the study of models in Biology. Monotone dynamical systems (which include cooperative and competitive systems) have naturally been introduced by models, especially in population dynamics (Lotka-Volterra, Kolmogoroff)[89, 62, 61, 92, 70]. As early as the 1920s-1930s, mathematicians began to build theoretical approaches (M. Muller 1927 [75], E. Kamke 1932 [49], J. Kingman 1961 [52]). But it is with Berkeley's school of dynamic systems and Hirsch's work (boundary sets, convergence almost everywhere, structural stability, closing lemma) [36, 38, 40, 39, 41, 42] and Smale (example of competitive dynamics with any type of attractor) [78, 79] that they are experiencing spectacular development. We must add references to the work of Hiroshi Matano [66, 67] and Hal L. Smith [43, 81, 82, 83], which extend to dynamic systems on Banach spaces and establish Perron-Frobenius theorems. The book by Josef Hofbauer and Karl Sigmund is also an important reference in the subject that links the theory of the Games to the dynamics of populations or dynamics of evolution [44]. In France, there have been contributions in applications to models in Biology (work of Jean-Luc Gouzé, L. Mailleret and V. Lemesle [31, 32, 33, 63, 34, 57, 64, 65, 77]).

Two fields of application are concerned in this thesis. The first is part of a series of works initiated by physiologists Agnès Aubert et Robert Costalat, Luc Pellerin and Pierre Magistretti concerning the dynamics of lactates in connection with cerebral energetic metabolism [4, 5]. The second concerns the study of insect population models with a significant seasonal threshold effect in relation to work developed at UPMC by Benoît Perthame and Martin Strugarek.

3.1 Lactate dynamics

A first model of compartmentalized dynamics coupling hemodynamics and cerebral energy metabolism (see [4]) was introduced by [5]. This is a two-variable dynamic x, standing for the extracellular lactate concentration and y representing the capil-

lary lactate concentration with a cotransport through the brain-blood boundary. The model reproduces with remarkable accuracy the experimental data obtained by Hu and Wilson [46]. In the thesis of Marion Lahutte and the series of works, see in [54, 56, 18], they have completely characterized the nature of the stationary point of the system and shown analytically the existence of an initial lactate depletion by asymptotic methods of slow-fast systems in the presence of a stimulation. They have also established the existence of a domain of viability. In two other articles, it has been proposed to study a natural extension of this model comprising two distinct intracellular compartments, one representing a neuron and the other an astrocyte in addition to the extracellular compartment (also called interstitial) and the capillary compartment. In these articles, they had not yet been able to determine the nature of the stationary point, but they had demonstrated its unicity.

In this thesis, we began by observing that the system (and even an extension of this system to N neurons and A astrocytes) is a cooperative system. It was then possible to apply the techniques developed by Hal L. Smith and demonstrate (in all dimensions) that the single stationary point is asymptotically stable. It has even been possible to obtain estimates of the basin of attraction. It should be noted that in this direction of work, we no longer need to consider the asymptotic of slow-fast systems. These results consist of chapter 2 of this thesis. They are the subject of the first article, in collaboration with Jean-Pierre Françoise accepted in Discrete and Continuous Dynamical Systems.

In the following, we study a piecewise smooth dynamical system inspired by a previous reduced system modeling compartimentalized brain metabolism in dimension 2. We consider a piecewise differentiable dynamic that has a jump when the variable x or the variable y exceeds a certain threshold. This type of dynamical systems is very much studied in applications. A general reference for this topic is for example the book [9]. This subject is also very well developed in the group of dynamic systems of Shanghai Jiao Tong University (SJTU). This article was done in collaboration with Dongmei Xiao, Jiang Yu and Jean-Pierre Françoise. This model makes it possible to introduce a auto-regulation induced by a retro-control of the concentrations of extracellular (interstitial) and capillary lactates on the capillary blood flow. We are discovering new dynamic phenomena. In particular, we discuss the presence of regimes with two stationary points (bistability), an attractive segment, a stationary point at the discontinuity boundary, and a pseudo-loop.These results form the whole of Chapter 2. They gave rise to an article accepted in QTDS (Qualitative Theory of Dynamical Systems) in 2018.

A. Gasull and J. Torregrosa have contributed much to the qualitative analysis of piecewise linear planar differential systems [11, 68, 15, 12, 29]. M. Desroches also contributed to the study of piecewise linear dynamical systems on canard solutions [19, 25, 24, 21, 20].

3.2 Dynamic with a sharp effect of seasonal threshold

In the last chapter, we consider, in contrast with the preceding chapters, a forced dynamical system (or in other words non-autonomous):

$$\dot{x} = f(t, x), x \in \mathbb{R}^n, t \in \mathbb{R}.$$

The dynamical system describes a population model whose environment varies periodically over time. We assume that there are two different seasons during a period, in which one is "favorable" and the other one is "unfavorable". The system is supposed to be monotone with concave nonlinearities. We will consider the following question. Suppose that the period T is fixed. In what condition is there a critical duration "maximum" for the unfavorable season? By critical duration "maximum", we mean that above some threshold, the population cannot sustain and extincts, while below this threshold, the system converges to a unique periodic and positive solution. We term this a "sharp seasonal threshold property" (SSTP, for short). We demonstrate the existence of sufficient conditions for systems in any dimension to satisfy SSTP property.

We assume that $F(t, x)$ is monotone and concave (in x). Such systems have well-known contraction properties when F is continuous [37, 52, 80, 48]. We extend these results to the case of continuous piecewise dynamics. This extension is motivated by applications. We assume that $F(t, 0) \equiv 0$. The problem of the existence of a maximal threshold is reduced to the study of the maximal value of the module of the linearization of $F(t, x)$ for $x = 0$. This eigenvalue is equal to the spectral radius of the Poincaré application which is computed here for a continuous piecewise system. The importance of this Perron-Frobenius eigenvalue for quantifying the effects of seasonality has been acknowledged continuously in mathematical biology in at least three application fields: circadian rhythms (in particular in connection with cell division and tumor growth), harvesting and epidemiology [7, 6, 14, 16, 30, 85, 88, 91].

In dimension 1, Dongmei Xiao has demonstrated the SSTP property for the logistic equation with harvesting, where the two distinct seasons correspond to the harvests ("unfavorable" season) and growing periods ("favorable" season). Our results extend a part of the results of Dongmei Xiao to any dimension for monotone and concave systems [85, 88].

We apply our theorem to the example of a population dynamics of insects (for example mosquitoes) with a juvenile stage exposed to a quadratic competition and a adult stage. This dynamic is subject to a seasonal periodic forcing. In particular, in temperate countries, mosquitoes are very rare in winter and grow explosively after the first rainy episodes of the hot season.

Chapter 4 was the subject of an article by Hongjun Ji and Martin Strugarek published in the Bulletin of Mathematical Sciences 147 (2018) 58–82 [47].

4 Main results

4.1 Model of Brain Lactate Metabolism in high dimension

In chapter 2, We focus on a cooperative non linear system of dimension $d = N + A + 2$, which is a system modeling brain lactate kinetics, with N neuron compartments, A astrocyte compartments, one interstitial compartment and one capilary compartment.

Let us consider a dynamical system equipped with forcing terms $J_i > 0, i = 0, 1, \ldots, N + A$, and input $F > 0$ and all parameters $C, C_n, D_a, E_a > 0$ with $n \in \{1, \ldots, N\}$, $a \in \{1, \ldots, A\}$:

$$\begin{aligned}
\frac{dx}{dt} &= J_0 + \sum_{n=1}^{N} C_n\left(\frac{u_n}{k_n + u_n} - \frac{x}{k + x}\right) + \sum_{a=1}^{A} D_a\left(\frac{v_a}{k_{N+a} + v_a} - \frac{x}{k + x}\right) \\
&\quad -C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right), \\
\frac{du_1}{dt} &= J_1 - C_1\left(\frac{u_1}{kn_1 + u_1} - \frac{x}{k + x}\right), \\
&\vdots \\
\frac{du_N}{dt} &= J_N - C_N\left(\frac{u_N}{kn_N + u_N} - \frac{x}{k + x}\right), \\
\frac{dv_1}{dt} &= J_{N+1} - D_1\left(\frac{v_1}{ka_1 + v_1} - \frac{x}{k + x}\right) - E_1\left(\frac{v_1}{ka_1 + v_1} - \frac{y}{k' + y}\right), \\
&\vdots \\
\frac{dv_A}{dt} &= J_{N+A} - D_A\left(\frac{v_A}{ka_A + v_A} - \frac{x}{k + x}\right) - E_A\left(\frac{v_A}{ka_A + v_A} - \frac{y}{k' + y}\right), \\
\frac{dy}{dt} &= F(L - y) + C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right) + \sum_{a=1}^{A} E_a\left(\frac{v_a}{ka_a + v_a} - \frac{y}{k' + y}\right).
\end{aligned} \tag{4.1}$$

For $N = A = 1$, this system coincides with the 4-dimensional system considered in [54, 55]. It can be considered as a model of brain lactate kinetics with co-transports (intracellular-extracellular) through the N neuron membranes and (intracellular-extracellular) through the astrocytes membranes and direct crossing (intracellular-capillary) from astrocyte to capillary. Variable x stands for the extracellular concentration. Variables $u_n, n = 1, \ldots, N$ stand for the intracellular concentration inside neurons. Variables $v_a, a = 1, \ldots, A$ represent the intracellular concentration in astrocytes. Variable y represents the concentration in capillary. For convenience, we denote as W the set of variables $W = (x, u_n, v_a, y) \in \mathbb{R}^d, d = N + A + 2$.

For our system (4.1), we have three main results as following:

Theorem 4.1 *The system* (4.1) *displays a unique stationary point denoted as* s^*.

Theorem 4.2 *The stationary point of system* (4.1) *is asymptotically stable.*

Theorem 4.3 *If the stationary point* $s^* \in int(\mathbb{R}^d_+)$*, then the system* (4.1) *has no periodic solution in* $\mathbb{R}^d_+$*.*

We discuss also the conditions for the positivity of the stationary point of our system. Assume that the positivity conditions for the unique stationary point are fullfilled. Then in that case, the basin of attraction of the stationary point provides a positive invariant set of non-empty interior of solutions which are bounded and positive. We give an explicit computation for the case $d = 4$, although it is not easy to proceed. See more detail in chapitre 2.

4.2 Model of Brain Lactate Metabolism with piecewise system

In chapter 3, 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 extracellular 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.

In [56], 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 of the two concentrations (x or y) on the Capillary Blood Flow F. This is discussed in chapter 3 where the autoregulation is represented by a piecewise variation of 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 $\mathcal{V}_F$:

$$\begin{aligned} \frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \\ \frac{dy}{dt} &= F(x,y)(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}). \end{aligned} \tag{4.2}$$

For this piecewise system (4.2), we give here some Theorems concerned with new dynamical phenomena.

Theorem 4.4 *Suppose $F^+ > F^-$ and $F(x,y)$ follows* (3.3.1)*, assume that $L + \frac{J}{F^+} < h \leq L + \frac{J}{F^-}$, then the piecewise system* (4.2) *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* (3.1.2) *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).*

Theorem 4.5 *Suppose $F^- > F^+$ and $F(x,y)$ follows* (3.3.1)*, and assume furthermore that $L + \frac{J}{F^-} < h \leq L + \frac{J}{F^+}$, then the piecewise system* (4.2) *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 $\mathbb{R}^2_+$.*

Theorem 4.6 *Suppose $F^+ > F^-$ and $F(x,y)$ follows* (3.4.1)*, then the piecewise system* (4.2) *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 (4.2) *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^-.*

Theorem 4.7 *Suppose $F^- > F^+$ and $F(x,y)$ is the piecewise function given by* (3.4.1)*, then*

(i) the piecewise system (4.2) *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.

In this chapter, we have introduced an autoregulation in the Neuron-Astrocyte-Capillary system preceedingly studied as a mathematical reduction of a compartimentalized Brain Lactate kinetics Model. 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.

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 were not present in the ODE model.

Within the conditions of Theorem 4.4 and 4.6 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 4.5, there exists an attracting set which is a sliding section.

With the conditions of Theorem 4.7, 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.

4.3 Sharp seasonal threshold property for cooperative population dynamics with concave nonlinearities

Chapter 4 is a theoretical contribution to the study of seasonal dynamics.

We study differential dynamical systems arising from nonlinear periodic positive differential equations of the form

$$\frac{dx}{dt} = F(t, x), \tag{4.3}$$

where F is monotone and concave (in x). These systems exhibit well-known contraction properties when F is continuous (see [46], [80], [48]). We extend in Theorem 4.3.1 these properties to non-linearities that are only piecewise-continuous in time. This extension is motivated by the study of typical seasonal systems in population dynamics.

We denote by $\theta \in [0, 1]$ the proportion of the year spent in unfavorable season. Then, we convene that time t belongs to an unfavorable (resp. a favorable) season if $nT \leq t < (n + \theta)T$ (resp. if $(n + \theta)T \leq t < (n + 1)T$) for some $n \in \mathbb{Z}_+$. In other words, we study the solutions to:

$$\frac{dX}{dt} = G(\pi_\theta(t), X), \quad \pi_\theta(t) = \begin{cases} \pi^U \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [0, \theta), \\ \pi^F \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [\theta, 1), \end{cases} \tag{4.4}$$

for some $G : \mathcal{P} \times \mathbb{R}^N \to \mathbb{R}^N$, with $\pi^U, \pi^F \in \mathcal{P}$ where $\mathcal{P}$ is the parameter space. We are looking for conditions ensuring that a sharp seasonal threshold property holds, that is:

$$\exists \theta_* \in [0, 1] \text{ such that } \begin{cases} \text{if } \theta < \theta_*, \exists! q : \mathbb{R}_+ \to \mathbb{R}^N, T\text{-periodic}, q \gg 0 \text{ and} \\ \forall X_0 \in \mathbb{R}^N_+ \backslash \{0\}, X \text{ converges to } q, \\ \text{if } \theta > \theta_*, \forall X_0 \in \mathbb{R}^N_+, \ X \text{ converges to } 0. \end{cases} \tag{SSTP}$$

Ecologically, the respective duration of dry and wet seasons is crucial for population sustainability in various species. The property (SSTP) means that if the dry season is

longer than $\theta_* T$ then the population collapses and if it is shorter then the population densities will tend to be periodic.

Firstly, we generalize a result by Smith [80] about continuous concave and cooperative nonlinearities to piecewise-continuous (in time) nonlinearities.

Theorem 4.8 *Let $F : \mathbb{R}_t \times \mathbb{R}_x^N \to \mathbb{R}^N$ be T-periodic and piecewise-continuous in t and such that for all $t \in \mathbb{R}_+$, $F(t, \cdot) \in \mathcal{C}^1(\mathbb{R}^N, \mathbb{R}^N)$. Assume that F satisfies assumptions* (P), (M), (C) *and* (I), *so that the associated differential system* (4.1.1) *is positive, monotone and concave with irreducible linearization at* 0. *Let $\lambda \in \mathbb{R}$ denote the Floquet multiplier with maximal modulus of* (4.1.3).

If $\lambda \leq 1$ then every non-negative solution of (4.1.1) *converges to* 0. *Otherwise,*

(i) either every non-negative solution of (4.1.1) *satisfies $\lim_{t\to\infty} x(t) = \infty$,*

(ii) or (4.1.1) *possesses a unique (nonzero) T-periodic solution $q(t)$.*

In case (ii), $q \gg 0$ and $\lim_{t\to\infty}(x(t)-q(t)) = 0$ for every non-negative solution of (4.1.1).

Secondly, we give the fairly general sufficient conditions for systems in any space dimension $N \in \mathbb{Z}_{>0}$ to satisfy (SSTP) see Theorem 4.3.2.

Finally, we present Theorem 4.3.3 an application to the two-dimensional system (4.1.2), for which we are able to show the threshold property (SSTP) for a wide range of parameters. By this we mean that the relative duration of the two seasons is a critical parameter: if it is above some threshold then the population extincts, and if it is a below then the dynamics converges toward a unique periodic profile.

4.4 Perspectives of developments of this work

- It seems natural to consider the 4-dimensional system rather than the 2-dimensional system because it distinguishes neurons from astrocytes. Now that we know that it is cooperative and that has a single stable stationary point, we can test the conditions for the existence of the lactate shuttle found by Pellerin and P. Magistretti [5]. The reader will also be able to refer to the book "l'homme glial" recently published by Y. Agid and P. Magistretti [2] to understand the importance of neurone-astrocyte coupling for brain metabolism.

- The two-variable model of lactate has recently undergone a significant development in the field of PDE Reaction-Diffusion systems [73, 35, 72, 71]. It is possible that the result of cooperation obtained in chapter 3 may give a new light on the system disturbed by a weak diffusion considered in these works. An interesting perspective would be to study a disturbance by a weak diffusion of the system of dimension 4.

- It can be seen that Dongmei Xiao's article [88] also investigates the maximum harvest in relation to a notion of sustainable development. It would be interesting to deepen this aspect with the tools that we introduced in any dimension for the system of chapter 4.

- The result of SSTP may be put in perspective with control problems associated with vector control methods. In particular, the study of the periodic limit cycle may prove useful. The extension to other types of nonlinearities should also be discussed, with a particular emphasis on the seasonal alternation of bistable and (extinction) monostable dynamics.

Chapter 1

Notations and Background

Contents

1.1 Notations **29**

1.1.1 Basic definition in Matrix Analysis 29

1.1.2 Basic definition of Dynamical Systems 32

1.1.3 Stability 34

1.1.4 Monotone Dynamical Systems 34

1.1.5 Positive Systems 36

1.1.6 Piecewise-smooth ODEs 37

1.2 Background of biological Model **41**

1.2.1 Model of concentration of brain lactate (neurosciences) . . . 41

1.2.2 Model for cooperative population dynamics 44

1.1 Notations

1.1.1 Basic definition in Matrix Analysis

Throughout this thesis, $\mathbb{R}$ denotes the field of real numbers, $M_n(\mathbb{R})$ denotes the space of $n \times n$ matrices with real entries. $\mathbb{R}^n$ is the space of column vectors of size n with real entries. For $x \in \mathbb{R}^n$ and $i = 1, \cdots, n$, x_i denotes the ith coordinate of x. For $A \in M_n(\mathbb{R})$, a_{ij} denotes the $(i,j)^{th}$ entry of A. A^T represents the transpose matrix of A and A^{-1} is the inverse matrix of A. Also, for $x \in \mathbb{R}^n$, $D = diag(x)$ is the $n \times n$ diagonal matrix in which $d_{ii} = x_i$. I refers to identity matrix of proper dimensions. We use 0 to refer to a vector or matrix of appropriate dimensions with all entries equal to zero.

We define:

$$\mathbb{R}_+ := \{x \in \mathbb{R} : x \geq 0\},$$

and

$$\mathbb{R}_+^n := \{x \in \mathbb{R}^n : x_i \geq 0, 1 \leq i \leq n\},$$

$\mathbb{R}_+^n$ is called the positive orthant of $\mathbb{R}^n$.

$$int(\mathbb{R}_+^n) := \{x \in \mathbb{R}^n : x_i > 0, 1 \leq i \leq n\}.$$

For a closed subset Ω of $\mathbb{R}_+^n$ the boundary of Ω is defined as:

$$bd(\Omega) := \Omega \backslash int(\Omega).$$

Definition 1.1.1 *Let A and B be two $n \times n$ matrices, we denote:*

$A \gg B \iff a_{ij} > b_{ij}$ *for all i,j* $\in \{1, \ldots, n\}$,

$A > B \iff a_{ij} \geq b_{ij}$ *for all i,j* $\in \{1, \ldots, n\}$ *and* $A \neq B$,

$A \geq B \iff a_{ij} \geq b_{ij}$ *for all i,j* $\in \{1, \ldots, n\}$.

In particular we define A a positive matrix if $A \geq 0$, strictly positive if $A > 0$ and strongly positive if $A \gg 0$. Clearly: $A \gg 0 \implies A > 0 \implies A \geq 0$.

A real $n \times n$ matrix $M = (m_{ij})$ is **Metzler** if its off-diagonal entries are nonnegative.

Clearly the positive matrices are Metzler matrices. Moreover, a strong link exists between the positive matrices and the Metzler matrices. Indeed, if M is a Metzler matrix, then:

$$\exists\, c \in \mathbb{R}^+ \quad and \quad \exists P \geq 0, P = M + cI.$$

Definition 1.1.2 *A Matrix A is said to be reducible when there exists a permutation matrix P such that*

$$P^T A P = \begin{pmatrix} X & Y \\ 0 & Z \end{pmatrix},$$

where X and Z are both square matrices.

In other terms, a matrix A is irreducible if and only if it is not equivalent to a block upper triangular matrix by permutations of row and columns.

Definition 1.1.3 *The graph of a $n \times n$ matrix A denoted by $G(A)$ is the directed graph on n nodes $\{N_1, N_2, \ldots, N_n\}$, in which there is a directed edge leading from N_i*

to N_j if and only if $a_{ij} \neq 0$.
The graph $G(A)$ is said ***strongly connected*** *if for each pair of nodes (N_i, N_j), there is a sequence of directed edges leading from N_i to N_j, where $i, j \in \{1, \ldots, n\}$.*

Proposition 1.1.1 ([69]) *A is an irreducible matrix if and only if its graph is strongly connected.*

Remark 1.1.1 *If a matrix $A \gg 0$, then A is irreducible.*

Lemma 1.1.1 ([45]) *Let $A \in M_n(\mathbb{R})$ nonnegative and irreducible, if A has a positive left eigenvector and there exists a vector $x > 0$ such that $Ax \geq \rho(A)x$, then $Ax = \rho(A)x$.*

Proof. let y as a positive left eigenvector (i.e.$y^T A$=λy^T). Since $y^T(A - \lambda I) = 0$ is same as $(A - \lambda I)^T y = 0$ (i.e. $(A^T - \lambda I)y = 0$). Hence $A^T y = \lambda y$, we know $y \gg 0$, so we obtain $\lambda = \rho(A^T) = \rho(A)$ write as $y^T A = \rho(A)y^T$, so $y^T Ax = \rho(A)y^T x$, $\forall x \geq 0$. On the other hand, by the condition there exista a x, such that$Ax \geq \rho(A)x$, so $y^T Ax \geq \rho(A)y^T x$. We can conclude $Ax = \rho(A)x$. □

Lemma 1.1.2 *Let $A \in M_n(\mathbb{R})$ nonnegative, then A is irreducible if only if A^T or I_n+ A is irreducible.*

Definition 1.1.4 *Given a $n \times n$ matrix, the spectral radius of A, denoted by $\rho(A)$ is: $\rho(A)$:=$max\{|\lambda| : \lambda \in \sigma(A)\}$ where $\sigma(A)$ is the set of all eigenvalues (spectrum) of the matrix A.*

Definition 1.1.5 *Given a $n \times n$ matrix, the spectral abscissa of A denoted by $\mu(A)$ is: $\mu(A)$:=$max\{Re(\lambda) : \lambda \in \sigma(A)\}$.*

A matrix A is called Hurwitz, if $\mu(A) < 0$.

Definition 1.1.6 *(Dominant Eigenvalue and Eigenvector)*

λ_F is dominant or Frobenius eigenvalue of A if and only if $Re(\lambda_F) = \mu(A)$. Eigenvectors corresponding to dominant eigenvalues are called the dominant or Frobenius eigenvectors of A.

Theorem 1.1.1 (Perron-Frobenius [83]) *Let $A \in M_n(\mathbb{R})$ is an nonnegative matrix, i.e. $A \geqslant 0$, then $\rho(A)$ is an eigenvalue of A and there is a corresponding eigenvector $v > 0$.*
In addition, if A is irreducible then:

i): $\rho(A) > 0$ and there is a corresponding eigenvector $v \gg 0$;
ii): $\rho(A)$ is a simple eigenvalue of A , and if $u > 0$ is eigenvector of A then there is a real number $s > 0$ such that u=sv;
iii): $\rho(A)$ increases when any entry of A increases;
iv): if $A \gg 0$, then $|\lambda| < \rho(A)$ for all other eigenvalue of A.

Remark 1.1.2 *There are many version of proof for Perron-Frobenius theorem, and we can see Berman and Plemmons (1979) [8] for a proof.*

Theorem 1.1.2 (Smith [83]) *Let $A \in M_n(\mathbb{R})$ be a matrix Metzler, then $\mu(A)$ is an eigenvalue of A and there is a corresponding eigenvector $v > 0$. Moreover $Re(\lambda) < \mu(A)$ for all other eigenvalue of A.*
In addition, if A is irreducible then:
i): $\mu(A)$ is an algebraically simple eigenvalue of A;
ii): $v \gg 0$ and any eigenvector $w > 0$ of A is a positive multiple of v;
iii): If B is a matrix satisfying $B > A$, then $\mu(B) > \mu(A)$;
iv): If $\mu(A) < 0$, then $-A^{-1} \gg 0$.

1.1.2 Basic definition of Dynamical Systems

Now we recall some basic definitions and results concerning dynamical systems. The systems we deal with in this subsection are autonomous continuous-time nonlinear systems of the form:

$$\begin{cases} \dot{x} = f(x), \\ x(0) = x_0, \end{cases} \tag{1.1.1}$$

where $f\colon \Omega \mapsto \mathbb{R}^n$ is a nonlinear vector field on a subset Ω of $\mathbb{R}^n$ and $x_0 \in \Omega$ is called the initial condition.

The forward solution (sometimes referred to as solution) or trajectory of (1.1.1) with initial condition x_0 at $t = 0$ is denoted by $x(t, x_0)$ and is defined on the maximal forward interval of existence $T_{max} := \big[0, T_{max}(x_0)\big)$ [51]. Hereafter, if we do not explicitly specify the maximal forward interval of existence for an initial condition x_0, we always assume $T_{max} := \big[0, +\infty\big)$.

For some $x_0 \in \Omega$, $x(t, x_0)$ is said to be decreasing, if for all $t \geq 0$ and $s > 0$ with $t + s \in T_{max}$, we have:

$$x(t + s, x_0) < x(t, x_0).$$

Also, $x(t, x_0)$ is said to be non-increasing, if

$$x(t + s, x_0) \leq x(t, x_0).$$

Increasing and non-decreasing trajectories are defined in the obvious manner.

A set $U \subset \Omega$ is forward invariant or positive invariant for system (1.1.1) if and only if $\forall x_0 \in \Omega$, $x(t, x_0) \in \Omega$ for all $t \in T_{max}$.

A point p is an omega limit point of x_0 if there exists an increasing sequence of time instances $\{t_k\}$, with $t_k \to +\infty$ when $k \to +\infty$, such that $\lim_{t_k \to +\infty} x(t_k, x_0)$. The set of all the omega limit points of x_0 is called its omega limit set and is represented by $\omega(x_0)$. Note that omega limit set of x_0 can be empty, for example if the solution starting from x_0 diverges.

If $T_{max} = +\infty$, then the set $\mathcal{O}(x_0) := \{x(t, x_0) | \, t \in \mathbb{R}_+\}$ is the forward orbit of the forward solution $x(t, x_0)$. $\mathcal{O}(x)$ is said to be a T-periodic orbit for some positive real number $T > 0$ if $x(T, x_0) = x_0$. In that case, $x(T, x_0) = x(t + T, x_0)$ for all $t \geq 0$, so $\mathcal{O}(x_0) = \{x(t, x_0) | \, 0 \leq t \leq T\}$ [83].

If the model (1.1.1) is to be a useful mathematical representation of a dynamical system, then it should have two important properties. The solution for every initial condition of interest should exist, and it should be unique. To state the condition for existence and uniqueness of the solution of system (1.1.1), we need to define the Lipschitz condition.

Definition 1.1.7 *(Lipschitz Condition) Let $\Omega \subset \mathbb{R}^n$ and let $f\colon \Omega \mapsto \mathbb{R}^n$ be a nonlinear vector field. We say f is locally Lipschitz in a closed subset U of Ω, if there exists a positive real L such that*

$$\|f(x) - f(y)\| \leq L\|x - y\|$$

for all $x, y \in U$ where $\|\cdot\|$ represents any p-norm.

The Lipschitz property is weaker than continuous differentiability, as stated in the next lemma which is Lemma 3.2 in [51].

Lemma 1.1.3 *If $f(a)$ and $\frac{\partial f}{\partial x}(a)$ are continuous in a subset U of Ω, then f is locally Lipschitz in U.*

The following theorem, states condition for existence and uniqueness of the solutions of (1.1.1) (Theorem 3.2 in [51]).

Theorem 1.1.3 *(Local Existence and Uniqueness). Let $\Omega \subset \mathbb{R}^n$ and let $f\colon \Omega \mapsto \mathbb{R}^n$ be a nonlinear vector field. Let f be continuous and Lipschitz in $B = \{x \in \Omega | \|x - x_0\| \leq r\}$ for some real r with $r > 0$. Then there exists some $\delta > 0$ such that system (1.1.1) with $x(0) = x_0$ has a unique solution over $[0, \delta]$.*

We now extend the concept of irreducibility to nonlinear dynamical systems. Following [1], system (1.1.1) is irreducible in $\mathbb{R}^n_+$, if

- For all $a \in int(\mathbb{R}^n)$, $\frac{\partial f}{\partial x}(a)$ is irreducible,
- For all $a \in bd(\mathbb{R}^n)\backslash 0$, either $\frac{\partial f}{\partial x}(a) > 0$ or $f_i(a) > 0$ for all i such that $a_i = 0$.

1.1.3 Stability

We next recall various fundamental stability concepts but before formally stating definitions of stability, we should define the concept of equilibrium of a system.

Definition 1.1.8 *(Equilibrium Point) Let $\Omega \subset \mathbb{R}^n$ and let $f\colon \Omega \mapsto \mathbb{R}^n$ be a nonlinear vector field. Any point $x^* \in \Omega$ that satisfies $f(x^*) = 0$ is an equilibrium point of the system* (1.1.1).

Now we are ready to define different concepts of stability.

Definition 1.1.9 *Let $f\colon \Omega \mapsto \mathbb{R}^n$ be a vector field on an open subset $\Omega \subset \mathbb{R}^n$. Let the system* (1.1.1) *have an equilibrium at p in a positive invariant and closed subset U of Ω. We consider U to be the state space of the system* (1.1.1). *Then we say that the equilibrium point p is*

- *stable, f for each $\epsilon > 0$, there is $\delta = \delta(\epsilon) > 0$ such that*

$$\|x_0 - p\| < \delta \implies \|x(t, x_0) - p\| < \epsilon, \quad t > 0;$$

- *unstable, if it is not stable;*
- *asymptotically stable if it is stable and there exists a neighbourhood N of p such that*

$$x_0 \in N \implies \lim_{t\to\infty} x(t, x_0) = p.$$

The set

$$A(p) := \{x_0 \in U | x(t, x_0) \to p, as\, t \to \infty\}$$

is the domain of attraction or region of attraction of p. If $A(p) = U$, then we say p is globally asymptotically stable (GAS for short).

1.1.4 Monotone Dynamical Systems

Monotone methods have been applied since at least the 1920s [75], [49], but not until the work of M. W. Hirsch in the 1980s was the potential of monotonicity widely appreciated in dynamical systems theory (see [39] and references therein). We start with the definition of monotone systems.

Definition 1.1.10 *(Monotonicity) Suppose $\Omega \subset \mathbb{R}^n$ is a forward invariant set for system* (1.1.1)*. The system* (1.1.1) *is monotone in Ω if and only if $\forall x_0, y_0 \in \Omega$ with $x_0 \leq y_0$,it holds that $x(t,x) \leq x(t,y)$ for all t.*

There is another property which is closely related to monotonicity.

Definition 1.1.11 *(Strong Monotonicity) Suppose $\Omega \subset \mathbb{R}^n$ is a forward invariant set for system* (1.1.1)*. The system* (1.1.1) *is strongly monotone in Ω if and only if $\forall x_0, y_0 \in \Omega$ with $x_0 \leq y_0$, it holds that $x(t,x) \ll x(t,y)$ for all t.*

Definition 1.1.12 *(Kamke Condition)*

The vector field f: $\Omega \mapsto \mathbb{R}^n$ on an open subset Ω of $\mathbb{R}^n$ is said to be of type K or to satisfy Kamke Condition, if for each i, $f_i(a) \leq f_i(b)$ for any two points a and b in Ω satisfying $a \leq b$ and $a_i = b_i$.

The following Proposition, which is a restatement of Proposition 3.1.1 in [82], links Kamke condition with monotonicity.

Proposition 1.1.2 *Let f be type K in an open subset Ω of $\mathbb{R}^n$. Then system* (1.1.1) *is monotone.*

Another concept that we will use repeatedly in this manuscript, and is closely tied with monotonicity, is the concept of cooperativity. A cooperative system is defined as follows.

Definition 1.1.13 *(Cooperative System) Consider a dynamic system of $\mathbb{R}^n$, which is continuous-time nonlinear systems of the form:*

$$\dot{x} = f(t,x). \tag{1.1.2}$$

System (1.1.2) *is called cooperative, if only if function $f(t,x)$ satisfy:*

$\forall i \neq j$, $\forall t \geq 0$, $\forall x \in \mathbb{R}^n$, $\frac{\partial f_i}{\partial x_j}(t,x) \geq 0$.

In other words, $Df(\cdot)$ Jacobien of system (1.1.2) *is Metzler matrix for all t and all point x.*

It can be proved that every cooperative system defined on a suitable set satisfies Kamke condition, hence, is monotone. The following remark, which is Remark 3.1.1 in [82], describes this relation.

Theorem 1.1.4 *(Kamke) Let $x(t)$ and $y(t)$ be solutions of*

$$\dot{x} = F(t,x)$$

and

$$\dot{x} = G(t, x)$$

respectively, where both systems are assumed to have the uniqueness property for initial value problems. Assume both $x(t)$ and $t(t)$ belong to a domain $D \subset \mathbb{R}^n$ for $[t_0, t_1]$ in which one of the two systems is cooperative and

$$F(t, z) \leq G(t, z) \quad (t, z) \in [t_0, t_1] \times D.$$

If $x(t_0) \leq y(t_0)$ then $x(t_1) \leq y(t_1)$. If $F = G$ and $x(t_0) < y(t_0)$, then $x(t_1) < y(t_1)$.

The above result may be found in [17] or [53]; the last assertion may be obtained from the first assertion and the fact that, by uniqueness, the solution operator is a homeomorphism.

Remark 1.1.3 *A subset Ω of $\mathbb{R}^n$ is said to be p-convex if $\alpha x + (1-\alpha)y \in \Omega$ for all $\alpha \in [0, 1]$ whenever $x, y \in \Omega$ and $x \leq y$. Obviously, if Ω is convex, then it is also p-convex. Let Ω be a p-convex subset of $\mathbb{R}^n$ and let $f : \Omega \mapsto \mathbb{R}^n$ be cooperative, which means we have*

$$\frac{\partial f_i}{\partial x_j}(a) \geq 0, \quad i \neq j, \quad \forall a \in \Omega. \tag{1.1.3}$$

Then the fundamental theorem of calculus, implies that f satisfies the Kamke condition in Ω. In fact, if $a \leq b$ and $a_i = b_i$, we have

$$f_i(b) - f_i(a) = \int_0^1 \sum_{i \neq j} \frac{\partial f_i}{\partial x_j}(a + r(b-a))(b_j - a_j)dr \geq 0$$

by (1.1.3).

Monotonicity is a powerful property and provides a range of different mathematical tools that will help us in the following chapters. One of the properties of monotone systems that we will repeatedly use is the following lemma which is a restatement of Proposition 3.2.1 in [82].

Lemma 1.1.4 *Let Ω be an open subset of $\mathbb{R}^n$ and let f: $\Omega \mapsto \mathbb{R}^n$ be a cooperative vector field. Assume there exists a vector x such that $f(x) \ll 0\,(resp. f(x) \gg 0)$. Then the trajectory $x(t, x)$ of system* (1.1.1) *is decreasing (resp. increasing) for $t \geq 0$. In the case of $f(x) \leq 0\,(resp. f(x) \geq 0)$, the trajectory will be non-increasing (resp. non-decreasing).*

1.1.5 Positive Systems

A system is called positive, if starting from any initial condition in the positive orthant $\mathbb{R}^n_+$, the trajectory of the system remains in the positive orthant. The formal

definition of a positive system is as follows.

Definition 1.1.14 *(Positive system) Consider a dynamic system of* $\mathbb{R}^n$*, which is continuous-time nonlinear systems of the form:*

$$\begin{cases} \dot{x} = f(t, x), \\ x(0) = x_0, \end{cases} \tag{1.1.4}$$

where $f(\cdot)$ *is a fonction* $\in \mathbb{C}^1$*.*

System (1.1.4) *is called positive, if*

$$x(t, x_0) \geq 0 \quad \forall t \geq 0, x_0 \geq 0. \tag{1.1.5}$$

In other words, if $\mathbb{R}^n_+$ *is an invariant set for the system* (1.1.4)*, then the system is positive.*

Theorem 1.1.5 *Consider a cooperative autonome dynamic system:*

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

this system is positive il only if $f(0) \geq 0$*.*

Theorem 1.1.6 *The dynamic system* (1.1.4) *is positive, if only if:*

$\forall i \in 1, 2, \ldots, n,$

$$\dot{x}_i = f_i(x_1 \geq 0, \ldots, x_i = 0, \ldots, x_n \geq 0) \geq 0. \tag{1.1.6}$$

Remark 1.1.4 *In particular, a linear autonomous (time-invariant) system is monotone, if and only if it is positive.*

1.1.6 Piecewise-smooth ODEs

In this subsection, we recall some definitions concerning Piecewise-smooth ODEs, which are from the book [9].

Definition 1.1.15 *(Piecewise-smooth flow) A piecewise-smooth flow is given by a finite set of ODEs*

$$\dot{x} = f_i(x, \mu), \quad \textit{for } x \in S_i,$$

where $\cup_i S_i = \Omega \subset \mathbb{R}^n$ *and each* S_i *has a non-empty interior. The intersection* $\sum_{ij} := S_i \cap S_j$ *is either an* $\mathbb{R}^{(n-1)}$*-dimensional manifold included in the boundaries*

∂S_j and ∂S_i, or is the empty set. Each vector field f_i is smooth in both the state x and the parameter μ, and defines a smooth flow $\phi_i(x,t)$ within any open set $U \supset S_i$. In particular, each flow ϕ_i is well defined on both sides of the boundary ∂S_j.

A non-empty border between two regions Σ_{ij} will be called a **discontinuity set, discontinuity boundary** or, sometimes, a **switching manifold**. We suppose that each piece of Σ_{ij} is of codimension-one, i.e., is an $(n-1)$-dimensional smooth manifold (something locally diffeomorphic to $\mathbb{R}^{n-1}$) embedded within the n-dimensional phase space. Moreover, we demand that each such Σ_{ij} is itself piecewise-smooth. That is, it is composed of finitely many pieces that are as smooth as the flow.

Note that Definition 1.1.15 does not uniquely specify a rule for the evolution of the dynamics within a discontinuity set. One possibility is to assign each Σ_{ij} as belonging to a single region S_i only. That is, F_i rather than F_j applies on Σ_{ij}. In fact, such notions make little difference except in the case where the flow becomes confined to the boundary (Filippov trajectories). Before we get to that case, let us first consider what might happen to the flow of the piecewise-smooth ODE as we cross a discontinuity boundary Σ_{ij}.

Definition 1.1.16 *The degree of smoothness at a point x_0 in a switching set Σ_{ij} of a piecewise-smooth ODE is the highest order r such the Taylor series expansions of $\phi_i(x_0,t)$ and $\phi_j(x_0,t)$ with respect to t, evaluated at $t=0$, agree up to terms of $O(t^{r-1})$. That is, the first non-zero partial derivative with respect to t of the difference $[\phi_i(x_0,t)-\phi_j(x_0,t)]|_{t=0}$ is of order r.*

Remark 1.1.5 *This definition almost agrees with the usual definition of smooth functions, thinking of the flow at a point as being a function of t. Thus, if we say that a piecewise-smooth flow has degree of smoothness r across a discontinuity boundary, then it is C^{r-1} but not C^r. The vector field is one degree less smooth (because it is by definition the time derivative of the flow). Thus for a flow with degree of smoothness r according to the definition, the vector field will be C^{r-2} but not C^{r-1}.*

Now, consider an ODE local to a single discontinuity set Σ_{ij} that can be written

$$\dot{x} = \begin{cases} F_1(x,\mu), & \text{if } x \in S_1, \\ F_2(x,\mu), & \text{if } x \in S_2, \end{cases}$$

where F_1 generates a flow ϕ_1, F_2 generates a flow ϕ_2. We have

$$\frac{\partial \phi_i(x,t)}{\partial t}\Big|_{t=0} = F_i(x),$$

$$\frac{\partial^2 \phi_i(x,t)}{\partial t^2}\Big|_{t=0} = \frac{\partial F_i}{\partial t} = \frac{\partial F_i}{\partial \phi_1}\frac{\partial \phi_i}{\partial t} = F_{i,x}F_i(x),$$

where a second subscript x means partial differentiation with respect to x. Similarly

$$\frac{\partial^3 \phi_i(x,t)}{\partial t^3}\Big|_{t=0} = F_{i,xx}F_i^2 + F_{i,x}^2 F_i,$$

etc. So, if F_1 and F_2 differ in an mth partial derivative with respect to the state x, we find that the flows ϕ_1 and ϕ_2 differ in their $(m+1)^{st}$ partial derivative with respect to t.

Therefore, if $F_1(x) \neq F_2(x)$ at a point $x \in \Sigma_{12}$, then we have degree of smoothness one there. Systems with degree one are said to be of **Filippov type**.

Alternatively if $F_1(x) = F_2(x)$ but there is a difference in the Jacobian derivatives $F_{1,x} \neq F_{2,x}$ at x, then the degree of smoothness is said to be 2. A difference in the second-derivative tensor $F_{1,xx} \neq F_{2,xx}$ gives smoothness of degree three, etc. Systems with smoothness of degree two or higher may be called **piecewise-smooth continuous systems**.

Definition 1.1.17 *A discontinuity boundary Σ_{ij} is said to be uniformly discontinuous in some domain D if the degree of smoothness of the system is the same for all points $x \in \Sigma_{ij} \cap D$. We say that the discontinuity is* ***uniform with degree m*** *if the first non-zero partial derivative of $F_i - F_j$ evaluated on Σ_{ij} is of order $m-1$. Furthermore, the degree of smoothness is one if $F_i(x) - F_j(x) \neq 0$ for $x \in \Sigma_{ij} \cap D$.*

In fact, the assumption of uniform discontinuity imposes a great restriction on the form that $F_i - F_j$ can take. Consider a general piecewise-smooth continuous system with a single boundary Σ that can be written as the zero set of a smooth function H

$$\dot{x} = \begin{cases} F_1(x), & H(x) > 0, \\ F_2(x), & H(x) < 0, \end{cases} \tag{1.1.7}$$

where $F_1(x) = F_2(x)$ if $H(x) = 0$. Suppose that the flow is uniformly discontinuous with degree m as in Definition 1.1.17.

The case of systems with uniform degree of smoothness one must be treated with great care since we have to allow the possibility of sliding motion. In order to define sliding, it is useful to think of a system (1.1.7) local to a discontinuity boundary between two regions defined by the zero set of a smooth function $H(x) = 0$, see Fig.1.1.

Definition 1.1.18 *The sliding region of the discontinuity set of a system of the form* (1.1.7) *with uniform degree of smoothness one is given by that portion of the boundary of $H(x)$ for which*

$$(H_x F_1) \cdot (H_x F_2) < 0.$$

That is, H_xF_1 (the component of F_1 normal to H) has the opposite sign to H_xF_2. Thus, the boundary is simultaneously attracting (or repelling) from both sides.

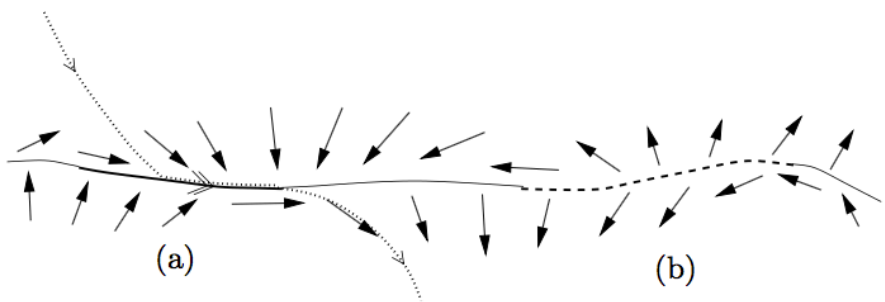


Figure 1.1: A typical discontinuity boundary of a two-dimensional Filippov system showing the behavior of the vector fields on both sides. Bold and dashed regions represent (a) attracting and (b) repelling sliding motion, respectively. Dotted lines indicate three individual trajectory segments.

Note that the case of most interest is when the sliding region is attracting since, as is clear from Fig.1.1, repelling sliding motion cannot be reached by following the system flow forward in time. However, attracting sliding motion can be reached in finite time. Henceforth, sliding will always be taken to mean 'attracting sliding' unless otherwise stated.

1.2 Background of biological Model

1.2.1 Model of concentration of brain lactate (neurosciences)

Our first model concerned with chapters 2 and 3 is inspired by the analysis of brain lactate metabolism developed in (Aubert-Costalat 2005; Aubert et al. 2005 [4, 5]). In this model the two state variables are the intracapillary lactate concentration LAC_c and the intracellular lactate concentration LAC_i. The model includes the following elements see Fig.1.2.

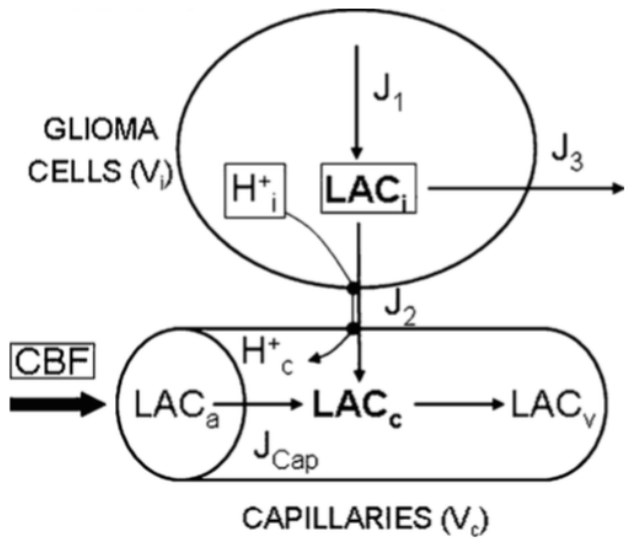


Figure 1.2: A comprehensive schematic representation of the flux exchanges, see [18].

The more detailed information are as following:

- intracellular lactate concentration LAC_i and pH, cell volume being V_i;
- cell lactate production J_1;
- flux of lactate diffusion from cells to capillaries J_2;
- flux J_3, which is the sum of: (1) lactate consumption by the metabolism, taking into account both the conversion lactate-pyruvate catalysed by lactate dehydrogenase and subsequent consumption of pyruvate by mitochondria, and a

possible consumption of lactate by remaining neurons (astrocyte-neuron lactate shuttle, as proposed by Pellerin-Magistretti 1994 [5], (2) lactate diffusion towards neighbouring regions; the diffusion term will be small with respect to lactate consumption by the metabolism.

- capillary lactate concentration (LAC_c) and pH, capillary volume being V_c;
- arterial lactate concentration LAC_a;
- cerebral blood flow (CBF);
- flux J_{cap}, which is the difference between lactate input to capillaries and output from capillaries, namely $J_{cap} = CBF \cdot LAC_a - CBF \cdot LAC_v$, where LAC_v is the venous lactate concentration.

Furthermore, volumes and blood flow values are expressed per unit tissue volume. As a consequence, V_c and V_i are dimensionless parameters, and the capillary blood flow CBF is expressed in s^{-1}. Thus the following mass balance equations can readily be obtained:

$$V_i \frac{dLAC_i}{dt} = J_1 - J_2 - J_3,$$
$$V_c \frac{dLAC_c}{dt} = J_{cap} + J_2.$$

We change to notations better adapted to the mathematical analysis. After some transformations [55, 56, 18, 54], for example the ϵ is come from the operation of $\frac{V_c}{V_i}$, we thus obtain the fast-slow system if ϵ is supposed very little:

$$\frac{dx}{dt} = J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \quad T,\ k,\ k',\ J > 0,$$
$$\epsilon \frac{dy}{dt} = F(L-y) - T(\frac{y}{k'+y} - \frac{x}{k+x}), \quad \epsilon,\ F,\ L > 0.$$

In this first paragraph, we consider F, L, k, k_0 as fixed and J, T as parameters. We discuss the existence and nature of the stationary point as well as eventual existence of periodic orbits. But we also decide that the system makes only sense in a fixed rectangle that we call the viable phase space:

$$V = \{(x, y),\ 0 \leq x \leq M, 0 \leq y \leq N\}.$$

This is motivated by the fact that the variables x and y must be positive as they represent concentrations and cannot assume very large values. We say that if an orbit leaves the domain V it is not viable. Our interpretation is that the biological viability of the system is no longer ensured, e.g. cell necrosis occurs.

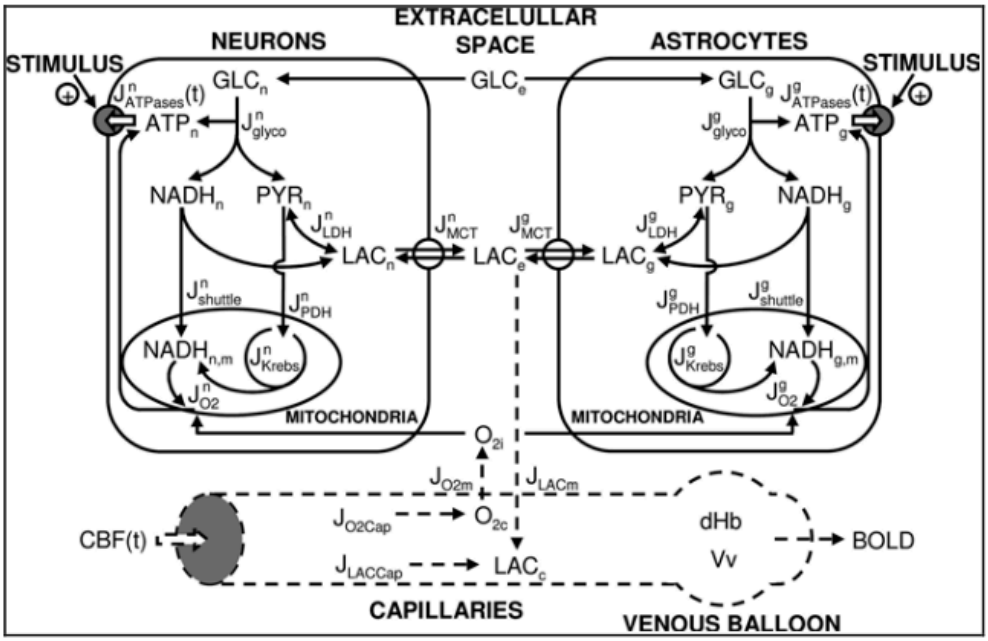


Figure 1.3: Model of comportment was proposed by Aubert and al, PNAS 2007 [5]. Introduction for the exchange of lactate, glucose, and oxygen.

After the research of biologists Aubert and Costalat, see Fig.1.3, we further discuss a natural extension of the system where the intracellular compartment splits into neurons and astrocytes and which includes transports through cell membranes. Following the choice made in [4], a direct transport from capillary to intracellular astrocytes is included. The input $F(t)$ is kept and we add to the forcing $J_0(t, x, u, v)$, still applied to the intracellular compartment, two other independent forcing terms $J_1(t, x, u, v)$ and $J_2(t, x, u, v)$ (resp.) responsible for the intracellular lactate dynamics inside the neurons (resp.) astrocytes.

A more general ODE's model for brain lactate kinetics, where the intracellular compartment splits into neuron and astrocyte, was considered in [54, 55]. It displays

$$
\begin{aligned}
\frac{dx}{dt} &= J_0 + T_1(-\frac{x}{k+x} + \frac{u}{k_n+u}) + T_2(-\frac{x}{k+x} + \frac{v}{k_a+v}) - T(\frac{x}{k+x} - \frac{y}{k'+y}),\\
\frac{du}{dt} &= J_1 - T_1(-\frac{x}{k+x} + \frac{u}{k_n+u}),\\
\frac{dv}{dt} &= J_2 - T_2(-\frac{x}{k+x} + \frac{v}{k_a+v}) - T_a(\frac{v}{k_a+v} - \frac{y}{k'+y}),\\
\epsilon\frac{dy}{dt} &= F(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}). + T_a(\frac{v}{k_a+v} - \frac{y}{k'+y}).
\end{aligned}
$$

1.2.2 Model for cooperative population dynamics

Our second model concerned with chapter 4 is a study of population dynamics of some insects, which is focused on the stage-structured biological population under a environment which varies periodically in time. The reason of studying this kind of problem is from the research of Martin Strugarek see in [76, 84] where they focused on the study of Wolbachia invasion to control the population of mosquitoes in order to reduce mosquito-borne disease transmission. Some more details for this study could be found in [22, 58, 60, 13, 90].

In fact, mosquito as a kind of insect is the vector of many diseases, like malaria, dengue, West Nile virus, etc. Mosquito-borne diseases (primarily malaria and dengue) are a heavy burden for public health in many countries, in particular in tropical areas. This is why so many scientists want to control the population of mosquitoes.

For this purpose, it is essential to understand mosquito population dynamics. Mosquito life includes four stages: egg, larva, pupa, and adult. Each of these stages can be easily recognized by their special appearance. The duration of the whole cycle, from egg laying to an adult mosquito, varies between 7 and 20 days, depending on the ambient temperature of the swamp and the mosquito species involved [27, 23].

Some mathematicians developed a few dynamical systems (as mentioned above) which include the immature mosquito stage. This stage is more sensitive to climate change and resource [10, 26, 59, 86, 87], which may help us understand mosquitoes from the point of view in mathematics. Our reference model is a simplistic description of the population dynamics of some insects, with a juvenile stage exposed to quadratic competition and an adult stage.

$$\begin{cases} \dfrac{dJ}{dt} = bA - J(h + d_J + c_J J), \\ \dfrac{dA}{dt} = hJ - d_A A, \end{cases} \tag{1.2.1}$$

where d_Y ($Y \in \{J, A\}$) stands for the (linear) death rate, b is the birth rate, h is the hatching rate and the parameter c_J tunes the only non-linearity: quadratic competition (=density-dependent death rate) among juveniles. This term effectively limits the total population size, as we will prove below. We use it to represent resource limitation both for breeding sites availability and for nutrient availability during growth. In principle, the parameters may depend on time:

$$\forall t \in \mathbb{R}, \quad \pi(t) := (b, h, d_J, c_J, d_A) \in \mathbb{R}^5_+.$$

The starting questions is: what are the effects of taking into account different seasons in the previous population dynamics? First we try to describe as precisely as possible the case when there are only two seasons, one being favorable and the

other one unfavorable. From the basic model below, we consider a non autonomous periodic vector field, which is a general form,

$$\begin{cases} \dfrac{dx}{dt} = f(t,x), \\ f(t,x) = f(t+T,x), \end{cases}$$

which represents a population whose environment varies periodically in time, exhibiting two "seasons". One is favorable and the other unfavorable. We address the question—Under which conditions there exists a critical duration for the unfavorable season?

Chapter 2

Application for model of Brain Lactate Metabolism in high dimension

Contents

2.1 Introduction **47**

2.2 Extension to N neuron compartments and A astrocyte compartments **49**

2.2.1 Introduction of the system and its positivity 49

2.2.2 Uniqueness of the stationary point 50

2.2.3 Conditions for the positivity of the stationary point 53

2.3 Asymptotic stability of the stationary point, cooperative dynamics and boundedness **53**

2.3.1 Asymptotic stability of the stationary point 53

2.3.2 Problem of boundedness 54

2.3.3 Sufficient condition for non periodic solution 55

2.4 Remarks and Perspectives **57**

2.1 Introduction

Our aim in this chapter is to study properties of a generalized dynamical system modeling brain lactate kinetics, with N neuron compartments and A astrocyte compartments. In particular, we prove the uniqueness of the stationary point and its asymptotic stability. Furthermore, we check that the system is positive and cooperative.

The system of ODE's

$$\begin{aligned}\frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \quad T,\ k,\ k',\ J > 0,\\ \epsilon\frac{dy}{dt} &= F(L-y) - T(\frac{y}{k'+y} - \frac{x}{k+x}), \quad \epsilon,\ F,\ L > 0,\end{aligned} \tag{2.1.1}$$

where ϵ is a small parameter, was proposed and studied as a model for brain lactate kinetics (see [18, 54, 55, 56]). 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 [50]). Finally, J and F are forcing and input terms, respectively, assumed frozen. The model has a unique stationary point which is asymptotically stable. Recently, in [72, 35], a PDE's system obtained by adding diffusion of lactate was introduced. The authors proved existence and uniqueneness of nonnegative solutions and obtained linear stability results. A more general ODE's model for brain lactate kinetics, where the intracellular compartment splits into neuron and astrocyte, was considered in [54, 55]. It displays

$$\begin{aligned}\frac{dx}{dt} &= J_0 + T_1(-\frac{x}{k+x} + \frac{u}{k_n+u}) + T_2(-\frac{x}{k+x} + \frac{v}{k_a+v}) - T(\frac{x}{k+x} - \frac{y}{k'+y}),\\ \frac{du}{dt} &= J_1 - T_1(-\frac{x}{k+x} + \frac{u}{k_n+u}),\\ \frac{dv}{dt} &= J_2 - T_2(-\frac{x}{k+x} + \frac{v}{k_a+v}) - T_a(\frac{v}{k_a+v} - \frac{y}{k'+y}),\\ \epsilon\frac{dy}{dt} &= F(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}) + T_a(\frac{v}{k_a+v} - \frac{y}{k'+y}),\end{aligned} \tag{2.1.2}$$

where all the constants are nonnegative. It also includes transports through cell membranes and a direct transport from capillary to intracellular astrocyte. It was proved in [54, 55] that this 4-dimensional system displays a unique stationary point but its nature was left open. The stability of the unique stationary point is an important issue as it relates with therapeutic protocols developped in the references [54, 55]. Another important issue is the boundedness of the lactate concentrations related with the viability domain (cf. [54, 55]). We can in fact consider a natural extension of this system into a more general $N + A + 2$ system. For this generalized system, we prove both unicity and asymptotic stability of the stationary point. In this article we do not consider fast-slow limits and absorb ϵ in the parameters.

2.2 Extension to N neuron compartments and A astrocyte compartments

2.2.1 Introduction of the system and its positivity

Let us consider a dynamical system equipped with forcing terms $J_i > 0, i = 0, 1, \ldots, N + A$, and input $F > 0$ and all parameters $C, C_n, D_a, E_a > 0$ with $n \in \{1, \ldots, N\}$, $a \in \{1, \ldots, A\}$:

$$\begin{aligned}
\frac{dx}{dt} &= J_0 + \sum_{n=1}^{N} C_n\left(\frac{u_n}{k_n + u_n} - \frac{x}{k + x}\right) + \sum_{a=1}^{A} D_a\left(\frac{v_a}{k_{N+a} + v_a} - \frac{x}{k + x}\right) \\
&\quad -C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right), \\
\frac{du_1}{dt} &= J_1 - C_1\left(\frac{u_1}{kn_1 + u_1} - \frac{x}{k + x}\right), \\
&\vdots \\
\frac{du_N}{dt} &= J_N - C_N\left(\frac{u_N}{kn_N + u_N} - \frac{x}{k + x}\right), \\
\frac{dv_1}{dt} &= J_{N+1} - D_1\left(\frac{v_1}{ka_1 + v_1} - \frac{x}{k + x}\right) - E_1\left(\frac{v_1}{ka_1 + v_1} - \frac{y}{k' + y}\right), \\
&\vdots \\
\frac{dv_A}{dt} &= J_{N+A} - D_A\left(\frac{v_A}{ka_A + v_A} - \frac{x}{k + x}\right) - E_A\left(\frac{v_A}{ka_A + v_A} - \frac{y}{k' + y}\right), \\
\frac{dy}{dt} &= F(L - y) + C\left(\frac{x}{k + x} - \frac{y}{k' + y}\right) + \sum_{a=1}^{A} E_a\left(\frac{v_a}{ka_a + v_a} - \frac{y}{k' + y}\right).
\end{aligned} \tag{2.2.1}$$

For $N = A = 1$, this system coincides with the 4-dimensional system considered in ([54, 55]). It can be considered as a model of brain lactate kinetics with co-transports (intracellular-extracellular) through the N neuron membranes and (intracellular-extracellular) through the astrocytes membranes and direct crossing (intracellular-capillary) from astrocyte to capillary. Variable x stands for the extracellular concentration. Variables $u_n, n = 1, \ldots, N$ stand for the intracellular concentration inside neurons. Variables $v_a, a = 1, \ldots, A$ represent the intracellular concentration in astrocytes. Variable y represents the concentration in capillary. For convenience, we denote as W the set of variables $W = (x, u_n, v_a, y) \in \mathbb{R}^d, d = N + A + 2$.

Recall that an autonomous continuous dynamical system associated with a vector field:

$$\frac{dW_i}{dt} = f_i(W), \quad i = 1, \ldots, d$$

is said to be positive if and only if: $\forall i \in 1, \ldots, d$

$$\dot{W}_i = f_i(W_1 \geq 0, \ldots, W_i = 0, \ldots, W_d \geq 0) \geq 0.$$

It is easy to check that the vector field defined by system (2.2.1) is positive. The geometrical meaning of this property is that the flow of the vector field can be restricted to the convex set $\Omega = \mathbb{R}^d_+$.

2.2.2 Uniqueness of the stationary point

Theorem 2.2.1 *The system (2.2.1) displays a unique stationary point denoted as s^*.*

Proof. The equations for finding a stationary point yield:

$$\begin{aligned}
0 &= J_0 + \sum_{n=1}^{N} C_n\left(\tfrac{u_n}{kn_n+u_n} - \tfrac{x}{x+k}\right) + \sum_{a=1}^{A} D_a\left(\tfrac{v_a}{ka_a+v_a} - \tfrac{x}{x+k}\right) - C\left(\tfrac{x}{k+x} - \tfrac{y}{k'+y}\right),\\
0 &= J_1 - C_1\left(\tfrac{u_1}{kn_1+u_1} - \tfrac{x}{x+k}\right),\\
&\vdots\\
0 &= J_n - C_n\left(\tfrac{u_n}{kn_n+u_n} - \tfrac{x}{x+k}\right),\\
&\vdots\\
0 &= J_N - C_N\left(\tfrac{u_N}{kn_N+u_N} - \tfrac{x}{x+k}\right),\\
0 &= J_{N+1} - D_1\left(\tfrac{v_1}{ka_1+v_1} - \tfrac{x}{x+k}\right) - E_1\left(\tfrac{v_1}{ka_1+v_1} - \tfrac{y}{k'+y}\right),\\
&\vdots\\
0 &= J_{N+a} - D_a\left(\tfrac{v_a}{ka_a+v_a} - \tfrac{x}{x+k}\right) - E_a\left(\tfrac{v_a}{ka_a+v_a} - \tfrac{y}{k'+y}\right),\\
&\vdots\\
0 &= J_{N+A} - D_A\left(\tfrac{v_a}{ka_A+v_A} - \tfrac{x}{x+k}\right) - E_A\left(\tfrac{v_A}{ka_A+v_A} - \tfrac{y}{k'+y}\right),\\
0 &= F(L-y) + C\left(\tfrac{x}{k+x} - \tfrac{y}{k'+y}\right) + \sum_{a=1}^{A} E_a\left(\tfrac{v_a}{ka_a+v_a} - \tfrac{y}{k'+y}\right).
\end{aligned} \tag{2.2.2}$$

Consider the following change of variable:

$$X = \frac{x}{k+x}, Y = \frac{y}{k'+y}, U_n = \frac{u_n}{kn_n+u_n}, V_a = \frac{v_a}{ka_a+v_a}, \tag{2.2.3}$$

for $n \in \{1, \ldots, N\}$ and $a \in \{1, \ldots, A\}$. So we can write the system in a matrix equation:

$$Ms = b, \tag{2.2.4}$$

where $M \in \mathbb{R}^{d \times d}$ displays:

$$s = \begin{pmatrix} U_1 \\ \vdots \\ U_N \\ V_1 \\ \vdots \\ V_A \\ X \\ Y \end{pmatrix} \in \mathbb{R}^d, \qquad b = \begin{pmatrix} J_1 \\ \vdots \\ J_N \\ J_{N+1} \\ \vdots \\ J_{N+A} \\ J_0 \\ F(L-y) \end{pmatrix} \in \mathbb{R}^d.$$

After summing up the d equations, this yields:

$$y = y^* = L + \frac{J_0 + J_1 + \cdots + J_{N+A}}{F}. \tag{2.2.5}$$

So we have a unique solution for y. In this case we can reduce equation (2.2.4) into a new matrix equation of dimension $d-1$ denoted:

$$M's' = b', \tag{2.2.6}$$

where

$$M' = \left(\begin{array}{ccc|ccc|c} C_1 & & & & & & -C_1 \\ & \ddots & & & 0 & & \vdots \\ & & C_N & & & & -C_N \\ \hline & 0 & & D_1+E_1 & & & -D_1 \\ & & & & \ddots & & \vdots \\ & & & & & D_A+E_A & -D_A \\ \hline -C_1 & \dots & -C_N & -D_1 & \dots & -D_A & \sum_{n=1}^{N} C_n + \sum_{a=1}^{A} D_a + C \end{array}\right),$$

$$s' = \begin{pmatrix} U_1 \\ \vdots \\ U_N \\ V_1 \\ \vdots \\ V_A \\ X \end{pmatrix} \in \mathbb{R}^{d-1}, \qquad b' = \begin{pmatrix} J_1 \\ \vdots \\ J_N \\ J_{N+1} + E_1 \frac{y^*}{k'+y^*} \\ \vdots \\ J_{N+A} + E_A \frac{y^*}{k'+y^*} \\ J_0 + Cy^* \end{pmatrix} \in \mathbb{R}^{d-1}.$$

We can write a block decomposition of the matrix M' as follows:

$$M' = \begin{pmatrix} M_1 & M_2 \\ M_3 & M_4 \end{pmatrix},$$

so

$$M_1 = \left(\begin{array}{ccc|ccc} C_1 & & & & & \\ & \ddots & & & 0 & \\ & & C_N & & & \\ \hline & & & D_1+E_1 & & \\ & 0 & & & \ddots & \\ & & & & & D_A+E_A \end{array}\right) \in \mathbb{R}^{(d-2)\times(d-2)},$$

$$M_2 = \begin{pmatrix} -C_1 & \dots & -C_N & -D_1 & \cdots & -D_A \end{pmatrix}^T \in \mathbb{R}^{(d-2)\times 1},$$

$$M_3 = \begin{pmatrix} -C_1 & \dots & -C_N & -D_1 & \cdots & -D_A \end{pmatrix} \in \mathbb{R}^{1\times(d-2)},$$

$$M_4 = \sum_{n=1}^{N} C_n + \sum_{a=1}^{A} D_a + C \in \mathbb{R}.$$

As M_1 is an invertible square matrix, we can write:

$$\det(M') = \det \begin{pmatrix} M_1 & M_2 \\ M_3 & M_4 \end{pmatrix} = \det(M_1)\det(M_4 - M_3 {M_1}^{-1} M_2).$$

The determinant of M_1 writes $\det(M_1) = \prod_{n=1}^{N} C_n \prod_{a=1}^{A} (D_a + E_a) > 0$.

Direct computation of the Matrix $(M_4 - M_3 {M_1}^{-1} M_2)$, which is a real number, yields:

$$\begin{aligned} \det(M_4 - M_3 {M_1}^{-1} M_2) &= \sum_{n=1}^{N} C_n + \sum_{a=1}^{A} D_a + C - (\sum_{n=1}^{N} C_n + \sum_{a=1}^{A} \frac{{D_a}^2}{(D_a+E_a)}) \\ &= \sum_{a=1}^{A} D_a + C - \sum_{a=1}^{A} \frac{{D_a}^2}{(D_a+E_a)} \\ &= \sum_{a=1}^{A} D_a (1 - \frac{{D_a}^2}{D_a+E_a}) + C \\ &= \sum_{a=1}^{A} \frac{D_a E_a}{D_a+E_a} + C > 0. \end{aligned}$$

Computation yields $\det(M') \neq 0$ and the equation (2.2.6) displays a unique solution s' which is as $s' = M'^{-1} b'$. With the change of variable (2.2.3), there is a unique solution for system (4.4.6) denoted as s'':

$$s'' = (x^*, u_1^*, \cdots, u_N^*, v_1^*, \cdots, v_A^*).$$

This proves the uniqueness of the stationary point $s^* = (s'', y^*)$ of system (2.2.1). □

In the next subsection, we discuss the positivity of this stationary point.

2.2.3 Conditions for the positivity of the stationary point

The stationary point $s^* = (s'', y^*)$ does not belong necessarily to $\mathbb{R}^d_+$ as it was observed already for the 2-dimensional system in [54, 18]. Following the notations of equation (2.1.1), the stationary point belongs to $\mathbb{R}^2_+$ if and only if:

$$T > J[1 + \frac{1}{k'}(L + \frac{J}{F})]. \tag{2.2.7}$$

Proof. Similar explicit conditions can be given for the 4-dimensional system as shown in [54, 55]. In any dimension d, even if these conditions are not easily obtained explicitly, they read, with vector $e = (1, 1, ..1)$, $0 \leq M'^{-1}b' \leq e$. □

2.3 Asymptotic stability of the stationary point, cooperative dynamics and boundedness

2.3.1 Asymptotic stability of the stationary point

We compute the Jacobian matrix of the vector field (2.2.1):
$J_F =$

$$\begin{pmatrix}
-(\sum_{n=1}^{N} C_n + \sum_{a=1}^{A} D_a + C)\frac{k}{(x+k)^2} & C_1\frac{kn_1}{(u_1+kn_1)^2} & \dots & C_N\frac{kn_N}{(u_N+kn_N)^2} & D_1\frac{ka_1}{(v_1+ka_1)^2} & \dots & D_A\frac{ka_A}{(v_A+ka_A)^2} & C\frac{k'}{(y+k')^2} \\
C_1\frac{k}{(x+k)^2} & -C_1\frac{kn_1}{(u_1+kn_1)^2} & & & & & & \\
\vdots & & \ddots & & & & & \\
C_N\frac{k}{(x+k)^2} & & & -C_N\frac{kn_N}{(u_N+kn_N)^2} & & & & \\
D_1\frac{k}{(x+k)^2} & & & & -(D_1+E_1)\frac{ka_1}{(v_1+ka_1)^2} & & & E_1\frac{k'}{(y+k')^2} \\
\vdots & & & & & \ddots & & \vdots \\
D_A\frac{k}{(x+k)^2} & & & & & & -(D_A+E_A)\frac{ka_A}{(v_A+ka_A)^2} & E_A\frac{k'}{(y+k')^2} \\
C\frac{k}{(x+k)^2} & & & & E_1\frac{ka_1}{(v_1+ka_1)^2} & \dots & E_A\frac{ka_A}{(v_A+ka_A)^2} & -F-(C+\sum_{a=1}^{A} E_a)\frac{k'}{(y+k')^2}
\end{pmatrix}$$

Denote J_0 the Jacobian matrix J_F for the input $F = 0$. All off-diagonal elements of the matrix J_F (and of J_0) are nonnegative. So we could use the theorem due to Hal.L. Smith which applies to the Metzler matrices.

We now prove the following theorem:

Theorem 2.3.1 *The stationary point of system (2.2.1) is asymptotically stable.*

Proof. As we can see, there are no zero elements at the first row and the first column in matrix J_F (and J_0). This means that in the graph associated to the matrix, there is a sequence of directed edges leading from N_i to N_j for all $i, j \in (1, 2..., d)$. Hence, $G(J_F)$ is strongly connected, so J_F (and J_0) is an irreducible matrix. Note that the strictly positive vector $w \in \mathbb{R}^d$:

$$w = \Big(\frac{(x+k)^2}{k}, \frac{(u_1+kn_1)^2}{kn_1}, \cdots, \frac{(u_N+kn_N)^2}{kn_N}, \frac{(v_1+ka_1)^2}{ka_1}, \cdots \\ \cdots, \frac{(v_A+ka_A)^2}{ka_A}, \frac{(y+k')^2}{k'}\Big)^T, \tag{2.3.1}$$

solves $J_0 w = 0$.
By (ii) in theorem (1.1.2), the vector w is necessarily proportional to the positive eigenvector v which corresponds to the spectral abscissa. Hence, we obtain that $\mu(J_0) = 0$.
By (iii) in theorem (1.1.2), $\mu(J_F) < \mu(J_0) = 0$.

This shows that all the real parts of eigenvalues of the Jacobian matrix J_F are negative, which means that the stationary point of system (2.2.1) is asymptotically stable. □

2.3.2 Problem of boundedness

Proposition 2.3.1 *Given a continuous dynamical system defined on the convex set $\Omega = \mathbb{R}^d_+$ which displays the Kamke property and two points x_0 and y_0 in Ω so that $x_0 \leq y_0$, then if the solutions $\phi_t(x_0)$ and $\phi_t(y_0)$ (ϕ_t is the flow at time t of the vector field) are defined then $\phi_t(x_0) \leq \phi_t(y_0)$.*

Such tools are useful to discuss the other important issue of boundedness of the lactate concentrations in relation with the viability domain (cf.[18, 54, 55, 56]).

Consider first the reduced 2-dimensional system. Assume that the condition $T > J[1 + \frac{1}{k'}(L + \frac{J}{F})]$ is not fullfilled. The domain Ω is invariant by the positive flow. Consider any initial point x_0 in Ω and assume that the closure of its orbit is contained in a compact set. Consider its ω limit set $\omega(x_0)$. By the Poincaré-Bendixson theorem it is either a stationary point, a periodic orbit or a polycyle (union of stationary point connected by heteroclinic connexions). All these cases are ruled out by the fact that the system does not display a stationary point inside the domain Ω. This shows that there is no bounded orbit inside the domain.

Consider now the d-dimensional system which distinguishes the neuron and astrocyte compartments. Assume that the positivity conditions for the unique stationary point are fullfilled. Then in that case, the basin of attraction of the stationary point

provides a positive invariant set of non-empty interior of solutions which are bounded and positive. Although it is not easy to proceed with explicit computations and we focus on the case $d = 4$.

Theorem 2.3.2 *There is a non-empty set of entries (J_0, J_1, J_2, L, F) so that the system (2.1.2) displays a full open set of solutions which are positive and bounded.*

Proof. It is enough to check that there are conditions on the entries so that the system (2.1.2) displays a positive stationary point. This yields:

$$\begin{aligned}
x^* &= \frac{k\big(T_a(J_0+J_1)+T_2(J_0+J_1+J_2)+(TT_2+TT_a+T_2T_a)\dfrac{y^*}{k'+y^*}\big)}{-T_a(J_0+J_1)-T_2(J_0+J_1+J_2)+(TT_2+TT_a+T_2T_a)\dfrac{k'}{k'+y^*}},\\
u^* &= \frac{k_n\big(\dfrac{J_1}{T_1}+\dfrac{T_a(J_0+J_1)+T_2(J_0+J_1+J_2)}{TT_2+TT_a+T_2T_a}+\dfrac{y^*}{k'+y^*}\big)}{1-\big(\dfrac{J_1}{T_1}+\dfrac{T_a(J_0+J_1)+T_2(J_0+J_1+J_2)}{TT_2+TT_a+T_2T_a}+\dfrac{y^*}{k'+y^*}\big)},\\
v^* &= \frac{k_a\big(TJ_2+T_2(J_0+J_1+J_2)+(TT_2+TT_a+T_2T_a)\dfrac{y^*}{k'+y^*}\big)}{-TJ_2-T_2(J_0+J_1+J_2)+(TT_2+TT_a+T_2T_a)\dfrac{k'}{k'+y^*}},\\
y^* &= L+\frac{J_0+J_1+J_2}{F}.
\end{aligned} \tag{2.3.2}$$

Note that, for instance in the limit where $J = (J_0, J_1, J_2) = O(\eta)$ is small, then $y^* = \frac{L}{k'+L} + O(\eta)$ and we check that the other coordinates are also positive. □

2.3.3 Sufficient condition for non periodic solution

Theorem 2.3.3 *If the stationary point $s^* \in int(\mathbb{R}^d_+)$, then the system* (2.2.1) *has no periodic solution in $\mathbb{R}^d_+$.*

Proof. Denote

$$s^* = (x^*, u_1^*, \cdots, u_N^*, v_1^*, \cdots, v_A^*, y^*) := (x^*, u^*, v^*, y^*),$$

where $u^* \in \mathbb{R}^N$ and $v^* \in \mathbb{R}^A$.

For all $t \geq 0$, $\Phi(t, s^0)$ denotes the solution of system for problem of the initial

value $s^0 \in \mathbb{R}_+^d$. Since $\forall t \geq 0$, $\Phi(t, s^0) \geq 0$, then

$$\frac{d}{dt}\|\Phi(t, s^0)\|_1 = \frac{dx}{dt} + \sum_{n=1}^{N} \frac{du_n}{dt} + \sum_{a=1}^{A} \frac{dv_a}{dt} + \frac{dy}{dt} = \sum_{i=1}^{N+A} J_i + F(L - y(t)).$$

Let $s^1 \geq s^0$ and $s^1 \geq s^*$, then $\forall t \geq 0$, $\Phi(t, s^1) \geq \Phi(t, s^*) = s^*$ because the system is cooperative. In particular, $y^1(t) \geq y^*$, hence

$$\frac{d}{dt}\|\Phi(t, s^1)\|_1 \leq 0.$$

In addition by cooperativeness, we have also $0 \leq \Phi(t, s^0) \leq \Phi(t, s^1)$, hence

$$\|\Phi(t, s^0)\|_1 \leq \|\Phi(t, s^1)\|_1 \leq s^1,$$

hence $\Phi(t, s^0)$ is uniformly bounded in $\mathbb{R}_+^d$ for all $t \geq 0$.

Second, suppose there exists a non constant T-periodic solution $S_{per}(t)$, $X_{per} := \{S_{per}(t) \,|\, t \in [0, T]\}$. X_{per} is obviously an invariant set for all $t \geq 0$, i.e. $\Phi_t(X_{per}) = X_{per}$. There exists two values such that $x_{min} \leq X_{per} \leq x_{max}$, where $x_{min} := \sup\{x \in \mathbb{R}_+^d \,|\, \forall t, x \leq X_{per}(t)\}$ and $x_{max} := \min\{x \in \mathbb{R}_+^d \,|\, \forall t, x \geq X_{per}(t)\}$, such that $x_{min} < x_{max}$ (since X_{per} contains at least two distinct points). By monotonicity, $\Phi_t(x_{min}) \leq X_{per}$, which implies $\Phi_t(x_{min}) \leq x_{min}$ by maximality of x_{min}, hence $\Phi_t(x_{min})$ decreases and is bounded. So it must tend to an equilibrium point in $\mathbb{R}_+^d$. For $\Phi_t(x_{max})$ increases and is bounded, it must tend to another equilibrium point for the same reason. This is a contradiction to our assumption that s^* is a unique positive equilibrium point. $\square$

2.4 Remarks and Perspectives

1- A natural question (for instance for the 4-dimensional system) is whether the conditions on the non-existence of stationary point inside the domain Ω implies that there is no bounded positive solutions.

2- There is a non-autonomous version of the Brain Lactate Dynamics for which the entries $J(t)$ and the forcing term $F(t)$ are time dependent. Further studies on the cooperative nature of these dynamics will be developed.

3- It should be interesting to analyse the reaction-diffusion PDE system obtained by adding diffusion to the 4-dimensional system (2.1.2) from the viewpoint of cooperative systems.

Chapter 3

Application for model of Brain Lactate Metabolism with piecewise system

Contents

3.1 Introduction **59**

3.2 Qualitative analysis of system (3.1.1) **61**

3.3 Global dynamics of system (3.1.2) **when** F **depends on the lactate concentration of Capillary domain** **67**

3.4 Global dynamics of system (3.1.2) **when** F **depends on the lactate concentration of the interstitial domain** . . **71**

3.4.1 An example of numerical simulation 78

3.5 Conclusions **78**

3.1 Introduction

In this chapter, 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 extracellular 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.

The nonlinear system of ODEs defined as follows:

$$\begin{aligned} \frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}) \qquad T,\ k,\ k',\ J > 0, \\ \frac{dy}{dt} &= F(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}) \qquad F,\ L > 0, \end{aligned} \tag{3.1.1}$$

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, Francoise, Guillevin, Lahutte-Auboin] (see [18, 54, 55, 56]). In this context, $x = x(t)$ and $y = y(t)$ correspond to the Lactate concentrations in an interstitial (i.e. extracellular) 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 [50]). 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 [73]). Here, our results are independent of this scaling. Recently, in [72, 35], 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 (3.1.1) the forcing term J and input terms F are assumed frozen.

In [56], 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 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 $\mathcal{V}_F$:

$$\begin{aligned} \frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \\ \frac{dy}{dt} &= F(x, y)(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}). \end{aligned} \tag{3.1.2}$$

If $\Omega^+ = \mathbb{R}^2_+$ and $\Omega^- = \varnothing$ (i.e. $F = F^+$ everywhere), we denote system (3.1.2) as $\mathcal{V}_{F^+}$. If $\Omega^- = \mathbb{R}^2_+$ and $\Omega^+ = \varnothing$ (i.e. $F = F^-$ everywhere), we denote system (3.1.2)

as $\mathcal{V}_{F^-}$. System $\mathcal{V}_{F^+}$ and system $\mathcal{V}_{F^-}$ are the two special cases of system (3.1.2) and they have same topological properties of trajectories as system (3.1.2). 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 [46]).

The chapter is organized as follows: we discuss two different choices of domains in (3.3.1) and (3.4.1). In section 3.2, we give some general properties of system (3.1.1) which are common to systems $\mathcal{V}_{F^\pm}$. In sections 3.3 and 3.4, 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 [9].

3.2 Qualitative analysis of system (3.1.1)

In this section, we study dynamics of system (3.1.1) in $\mathbb{R}^2_+$ for a given constant F [56, 18, 28]. 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 (3.1.2) in $\mathbb{R}^2_+$.

Proposition 3.2.1 *System* (3.1.1) *is cooperative in* $\mathbb{R}^2_+$ *and all solutions of system* (3.1.1) *are positive if the initial points are in the interior of the first quadrant* $\mathbb{R}^2_+$.

Proof. Let

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

Then the Jacobian matrix A of the vector field of system (3.1.1) is

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

Since 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 [83]). 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 3.2.1 *System* (3.1.1) *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* (3.1.1) *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* (3.1.1) *are positively unbounded in* $\mathbb{R}^2_+$.

Proof. The existence of equilibrium points of system (3.1.1) in $\mathbb{R}^2_+$ is given by non-negative 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 (3.1.1) 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 (3.1.1) is a locally stable node.

Note that the divergence of system (3.1.1) 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 (3.1.1) 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 (3.1.1) is globally stable in $\mathbb{R}^2_+$, we only need to prove that all solutions of system (3.1.1) 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.3.1) surrounded by four line segments:

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

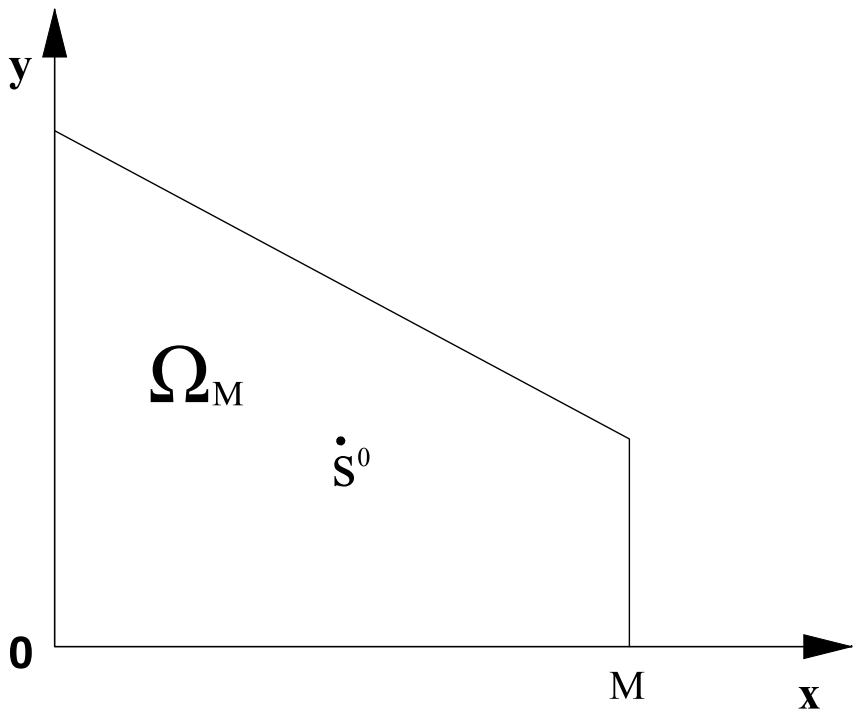


Figure 3.1: The convex set Ω_M

Clearly, the restriction of the vector field (3.1.1) on the boundary of Ω_M is $\frac{d(\ell_1)}{dt}|_{(3.1.1)} > 0$, $\frac{d(\ell_3)}{dt}|_{(3.1.1)} > 0$, furthermore,

$$\begin{aligned}
\frac{d(\ell_2)}{dt}|_{(3.1.1)} &= J - T(\frac{M}{k+M} - \frac{y}{k'+y}) \le J - T(\frac{M}{k+M} - \frac{y^0}{k'+y^0}) < 0,\\
\frac{d(\ell_4)}{dt}|_{(3.1.1)} &= F(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}) + \left(J - T(\frac{x}{k+x} - \frac{y}{k'+y})\right)\\
&= J + F(L-y) \le J + F(L-y^0) = 0.
\end{aligned}$$

Thus, Ω_M is a positively invariant subset of the system (3.1.1) in $\mathbb{R}^2_+$, and all solutions of system (3.1.1) in $\mathbb{R}^2_+$ enter the convex set Ω_M as t tends to $+\infty$ as system (3.1.1) has a unique equilibrium point in $\mathbb{R}^2_+$.

On the other hand, if system (3.1.1) has no equilibrium points in $\mathbb{R}^2_+$, then all solutions of system (3.1.1) are unbounded as t tends to $+\infty$ since the direction of vector field of system (3.1.1) on the positive x-axis (y-axis) is from down (left, resp.) to up (right, resp.) and system (3.1.1) has no closed orbits in $\mathbb{R}^2_+$.

Below, Fig.3.2 is a preliminary sketch of orbits of system (3.1.1) when $s^0 \in \mathbb{R}^2_+$. $\square$

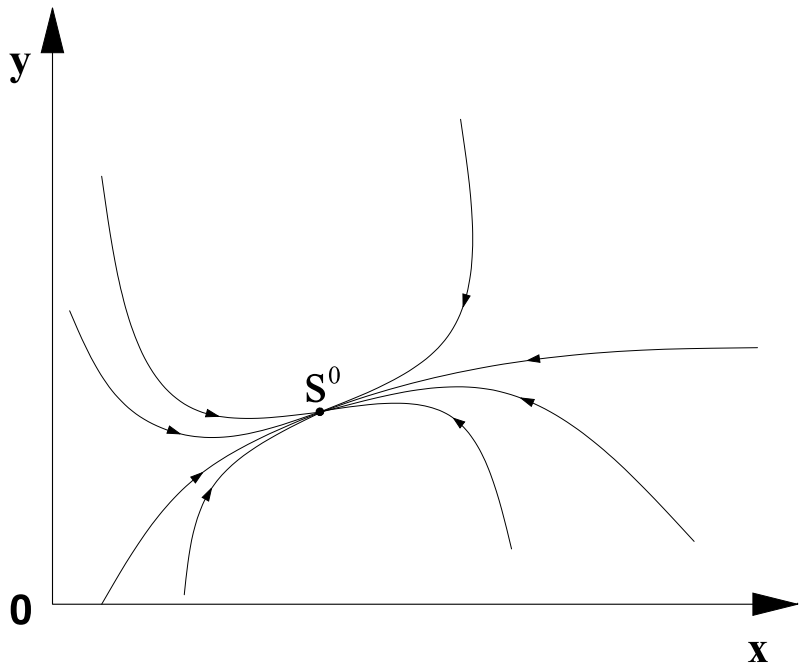


Figure 3.2: Orbits of system (3.1.1) when $s^0 \in \mathbb{R}^2_+$

Lemma 3.2.2 *When the system* (3.1.1) *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*

$$\begin{aligned} v_1 &= \left(\tfrac{1}{2a}(F+b-a) - \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right), \\ v_2 &= \left(\tfrac{1}{2a}(F+b-a) + \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab}, \quad 1 \quad\right), \end{aligned} \tag{3.2.1}$$

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:

$$\begin{aligned} &\tfrac{1}{2a}(F+b-a) - \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab} < 0, \\ &\tfrac{1}{2a}(F+b-a) + \tfrac{1}{2a}\sqrt{(F+b-a)^2+4ab} > 0. \end{aligned}$$

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 3.2.1, 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 3.2.1, 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

$$\begin{aligned} x^{\pm} &= \frac{k(\frac{J}{T} + \frac{y^{\pm}}{k'+y^{\pm}})}{1 - (\frac{J}{T} + \frac{y^{\pm}}{k'+y^{\pm}})}, \\ y^{\pm} &= L + \frac{J}{F^{\pm}}. \end{aligned} \tag{3.2.2}$$

We consider the following problem of the initial value

$$\begin{aligned} \frac{dx}{dt} &= J - T(\frac{x}{k+x} - \frac{y}{k'+y}), \\ \frac{dy}{dt} &= F^+(L-y) + T(\frac{x}{k+x} - \frac{y}{k'+y}), \\ x(0) &= x^-, y(0) = y^-. \end{aligned} \tag{3.2.3}$$

Then there exists a unique orbit $\varphi^+(t; s^-)$ of system (3.2.3) 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 3.2.1. 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 (3.1.2).

Proposition 3.2.2 *(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 3.2.1 and the expressions (3.2.2), we can obtain the following 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.

3.3 Global dynamics of system (3.1.2) 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:

$$F(x,y) = \begin{cases} F^+, & y < h, \\ F^-, & y \geq h. \end{cases} \tag{3.3.1}$$

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**.

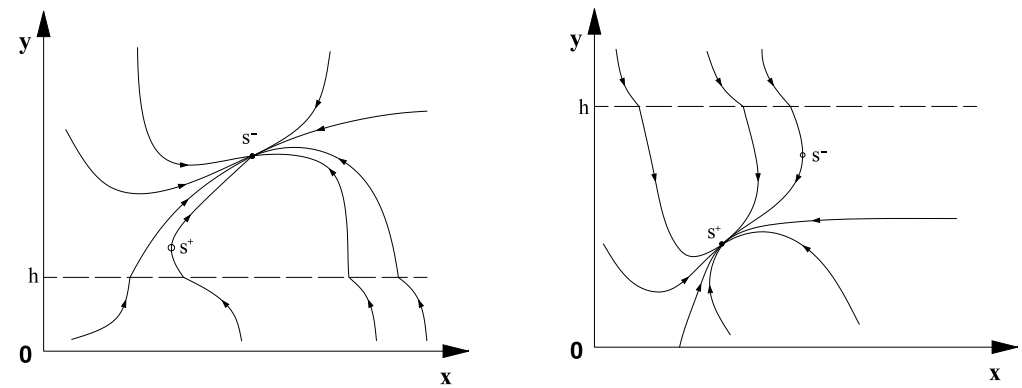
Theorem 3.3.1 *Suppose $F^+ > F^-$ ($F^- > F^+$, respectively) and $F(x, y)$ follows (3.3.1), then the piecewise system* (3.1.2) *displays one equilibrium point in $\mathbb{R}^2_+$ if $h \leqslant L + \frac{J}{F^+}$ or $h > L + \frac{J}{F^-}$.*

(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 (3.1.2)*.*

(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 (3.1.2)*.*

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 3.2.2 and Lemma 3.3.2, 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.3.3(a) is the case when $h \leqslant L + \frac{J}{F^+}$ and Fig.3.3(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 3.3: Piecewise system (3.1.2) has one globally asymptotically stable equilibrium point in $\mathbb{R}^2_+$

Lemma 3.3.1 *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

$$F^+(L-h) + T(\frac{x}{k+x} - \frac{h}{k'+h}) = 0, \tag{3.3.2}$$

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 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

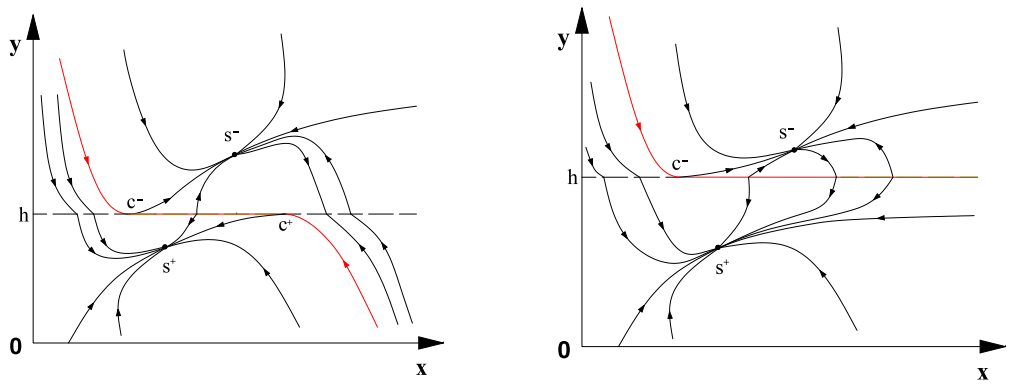
$$h_2^+ = -\frac{1}{2}(k' - L) + \frac{1}{2}\sqrt{(k' - L)^2 + 4(Lk' + \frac{Tk'}{F^+})}.$$

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 3.3.2 *Suppose $F^+ > F^-$ and $F(x, y)$ follows* (3.3.1)*, Assume that $L + \frac{J}{F^+} < h \leqslant L + \frac{J}{F^-}$, then the piecewise system* (3.1.2) *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* (3.1.2) *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 3.2.1 and 3.2.2, 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 3.3.1, there is a tangent point $c^- \in \mathbb{R}_+^2$ if $y^+ = L + \frac{J}{F^+} < h \leqslant h_2^+$ see Fig.3.4(a) and the tangent point $c^+ \notin \mathbb{R}_+^2$ if $h_2^+ < h \leqslant y^- = L + \frac{J}{F^-}$ see Fig.3.4(b). In Fig.3.4, $\mathcal{A}^-$ 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 3.2.1. 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.3.4. 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 $y = h$. □



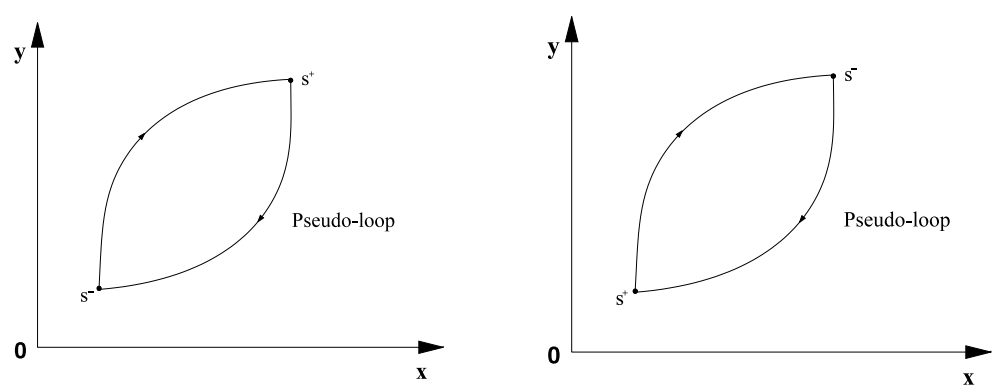
(a) The case $y^+ < h \leqslant h_2^+$ (b) The case $h_2^+ < h \leqslant y^-$

Figure 3.4: Basins of attraction separated by the boundary curve

Lemma 3.3.2 *(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 3.2.2. 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 (3.1.2). There exist two types of pseudo-loop according to the relative values of F^- and F^+. Fig.3.5 provides two examples of pseudo-loop for $F^- > F^+$ and $F^+ > F^-$.



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

Figure 3.5: Two examples of pseudo-loop

Theorem 3.3.3 *Suppose $F^- > F^+$ and $F(x,y)$ follows* (3.3.1)*, and assume furthermore that $L + \frac{J}{F^-} < h \leq L + \frac{J}{F^+}$, then the piecewise system* (3.1.2) *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 3.3.2 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 3.3.1. 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 (3.2.1) 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 (3.1.2).

Finally, if there is a piecewise periodic orbit of (3.1.2), 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.3.6: □

3.4 Global dynamics of system (3.1.2) when F depends on the lactate concentration of the interstitial domain

We consider in this section 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

$$F(x,y) = \begin{cases} F^+, & x < h, \\ F^-, & x \geq h. \end{cases} \tag{3.4.1}$$

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 3.4.1 *Suppose $F^+ > F^-$ ($F^- > F^+$, respectively) and $F(x,y)$ follows* (3.4.1)*, then the piecewise system* (3.1.2) *has one equilibrium point in $\mathbb{R}^2_+$ if $h \leqslant x^+$ or $h > x^-$. In addition,*

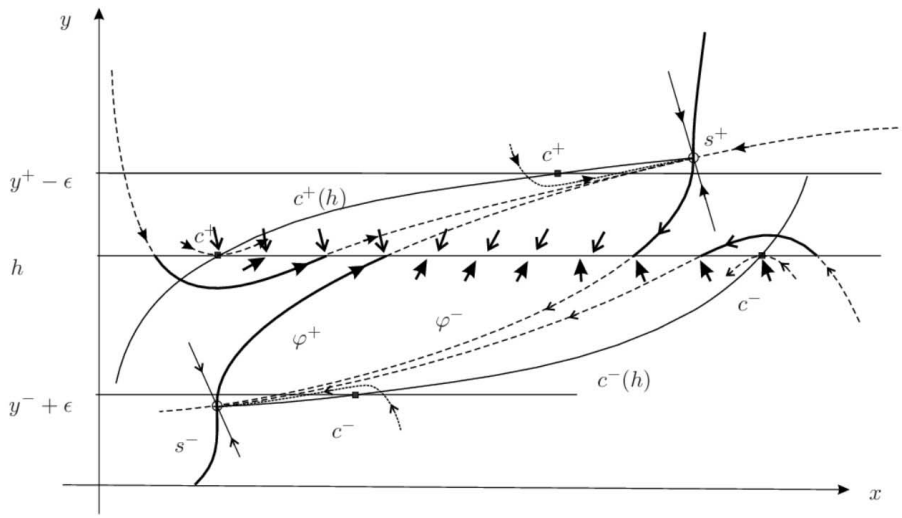


Figure 3.6: Piecewise system (3.1.2) has non equilibrium point but an attracting set in $\mathbb{R}^2_+$ with $F^- > F^+$

(i) When $h \leqslant x^+$ ($h \leqslant x^-$, respectively), s^- (s^+, respectively) is the unique globally stable equilibrium point of the piecewise system (3.1.2).

(ii) When $h > x^-$ ($h > x^+$, respectively), s^+ (s^-, respectively) is the unique globally stable equilibrium point of the piecewise system (3.1.2).

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

Proof. The proof follows the lines of the proof of Theorem 3.3.1. □

Lemma 3.4.1 *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 is 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 3.4.2 *Suppose $F^+ > F^-$ and $F(x, y)$ follows* (3.4.1)*, then the piecewise system* (3.1.2) *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* (3.1.2) *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 3.3.2, 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 3.4.1, there exists a unique tangent point c for both the right and left subsystem, which is a point located at the boundary curve (the red curve in Fig.3.7). In Fig.3.7, $\mathcal{A}^-$ 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. □

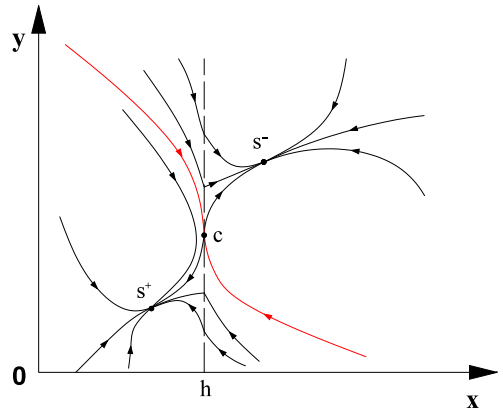


Figure 3.7: $F(x, y)$ is a piecewise function follows (3.4.1) with $F^+ > F^-$

Theorem 3.4.3 *Suppose $F^- > F^+$ and $F(x, y)$ is the piecewise function given by* (3.4.1)*, then*

(i) the piecewise system (3.1.2) *has no equilibrium in $\mathbb{R}^2_+$ for $x^- < h < x^+$, and a unique boundary equilibrium c on $x = h$.*

(ii) the segments $(x = h)\backslash c$ 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 3.4.1. 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 (3.2.1) 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, 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.3.8. 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.3.8. 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.

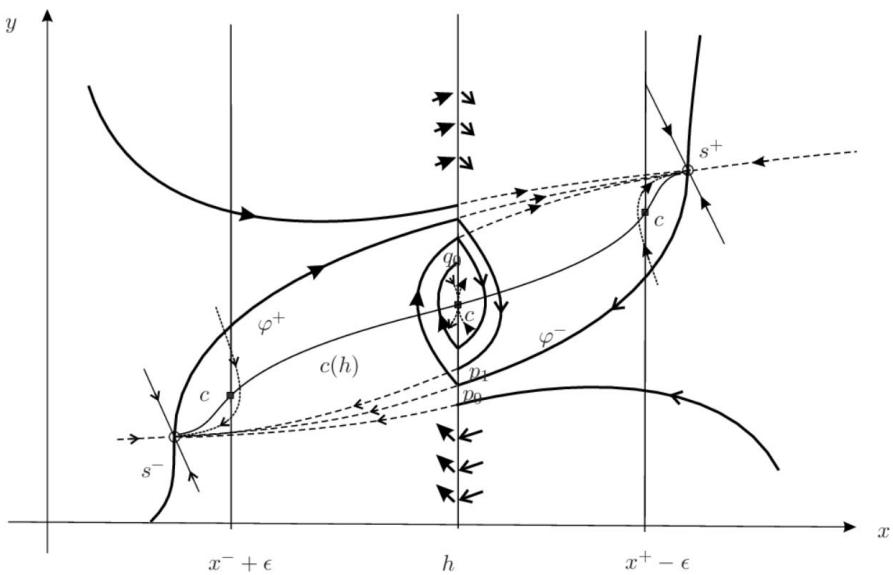


Figure 3.8: The piecewise system (3.1.2) displays a Poincaré mapping associated to the sawing section $\{x = h\} \setminus h$ surrounding the unique boundary equilibrium point c inside the pseudo-loop.

Finally, it follows from Lemma 3.2.1 that the pseudo-nodes s^+ and s^- are globally stable, which implies that any orbit of (3.1.2) shall go through the separating line $x = h$, then tend to c or a limit cycle as $t \to \infty$.

□

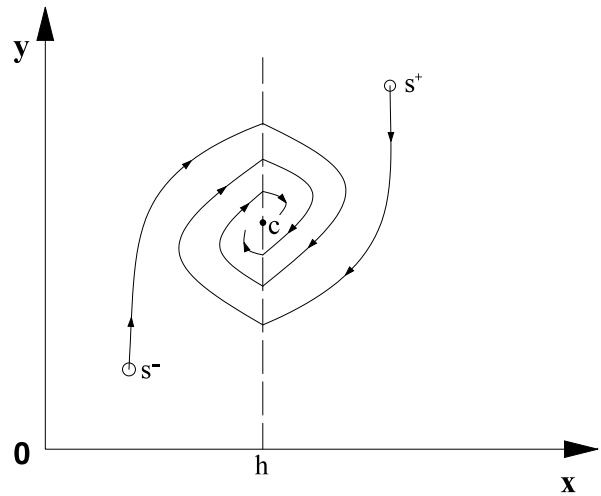


Figure 3.9: Two orbits connecting the pseudo equilibrium points s^+ and s^- with the boundary equilibrium

Theorem 3.4.4 *With the condition of theorem* (3.4.3)*, the piecewise system* (3.1.2) *has no periodic solution in* $\mathbb{R}^2_+$

Proof. We suppose there is a periodic solution in $\mathbb{R}^2_+$ referred as Γ . We denote the part on the right side of the separator line $\{(x,y)|x=h, y\geq 0\}$ as Γ^+ and the part on the left side of the separator line as Γ^-. We denote also Γ^h the part of the separator line which is inside the Γ, which represents go from bottom to top. $-\Gamma^h$ means go from top to bottom. The domain which is surrounded by Γ^+ and Γ^h is called D^+ and the domain which is surrounded by Γ^- and Γ^h is called D^-, see Fig.3.10.

In piecewise system, we denote $f^+ = (f_1^+, f_2^+)$ (resp. $f^- = (f_1^-, f_2^-)$) as the vector field on the right-hand side (resp. left-hand side) of the separator line. By Green's formula, we have

$$\begin{aligned}
&\iint_{D^+} (\frac{\partial f_1^+}{\partial x} + \frac{\partial f_2^+}{\partial y}) dxdy \\
=&\int_{\Gamma^+\cup\Gamma^h} f_1^+ dy - f_2^+ dx \\
=&\int_{\Gamma^+} f_1^+ dy - f_2^+ dx + \int_{\Gamma^h} f_1^+ dy - f_2^+ dx \\
=&\int_{\Gamma^+} f_1^+ f_2^+ dt - f_2^+ f_1^+ dt + \int_{\Gamma^h} f_1^+ dy - f_2^+ dx \\
=&\int_{\Gamma^h} f_1^+ dy - f_2^+ dx,
\end{aligned} \tag{3.4.2}$$

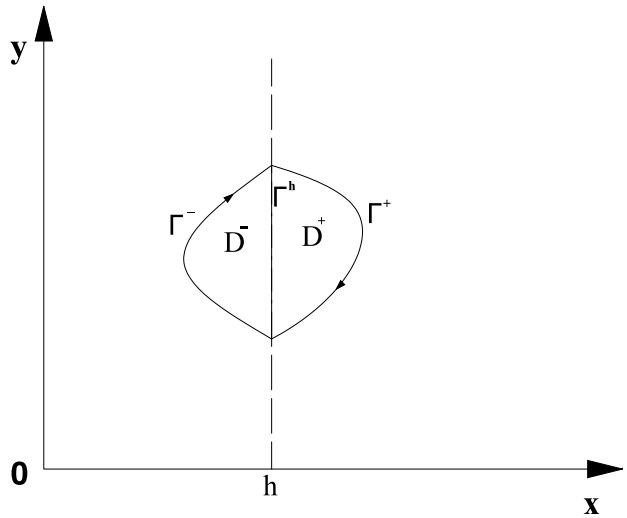


Figure 3.10: Suppose there exists a periodic solution Γ which contain Γ^+ and Γ^-

and

$$\begin{aligned}
&\iint_{D^-}(\frac{\partial f_1^-}{\partial x}+\frac{\partial f_2^-}{\partial y})dxdy\\
=&\int_{\Gamma^+\cup-\Gamma^h} f_1^- dy - f_2^- dx\\
=&\int_{\Gamma^+} f_1^- dy - f_2^- dx + \int_{-\Gamma^h} f_1^- dy - f_2^- dx \qquad (3.4.3)\\
=&\int_{\Gamma^+} f_1^- f_2^- dt - f_2^- f_1^- dt + \int_{-\Gamma^h} f_1^- dy - f_2^- dx\\
=&\int_{-\Gamma^h} f_1^- dy - f_2^- dx.
\end{aligned}$$

As $dx = 0$ on Γ^h and $f_1^+ = f_1^-$, so

$$\int_{\Gamma^h} f_1^+ dy - f_2^+ dx + \int_{-\Gamma^h} f_1^- dy - f_2^- dx = \int_{\Gamma^h} f_1^+ dy - \int_{\Gamma^h} f_1^- dy = 0, \qquad (3.4.4)$$

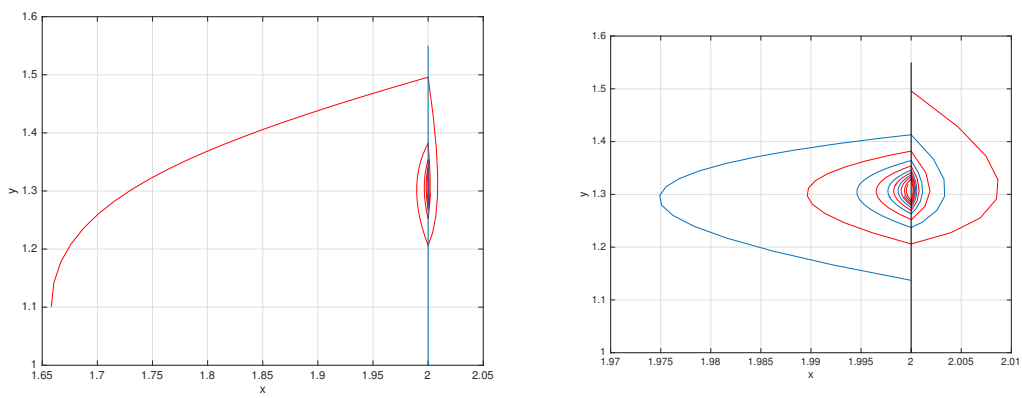
which is contradict with

$$\iint_{D^+}(\frac{\partial f_1^+}{\partial x}+\frac{\partial f_2^+}{\partial y})dxdy + \iint_{D^-}(\frac{\partial f_1^-}{\partial x}+\frac{\partial f_2^-}{\partial y})dxdy < 0. \qquad (3.4.5)$$

So there is no periodic solution in $\mathbb{R}^2_+$. $\square$

3.4.1 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 (3.4.1) (see Fig.3.11). 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.3.11 (a), we draw one orbit which begins with the initial point $s^- = (1.658, 1.1)$ and in Fig.3.11 (b), we draw two orbits which begin with the two different intersection points between the pseudo-loop and the separator line $x = 2$.



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

Figure 3.11: Numerical simulation of orbits for $F^- > F^+$ and $F(x, y)$ follows (3.4.1)

3.5 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. [4, 5, 18, 54, 56, 55]). 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 [56, 54]).

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 were not present in the ODE model.

Within the conditions of Theorem 3.3.2 and 3.4.2 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 3.3.3, there exists an attracting set which is a sliding section.

With the conditions of Theorem 3.4.3, 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.

Chapter 4

Sharp seasonal threshold property for cooperative population dynamics with concave nonlinearities

Contents

4.1 Introduction **81**
4.2 Context and motivation **84**
4.3 Results **86**
4.3.1 General results 86
4.3.2 Application to a two-dimensional model of insect population dynamics 88
4.4 Proofs **89**
4.4.1 Proof of Theorem 4.3.1 89
4.4.2 Proof of Theorem 4.3.2 92
4.4.3 Proofs of Proposition 4.3.1 and Proposition 4.3.2 93
4.4.4 Proof of Theorem 4.3.3 98
4.4.5 An example of numerical simulation 101
4.5 Discussion and extensions **101**

4.1 Introduction

We consider a biological population whose environment varies periodically in time, exhibiting two very different "seasons": one is favorable and the other one is unfavor-

able. For monotone differential models with concave nonlinearities, we address the following question: the system's period being fixed, under what conditions does there exist a critical duration for the unfavorable season? By "critical duration" we mean that above some threshold, the population cannot sustain and extincts, while below this threshold, the system converges to a unique periodic and positive solution. We term this a "sharp seasonal threshold property" (SSTP, for short).

We study differential dynamical systems arising from nonlinear periodic positive differential equations of the form

$$\frac{dx}{dt} = F(t, x), \tag{4.1.1}$$

where F is monotone and concave (in x). These systems exhibit well-known contraction properties when F is continuous (see [46], [80], [48]). We extend in Theorem 4.3.1 these properties to non-linearities that are only piecewise-continuous in time. This extension is motivated by the study of typical seasonal systems in population dynamics.

We denote by $\theta \in [0, 1]$ the proportion of the year spent in unfavorable season. Then, we convene that time t belongs to an unfavorable (resp. a favorable) season if $nT \leq t < (n + \theta)T$ (resp. if $(n + \theta)T \leq t < (n + 1)T$) for some $n \in \mathbb{Z}_+$. In other words, we study the solutions to:

$$\frac{dX}{dt} = G(\pi_\theta(t), X), \quad \pi_\theta(t) = \begin{cases} \pi^U \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [0, \theta), \\ \pi^F \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [\theta, 1), \end{cases} \tag{4.1.2}$$

for some $G : \mathcal{P} \times \mathbb{R}^N \to \mathbb{R}^N$, with $\pi^U, \pi^F \in \mathcal{P}$ where $\mathcal{P}$ is the parameter space. We are looking for conditions ensuring that a sharp seasonal threshold property holds, that is:

$$\exists \theta_* \in [0, 1] \text{ such that } \begin{cases} \text{if } \theta < \theta_*, \exists\, !\, q : \mathbb{R}_+ \to \mathbb{R}^N, T\text{-periodic}, q \gg 0 \text{ and} \\ \forall X_0 \in \mathbb{R}^N_+ \backslash \{0\}, X \text{ converges to } q, \\ \text{if } \theta > \theta_*, \forall X_0 \in \mathbb{R}^N_+,\ X \text{ converges to } 0. \end{cases} \tag{SSTP}$$

Ecologically, the respective duration of dry and wet seasons is crucial for population sustainability in various species. The property (SSTP) means that if the dry season is longer than $\theta_* T$ then the population collapses and if it is shorter then the population densities will tend to be periodic.

Assume that $F(t, 0) \equiv 0$. Thanks to the contraction properties of concave nonlinearities, the whole problem reduces to the study of the Floquet eigenvalue with maximum modulus of the linearization of (4.1.1) at $X = 0$:

$$\frac{dz}{dt} = D_x F(t, 0) z. \tag{4.1.3}$$

In fact, this eigenvalue is equal to the spectral radius of the Poincaré application for (4.1.3), which we compute here for piecewise-autonomous systems.

Our proof uses the Perron-Frobenius theorem and relies on the Perron eigenvalue and (left and right) eigenvectors. The importance of this eigenvalue for quantifying the effects of seasonality has been acknowledged continuously in mathematical biology in at least three application fields: circadian rhythms (in particular in connection with cell division and tumor growth), harvesting and epidemiology.

It was noted in [16] that Floquet eigenvalue with maximum modulus of (4.1.3) is always larger that the Perron eigenvalue of some averaged (over a period) matrix $\overline{F}$ defined from the entries of $D_xF(t,0)$. There has been a continued interest in this eigenvalue for linear models of cell division since and we refer to [30] in particular for a detailed study of the monotonicity of the Perron eigenvalue with respect to parameters of a structured model for cell division. In a stochastic framework for growth and fragmentation, [14] establishes a similar monotonicity property. In this context, the Perron eigenvalue is seen as the cell growth rate, and this is why its dependence in the model parameters is important. Here, we connect the eigenvalue monotonicity with a non-extinction condition to derive the (SSTP). We emphasize that our Theorem 4.3.2 gives some sufficient conditions for the monotonicity of the Perron eigenvalue, in the case when there are only two different seasons.

In dimension 1, for the logistic equation with harvesting, Xiao has shown in [88] a sharp threshold property, where the two different "seasons" correspond to one harvesting period ("unfavorable season") and one rest period ("favorable season"). Contrary to the case of cell division, the model treated there is non-linear, though 1-dimensional. Our results extend a part of those of [88] to n-dimensional concave monotone systems. Note that the cited article also studies the maximal sustainable yield, which can be seen as an objective function of the periodic solution q. On this topic, [74, Section 5] studies a structured problem of adaptive dynamics with concave nonlinearity and periodic forcing to show a similar effect as in [88] (there, for population size): in both cases, time fluctuations can improve an objective value.

For applications in epidemiology, where seasonality often has dramatic effects, we refer to [7] and [6] for the computation of case reproduction numbers with seasonal forcing.

The organization of the paper is as follows. The motivating model is detailed in Section 4.2, where we also define some notations. In Section 4.3 we state our results: first Theorem 4.3.1 an extension to piecewise-continuous nonlinearities of the well-known results on monotone concave nonlinearities, then Theorem 4.3.2 fairly general sufficient conditions for systems in any space dimension $N \in \mathbb{Z}_{>0}$ to satisfy (SSTP), and finally Theorem 4.3.3 an application to the two-dimensional system (4.1.2), for which we are able to show the threshold property (SSTP) for a wide range of parameters. The proofs are detailed in Section 4.4, while extensions and possible research directions are gathered in Section 4.5.

4.2 Context and motivation

Our reference model is a simplistic description of the population dynamics of some insects, with a juvenile stage exposed to quadratic competition and an adult stage. Let $J(t), A(t)$ represent the populations of juveniles and adults at time t, respectively. A very simple dynamic is defined by

$$\begin{cases} \dfrac{dJ}{dt} = bA - J(h + d_J + c_J J), \\ \dfrac{dA}{dt} = hJ - d_A A, \end{cases} \tag{4.2.1}$$

where d_Y ($Y \in \{J, A\}$) stands for the (linear) death rate, b is the birth rate, h is the hatching rate and the parameter c_J tunes the only non-linearity: quadratic competition (=density-dependent death rate) among juveniles. This term effectively limits the total population size, as we will prove below. We use it to represent resource limitation both for breeding sites availability and for nutrient availability during growth. In principle, the parameters may depend on time:

$$\forall t \in \mathbb{R}, \quad \pi(t) := (b, h, d_J, c_J, d_A) \in \mathbb{R}^5_+. \tag{4.2.2}$$

For convenience, we rewrite the right-hand side of (4.2.1) as $G(\pi, X)$ with $X = (J, A) \in \mathbb{R}^2$, and $G : \mathbb{R}^5_+ \times \mathbb{R}^2 \to \mathbb{R}^2$.

In the tempered areas where mosquito populations are established, dramatic seasonal variations in population abundance are usually observed. Namely, there is explosive growth in summer after rain events, whereas mosquitoes are very scarce in winter. This phenomenon is possible thanks to dormant (or "quiescent" or "refuge") phases in the mosquito's life-cycle. These seasonal variations imply that the natural environment (temperature, rainfall, humidity etc.) is very important for the mosquito.

We propose to study population dynamics in simple models such as (4.2.1) under periodic seasonal forcing. As a rough approximation, we set up (4.2.1) with periodic piecewise-constant coefficients of period $T = 1$ year, each one possibly taking two different values over one period. Thus, the year is divided into unfavorable and favorable seasons, defined by parameter values $\pi^U, \pi^F \in \mathbb{R}^5_+$ such that

$$\begin{pmatrix} -d_J^F + d_J^U & b^F - d_A^F - (b^U - d_A^U) \\ h^F - h^U & -d_A^F + d_A^U \end{pmatrix} > 0. \tag{4.2.3}$$

The four scalar inequalities of condition (4.2.3) deserve a biological justification. It implies that during the favorable season, the hatching rate is larger than during the unfavorable season, while death rates (for juveniles, and adults) are smaller. These

assumptions rely on the facts that breeding sites availability and quality is much higher in good season (whence higher hatching rate and birth rate and lower juvenile competition), while the temperature increase can be expected to extend the life-span of both adults and juveniles. The first component in (4.2.3) implies that the growth coefficients $b-d_A$ are ordered: $b^F-d_A^F > b^U-d_A^U$. This is true in particular if $b^F > b^U$, but holds in more generality.

We emphasize that the systems under study are excessively simple because, in mathematical terms, they are cooperative with concave nonlinearity, and as such they have strong asymptotic convergence properties.

Notations. For X, Y two real finite-dimensional vector spaces embedded in $\mathbb{R}^d$ ($d \geq 1$), we denote by $\mathcal{L}(X,Y)$ the space of linear applications from X to Y, with the convention $\mathcal{L}(X) = \mathcal{L}(X,X)$. We denote the adjoint of $A \in \mathcal{L}(X,Y)$ by $A^* \in \mathcal{L}(Y,X)$, defined by

$$\forall (v,w) \in X \times Y, \quad \langle Av, w\rangle = \langle v, A^* w\rangle,$$

where $\langle \cdot, \cdot \rangle$ denoted the euclidean scalar product in $\mathbb{R}^d$. For $x \in \mathbb{R}$, the notation $\lfloor x \rfloor$ stands for the largest integer $n \in \mathbb{Z}$ such that $n \leq x$.

Let $F : \mathbb{R}_t \times \mathbb{R}_x^N \to \mathbb{R}^N$ be piecewise continuous in t and continuously differentiable in x. The system (4.1.1) is *cooperative* if its Jacobian matrix is Metzler:

$$\forall (t,x) \in \mathbb{R}_+ \times \mathbb{R}_+^N,\ i \neq j \implies \frac{\partial F_i}{\partial x_j}(t,x) \geq 0, \tag{M}$$

It is *positive* (*i.e.*, $\mathbb{R}_+^N$ is an invariant set) if

$$\forall t \in \mathbb{R}_+,\ \forall 1 \leq i \leq N,\ \forall x \geq 0, \quad x_i = 0 \implies F_i(t,x) \geq 0. \tag{P}$$

Under condition (M), (4.1.1) is positive if $\forall t \in \mathbb{R}_+$, $F(t,0) \geq 0$. We say that (4.1.1) defines a *concave dynamics* on $\mathbb{R}_+^N$ if

$$\forall 0 \ll x \ll y,\ D_x F(t,x) \geq D_x F(t,y), \tag{C}$$

and that (4.1.3) is *irreducible* if

$$\forall t \in \mathbb{R}_+,\ D_x F(t,0) \text{ is irreducible in } \mathcal{M}_N(\mathbb{R}). \tag{I}$$

4.3 Results

4.3.1 General results

In order to study the asymptotic behavior of (4.1.2), we generalize a result by Smith [80] (refined by Jiang in [48]) about continuous concave and cooperative non-linearities to piecewise-continuous (in time) nonlinearities.

Theorem 4.3.1 *Let $F : \mathbb{R}_t \times \mathbb{R}^N_x \to \mathbb{R}^N$ be T-periodic and piecewise-continuous in t and such that for all $t \in \mathbb{R}_+$, $F(t,\cdot) \in \mathcal{C}^1(\mathbb{R}^N, \mathbb{R}^N)$. Assume that F satisfies assumptions* (P), (M), (C) *and* (I), *so that the associated differential system* (4.1.1) *is positive, monotone and concave with irreducible linearization at* 0. *Let $\lambda \in \mathbb{R}$ denote the Floquet multiplier with maximal modulus of* (4.1.3).

If $\lambda \leq 1$ then every non-negative solution of (4.1.1) *converges to* 0. *Otherwise,*

(i) either every non-negative solution of (4.1.1) *satisfies $\lim_{t\to\infty} x(t) = \infty$,*

(ii) or (4.1.1) *possesses a unique (nonzero) T-periodic solution $q(t)$.*

In case (ii), $q \gg 0$ and $\lim_{t\to\infty}(x(t)-q(t)) = 0$ for every non-negative solution of (4.1.1).

The proof of Theorem 4.3.1 follows closely the lines of [80] and [48].

An illuminating example when Theorem 4.3.1 applies is for T-periodic piecewise autonomous differential systems, where for all $x \in \mathbb{R}^N$, $F(\cdot, x)$ is a piecewise-constant function. Namely, we assume that there exists $K \in \mathbb{Z}_{>0}$ and functions $(F^k)_{1\leq k\leq K} : \mathbb{R}^N_+ \to \mathbb{R}^N_+$ such that:

$$F(t,x) = F^k(x) \text{ if } \frac{t}{T} - \left\lfloor \frac{t}{T} \right\rfloor \in [\theta_{k-1}, \theta_k), \tag{4.3.1}$$

where $(\theta_k)_{0\leq k\leq K} \in [0,1]^{K+1}$ is a non-decreasing family such that $\theta_0 = 0$ and $\theta_K = 1$. To verify the hypotheses of Theorem 4.3.1, we need to assume that for all $1 \leq k \leq K$, F^k is continuously differentiable, monotone, concave and satisfies $F^k(0) = 0$; and in addition that $DF^k(0)$ is irreducible for all $1 \leq k \leq K$.

The main advantage of piecewise-constant non-linearities is that for such dynamics (and almost only for these dynamics), the Floquet multiplier with maximal modulus λ can be computed explicitly as the following spectral radius:

$$\lambda = \rho\big(e^{(\theta_K-\theta_{K-1})T\cdot DF^K(0)} \cdots e^{(\theta_1-\theta_0)T\cdot DF^1(0)}\big). \tag{4.3.2}$$

In the case $K = 2$, with $\theta := \theta_1$, the Perron-Frobenius theorem applies to

$$M(\theta) := e^{(1-\theta)T\cdot DF^2(0)} e^{\theta T\cdot DF^1(0)},$$

which is positive since $DF^k(0)$ are (irreducible) Metzler matrix by (M) (and (I)). Therefore there exists unique vectors $V(\theta), V_*(\theta) \gg 0$ with $\|V(\theta)\| = 1$ and $\langle V(\theta), V_*(\theta)\rangle = 1$, and a unique positive number $\rho(\theta)$ such that

$$M(\theta)V(\theta) = \rho(\theta)V(\theta), \quad M(\theta)^*V_*(\theta) = \rho(\theta)V_*(\theta). \tag{4.3.3}$$

In this setting, assume without loss of generality that $\mu(DF^2(0)) \geq \mu(DF^1(0))$, and denote $S := DF^1(0) - DF^2(0)$. We consider two specific cases:

(A) $DF^1(0)$ and $DF^2(0)$ have the same principal right or left eigenvector;

(B) for all $\theta \in [0,1]$, one of the following holds:

(B-1) $\exists P \in GL_N(\mathbb{R})$, $PS < 0$ and $(P^{-1})^*V_*(\theta) > 0$;

(B-2) $\exists P \in GL_N(\mathbb{R})$, $SP < 0$ and $P^{-1}V(\theta) > 0$;

(B-3) $\exists P, Q \in \mathcal{M}_N(\mathbb{R})$, $S < P^*Q$ and $PV_*(\theta) = -QV(\theta)$.

Theorem 4.3.2 *Let F of the form* (4.3.1) *with $K = 2$ satisfy the assumptions of Theorem 4.3.1. Assume that the forward orbits of* (4.1.1) *are bounded. Then under* (A) *or* (B), (SSTP) *holds.*

Remark 4.3.1 *In addition, condition* $(B-1)$ *(resp.* $(B-2)$*) is equivalent to*

$$S^*V_*(\theta) < 0 \text{ (resp. } SV(\theta) < 0\text{)},$$

and if condition (A) *holds then $V(\theta) \equiv V$ or $V_*(\theta) \equiv V_*$, where V (resp. V_*) is the right (resp. left) principal eigenvector of $DF^i(0)$, $i \in \{1,2\}$.*

Proof. We apply Theorem 4.3.1 and check that the value of λ (determining if case (i) or (ii) occurs) is a decreasing function of θ under assumptions (A) or (B). The forward-boundedness of orbits rules out the case $x \to +\infty$, thus leading to the result. More details in Section 4.4.2. □

Remark 4.3.2 *In the case $DF^2(0) > DF^1(0)$, we note that conditions* $(B-1)$ *and* $(B-2)$ *are obviously satisfied with $P = I$ (identity matrix), and condition* $(B-3)$ *is obviously satisfied with $P = Q = 0$.*

Remark 4.3.3 *As will be seen below, in practical situations it is sometimes easier to check condition* $(B-1)$ *rather than computing $S^*V_*(\theta)$.*

4.3.2 Application to a two-dimensional model of insect population dynamics

We can now specify Theorem 4.3.2 to the two-dimensional ($N = 2$) case of (4.2.1). First we describe the general properties of this system

Proposition 4.3.1 *For system* (4.2.1) *written as* $\dot{X} = G(\pi(t), X) =: F(t, X)$, *where* π *is defined by* (4.2.2), *assume that* $\pi(t) \gg 0$, *there exists* $c, C \in \mathbb{R}_+^*$ *such that* $\pi_i(t) \geq c$ *for* $i \in \{4, 5\}$ *and* $\pi(t) \leq C\mathbb{1}$. *Then, it is positive, forward-bounded, cooperative and concave.*

Then, we give the dynamics of the non-seasonal (=autonomous) system (4.2.1) with $\pi(t) \equiv \pi = (b, h, d_J, c_J, d_A)$. We define the basic offspring number:

$$\mathcal{R}_0 = \mathcal{R}(\pi) := \frac{bh}{d_A(h + d_J)}. \tag{4.3.4}$$

Proposition 4.3.2 *If* $\mathcal{R}_0 \leq 1$, *then* (4.2.1) *has no positive steady state and the trivial equilibrium is a global attractor. If* $\mathcal{R}_0 > 1$ *then* (4.2.1) *has exactly one positive steady state* $S_1^* = (\mathcal{R}_0 - 1)\big(\frac{h+d_J}{c_J}, \frac{h(h+d_J)}{c_J d_A}\big)$, *which is a global attractor in* $\mathbb{R}_+^2 \backslash \{0\}$.

The proofs of Proposition 4.3.2 and Proposition 4.3.1 are to be found in Section 4.4.3.

We finally state the sharp seasonal threshold property for (4.1.2):

Theorem 4.3.3 *For* (4.1.2) *under assumption* (4.2.3), *if* $\mathcal{R}_0(\pi^U) < 1 < \mathcal{R}_0(\pi^F)$ *and* $b^U + d_J^U > d_A^U$ *(where* $\pi^U = (b^U, h^U, d_J^U, c_J^U, d_A^U)$*) then* (SSTP) *holds with* $\theta_* \in (0, 1)$.

Proof. We check assumption $(B - 1)$ with

$$P = \begin{pmatrix} 1 & 1 \\ 0 & 1 \end{pmatrix}, \quad (P^{-1})^* = \begin{pmatrix} 1 & 0 \\ -1 & 1 \end{pmatrix}.$$

More details in Section 4.4.4. □

Remark 4.3.4 *If instead of* (4.2.3) *we assume the stronger condition*

$$\begin{pmatrix} -(h^F + d_J^F) + h^U + d_J^U & b^F - b^U \\ h^F - h^U & -d_A^F + d_A^U \end{pmatrix} > 0, \tag{4.3.5}$$

then assumption $(B - 1)$ *(or* $(B - 2)$*) of Theorem 4.3.2 applies with* $P = I$ *and no further computations are needed.*

We emphasize that (4.2.3) *is more biologically relevant than* (4.3.5)*. The latter requires that the increase of the hatching rate between favorable and unfavorable season does more than compensate the decrease of juvenile death rate, which is highly debatable. This justifies the technical computations of Section 4.4.4.*

Note that in any case, no assumptions are made on c_J^U *and* c_J^F*, since the behavior is only determined by the linearization at* 0*.*

4.4 Proofs

4.4.1 Proof of Theorem 4.3.1

We consider the following T-periodic piecewise-autonomous differential equation

$$\frac{dx}{dt} = F(t,x), \tag{4.4.1}$$

where for all $x \in \mathbb{R}^N$, $F(\cdot, x)$ is a piecewise-constant function. We assume that there is a family of functions $(F^k)_k : \mathbb{R}_+^N \to \mathbb{R}_+^N$ such that:

$$F(t,x) = F^k(x) \text{ if } \frac{t}{T} - \lfloor \frac{t}{T} \rfloor \in [\theta_{k-1}, \theta_k)$$

where $(\theta_i)_{0 \le i \le N} \in [0,1]^{N+1}$ is a non-decreasing family such that $\theta_0 = 0$ and $\theta_N = 1$. For $x \in \mathbb{R}$, the notation $\lfloor x \rfloor$ stands for the largest integer $n \in \mathbb{Z}$ such that $n \le x$.

We assume that for all $1 \le k \le K$, $F^k : \mathbb{R}_+^N \to \mathbb{R}_+^N$ is continuously differentiable, monotone (that is, if $x \ll y$ then $F^k(x) \ll F^k(y)$), concave (that is, if $x \ll y$ then $DF^k(x) \gg DF^k(y)$) and satisfies $F^k(0) = 0$.

Following the lines of [80] and [48], to prove Theorem 4.3.1 we split into four assertions the various hypotheses of [80, Theorem 2.1], to check that they hold for the Poincare map for (4.4.1). We begin with:

Lemma 4.4.1 *If* $x(t)$ *is a solution of* (4.4.1) *with* $x(t_0) \ge 0$*, then* $x(t)$ *can be extended to* $[t_0, +\infty]$ *and* $x(t) \ge 0$ *for* $t \ge t_0$*.*

Proof. Let $t \ge 0$. For all $y \ge 0$, by concavity of all F^k $(1 \le k \le K)$, we have $D_xF(t,y) \le D_xF(t,0)$. Hence for all $t \ge 0$ and $x \ge 0$,

$$\begin{aligned} F(t,x) &= F(t,0) + \big(\int_0^1 D_xF(t,sx)ds\big)x \\ &\le F(t,0) + D_xF(t,0)x \quad \text{ since } x \ge 0. \end{aligned}$$

Let y be the solution to the affine differential equation $y' = F(t,0) + D_xF(t,0)y$, $y(t_0) = x(t_0)$. From Kamke's theorem, we deduce that $x(t) \leq y(t)$ on the maximal interval of existence $[t_0, w)$ of $x(t)$. Since $y(t)$ is defined for all $t \geq t_0$, it follows that $w = +\infty$.

The standard positivity property (P) implies $x(t) \geq 0$ for $t \geq t_0$. □

Then, as an immediate consequence of monotonicity and Kamke's theorem:

Lemma 4.4.2 *If $x(t)$ and $y(t)$ are solutions of* (4.4.1) *with $0 \leq y(t_0) \ll x(t_0)$, then $y(t) \ll x(t)$ for $t > t_0$.*

For all $s \in \mathbb{R}$ and $x_0 \in \mathbb{R}^N$, we denote by $t \mapsto \phi(t; s, x_0)$ the solution of (4.4.1) which satisfies $x(s) = x_0$. In particular, $\phi(s; s, x) = x$. For all $1 \leq k \leq K$, we also introduce $t \mapsto \phi^k(t; s, x_0)$ as the solution to

$$\frac{dx}{dt} = F^k(x), \quad x(s) = x_0.$$

By regularity of F^k, each $\phi^k(\theta_k T, \theta_{k-1}T, \cdot)$ is a C^1 function.

With these notations it follows from Lemmas 4.4.1 and 4.4.2 that the Poincare map

$$P(x) := \phi(T; 0, x) = \phi^K\big(\theta_K T; \theta_{K-1}T, \phi^{K-1}\big(\cdots \phi^1(\theta_1 T; 0, x)\big)\big), \quad x \geq 0 \tag{4.4.2}$$

is well defined as a C^1 map $P : \mathbb{R}^N_+ \to \mathbb{R}^N_+$ because it is a composition of functions of class C^1. In order to apply [80, Theorem 2.1], we must verify that the differential DP satisfies:

$$DP(0) \gg 0 \text{ and } DP(x) \geq 0 \text{ if } x \gg 0, \tag{M_0}$$
$$DP(y) < DP(x) \text{ if } 0 \ll x \ll y. \tag{C_0}$$

Introducing the notations, for $x \in \mathbb{R}^N$

$$\widetilde{\phi}^k(x) := \phi^k\big(\theta_k T; \theta_{k-1}T, \widetilde{\phi}^{k-1}(x)\big) \in \mathbb{R}^N \text{ for } 1 \leq k \leq K, \quad \widetilde{\phi}_0(x) := x,$$
$$\widehat{\phi}^k(x) := \frac{\partial \phi^k}{\partial x}(\theta_k T; \theta_{k-1}T, x) \in \mathbb{R}^{N\times N},$$

we can compute

$$DP(x) = \frac{\partial \phi}{\partial x}(T; 0, x) = \prod_{k=1}^{K} \widehat{\phi}^k \circ \widetilde{\phi}^{k-1}(x). \tag{4.4.3}$$

We write $\Phi(t, x) := \frac{\partial \phi}{\partial x}(t; 0, x)$, so that $DP = \Phi(T, \cdot)$. By construction, $\Phi(t, x)$ is

the fundamental matrix for the variational equation

$$X' = D_x F(t, \phi(t; 0, x))X, \quad X(0) = I \tag{4.4.4}$$

where I is the $N \times N$ identity matrix. Lemma 4.4.3 below is a direct consequence of (M)

Lemma 4.4.3 *If $x \gg 0$, then $\Phi(t, x) > 0$ for $t > 0$. In addition, $\Phi(t, 0) \gg 0$ for $t > 0$.*

Proof. Let $T > 0$ and $x \in \mathbb{R}^N$. Let $M = M_{T,x} \in (0, +\infty)$ such that $D_x F(t, \phi(t; 0, x)) + MI \geq 0$ for all $t \in [0, T]$. As long as $\Phi(t, x) \geq 0$ on $[0, T]$ we have on this interval $\frac{d}{dt}\Phi(t, x) \geq -M\Phi(t, x)$, hence $\Phi(t, x) \geq e^{-Mt} I > 0$.

Then, $\Phi(t, 0)$ solves (4.1.3) with $\Phi(0, 0) = I$. Since $D_x F(t, 0)$ is an irreducible (by (I)) Metzler matrix, $\Phi(t, 0) \gg 0$ for $t > 0$. □

Applying Lemma 4.4.3 with $t = T$ yields (M_0). It remains only to verify (C_0), which is the object of the next lemma

Lemma 4.4.4 *If $0 \ll x \ll y$, then $DP(x) > DP(y)$.*

Proof. We write $Z(t, x) = D_x F(t, \phi(t; 0, x))$ for short. If $0 \ll x \ll y$, from Lemma 4.4.2, we have $\phi(t; 0, x) \ll \phi(t; 0, y)$ for all $t \geq 0$. By (C), we deduce that $Z(t, x) > Z(t, y)$. Hence

$$\begin{aligned} \Phi'(t, x) &= Z(t, x)\Phi(t, x) \\ &\geq Z(t, y)\Phi(t, x), \end{aligned}$$

since $\Phi(t, x) \geq 0$ by Lemma 4.4.3. Therefore, it follows from Kamke's theorem that $\Phi(t, x) \geq \Phi(t, y)$.

Then, we follow ([3], lemma l) by letting $Y(t) = \Phi(t, x) - \Phi(t, y)$. $Y(t)$ satisfies

$$Y'(t) = Z(t, x)Y(t) + [Z(t, x) - Z(t, y)]\Phi(t, y), \quad Y(0) = 0.$$

Using the fundamental matrix Φ we get

$$Y(T) = \int_0^T \Phi(T, x)\Phi(s, x)^{-1}[Z(s, x) - Z(s, y)]\Phi(s, y)ds$$

Now, $Z(t, s) \equiv \Phi(t, x)\Phi(s, x)^{-1} > 0$ for $t > s$ since it is the fundamental matrix at $t = s$ of $z' = Z(t, x)z$ (exactly as in Lemma 4.4.3). Since $\Phi(s, y) > 0$ for $0 < s \leq T$ and $Z(s, x) - Z(s, y) \gg 0$ for $0 \leq s \leq T$, it follows that $Y(T) > 0$. This is the desired conclusion. □

We have verified all assumptions and can apply [80, Theorem 2.1] and Theorem 4.3.1 follows immediately on noting that $\lambda = \rho(DP(0)) = \rho(\Phi(T,0))$ is the characteristic multiplier of (4.1.3) of maximum modulus.

4.4.2 Proof of Theorem 4.3.2

When there are only two dynamics within a period, that is when $K = 2$, we notice that the alternative $(i) - (ii)$ from Theorem 4.3.1 is uniquely determined by the sign of the real function:

$$\theta \quad \mapsto \quad \rho\big(e^{(1-\theta)T\cdot DF^2(0)}e^{\theta T\cdot DF^1(0)}\big) - 1.$$

We notice that

Lemma 4.4.5 *The function $\rho : [0,1] \to \mathbb{R}$ is $\mathcal{C}^1$ and satisfies*

$$\rho'(\theta) = T\rho(\theta)\langle (DF^1(0) - DF^2(0))V(\theta), V_*(\theta)\rangle. \tag{4.4.5}$$

Proof. By Perron-Frobenius theorem, $\rho(\theta)$ is the maximal root of the characteristic polynomial of $M(\theta)$, whose entries are analytic functions of θ. In particular, it is $\mathcal{C}^1$.

The principal eigenvector of norm 1 of $M(\theta)$, that is $V(\theta)$, depends smoothly of θ, as can be seen by uniqueness for all θ. Then, $V_*(\theta)$ also depends smoothly of θ since the same argument applies to $M^*(\theta)$ and $V_*(\theta)$ is equal to the principal eigenvector $Y_*(\theta)$ of $M^*(\theta)$ divided by $\langle V(\theta), Y_*(\theta)\rangle > 0$, which is a smooth function of θ.

Let us write $M_i := DF^i(0)$ for $i \in \{1,2\}$. We differentiate the identity $\rho(\theta) = \langle M(\theta)V(\theta), V_*(\theta)\rangle$ to obtain

$$\begin{aligned}
\rho'(\theta) &= \langle M(\theta)V'(\theta), V_*(\theta)\rangle + \langle M'(\theta)V(\theta), V_*(\theta)\rangle + \langle M(\theta)V(\theta), V_*'(\theta)\rangle,\\
&= \rho(\theta)\Big(\langle V'(\theta), V_*(\theta)\rangle + T\big(\langle V(\theta), M_1^*V_*(\theta)\rangle - \langle M_2V(\theta), V_*(\theta)\rangle\big) + \langle V(\theta), V_*'(\theta)\rangle\Big),\\
&= T\rho(\theta)\langle (M_1 - M_2)V(\theta), V_*(\theta)\rangle,
\end{aligned}$$

since $M'(\theta) = Te^{(1-\theta)TM_2}\big(M_1 - M_2\big)e^{\theta TM_1}$ and $\langle V(\theta), V_*(\theta)\rangle \equiv 1$. □

Applying Theorem 4.3.1 with the assumption that the forward orbits are bounded, we are left with either global asymptotic stability of 0 is $\lambda \leq 1$, or the global stability of the unique positive periodic solution, if $\lambda > 1$. Using formula (4.3.2), we obtain (SSTP) with $\rho(\theta_*) = 1$ (or $\theta_* = 0$ if $\rho(0) > 1$, and $\theta_* = 1$ if $\rho(1) \leq 1$) if ρ is a decreasing function of θ.

It remains to prove that any of the conditions (A) or (B) implies that ρ is decreasing. Under assumption $(B-1)$, with $S = DF^1(0) - DF^2(0)$ we get by Lemma 4.4.5

$$\frac{\rho'(\theta)}{T\rho(\theta)} = \langle SV(\theta), V_*(\theta)\rangle = \langle PSV(\theta), (P^{-1})^* V_*(\theta)\rangle < 0,$$

since $PS < 0$, $V(\theta) \gg 0$ and $(P^{-1})^* V_*(\theta) > 0$ by assumption. Note that this condition is equivalent to $S^* V_*(\theta) < 0$. Reasoning by density of $GL_N(\mathbb{R})$ in $\mathcal{M}_N(\mathbb{R})$, we assume that S is invertible and check that if $S^* V_* < 0$ then $P = -S^{-1}$ satisfies the assumption, and conversely if $PS = Q < 0$, upon writing $(P^{-1})^* = (Q^{-1})^* S^*$ we get $(Q^{-1})^* S^* V_* > 0$, and by multiplication by $Q^* < 0$ this implies $S^* V_* < 0$. The argument is symmetrical for assumption $(B-2)$ and is omitted here.

Under assumption $(B-3)$ we get by Lemma 4.4.5

$$\frac{\rho'(\theta)}{T\rho(\theta)} = \langle SV(\theta), V_*(\theta)\rangle < \langle P_*(\theta)Q(\theta)V(\theta), V_*(\theta)\rangle = -\|Q(\theta)V(\theta)\|^2 \leq 0,$$

since $V(\theta), V_*(\theta) \gg 0$ (for the inequality), and $PV_* = -QV$ (for the equality).

Finally, under assumption (A) we get that $V(\theta) \equiv V$ and $V_*(\theta) \equiv V_*$ where V (resp. V_*) is the principal eigenvector (resp. left principal eigenvector) of $DF^1(0)$ (which is the same as the one of $DF^2(0)$). In this case,

$$\frac{\rho'(\theta)}{T\rho(\theta)} = \langle SV, V_*\rangle = \mu(DF^1(0)) - \mu(DF^2(0)),$$

whence the result.

4.4.3 Proofs of Proposition 4.3.1 and Proposition 4.3.2

Recall that by definition,

$$\forall X \in \mathbb{R}^2, \quad F(t,X) = G(\pi(t), X) := \begin{pmatrix} \pi_1 X_2 - (\pi_2 + \pi_3 + \pi_4 X_1)X_1 \\ \pi_2 X_1 - \pi_5 X_2 \end{pmatrix}.$$

We first proceed to the proof of Proposition 4.3.1. If $X_i = 0$ for some $i \in \{1,2\}$, then since $\pi(t) \geq 0$, $F_i(t,X) \geq 0$. Therefore the system is positive.

We recall the notation $\pi = (b, h, d_J, c_J, d_A)$. We have:

$$D_X F = \begin{pmatrix} -h - d_J - 2c_J J & b \\ h & -d_A \end{pmatrix}.$$

Thus, $D_X F$ is a Metzler matrix, so (4.2.1) is monotone cooperative.

To check the concavity property, let $X \gg Y$. We simply compute

$$D_X F(t,X) - D_X F(t,Y) = \begin{pmatrix} 2c_J(Y_1 - X_1) & 0 \\ 0 & 0 \end{pmatrix} > 0.$$

Then, we proceed to the proof of Proposition 4.3.2. Calculating the equations of nullclines

$$\begin{aligned} &bA - hJ - d_J J - c_J J^2 = 0, \\ &hJ - d_A A = 0, \end{aligned}$$

immediately yields all steady states as:

$$S_0^* = (0,0), \quad S_1^* = (\frac{bh}{d_J} - h - d_J)(\frac{1}{c_J}, \frac{h}{c_J d_A}).$$

Then, the sign of both components of S_1^* is equal to the sign of $\mathcal{R}_0 - 1$, whence the result.

The stability and local behavior of solutions is detailed in

Proposition 4.4.1 *If $\mathcal{R}_0 \leq 1$ the unique equilibrium point $S_0^* = (0,0)$ is either a stable node (when $\mathcal{R}_0 < 1$) or a singular point of superior order and of attracting type (when $\mathcal{R}_0 = 1$), in which case all the orbits in the neighborhood of the S_0^* tend to S_0^* along direction $\theta_1 := \arctan \frac{h+d_J}{b}$.*

If $\mathcal{R}_0 > 1$, the equilibrium point $S_0^* = (0,0)$ is of saddle type, and the direction of unstable manifold is $\frac{h+d_J-d_A+\sqrt{(h+d_J-d_A)^2+4bh}}{2b}$. The equilibrium point S_1^* is a stable node.

Proof. We divide the proof into three parts, depending on the sign of $\mathcal{R}_0 - 1$.

When $\mathcal{R}_0 = 1$. Then (4.2.1) becomes

$$\begin{aligned} \frac{dJ}{dt} &= -\frac{bh}{d_A} J + bA - c_J J^2, \\ \frac{dA}{dt} &= hA - d_A A. \end{aligned} \tag{4.4.6}$$

The determinant of its Jacobian matrix is

$$\begin{vmatrix} -\frac{bh}{d_A} & b \\ h & -d_A \end{vmatrix} = 0.$$

Hence, the equilibrium point S_0^* of system (4.4.6) is an isolated critical point of higher order.

Obviously, system (4.4.6) is analytic in a neighborhood of the origin. By Theorem

3.10 on page 79 of [91], any orbit of (4.4.6) tending to the origin must tend to it spirally or along a fixed direction, which depends on the characteristic equation of system (4.4.6). First of all, we introduce the polar coordinates $J = r\cos\delta$, $A = r\sin\delta$, where $\delta \in [0, \frac{\pi}{2}]$, $r \in \mathbb{R}_+$ and we get the relation

$$\begin{cases} \dot{r} = r^{-1}(J\dot{J} + A\dot{A}) = r^m[R(\delta) + o(1)], \\ \dot{\delta} = r^{-2}(J\dot{A} - A\dot{J}) = r^{m-1}[G(\delta) + o(1)]. \end{cases}$$

This yields

$$\begin{cases} \dot{r} = r(-\frac{bh}{d_A}\cos^2\delta + b\cos\delta\sin\delta + h\cos\delta\sin\delta - d_A\sin^2\delta - c_J r\cos^3\delta), \\ \dot{\delta} = h\cos^2\delta - d_A\cos\delta\sin\delta + (h + d_J)\cos\delta\sin\delta - b\sin^2\delta + c_J r\cos^2\delta\sin\delta. \end{cases}$$

Then the characteristic equation of system (4.4.6) takes the form

$$G(\delta) = h\cos^2\delta - d_A\cos\delta\sin\delta + (h + d_J)\cos\delta\sin\delta - b\sin^2\delta = 0, \tag{4.4.7}$$

and we have

$$R(\delta) = -\frac{bh}{d_A}\cos^2\delta + b\cos\delta\sin\delta + h\cos\delta\sin\delta - d_A\sin^2\delta.$$

After equation (4.4.7), we get

$$(\frac{h + d_J}{b}\cos\delta - \sin\delta)(d_A\cos\delta + b\sin\delta) = 0. \tag{4.4.8}$$

Thus

$$\begin{cases} \tan\ \delta_1 = \frac{h+d_J}{b}, \\ \tan\delta_2 = -\frac{d_A}{b}. \end{cases}$$

Clearly, $G(\delta) = 0$ has two real roots which we denote by δ_1 and δ_2. By the results in section 2 of [91], we know that neither the case no orbit of system (4.4.6) can tend to the critical point S_0^* spirally nor the singular case (if $G(\delta) \equiv 0$).

The orbits of the system tend to the origin along a characteristic direction δ_i, given by solutions of the equation (4.4.7). Since the system is positive we need to consider $\delta \in [0, \frac{\pi}{2}]$, so $\delta_1 = \arctan\frac{h+d_J}{b}$ is in first orthant and the orbits of the system approach the origin along the direction $\delta = \delta_J$.

When $\mathcal{R}_0 > 1$. We now write the Jacobian matrix **Jac** of the system

$$\mathbf{Jac} := \begin{pmatrix} -h - d_J - 2c_J E & b \\ h & -d_A \end{pmatrix},$$

and consider $\mathbf{Jac}_0$ and $\mathbf{Jac}_1$ are the Jacobian matrices respectively at equilibrium point S_0^* and S_1^*. At ${S_0}^*$,

$$\mathbf{Jac}_0 = \begin{pmatrix} -h - d_J & b \\ h & -d_J \end{pmatrix},$$

whose eigenvalues read

$$\begin{aligned} \lambda_1 &= \tfrac{-(h+d_J+d_A)+\sqrt{\Delta}}{2}, \\ \lambda_2 &= \tfrac{-(h+d_J+d_A)-\sqrt{\Delta}}{2}, \end{aligned}$$

where $\Delta := (h+d_J+d_A)^2 - 4[(h+d_J)d_A - hb] > 0$ (since $(h+d_J)d_A - hb < 0$). Then

$$\begin{aligned} \lambda_1 + \lambda_2 &= -(h + d_J + d_A) < 0, \\ \lambda_1\lambda_2 &= (h + d_J)d_A - hb < 0, \end{aligned}$$

so that one eigenvalue is positive and the another one is negative: S_0^* is a saddle point.

To find the direction of the stable manifold or unstable manifold at S_0^*, we write

$$\frac{\dot{A}}{\dot{J}} = \frac{dA}{dt} = \frac{hJ - d_A A}{-hJ - d_J J + bA - c_J J^2} = \frac{h - \frac{A}{J}}{-h - d_J + b\frac{A}{J} - c_J J}.$$

Consider (J, A) tending to S_0^* and let $k := \frac{A}{J}$. Then k is a solution to

$$k = \frac{h - d_A k}{-h - d_J + bk},$$

which leads to two solutions $(k_1, k_2) \in \mathbb{R}_+^* \times \mathbb{R}_-^*$ given by

$$\frac{h + d_J - d_A \pm \sqrt{(h + d_J - d_A)^2 + 4bh}}{2b}.$$

Hence, the boundary lines are $A = k_1 J$ and $A = k_2 J$ and by unstable manifold theorem we know that k_1 is the direction of unstable manifold at $(0, 0)$

Then, at equilibrium point S_1^*,

$$\mathbf{Jac}_1 = \begin{pmatrix} h + d_J - \frac{2bh}{d_A} & b \\ h & -d_A \end{pmatrix},$$

whose eigenvalues λ_1, λ_2 are real and satisfy

$$\begin{aligned} \lambda_1 + \lambda_2 &= h + d_J - \tfrac{2bh}{d_A} - d_A < 0, \\ \lambda_1\lambda_2 &= -d_A(h + d_J) + bh > 0. \end{aligned}$$

This implies that the two eigenvalues are real and negative, hence S_1^* is a stable node.

Finally, if $\mathcal{R}_0 < 1$. Then at equilibrium point S_0^*

$$\mathbf{Jac}_0 = \begin{pmatrix} -h - d_J & b \\ h & -d_A \end{pmatrix}.$$

Because $(h + d_J)d_A - hb > 0$, the eigenvalues are such that

$$\begin{aligned} \lambda_1 + \lambda_2 &= -(h + d_J + d_A) < 0, \\ \lambda_1\lambda_2 &= (h + d_J)d_A - hb > 0, \end{aligned}$$

with also the discriminant $(-h - d_J + d_A)^2 + 4bh > 0$, hence they are both negative and the equilibrium point S_0^* is a stable node. □

Remark 4.4.1 *In particular when $h = 0$ (no hatching), and the trivial equilibrium point S_0^* is a stable node.*

We now prove that all the orbits of (4.2.1) are forward bounded.

Lemma 4.4.6 *Let*

$$\tau^* := \sup_{t\geq 0} \frac{h(t)}{d_A(t)}, \quad J^* := \sup_{t\geq 0} \frac{b(t)\tau^* - h(t) - d_J(t)}{c_J(t)}.$$

Under the assumptions of Proposition 4.3.1, τ^* and J^* are finite. For all $X_0 \in \mathbb{R}_+^2$ and all real number $L \geq \max(0, J^*)$ such that $X_0 \in \Omega_L := [0, L]\times[0, \tau^* L]$, the solution $X(t)$ of (4.2.1) with initial data X_0 belongs to Ω_M.

Proof. Under the assumptions of Proposition 4.3.1, $c_J \geq c > 0$ and $d_A \geq c$ while all parameters are smaller than $C > 0$, hence J^* and ρ^* are finite.

For $L > 0$ we define the area rectangle Ω_L surrounded by four line segments ℓ_i with outward normal vector ν_i:

$$\begin{aligned} \ell_1 &= \{(J, A)|J = 0, 0 \leq A \leq \tau^* L)\}, \quad \nu_1 = (-1, 0), \\ \ell_2 &= \{(J, A)|J = L, 0 \leq A \leq \tau^* L)\}, \quad \nu_2 = (1, 0), \\ \ell_3 &= \{(J, A)|0 \leq J \leq L, A = 0\}, \quad \nu_3 = (0, -1), \\ \ell_4 &= \{(J, A)|0 \leq J \leq L, A = \tau^* L\}, \quad \nu_4 = (0, 1). \end{aligned}$$

To prove that Ω_L is positively invariant, since the system is positive, we only need to show that the scalar products of $\frac{dX}{dt}$ and ν_i on ℓ_i for $i \in \{2, 4\}$ are non-positive:

$$\begin{aligned} \nu_4 \cdot G(\pi, X) &= hJ - d_A\tau^* L \leq 0 \text{ since } J \leq L \text{ and } d_A\tau^* \geq h, \\ \nu_2 \cdot G(\pi, X) &= bA - hL - d_J L - c_J L^2. \end{aligned}$$

Since $A < \tau^* L$, $\nu_2 \cdot G(\pi, X) \leq 0$ on ℓ_2 as soon as $b\tau^* - h - d_J - c_J L \leq 0$, that is

$$L \geq \frac{b\tau^* - h - d_J}{c_J}.$$

Upon taking $L \geq J^*$ this inequality is satisfied. For L large enough such that $X_0 \in \Omega_L$, we have proved that for all $t > 0$, the solution $X(t)$ of (4.2.1) belongs to Ω_L. $\square$

The Dulac (divergence) criterion ensures that the system has no limit cycle, since:

$$\operatorname{div}(F) = -(h + d_J + c_J J + d_A) < 0.$$

This concludes the proof.

4.4.4 Proof of Theorem 4.3.3

Theorem 4.3.3 is a consequence of Theorem 4.3.2, condition $(B-1)$. To check this condition, we apply the following result (specific to the dimension $N = 2$) to the positive matrix $M(\theta)$:

Lemma 4.4.7 *Let $S \in \mathcal{M}_2(\mathbb{R})$ be a positive matrix, and assume vector $W = (w_1, w_2) \gg 0$ satisfies $S^* W = \mu W$ for some $\mu > 0$ (i.e. W is the principal eigenvector of S^*). Then, $w_2 > w_1$ if and only if*

$$s_{11} + s_{21} < s_{12} + s_{22}, \tag{4.4.9}$$

Where s_{11}, s_{21}, s_{12} and s_{22} are the elements of matrix S.

Proof. We write $SW = \mu W$ as

$$\begin{cases} s_{11} w_1 + s_{21} w_2 = \mu w_1, \\ s_{12} w_1 + s_{22} w_2 = \mu w_2, \end{cases} \iff \begin{cases} s_{11} + s_{21} \frac{w_2}{w_1} = \mu, \\ s_{12} \frac{w_1}{w_2} + s_{22} = \mu. \end{cases}$$

If $0 < w_1 < w_2$, since $S \gg 0$ we deduce that $s_{11} + s_{21} < \rho < s_{12} + s_{22}$.

Conversely, if $s_{11} + s_{21} < s_{12} + s_{22}$, subtracting the previous equalities we obtain

$$\mu(1 - \frac{w_2}{w_1}) = s_{11} - s_{12} + \frac{w_2}{w_1}(s_{21} - s_{22}) < (s_{22} - s_{21})(1 - \frac{w_2}{w_1}).$$

By contradiction, we assume that $w_2 < w_1$. Then $\mu < s_{22} - s_{21}$. Injecting this inequality into the previous equality we obtain

$$s_{12} + \frac{w_2}{w_1} s_{22} < (s_{22} - s_{21}) \frac{w_2}{w_1},$$

whence $s_{12} < -\frac{w_2}{w_1} s_{21}$, which contradicts $S > 0$. Hence $w_2 > w_1$. □

Lemma 4.4.7 is satisfied by $M(\theta)$, so that condition $(B-1)$ holds with $P = \begin{pmatrix} 1 & 1 \\ 0 & 1 \end{pmatrix}$. Indeed, $(P^{-1})^* = \begin{pmatrix} 1 & 0 \\ -1 & 1 \end{pmatrix}$ and $(P^{-1})^* V_* > 0$ with $V_* \gg 0$ if and only if $[V_*]_2 > [V_*]_1$, hence by (4.2.3) we have $P\big(DF^2(0) - DF^1(0)\big) < 0$.

The remaining of the proof is devoted to checking that $M_{12}(\theta) + M_{22}(\theta) - M_{11}(\theta) - M_{21}(\theta) > 0$. To this aim, we diagonalize

$$DF^1(0) = \begin{pmatrix} -h^U - d_J^U & b^U \\ h^U & -d_A^U \end{pmatrix} \text{ and } DF^2(0) = \begin{pmatrix} -h^F - d_J^F & b^F \\ h^F & -d_A^F \end{pmatrix}$$

by

$$DF^1(0) = P_U \begin{pmatrix} \lambda_U^+ & 0 \\ 0 & \lambda_U^- \end{pmatrix} P_U^{-1}, \quad DF^2(0) = P_F \begin{pmatrix} \lambda_F^+ & 0 \\ 0 & \lambda_F^- \end{pmatrix} P_F^{-1},$$

where for $\sharp \in \{U, F\}$,

$$P_\sharp = \begin{pmatrix} 1 & 1 \\ x_\sharp^+ & x_\sharp^- \end{pmatrix}, \quad P_\sharp^{-1} = \frac{1}{x_\sharp^- - x_\sharp^+} \begin{pmatrix} x_\sharp^- & -1 \\ -x_\sharp^+ & 1 \end{pmatrix}$$

and

$$\begin{aligned} \lambda_\sharp^\pm &= -\frac{1}{2}(h^\sharp + d_J^\sharp + d_A^\sharp) \pm \frac{1}{2}\sqrt{(h^\sharp + d_J^\sharp - d_A^\sharp)^2 + 4h^\sharp b^\sharp}, \\ x_\sharp^\pm &= \frac{\lambda_\sharp^\pm + h^\sharp + d_J^\sharp}{b^\sharp}, \\ &= \frac{1}{2b^\sharp}(h^\sharp + d_J^\sharp - d_A^\sharp) \pm \frac{1}{2b^\sharp}\sqrt{(h^\sharp + d_J^\sharp - d_A^\sharp)^2 + 4h^\sharp b^\sharp}. \end{aligned}$$

The condition of Lemma 4.4.7 will follow from:

Lemma 4.4.8 *For $\sharp \in \{U, F\}$, we have $x_\sharp^- < 0 < x_\sharp^+$ and $1 + x_\sharp^- > 0$.*

Proof. The first inequalities follow directly from the above expression of $x_\sharp^\pm$. Then, we compute $1 + x_\sharp^- = \frac{2b^\sharp + h^\sharp + d_J^\sharp - d_A^\sharp - \sqrt{(h^\sharp + d_J^\sharp - d_A^\sharp)^2 + 4h^\sharp b^\sharp}}{2b^\sharp}$. We have

$$\begin{aligned} (2b^\sharp + h^\sharp + d_J^\sharp - d_A^\sharp)^2 &= 4(b^\sharp)^2 + 4b^\sharp(h^\sharp + d_J^\sharp - d_A^\sharp) + (h^\sharp + d_J^\sharp - d_A^\sharp)^2 \\ &> (h^\sharp + d_J^\sharp - d_A^\sharp)^2 + 4h^\sharp b^\sharp \end{aligned}$$

since $b^\sharp + d_J^\sharp - d_A^\sharp > 0$ (explicit assumption in Proposition 4.3.2 for $\sharp = U$, and from $\mathcal{R}(\pi^F) > 1$ for $\sharp = F$). It implies $1 + x_\sharp^- > 0$.

□

Thanks to the above diagonalization, we can write $M = M(\theta) = (m_{ij})_{1\le i,j\le 2}$ as

$$\begin{aligned}
m_{11} &= (\beta^+ x_F^- - \beta^- x_F^+)(\gamma^+ x_U^- - \gamma^- x_U^+) + (-\beta^+ + \beta^-)(x_U^+ x_U^- \gamma^+ - x_U^+ x_U^- \gamma^-),\\
m_{12} &= (\beta^+ x_F^- - \beta^- x_F^+)(-\gamma^+ + \gamma^-) + (-\beta^+ + \beta^-)(-x_U^+ \gamma^+ + x_U^- \gamma^-),\\
m_{21} &= (x_F^+ x_F^- \beta^+ - x_F^+ x_F^- \beta^-)(\gamma^+ x_U^- - \gamma^- x_U^+) + (-x_F^+ \beta^+ + x_F^- \beta^-)(x_U^+ x_U^- \gamma^+ - x_U^+ x_U^- \gamma^-),\\
m_{22} &= (x_F^+ x_F^- \beta^+ - x_F^+ x_F^- \beta^-)(-\gamma^+ + \gamma^-) + (-x_F^+ \beta^+ + x_F^- \beta^-)(-x_U^+ \gamma^+ + x_U^- \gamma^-),
\end{aligned}$$

where

$$\begin{aligned}
&\beta^+ := e^{\lambda_F^+(1-\theta)T}, \quad \beta^- := e^{\lambda_F^-(1-\theta)T},\\
&\gamma^+ := e^{\lambda_U^+\theta T}, \quad \gamma^- := e^{\lambda_U^-\theta T},\\
&\alpha := \frac{b^U b^F}{\sqrt{\big((h^U + d_J^U - d_A^U)^2 + 4h^U b^U\big)\big((h^F + d_J^F - d_A^F)^2 + 4h^F b^F\big)}}.
\end{aligned}$$

Proving $m_{11} + m_{21} < m_{12} + m_{22}$ therefore amounts to checking

$$\begin{aligned}
&\beta^+\gamma^+(x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + \beta^+\gamma^-(x_U^- - x_F^-)(1 + x_F^+)(1 + x_U^+)\\
&\quad + \beta^-\gamma^+(x_U^+ - x_F^+)(1 + x_U^-)(1 + x_F^-) + \beta^-\gamma^-(x_F^+ - x_U^-)(1 + x_F^-)(1 + x_U^+) < 0.
\end{aligned} \tag{4.4.10}$$

We introduce $\Psi : \mathbb{R}_+^2 \to \mathbb{R}$ as

$$\begin{aligned}
\Psi(\beta,\gamma) := {}& \beta\gamma(x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + \beta(x_U^- - x_F^-)(1 + x_F^+)(1 + x_U^+)\\
&+ \gamma(x_U^+ - x_F^+)(1 + x_U^-)(1 + x_F^-) + (x_F^+ - x_U^-)(1 + x_F^-)(1 + x_U^+),
\end{aligned}$$

so that (4.4.10) is equivalent to $\Psi(\frac{\beta^+}{\beta^-}, \frac{\gamma^+}{\gamma^-}) < 0$. First, it is easily checked that $\Psi(1,1) = 0$, $\beta^+ > \beta^-$ and $\gamma^+ > \gamma^-$. Then, by Lemma 4.4.8, $x_F^- < 0 < x_U^+$ and $1 + x_\sharp^\flat > 0$ for $\sharp \in \{U, F\}$ and $\flat \in \{+, -\}$. Hence for $\beta > 1$, we have

$$\begin{aligned}
\frac{\partial\Psi(\beta,\gamma)}{\partial\gamma} &= \beta(x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + (x_U^+ - x_F^+)(1 + x_U^-)(1 + x_F^-)\\
&< (x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + (x_U^+ - x_F^+)(1 + x_U^-)(1 + x_F^-)\\
&= (x_F^- - x_F^+)(1 + x_U^-)(1 + x_U^+).
\end{aligned}$$

Symmetrically, for $\gamma > 1$ we have

$$\begin{aligned}
\frac{\partial\Psi(\beta,\gamma)}{\partial\beta} &= \gamma(x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + (x_U^- - x_F^-)(1 + x_F^+)(1 + x_U^+)\\
&< (x_F^- - x_U^+)(1 + x_F^+)(1 + x_U^-) + (x_U^- - x_F^-)(1 + x_F^+)(1 + x_U^+)\\
&= (x_U^- - x_U^+)(1 + x_F^-)(1 + x_F^+).
\end{aligned}$$

Applying Lemma 4.4.8 again, we deduce that if $\beta, \gamma > 1$ then

$$\frac{\partial \Psi}{\partial \gamma}, \frac{\partial \Psi}{\partial \beta} < 0.$$

In particular $\Psi(\frac{\beta^+}{\beta^-}, \frac{\gamma^+}{\gamma^-}) < 0$, and this concludes the proof.

4.4.5 An example of numerical simulation

Here we give an example of numerical simulations for our reference model 4.2.1, We suppose that:
In favorable season, the death rate of juveniles d_J^F is 0.5; the death rate of adults d_A^F is 0.4; the birth rate b^F is 10; the hatching rate h^F is 1.

In unfavorable season, the death rate of juveniles d_J^U is 0.8; the death rate of adults d_A^U is 0.4; the birth rate b^U is 0.5; the hatching rate h^U is 0.2.

The following Fig.4.1 shows $\rho(\theta)$, the maximal root of the characteristic polynomial of $M(\theta)$, decreases with respect to $\theta \in [0, 1]$ and it show that $\rho(0) > 1$ and $\rho(1) < 1$

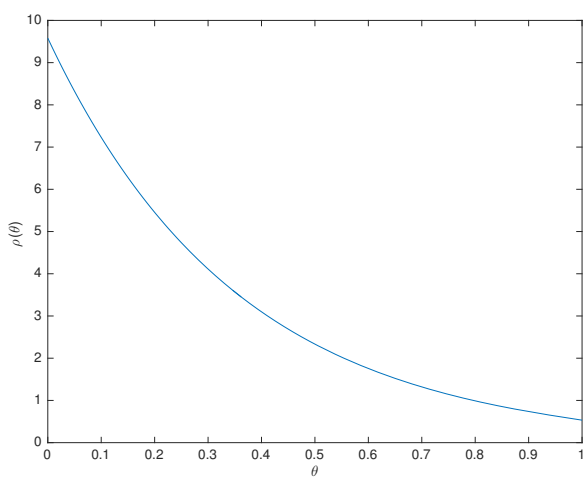


Figure 4.1: A numerical simulation with two seasons

4.5 Discussion and extensions

Geometric viewpoint. We denote by $\Upsilon \times \Upsilon_*$ the graph of $\upsilon := (V, V_*) : [0, 1] \to (\mathbb{R}_+^*)^{2N}$. Then we define $r(\theta) := \frac{\rho'(\theta)}{T\rho(\theta)} = \langle SV(\theta), V_*(\theta)\rangle$. Denoting by $\psi_S : \mathbb{R}^N \times \mathbb{R}^N \to$

$\mathbb{R}$ the bilinear form $(V,W) \mapsto \langle AV, W\rangle$, we get $r = \psi_S \circ \upsilon$. Let $X_S := \{\psi_S < 0\}$, it is an open and radial subset of $\mathbb{R}^{2N}$ (if $Y \in X_S$ and $\lambda > 0$, then $\lambda Y \in X_S$). $\rho(M)$ is decreasing if and only if r is decreasing, which is equivalent to $\Upsilon \times \Upsilon_* \subset X_S$. Up to changing S into $-S$, assumption (4.5.1) amounts to $\upsilon(0), \upsilon(1) \in X_S$.

The case (A) implies that $\Upsilon \times \Upsilon_*$ is a singleton, in which case (4.5.1) simply rewrites $(\mu_2 - \mu_1)^2 > 0$.

Practical computations in higher dimension. Theorem 4.3.2 suggests 4 different sufficient conditions on $DF^1(0)$ and $DF^2(0)$ to obtain (SSTP). Apart from the trivial situations when $DF^1(0) - DF^2(0)$ has a sign or when the two matrices share the same principal eigenvector, how applicable are these conditions when $N > 2$ If $DF^i(0)$ is diagonalizable for $i \in \{1,2\}$, which we write

$$DF^i(0) = P_i^{-1}\mathbf{diag}((\lambda_i^{(k)})_{1\le k\le N})P_i,$$

then we can compute

$$M_{i,j}(\theta) = \sum_{j',j''=1}^{N} P_1^{-1}(i,j')Q(j',j'')P_2(j'',j)e^{T\left(\theta\lambda_1^{(j')}+(1-\theta)\lambda_2^{(j'')}\right)},$$

where $Q(j',j'') = \sum_{k=1}^N P_1(j',k)P_2^{-1}(k,j'')$. For any matrix $\Gamma = (\gamma(i,j))_{1\le i,j\le N} \in GL_N(\mathbb{R})$ such that $\Gamma M(\theta) > 0$, we obtain $\Gamma V(\theta) > 0$ (where $V(\theta)$ is the principal eigenvector of $M(\theta)$). Then, a sufficient condition for (SSTP) is given by $(DF^2(0) - DF^1(0))\Gamma^{-1} < 0$. Symmetrically, if $M(\theta)\Gamma > 0$ then a sufficient condition is given by $\Gamma^{-1}(DF^2(0) - DF^1(0)) < 0$.

In order to get better conditions than the obvious ones, we require that $\Gamma \not\geq 0$. We note that

$$\left[\Gamma M(\theta)\right]_{i,j} = \sum_{k,j',j''=1}^{N} \gamma(i,k)P_1^{-1}(k,j')P_2(j'',j)Q(j',j'')e^{T\left(\theta\lambda_1^{(j')}+(1-\theta)\lambda_2^{(j'')}\right)}.$$

Log-convexity of the spectral radius. A celebrated result of Kingman [52] asserts that if the entries of a nonnegative matrix are log convex functions of a variable then so is the spectral radius of the matrix. If this property applies to the positive matrix $M(\theta)$, $\theta \mapsto \rho(M(\theta))$ is log-convex. In this case, it is monotone (yielding (SSTP)) provided that the derivatives at 0 and 1 have the same sign, that is:

$$\left(\mu_2 - \langle DF^1(0)V^2, V_*^2\rangle\right)\left(\langle DF^2(0)V^1, V_*^1\rangle - \mu_1\right) > 0, \tag{4.5.1}$$

where $\mu_i = \mu(DF^i(0))$, and V^i (resp. V_*^i) is the principal eigenvector of $DF^i(0)$ (resp. of $DF^i(0)^*$) with $V^i, V_*^i \gg 0$ and $\langle V^i, V^i\rangle = 1 = \langle V^i, V_*^i\rangle$.

When $DF^i(0)$ are diagonalizable ($i \in \{1,2\}$), the above formula shows that

$$M_{i,j}(\theta) = \sum_{n=1}^{N^2} \alpha_n(i,j) e^{\beta_n(i,j)\theta}$$

for some α, β. In cases when $M_{i,j}$ can be proved to be a log-convex function of θ, (SSTP) holds under assumption (4.5.1).

Computation of the second-order derivative. A more general condition for (SSTP) than the monotonicity of ρ would be that ρ is either concave or convex (or log-concave, or log-convex). To formulate this condition we compute the second-order derivative of $\log(\rho)$ from (4.4.5) as

$$\frac{d}{d\theta}\big(\log(\rho(\theta))\big) = r'(\theta) = \underbrace{\langle SV'(\theta), V_*(\theta)\rangle}_{=:R_1} + \underbrace{\langle SV(\theta), V_*'(\theta)\rangle}_{=:R_2},$$

where

$$S = DF^1(0) - DF^2(0). \tag{4.5.2}$$

Differentiating with respect to θ the eigenvector equations for $V(\theta)$ and $V_*(\theta)$ along with their normalizations $\langle V(\theta), V(\theta)\rangle = 1$ and $\langle V(\theta), V_*(\theta)\rangle = 1$ yields:

$$\begin{aligned}
(M(\theta) - \rho(\theta)I)V'(\theta) &= (\rho'(\theta)I - M'(\theta))V(\theta),\\
(M^*(\theta) - \rho(\theta)I)V_*'(\theta) &= (\rho'(\theta)I - (M^*)'(\theta))V_*(\theta),\\
\langle V(\theta), V'(\theta)\rangle &= 0 = \langle V'(\theta), V_*(\theta)\rangle + \langle V(\theta), V_*'(\theta)\rangle.
\end{aligned}$$

Dropping the argument θ, we note that V', V_*' are well-defined from these linear equations since $\mathrm{Im}(M - \rho I) = (V_*\mathbb{R})^\perp$ (and symmetrically $\mathrm{Im}(M^* - \rho I) = (V\mathbb{R})^\perp$) and the scalar product conditions give uniqueness. We introduce the notation $H := (V\mathbb{R})^\perp$ (resp. $H_* := (V_*\mathbb{R})^\perp$) for the hyperplane with normal vector V (resp. V_*). We also introduce the Perron projection operator $\Pi := V_* V^* \in \mathcal{L}(\mathbb{R}^N)$, and its adjoint $\Pi^* = V {V_*}^*$.

In particular, $M - \rho I \in \mathcal{L}(H, H_*)$ is an invertible linear application, whose inverse is denoted $M_r \in \mathcal{L}(H_*, H)$, and we have

$$V' = M_r\big((\rho' I - M')V\big).$$

Symmetrically, $M^* - \rho I \in \mathcal{L}(H)$ is invertible (since $V_* \notin H$), its inverse is denoted $M_a^* \in \mathcal{L}(H)$ and

$$V_*' = M_a^*\big((\rho' I - M_*')V_*\big) - \langle V_*, V'\rangle V_*.$$

Using the notation $M_i = DF^i(0)$ ($i \in \{1,2\}$), from the definition $M(\theta) = e^{T(1-\theta)M_2} e^{T\theta M_1}$

we also have:

$$M' = T(MM_1 - M_2M), \tag{4.5.3}$$
$$(M^*)' = T\big((M_1)^*M^* - M^*(M_2)^*\big). \tag{4.5.4}$$

In order to compute the two terms in r', we note two preliminary identities. First, using (4.5.3) and (4.4.5) we get

$$\frac{1}{T}(\rho' I - M')V = \rho(\Pi^* - I)SV - (M - \rho I)M_1V, \tag{4.5.5}$$

where both terms in the right-hand side belong to H_*. Symmetrically, using (4.5.4) and (4.4.5) we get

$$\frac{1}{T}(\rho' I - (M^*)')V_* = (M^* - \rho I)M_2^*V_* + \rho(\Pi - I)S^*V_*, \tag{4.5.6}$$

where both terms in the right-hand side belong to H.

Then, using (4.5.5), $M_r \in \mathcal{L}(H_*, H)$ and $M_r \circ (M - \rho I) = I_H$ we can compute

$$\begin{aligned} R_1 &= \big\langle M_r\big((\rho' I - M')V\big), S^*V_*\big\rangle, \\ &= T\rho\big\langle M_r(\Pi^* - I)SV, S^*V_*\big\rangle - T\langle M_1V, S^*V_*\rangle. \end{aligned}$$

Symmetrically, using (4.5.6), $M_a^* \in \mathcal{L}(H)$ and $M_a^* \circ (M^* - \rho I) = I_H$ we obtain

$$\begin{aligned} R_2 &= \langle SV, M_a^*\big((\rho' I - M_*')V_*\big) - \langle V_*, V'\rangle V_*\rangle, \\ &= T\rho\big\langle SV, M_a^*(\Pi - I)S^*V_*\big\rangle + T\langle SV, M_2^*V_*\rangle - \langle SV, V_*\rangle\langle V_*, V'\rangle. \end{aligned}$$

Using (4.5.5) with $M_r \in \mathcal{L}(H_*, H)$ and $(M - \rho I) \circ M_r = I_H$ we also get

$$\begin{aligned} \langle V_*, V'\rangle &= \langle V_*, M_r\big((\rho' I - M')V\big)\rangle, \\ &= T\rho\big\langle V_*, M_r(\Pi^* - I)SV\big\rangle - T\langle V_*, M_1V\rangle. \end{aligned}$$

Gathering R_1 and R_2 we obtain

$$\frac{r'}{T} = \overbrace{\big(\langle SV, V_*\rangle\big)^2 + \big\langle (M_2S - SM_1)V, V_*\big\rangle}^{r_1} + \underbrace{\rho\big\langle M_r(\Pi^* - I)SV, (S^* - \langle SV, V_*\rangle I)V_*\big\rangle}_{r_2} + \underbrace{\rho\big\langle M_a^*(\Pi - I)S^*V_*, SV\big\rangle}_{r_3}.$$

We notice that

$$r_2 = \rho\big\langle M_r(\Pi^* - I)SV, (I - \Pi)S^*V_*\big\rangle = \rho\big\langle SV, (I - \Pi)M_r^*(\Pi - I)S^*V_*\big\rangle$$

and

$$r_3 = \rho\big\langle SV, M_a^*(\Pi - I)S^*V_*\big\rangle,$$

so $r_2 = r_3$, since $(M^* - \rho I)\circ M_a^* = I_H$, $(M^* - \rho I)\circ M_r^* = I_H$ and $(M^* - \rho I)\circ \Pi M_r^* = 0$

Finally $\rho'' = T^2\rho r^2 + T\rho r'$ whence

$$\frac{\rho''}{T^2\rho} = 2\big(\langle SV, V_*\rangle\big)^2 + \big\langle (M_2S - SM_1)V, V_*\big\rangle + 2\rho\big\langle M_a^*(\Pi - I)S^*V_*, SV\big\rangle. \tag{4.5.7}$$

In principle, the identity (4.5.7) could be used to derive (SSTP) under more general conditions on $M_1 = DF^1(0), M_2 = DF^2(0)$ than those given in Theorem 4.3.2. However, we do not explore such conditions in the present article.

Time scaling. Until now we have considered that the period $T > 0$ was fixed. Letting T go to 0 or $+\infty$ yields interesting limits. For an irreducible Metzler matrix U,

$$e^{-T\mu(U)}e^{TU} \xrightarrow[T\to+\infty]{} VV_*^*$$

where V is the principal eigenvector of U and V_* is the principal eigenvector of U^*, normalized by $V_*^*V = 1$. From this fact, we have

$$e^{-T(\theta\mu(DF^1(0))+(1-\theta)\mu(DF^2(0))}M(\theta) \xrightarrow[T\to+\infty]{} V(0)V_*(0)^*V(1)V_*(1)^*,$$

from which we deduce that

$$\frac{1}{T}\log(\rho(\theta)) \sim_{T\to+\infty} \theta\mu(DF^1(0)) + (1-\theta)\mu(DF^2(0)).$$

In fact, we even get the next term in the asymptotic development:

$$\log(\rho(\theta)) - T\big(\theta\mu(DF^1(0)) + (1-\theta)\mu(DF^2(0))\big) - \log\big(V_*(0)^*V(1)V_*(1)^*V(0)\big) = o_{T\to\infty}(1).$$

Therefore, for T large enough, ρ is close to be monotone, and even close to be equal to the exponential interpolation of $T\mu(DF^1(0))$ and $T\mu(DF^2(0))$.

Meanwhile, $\lim_{T\to 0}\rho(\theta) \equiv 1$.

Optimization problems. For a general two-seasonal model defined by a monotone and concave map $G : \mathcal{P}\times\mathbb{R}^N \to \mathbb{R}^N$ and $\pi^U, \pi^F \in \mathcal{P}$, a natural question is the optimization of the spectral radius when the favorable and unfavorable seasons can be split throughout the year. Let $M_\sharp := T\cdot DG(\pi_\sharp, 0)$ (with $\sharp \in \{U, F\}$). For $K \in \mathbb{Z}_+$, we define:

$$\overline{\rho}_{M_U,M_F}(\theta, K) = \max_{(\sigma,\sigma')\in\varphi_K(\theta)} \rho(M_{M_U,M_F}(\sigma,\sigma')), \tag{4.5.8}$$

$$\underline{\rho}_{M_U,M_F}(\theta,K) = \min_{(\sigma,\sigma')\in\varphi_K(\theta)} \rho(M_{M_U,M_F}(\sigma,\sigma')), \tag{4.5.9}$$

where

$$\varphi_K(\theta) := \Big\{\big((\theta_k)_k,(\theta'_k)_k\big) \in [0,1]^{2K},\ \sum_{k=1}^K \theta_k = \theta,\ \sum_{k=1}^K \theta'_k = 1-\theta\Big\}$$

is compact and for $(\sigma,\sigma') \in \varphi_K(\theta)$ and $M_1, M_2 \in \mathcal{M}_N(\mathbb{R})$,

$$M_{M_1,M_2}(\sigma,\sigma') := e^{\theta'_K M_2} e^{\theta_K M_1} \cdots e^{\theta'_1 M_2} e^{\theta_1 M_1}.$$

Note that by Gelfand's formula,

$$\rho(M(\sigma,\sigma')) \le \prod_k \rho(e^{\theta'_k M_2})\rho(e^{\theta_k M_1}) = e^{\theta\mu_1+(1-\theta)\mu_2},$$

where $\mu_i = \mu(M_i)$.

Remark 4.5.1 *In the specific case when M_U and M_F are irreducible Metzler matrices with the same principal eigenvector (that is, condition (A)) , $\rho(M(\sigma,\sigma'))$ does not depend on $(\sigma,\sigma') \in S_K(\theta)$ and does even not depend on $K \in \mathbb{Z}_+$: we have*

$$\forall K \in \mathbb{Z}_+, \forall\theta \in [0,1], \quad \overline{\rho}_{M_U,M_F}(\theta,K) = e^{\left(\theta\mu_U+(1-\theta)\mu_F\right)} = \underline{\rho}_{M_U,M_F}(\theta,K),$$

with $\mu_\sharp = \mu(M_\sharp)$.

In this case, assuming $\mu_F > 0 > \mu_U$ we recover Theorem 4.3.3 with

$$\theta_* = \frac{\mu_F}{\mu_F - \mu_U}.$$

Bibliography

[1] D. Aeyels and P. De Leenheer. Extension of the Perron-Frobenius theorem to homogeneous systems. *SIAM Journal on Control and Optimization*, 41(2):563–582, 2002.

[2] Y. Agid and P. Magistretti. *L'Homme glial: Une révolution dans les sciences du cerveau*. Odile Jacob, 2018.

[3] G. Aronsson and I. Mellander. A deterministic model in biomathematics. asymptotic behavior and threshold conditions. *Mathematical Biosciences*, 49(3-4):207–222, 1980.

[4] A. Aubert and R. Costalat. Interaction between astrocytes and neurons studied using a mathematical model of compartmentalized energy metabolism. *Journal of Cerebral Blood Flow Metabolism*, 25(11):1476–1490, 2005.

[5] A. Aubert, R. Costalat, P.J. Magistretti, and L. Pellerin. Brain lactate kinetics: modeling evidence for neuronal lactate uptake upon activation. *Proceedings of the National Academy of Sciences of the United States of America*, 102(45):16448–16453, 2005.

[6] N. Bacaër. On the stochastic sis epidemic model in a periodic environment. *Journal of Mathematical Biology*, 71(2):491–511, 2015.

[7] N. Bacaër and N. Ait Dads. Sur l'interprétation biologique d'une définition du paramètre r0 pour les modèles de population périodiques. *Journal of Mathematical Biology*, 65(4):601–621, 2012.

[8] A. Berman and R.J. Plemmons. Nonnegative matrices in the mathematical sciences. *MR 95e*, 9, 1994.

[9] M. Bernardo, C. Budd, A.R. Champneys, and P. Kowalczyk. *Piecewise-smooth dynamical systems: theory and applications*, volume 163. Springer Science & Business Media, 2008.

[10] C.J. Briggs and H.C.J. Godfray. The dynamics of insect-pathogen interactions in stage-structured populations. *The American Naturalist*, 145(6):855–887, 1995.

[11] C. Buzzi, A. Gasull, and J. Torregrosa. Algebraic limit cycles in piecewise linear differential systems. *International Journal of Bifurcation and Chaos*, 28(03):1850039, 2018.

[12] C. Buzzi, C. Pessoa, and J. Torregrosa. Piecewise linear perturbations of a linear center. *Discrete & Continuous Dynamical Systems-A*, 33(9):3915–3936, 2013.

[13] L.M. Cai, S.B. Ai, and J. Li. Dynamics of mosquitoes populations with different strategies for releasing sterile mosquitoes. *SIAM Journal on Applied Mathematics*, 74(6):1786–1809, 2014.

[14] F. Campillo, N. Champagnat, and C. Fritsch. On the variations of the principal eigenvalue with respect to a parameter in growth-fragmentation models. *Communications in Mathematical Sciences*, 15(7):1801–1819, 2017.

[15] P.T. Cardin and J. Torregrosa. Limit cycles in planar piecewise linear differential systems with nonregular separation line. *Physica D: Nonlinear Phenomena*, 337:67–82, 2016.

[16] J. Clairambault, S. Gaubert, and B. Perthame. An inequality for the Perron and Floquet eigenvalues of monotone differential systems and age structured equations. *Comptes Rendus Mathematique*, 345(10):549–554, 2007.

[17] W.A. Coppel. *Stability and asymptotic behavior of differential equations*. Heath, 1965.

[18] R. Costalat, J.-P. Françoise, C. Menuel, M. Lahutte, J.-N. Vallée, G.De Marco, J. Chiras, and R. Guillevin. Mathematical modeling of metabolism and hemodynamics. *Acta Biotheoretica*, 60(1-2):99–107, 2012.

[19] M. Desroches, S. Fernández-García, and M. Krupa. Canards in a minimal piecewise-linear square-wave burster. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, 26(7):073111, 2016.

[20] M. Desroches, E. Freire, S.J. Hogan, E. Ponce, and P. Thota. Canards in piecewise-linear systems: explosions and super-explosions. *Proc. R. Soc. A*, 469(2154):20120603, 2013.

[21] M. Desroches, A. Guillamon, E. Ponce, R. Prohens, S. Rodrigues, and A.E.Teruel. Canards, folded nodes, and mixed-mode oscillations in piecewise-linear slow-fast systems. *SIAM Review*, 58(4):653–691, 2016.

[22] C. Dye and G. Hasibeder. Population dynamics of mosquito-borne disease: effects of flies which bite some people more frequently than others. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 80(1):69–77, 1986.

[23] P.A. Eckhoff. A malaria transmission-directed model of mosquito life cycle and ecology. *Malaria journal*, 10(1):303, 2011.

[24] S. Fernández-García, M. Desroches, M. Krupa, and F. Clément. A multiple time scale coupling of piecewise linear oscillators. application to a neuroendocrine system. *SIAM Journal on Applied Dynamical Systems*, 14(2):643–673, 2015.

[25] S. Fernández-García, M. Desroches, M. Krupa, and A. E. Teruel. Canard solutions in planar piecewise linear systems with three zones. *Dynamical Systems*, 31(2):173–197, 2016.

[26] D. Fish and S.R. Carpenter. Leaf litter and larval mosquito dynamics in tree-hole ecosystems. *Ecology*, 63(2):283–288, 1982.

[27] L. Florens, M.P. Washburn, J.D. Raine, et al. A proteomic view of the plasmodium falciparum life cycle. *Nature*, 419(6906):520, 2002.

[28] J.-P. Françoise and H. Ji. The stability analysis of brain lactate kinetics. *Discrete and Continuous Dynamical Systems-S*, 2018.

[29] A. Gasull and J. Torregrosa. Center-focus problem for discontinuous planar differential equations. *International Journal of Bifurcation and Chaos*, 13(07):1755–1765, 2003.

[30] S. Gaubert and T. Lepoutre. Discrete limit and monotonicity properties of the Floquet eigenvalue in an age structured cell division cycle model. *Journal of Mathematical Biology*, 71(6-7):1663–1703, 2015.

[31] J.-L. Gouzé. Structure des modèles mathématiques en biologie. In *Analysis and optimization of systems*, pages 1152–1163. Springer, 1988.

[32] J.-L. Gouzé. *Global behaviour of polynomial differential systems in the positive orthant*. PhD thesis, INRIA, 1990.

[33] J.-L. Gouzé. Differential systems with positive variables. In *Positive Systems*, pages 151–158. Springer, 2003.

[34] J.-L. Gouzé and K. P. Hadeler. Monotone flows and order intervals. *Nonlinear World*, 1:23–34, 1994.

[35] R. Guillevin, A. Miranville, and A. Perrillat-Mercerot. On a reaction-diffusion system associated with brain lactate kinetics. *Electron. J. Differ. Equation*, pages 1–16, 2017.

[36] Morris W. Hirsch. Systems of differential equations which are competitive or cooperative: I. limit sets. *SIAM Journal on Mathematical Analysis*, 13(2):167–179, 1982.

[37] Morris W. Hirsch. The dynamical systems approach to differential equations. *Bulletin of the American Mathematical Society*, 11(1):1–64, 1984.

[38] Morris W. Hirsch. Systems of differential equations that are competitive or cooperative: II. convergence almost everywhere. *SIAM Journal on Mathematical Analysis*, 16(3):423–439, 1985.

[39] Morris W. Hirsch. Systems of differential equations which are competitive or cooperative: III. competing species. *Nonlinearity*, 1(1):51, 1988.

[40] Morris W. Hirsch. Systems of differential equations that are competitive or cooperative. V. convergence in 3-dimensional systems. *Journal of Differential Equations*, 80(1):94–106, 1989.

[41] Morris W. Hirsch. Systems of differential equations that are competitive or cooperative. VI. structural stability in three-dimensional systems. *SIAM Journal on Mathematical Analysis*, 21(5):1225–1234, 1990.

[42] Morris W. Hirsch. Systems of differential equations that are competitive or cooperative. VI: A local c^r closing lemma for 3-dimensional systems. *Ergodic Theory and Dynamical Systems*, 11(3):443–454, 1991.

[43] Morris W. Hirsch and H. L. Smith. Competitive and cooperative systems: a mini-review. positive systems, 2003.

[44] J. Hofbauer and K. Sigmund. *Evolutionary games and population dynamics*. Cambridge university press, 1998.

[45] R.A. Horn and C.R. Johnson. *Matrix analysis*. Cambridge university press, 1990.

[46] Y. Hu and G.S. Wilson. A temporary local energy pool coupled to neuronal activity: Fluctuations of extracellular lactate levels in rat brain monitored with rapid-response enzyme-based sensor. *Journal of neurochemistry*, 69(4):1484–1490, 1997.

[47] H. Ji and M. Strugarek. Sharp seasonal threshold property for cooperative population dynamics with concave nonlinearities. *Bulletin des Sciences Mathématiques*, 147:58–82, 2018.

[48] J. Jiang. The algebraic criteria for the asymptotic behavior of cooperative systems with concave nonlinearities. *J. Systems Sci. Math. Sci.*, 6:193–208, 1993.

[49] E. Kamke. Zur theorie der systeme gewöhnlicher differentialgleichungen. ii. *Acta Mathematica*, 58(1):57–85, 1932.

[50] J.P. Keener and J. Sneyd. *Mathematical physiology*, volume 1. Springer, 1998.

[51] H.K. Khalil. Nonlinear systems, 3rd. *New Jewsey, Prentice Hall*, 9(4.2), 2002.

[52] J.F.C. Kingman. A convexity property of positive matrices. *The Quarterly Journal of Mathematics*, 12(1):283–284, 1961.

[53] M.A. Krasnosel'skii. *The operator of translation along the trajectories of differential equations*, volume 19. American Mathematical Soc., 1968.

[54] M. Lahutte-Auboin. *Modélisation biomathématique du métabolisme énergétique cérébral: réduction de modèle et approche multi-échelle, application à l'aide à la décision pour la pathologie des gliomes*. PhD thesis, UPMC, 2015.

[55] M. Lahutte-Auboin, R. Costalat, J.-P. Françoise, and R. Guillevin. Dip and buffering in a fast-slow system associated to brain lactacte kinetics. *arXiv preprint arXiv:1308.0486*, 2013.

[56] M. Lahutte-Auboin, R. Guillevin, J.-P. Françoise, J.-N.Vallée, and R. Costalat. On a minimal model for hemodynamics and metabolism of lactate: application to low grade glioma and therapeutic strategies. *Acta Biotheoretica*, 61(1):79–89, 2013.

[57] V. Lemesle and J.-L. Gouzé. A simple unforced oscillatory growth model in the chemostat. *Bulletin of Mathematical Biology*, 70(2):344–357, 2008.

[58] J. Li. New revised simple models for interactive wild and sterile mosquito populations and their dynamics. *Journal of Biological Dynamics*, 11(sup2):316–333, 2017.

[59] J. Li, L.M. Cai, and Y. Li. Stage-structured wild and sterile mosquito population models and their dynamics. *Journal of Biological Dynamics*, 11(sup1):79–101, 2017.

[60] J. Li and Z.L. Yuan. Modelling releases of sterile mosquitoes with different strategies. *Journal of Biological Dynamics*, 9(1):1–14, 2015.

[61] J. Llibre and D. Xiao. Global dynamics of a Lotka-Volterra model with two predators competing for one prey. *SIAM Journal on Applied Mathematics*, 74(2):434–453, 2014.

[62] J. Llibre and D. Xiao. Dynamics, integrability and topology for some classes of kolmogorov hamiltonian systems in R^4_+. *Journal of Differential Equations*, 262(3):2231–2253, 2017.

[63] L. Mailleret, J.-L. Gouzé, and O. Bernard. Global stabilization of a class of partially known nonnegative systems. *Automatica*, 44(8):2128–2134, 2008.

[64] L. Mailleret and F. Grognard. Global stability and optimisation of a general impulsive biological control model. *Mathematical Biosciences*, 221(2):91–100, 2009.

[65] L. Mailleret and V. Lemesle. A note on semi-discrete modelling in the life sciences. *Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, 367(1908):4779–4799, 2009.

[66] H. Matano. Existence of nontrivial unstable sets for equilibriums of strongly orderpreserving systems. *J. Fac. Sci. Univ.*, 30:645–673, 1984.

[67] H. Matano. Strongly order-preserving local semi-dynamical systems-theory and applications. *Semigroups, theory and applications*, 1:178–185, 1986.

[68] J.C. Medrado and J. Torregrosa. Uniqueness of limit cycles for sewing planar piecewise linear systems. *Journal of Mathematical Analysis and Applications*, 431(1):529–544, 2015.

[69] C.D. Meyer. *Matrix analysis and applied linear algebra*, volume 71. SIAM, 2000.

[70] J. Mierczyński, W.Shen, and X.Q. Zhao. Uniform persistence for nonautonomous and random parabolic kolmogorov systems. *Journal of Differential Equations*, 204(2):471–510, 2004.

[71] A. Miranville. Mathematical analysis of a parabolic-elliptic model for brain lactate kinetics. In *Solvability, Regularity, and Optimal Control of Boundary Value Problems for PDEs*, pages 379–403. Springer, 2017.

[72] A. Miranville. A singular reaction-diffusion equation associated with brain lactate kinetics. *Mathematical Methods in the Applied Sciences*, 40(7):2454–2465, 2017.

[73] A. Miranville, C. Guillevin, R. Guillevin, and A. Perrillat-Mercerot. Analysis of a mathematical model for brain lactate kinetics. *Mathematical Biosciences & Engineering*, 15(5):1225–1242, 2018.

[74] S. Mirrahimi, B. Perthame, and P. E. Souganidis. Time fluctuations in a population model of adaptive dynamics. *Annales de l'Institut Henri Poincaré (C) Non Linear Analysis*, 32(1):41–58, 2015.

[75] M. Müller. Über das fundamentaltheorem in der theorie der gewöhnlichen differentialgleichungen. *Mathematische Zeitschrift*, 26(1):619–645, 1927.

[76] G. Nadin, M. Strugarek, and N. Vauchelet. Hindrances to bistable front propagation: application to wolbachia invasion. *Journal of Mathematical Biology*, pages 1–45, 2017.

[77] J. Pizzol, D. Nammour, P. Hervouet, A. Bout, N. Desneux, and L. Mailleret. Comparison of two methods of monitoring thrips populations in a greenhouse rose crop. *Journal of pest science*, 83(2):191–196, 2010.

[78] S. Smale. On the differential equations of species in competition. *Journal of Mathematical Biology*, 3(1):5–7, 1976.

[79] S. Smale. On the differential equations of species in competition. In *The Collected Papers of Stephen Smale: Volume 2*, pages 997–999. World Scientific, 2000.

[80] H.L. Smith. Cooperative systems of differential equations with concave nonlinearities. *Nonlinear Analysis: Theory, Methods & Applications*, 10(10):1037–1052, 1986.

[81] H.L. Smith. On the asymptotic behavior of a class of deterministic models of cooperating species. *SIAM Journal on Applied Mathematics*, 46(3):368–375, 1986.

[82] H.L. Smith. Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems. *Bulletin (New Series) of the American Mathematical Society*, 33:203–209, 1996.

[83] H.L. Smith. *Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems*. Number 41. American Mathematical Soc., 2008.

[84] M. Strugarek and N. Vauchelet. Reduction to a single closed equation for 2-by-2 reaction-diffusion systems of lotka–volterra type. *SIAM Journal on Applied Mathematics*, 76(5):2060–2080, 2016.

[85] Y. Tang, D. Xiao, W. Zhang, and D. Zhu. Dynamics of epidemic models with asymptomatic infection and seasonal succession. *Math. Biosci. Eng.*, 14(5-6):1407–1424, 2017.

[86] M. Walker, J.C. Blackwood, V. Brown, and L.M. Childs. Modelling *a*llee effects in a transgenic mosquito population during range expansion. *Journal of Biological Dynamics*, pages 1–21, 2018.

[87] H.J. Wearing, S.M. Sait, T.C. Cameron, and P. Rohani. Stage-structured competition and the cyclic dynamics of host–parasitoid populations. *Journal of Animal Ecology*, 73(4):706–722, 2004.

[88] D. Xiao. Dynamics and bifurcations on a class of population model with seasonal constant-yield harvesting. *Discrete Continuous Dynamical Systems-Series B*, 21(2), 2016.

[89] D. Xiao and S. Ruan. Global analysis in a predator-prey system with nonmonotonic functional response. *SIAM Journal on Applied Mathematics*, 61(4):1445–1472, 2001.

[90] L. Xue, C. Manore, P. Thongsripong, and J.M. Hyman. Two-sex mosquito model for the persistence of wolbachia. *Journal of Biological Dynamics*, 11(sup1):216–237, 2017.

[91] Z.F. Zhang, T.R. Ding, W.Z. Huang, and Z.X. Dong. *Qualitative theory of differential equations*, volume 101. American Mathematical Soc., 2006.

[92] X.Q. Zhao, J. Borwein, and P. Borwein. *Dynamical systems in population biology.* Springer, 2003.

Résumé

Ce travail de thèse est constitué de nouvelles applications de la théorie des systèmes dynamiques coopératifs à l'étude de modèles en Biologie. Un premier modèle réduit d'une dynamique compartimentalisée couplant l'hémodynamique et le métabolisme énergétique cérébral. Nous avons proposé l'étude d'une extension naturelle de ce modèle comprenant deux compartiments intracellulaires distincts, l'un représentant un neurone et l'autre un astrocyte en plus du compartiment extracellulaire (aussi appelé interstitiel) et du compartiment capillaire. Nous avons commencé par observer que ce système (et même une extension de ce système à N neurones et A astrocytes) est un système coopératif. On a pu alors appliquer les techniques dévelopées par Hal L. Smith et démontrer (en toutes dimensions) que l'unique point stationnaire est asymptotiquement stable. Dans la suite, nous avons considéré une variante du système réduit de dimension 2 dans laquelle on considère une dynamique différentiable par morceaux qui présente un saut lorsque la variable x ou la variable y dépasse un certain seuil. Ce système par morceaux permet l'introduction d'une autorégulation induite par un retour des concentrations de lactate extracellulaire ou capillaire sur le flux sanguin capillaire. De nouveaux phénomènes dynamiques sont découverts et nous discutons de l'existence et de la nature de deux points d'équilibre, d'un segment attractif, d'un équilibre frontalier et d'orbites périodiques en fonction du flux sanguin capillaire. Dans le dernier chapitre, on considère, en contraste avec les chapitres précédents, un système dynamique forcé. Ce système dynamique modélise une population dont l'environnement varie périodiquement dans le temps. Nous appliquons notre théorème à l'exemple d'une dynamique de population d'insectes (moustiques) avec un stade juvénile exposé à une compétition quadratique et un stade adulte. Cette dynamique est sujette à un forçage périodique saisonnier. En particulier, dans les pays tempérés, les moustiques sont très rares en hiver et connaissent une croissance explosive après les premiers épisodes pluvieux de la saison chaude.

Mots-clés: Systèmes dynamiques coopératifs; systèmes continus par morceaux; analyse qualitative; métabolisme du lactate du cerveau; dynamique de populations; saisonnalité

Abstract

This thesis work consists of new applications of the theory of cooperative dynamical systems to the study of models in Biology. A first model of compartmentalized dynamics coupling hemodynamics and cerebral energy metabolism. It has been proposed to study a natural extension of this model comprising two distinct intracellular compartments, one representing a neuron and the other an astrocyte in addition to the extracellular compartment (also called interstitial) and the capillary compartment. We began by observing that this system (even an extension of this system to N neurons and A astrocytes) is a cooperative system. It was then possible to apply the techniques developed by Hal L. Smith and demonstrate (in all dimensions) that the single stationary point is asymptotically stable. In the following, we have considered a variant of the reduced system of dimension 2 in which we consider a piecewise differentiable dynamic that has a jump when the variable x or the variable y exceeds a certain threshold. This piecewise system allows the introduction of an autoregulation induced by a feedback of the extracellular 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. In the last chapter, we consider, in contrast with the preceding chapters, a forced dynamical system. This dynamical system models a population whose environment varies periodically over time. We apply our theorem to the example of a population dynamics of insects (for example mosquitoes) with a juvenile stage exposed to a quadratic competition and an adult stage. These dynamics are subject to a seasonal periodic forcing. In particular, in temperate countries, mosquitoes are very rare in winter and grow explosively after the first rainy episodes of the hot season.

Keywords: Cooperative dynamical systems; piecewise smooth system; qualitative analysis; brain lactate metabolism; population dynamics; seasonality