# Laurent Pujo-Menjouet

Enseignant-chercheur
Maître de conférences
en mathématiques appliquées section 26
Habilité à diriger les recherches
Hors classe

Université Claude Bernard Lyon 1

Math rd

Inria
INVENTEURS DU MONDE NUMÉRIQUE

# Enseignement
# responsable de TOUTES mes UE

## Licence

**Maths**

**L1, L2, L3**
**responsable d'UE:**
analyse, analyse numérique, systèmes dynamiques, équations différentielles, calcul différentiel

**Polytech**

**L1**
**Peip C:**
étudiants post-pass

**LBBE**
**L3**
**Peip C:**
équations de réaction-diffusion appliquées à la biologie

## Master

**Master 1**
mathématiques appliquées et statistiques

Systèmes dynamiques

**Master 2**
Statistiques, Modélisation et Science des Données

Mathématiques et statistiques pour la santé

**Master 2**
Maths en action

Responsable de la filière maths pour la biologie et la médecine

**ENS: Master IXXI**

**INSA**
3e et 4e années de Biosciences

## NOUVEAU !

**Projet**

**Double Licence Mathématiques-Biologie**

**1 double diplôme**
avec débouchés possibles sur un master biosciences, ou un master de mathématiques appliquées

**en construction**


Céline Brochier


Philippe Malbos

# Prises de responsabilité

**C**orrespondant **M**obilité **I**nternationale (**CMI)**
(créations de nouveaux accords)

**Directeur du portail Mathématiques et Informatique**

**R**esponsable **A**ide à l'**E**ducation en **P**ré-professionnalisation (AED)
**(avec le rectorat)**

**R**esponsable de la **L1 Aménagée** (OUI-SI)

**R**esponsable des LAS et PASS en mathématiques

**Directeur Adjoint de la Faculté des Sciences**
(en charge de la formation)

**Président de la commission formation de la Faculté des Sciences**

**NOUVEAU !**

**Projet**

implication dans la construction du nouveau

**Pôle Sciences**

rapprochement entre Faculté des Sciences et pôle Biosciences

**I**nclude

**F**ormation alternance renforcée

**E**valuations blocs de compétences

**P**ersonnalisation des cursus, **F**ormation à distance

# Encadrement

## Stages Masters

Depuis 2007

**44 master 1**

**25 master 2**
**+**
**2022/2023**
**1 master 1**

**Camille Jacquié** (4BIM -INSA)
minéralisation de l'os

**3 master 2**

**Julien Blohm** (Master 2)
Prion - Alzheimer

**Marion Charmasson** (Master 2)
Sang -Dialyse

**Pauline Mazel** (Master 2)
Radiobiologie-Alzheimer

## Thèses

Depuis 2007

**8 étudiants en thèse**

**5 ont soutenu**
**et ont un poste**
**+**
**3 en cours**

**Basile Fornara**
(2021- )

**Cheikh Gaye**
(2018- 2023)

**Grégoire Ranson**
( Janvier 2022- )

**+**
**1 janvier 2023**

**Théo Loureau**

## Post-doctorats

Depuis 2007

**2 post-doctorants**

# Recherche: équipe à Lyon

Institut Camille Jordan

**291 permanents et non permanents**

regroupés en

**6 équipes**

Algèbre, Géométrie, Logique (AGL)

Combinatoire, Théorie des Nombres (CTN)

Équations aux dérivées partielles, Analyse (EDPA)

Histoire des Mathématiques (HM)

**Modélisation Mathématique, Calcul Scientifique (MMCS)**

Probabilités, Statistique, Physique Mathématique (PSPM).

## Équipe

Modélisation Mathématique, Calcul Scientifique **(MMCS)**

**81 permanents et non permanents**
**27%** du laboratoire

**dont**

**18 professeurs d'université** soit
**31%** du laboratoire

## Équipe

Modélisation Mathématique pour la Biologie et la Médecine

**14 permanents et non permanents**

**dont**

**0 professeurs d'université soit**
**0% du laboratoire**

# Dans la lignée de SHAPE-Med

## Équipe

**M**odélisation **M**athématique pour la **B**iologie et la **M**édecine

**14 permanents et non permanents**

**dont**

**0 professeurs d'université soit 0% du laboratoire**

## SHAPE-Med@Lyon

**PIA4** ExcellencES, sept institutions lyonnaises **S**tructuring one **H**ealth **A**pproach for **Pe**rsonalized **Med**icine in **Lyon**)

**pour renforcer la recherche et les formations dans le domaine de la santé**.

**Universités Claude Bernard Lyon 1** (UCBL) et **Lumière Lyon 2**, Hospices Civils de Lyon (HCL), **Centre Léon Bérard**, Centre hospitalier Le Vinatier, VétAgro Sup, CPE Lyon, avec les organismes nationaux de recherche **Inserm**, **CNRS**, **INRAé**, **Inria** et le Centre International de Recherche sur le Cancer-OMS.

**conforter la position de Lyon en tant que centre international majeur de recherche, d'innovation et de formation en santé**.

# Dans la lignée de Pluriel 2024 et de SHAPE-Med@Lyon (recherche)

cnrs

Math rd

Université Claude Bernard Lyon 1

Université Lumière Lyon 2

Laboratoire Dynamique du Langage (DDL)

*François Pelligrino*

Inria
INVENTEURS DU MONDE NUMÉRIQUE

*équipe DRACULA*

INRAE

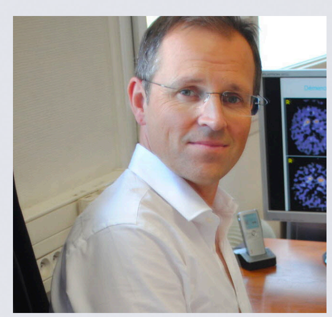

*Vincent Béringue*
*Human Rezaei*

Inserm
La science pour la santé
From science to health

*Hélène Follet*

*Laurent Juillard*

*Pierre Krolak-Salmon*



*Charles Dumontet*

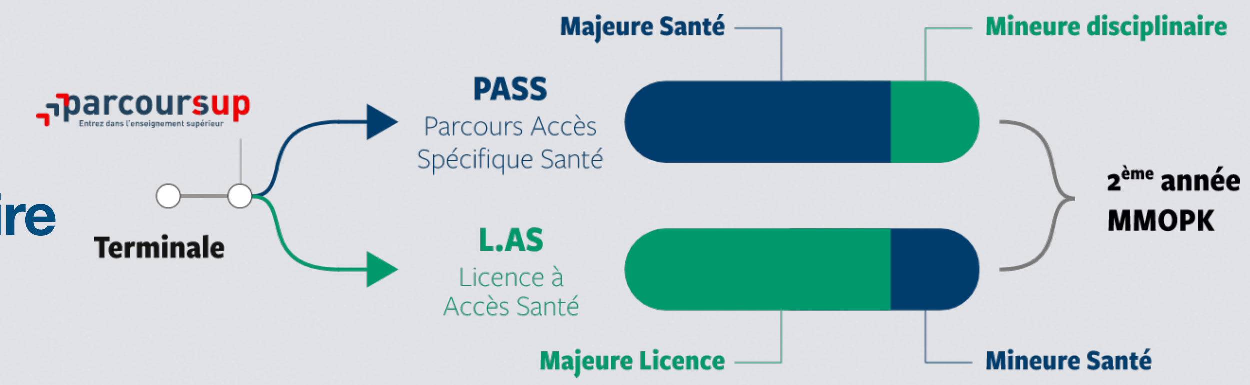
HCL HOSPICES CIVILS DE LYON

*Nicolas Foray*


CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

# Dans la lignée de Pluriel 2024 et de SHAPE-Med@Lyon (formation)

**PASS/LAS**
impliqué dans la construction
et responsable de la mineure disciplinaire




**Licence Sciences pour la Santé (SPS)**
responsables des mathématiques en L1, L2 et L3

**Bio-informatique, statistiques et modélisation (BISM)**
intervenant mathématiques en L3

**Filière mathématiques appliquées à la biologie et médecine**
responsable de cette filière du master 2 Maths en Action (vivier de stages et thèses pour notre équipe

**Master Systèmes Complexes (IXXI) (ENS) - master 2**
responsable du cours Mathematics in Biology and Medicine

**Biosciences INSA - 3BS-3BIM-4BIM**
responsable d'UE en 3ème et 4ème année (vacataire INSA)


Jianhong Wu
York University
Michael Mackey McGill
Jacques Bélair UdM
Tony Humphries MCGill
Adolfo Poma IPPT PAN
Suzanne Sindi UC MERCED
Mike Lindstrom UCLA / The University of Texas Rio Grande Valley
Glenn Webb Vanderbilt University
Jean-Philippe Berteau CUNY
Abdennasser Chekroun Tlemcen
Mohamed Helal Sidi-Bel-Abbes
Abennasser Lakmeche Sidi-Bel-Abbes
Malay Banerjee

# Bourses de recherche

**IXXI:**
Mecanos -> Fin 2025

**Labex MiLyon:**
Micr’os - Macr’os  -> Mars 2023

**BQR Insa (partenaire):**
Neurinfo  -> Fin 2025

**ANR (partenaire):**
PrionDiff  -> Fin 2025

**DÉPOSÉ: ANR (2022)**
GRACE (porteur) et MAHATMA (partenaire)

# VALORISATION ET DIFFUSION - conférences, publications et vulgarisation

## Conférences

- plus de 140 conférences
- **organisation et participation**
- **Bonitos**
**BO**Ne **In****T**erdisciplinary symp**OS**ium
organisation d'un symposium récurrent

- **En 2022:**
6 conférences

- **Pour 2023:**
**USA** (Vanderbilt)
**Italie** (Arpino)
**Algérie** (Side-Bel-Abbes)
**Lyon** (Bonitos 2023)
**Lyon** (Carte Blanche)

## Publications

- **52** publications

**Thématiques:**
- mathématiques théoriques,
- mathématiques appliquées à la biologie,
- biologie théorique

**Responsabilités éditoriales**: revues internationales

- **dernière publication:**
novembre 2022: SIADS

- **pour 2023:**
soumis (3 articles)
en préparation (10 articles)

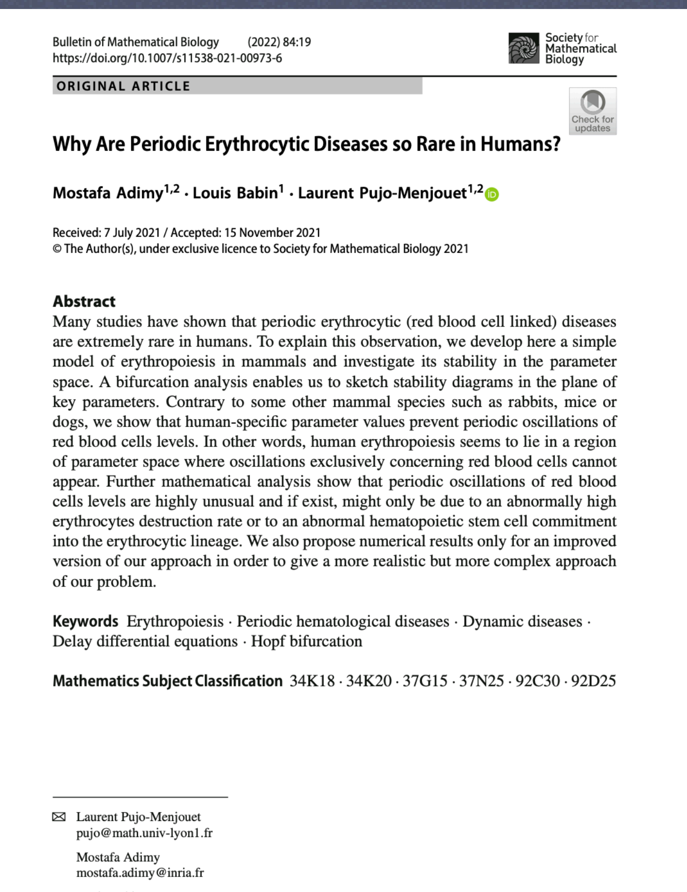
## Vulgarisation

- **MATh.en.JEANS**
- **Intervention** dans les lycées, les collèges
- **Time World**
- **TedX, …**
- **Livre (télé, radio, journaux)**


- **pour 2023:**
Lyon (Carte Blanche)
Deuxième livre

# Publications 2022

## SANG



Bulletin of Mathematical Biology (2022) 84:19
https://doi.org/10.1007/s11538-021-00973-6

Society for Mathematical Biology

ORIGINAL ARTICLE

### Why Are Periodic Erythrocytic Diseases so Rare in Humans?

Mostafa Adimy[1,2] · Louis Babin[1] · Laurent Pujo-Menjouet[1,2]

Received: 7 July 2021 / Accepted: 15 November 2021


**Abstract**
Many studies have shown that periodic erythrocytic (red blood cell linked) diseases are extremely rare in humans. To explain this observation, we develop here a simple model of erythropoiesis in mammals and investigate its stability in the parameter space. A bifurcation analysis enables us to sketch stability diagrams in the plane of key parameters. Contrary to some other mammal species such as rabbits, mice or dogs, we show that human-specific parameter values prevent periodic oscillations of red blood cells levels. In other words, human erythropoiesis seems to lie in a region of parameter space where oscillations exclusively concerning red blood cells cannot appear. Further mathematical analysis show that periodic oscillations of red blood cells levels are highly unusual and if exist, might only be due to an abnormally high erythrocytes destruction rate or to an abnormal hematopoietic stem cell commitment into the erythrocytic lineage. We also propose numerical results only for an improved version of our approach in order to give a more realistic but more complex approach of our problem.

**Keywords** Erythropoiesis · Periodic hematological diseases · Dynamic diseases · Delay differential equations · Hopf bifurcation

**Mathematics Subject Classification** 34K18 · 34K20 · 37G15 · 37N25 · 92C30 · 92D25

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Mostafa Adimy
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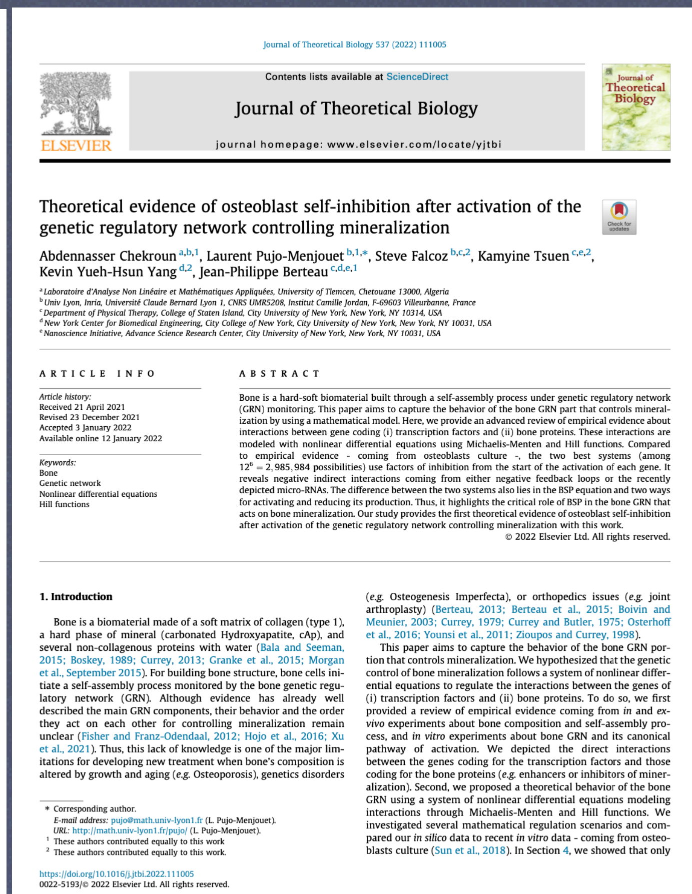
Louis Babin

## OS



Journal of Theoretical Biology 537 (2022) 111005

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journal homepage: www.elsevier.com/locate/yjtbi

ELSEVIER

### Theoretical evidence of osteoblast self-inhibition after activation of the genetic regulatory network controlling mineralization

Abdennasser Chekroun[a,b,1], Laurent Pujo-Menjouet[b,1,*], Steve Falcoz[b,c,2], Kamyine Tsuen[c,e,2], Kevin Yueh-Hsun Yang[d,2], Jean-Philippe Berteau[c,d,e,1]

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[b] Univ Lyon, Inria, Université Claude Bernard Lyon 1, CNRS UMR5208, Institut Camille Jordan, F-69603 Villeurbanne, France
[c] Department of Physical Therapy, College of Staten Island, City University of New York, New York, NY 10314, USA
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*Keywords:*
Bone
Genetic network
Nonlinear differential equations
Hill functions

ABSTRACT

Bone is a hard-soft biomaterial built through a self-assembly process under genetic regulatory network (GRN) monitoring. This paper aims to capture the behavior of the bone GRN part that controls mineralization by using a mathematical model. Here, we provide an advanced review of empirical evidence about interactions between gene coding (i) transcription factors and (ii) bone proteins. These interactions are modeled with nonlinear differential equations using Michaelis-Menten and Hill functions. Compared to empirical evidence - coming from osteoblasts culture -, the two best systems (among $12^6 = 2,985,984$ possibilities) use factors of inhibition from the start of the activation of each gene. It reveals negative indirect interactions coming from either negative feedback loops or the recently depicted micro-RNAs. The difference between the two systems also lies in the BSP equation and two ways for activating and reducing its production. Thus, it highlights the critical role of BSP in the bone GRN that acts on bone mineralization. Our study provides the first theoretical evidence of osteoblast self-inhibition after activation of the genetic regulatory network controlling mineralization with this work.


#### 1. Introduction

Bone is a biomaterial made of a soft matrix of collagen (type 1), a hard phase of mineral (carbonated Hydroxyapatite, cAp), and several non-collagenous proteins with water (Bala and Seeman, 2015; Boskey, 1989; Currey, 2013; Granke et al., 2015; Morgan et al., September 2015). For building bone structure, bone cells initiate a self-assembly process monitored by the bone genetic regulatory network (GRN). Although evidence has already well described the main GRN components, their behavior and the order they act on each other for controlling mineralization remain unclear (Fisher and Franz-Odendaal, 2012; Hojo et al., 2016; Xu et al., 2021). Thus, this lack of knowledge is one of the major limitations for developing new treatment when bone's composition is altered by growth and aging (*e.g.* Osteoporosis), genetics disorders (*e.g.* Osteogenesis Imperfecta), or orthopedics issues (*e.g.* joint arthroplasty) (Berteau, 2013; Berteau et al., 2015; Boivin and Meunier, 2003; Currey, 1979; Currey and Butler, 1975; Osterhoff et al., 2016; Younsi et al., 2011; Zioupos and Currey, 1998).

This paper aims to capture the behavior of the bone GRN portion that controls mineralization. We hypothesized that the genetic control of bone mineralization follows a system of nonlinear differential equations to regulate the interactions between the genes of (i) transcription factors and (ii) bone proteins. To do so, we first provided a review of empirical evidence coming from *in* and *ex-vivo* experiments about bone composition and self-assembly process, and *in vitro* experiments about bone GRN and its canonical pathway of activation. We depicted the direct interactions between the genes coding for the transcription factors and those coding for the bone proteins (*e.g.* enhancers or inhibitors of mineralization). Second, we proposed a theoretical behavior of the bone GRN using a system of nonlinear differential equations modeling interactions through Michaelis-Menten and Hill functions. We investigated several mathematical regulation scenarios and compared our *in silico* data to recent *in vitro* data - coming from osteoblasts culture (Sun et al., 2018). In Section 4, we showed that only

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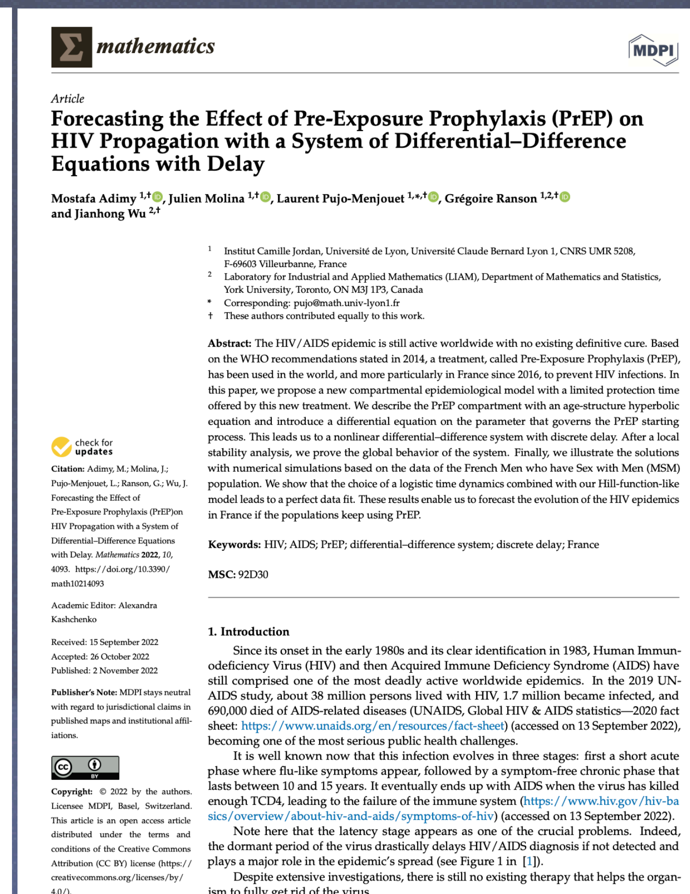
[1] These authors contributed equally to this work
[2] These authors contributed equally to this work.

https://doi.org/10.1016/j.jtbi.2022.111005


## VIH



mathematics

MDPI

*Article*

### Forecasting the Effect of Pre-Exposure Prophylaxis (PrEP) on HIV Propagation with a System of Differential–Difference Equations with Delay

Mostafa Adimy[1,†], Julien Molina[1,†], Laurent Pujo-Menjouet[1,*,†], Grégoire Ranson[1,2,†] and Jianhong Wu[2,†]

[1] Institut Camille Jordan, Université de Lyon, Université Claude Bernard Lyon 1, CNRS UMR 5208, F-69603 Villeurbanne, France
[2] Laboratory for Industrial and Applied Mathematics (LIAM), Department of Mathematics and Statistics, York University, Toronto, ON M3J 1P3, Canada
* Corresponding: pujo@math.univ-lyon1.fr
† These authors contributed equally to this work.

check for updates

**Citation:** Adimy, M.; Molina, J.; Pujo-Menjouet, L.; Ranson, G.; Wu, J. Forecasting the Effect of Pre-Exposure Prophylaxis (PrEP)on HIV Propagation with a System of Differential–Difference Equations with Delay. *Mathematics* **2022**, *10*, 4093. https://doi.org/10.3390/math10214093

Academic Editor: Alexandra Kashchenko

Received: 15 September 2022
Accepted: 26 October 2022
Published: 2 November 2022



**Abstract:** The HIV/AIDS epidemic is still active worldwide with no existing definitive cure. Based on the WHO recommendations stated in 2014, a treatment, called Pre-Exposure Prophylaxis (PrEP), has been used in the world, and more particularly in France since 2016, to prevent HIV infections. In this paper, we propose a new compartmental epidemiological model with a limited protection time offered by this new treatment. We describe the PrEP compartment with an age-structure hyperbolic equation and introduce a differential equation on the parameter that governs the PrEP starting process. This leads us to a nonlinear differential–difference system with discrete delay. After a local stability analysis, we prove the global behavior of the system. Finally, we illustrate the solutions with numerical simulations based on the data of the French Men who have Sex with Men (MSM) population. We show that the choice of a logistic time dynamics combined with our Hill-function-like model leads to a perfect data fit. These results enable us to forecast the evolution of the HIV epidemics in France if the populations keep using PrEP.

**Keywords:** HIV; AIDS; PrEP; differential–difference system; discrete delay; France

**MSC:** 92D30

#### 1. Introduction

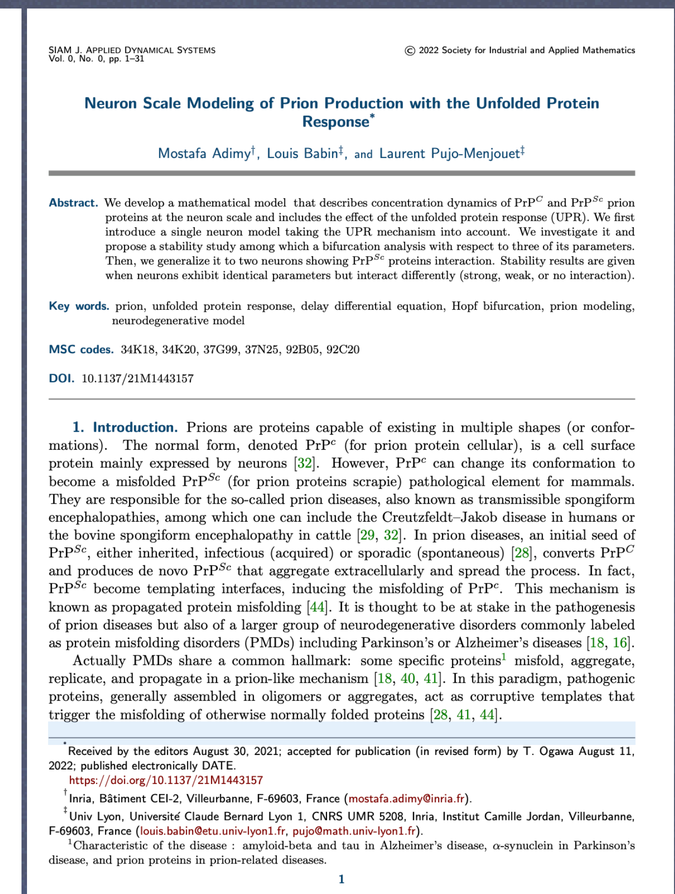
Since its onset in the early 1980s and its clear identification in 1983, Human Immunodeficiency Virus (HIV) and then Acquired Immune Deficiency Syndrome (AIDS) have still comprised one of the most deadly active worldwide epidemics. In the 2019 UNAIDS study, about 38 million persons lived with HIV, 1.7 million became infected, and 690,000 died of AIDS-related diseases (UNAIDS, Global HIV & AIDS statistics—2020 fact sheet: https://www.unaids.org/en/resources/fact-sheet) (accessed on 13 September 2022), becoming one of the most serious public health challenges.

It is well known now that this infection evolves in three stages: first a short acute phase where flu-like symptoms appear, followed by a symptom-free chronic phase that lasts between 10 and 15 years. It eventually ends up with AIDS when the virus has killed enough TCD4, leading to the failure of the immune system (https://www.hiv.gov/hiv-basics/overview/about-hiv-and-aids/symptoms-of-hiv) (accessed on 13 September 2022).

Note here that the latency stage appears as one of the crucial problems. Indeed, the dormant period of the virus drastically delays HIV/AIDS diagnosis if not detected and plays a major role in the epidemic's spread (see Figure 1 in [1]).

Despite extensive investigations, there is still no existing therapy that helps the organism to fully get rid of the virus.

## PRION



SIAM J. Applied Dynamical Systems
Vol. 0, No. 0, pp. 1–31


### Neuron Scale Modeling of Prion Production with the Unfolded Protein Response*

Mostafa Adimy†, Louis Babin‡, and Laurent Pujo-Menjouet‡

**Abstract.** We develop a mathematical model that describes concentration dynamics of $\mathrm{PrP}^C$ and $\mathrm{PrP}^{Sc}$ prion proteins at the neuron scale and includes the effect of the unfolded protein response (UPR). We first introduce a single neuron model taking the UPR mechanism into account. We investigate it and propose a stability study among which a bifurcation analysis with respect to three of its parameters. Then, we generalize it to two neurons showing $\mathrm{PrP}^{Sc}$ proteins interaction. Stability results are given when neurons exhibit identical parameters but interact differently (strong, weak, or no interaction).

**Key words.** prion, unfolded protein response, delay differential equation, Hopf bifurcation, prion modeling, neurodegenerative model

**MSC codes.** 34K18, 34K20, 37G99, 37N25, 92B05, 92C20

**DOI.** 10.1137/21M1443157

**1. Introduction.** Prions are proteins capable of existing in multiple shapes (or conformations). The normal form, denoted $\mathrm{PrP}^c$ (for prion protein cellular), is a cell surface protein mainly expressed by neurons [32]. However, $\mathrm{PrP}^c$ can change its conformation to become a misfolded $\mathrm{PrP}^{Sc}$ (for prion proteins scrapie) pathological element for mammals. They are responsible for the so-called prion diseases, also known as transmissible spongiform encephalopathies, among which one can include the Creutzfeldt–Jakob disease in humans or the bovine spongiform encephalopathy in cattle [29, 32]. In prion diseases, an initial seed of $\mathrm{PrP}^{Sc}$, either inherited, infectious (acquired) or sporadic (spontaneous) [28], converts $\mathrm{PrP}^C$ and produces de novo $\mathrm{PrP}^{Sc}$ that aggregate extracellularly and spread the process. In fact, $\mathrm{PrP}^{Sc}$ become templating interfaces, inducing the misfolding of $\mathrm{PrP}^c$. This mechanism is known as propagated protein misfolding [44]. It is thought to be at stake in the pathogenesis of prion diseases but also of a larger group of neurodegenerative disorders commonly labeled as protein misfolding disorders (PMDs) including Parkinson's or Alzheimer's diseases [18, 16].

Actually PMDs share a common hallmark: some specific proteins[1] misfold, aggregate, replicate, and propagate in a prion-like mechanism [18, 40, 41]. In this paradigm, pathogenic proteins, generally assembled in oligomers or aggregates, act as corruptive templates that trigger the misfolding of otherwise normally folded proteins [28, 41, 44].

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https://doi.org/10.1137/21M1443157
†Inria, Bâtiment CEI-2, Villeurbanne, F-69603, France (mostafa.adimy@inria.fr).
‡Univ Lyon, Université Claude Bernard Lyon 1, CNRS UMR 5208, Inria, Institut Camille Jordan, Villeurbanne, F-69603, France (louis.babin@etu.univ-lyon1.fr, pujo@math.univ-lyon1.fr).
[1] Characteristic of the disease : amyloid-beta and tau in Alzheimer's disease, α-synuclein in Parkinson's disease, and prion proteins in prion-related diseases.



Equations aux dérivées partielles et équations différentielles à retards

Equations différentielles

Equations au dérivées partielles et équations différentielles et aux différences avec retard

Equations au dérivées partielles et équations différentielles avec retard

Intervention de mon étudiant en thèse:

**Grégoire Ranson**

3 décembre 2022
Institut Fields - Toronto

(thèse co-financée par Sanofi)