RESEARCH CENTRE

Inria Lyon Centre

IN PARTNERSHIP WITH:

Université Claude Bernard (Lyon 1), CNRS, Ecole normale supérieure de Lyon

2024

ACTIVITY REPORT

Project-Team

MUSICS

MUltiScale Interacting Cell Systems

IN COLLABORATION WITH: Institut Camille Jordan, Laboratoire de Biologie et Modélisation de la Cellule

DOMAIN

Digital Health, Biology and Earth

THEME

Modeling and Control for Life Sciences

Inria

Contents

Project-Team MUSICS 1

1 Team members, visitors, external collaborators 2

2 Overall objectives 2

3 Research program 3

4 Application domains 4

5 Highlights of the year 4
5.1 Awards . . . 5

6 New software, platforms, open data 5
6.1 New software . . . 5
6.1.1 Simuscale . . . 5

7 New results 5
7.1 Mathematical modelling of the motility regime switching in Myxobacteria . . . 6
7.2 Results on stability for HIV . . . 6
7.3 Modelling the antigen–antibody complex activity . . . 6
7.4 Mathematical modelling of dialog between yeast cells . . . 6
7.5 Modelling prion and Alzheimer . . . 7
7.5.1 Alzheimer and inflammation . . . 7
7.5.2 Prion replication . . . 7
7.5.3 Estimation of nucleation . . . 7
7.6 In silico modelling of CD8 T cell immune response . . . 8
7.7 Selection and refinement in ensembles of executable gene regulatory networks . . . 8
7.8 A new collision avoidance model with semi implicit random batch resolution . . . 8
7.9 Steady state large deviations for one-dimensional, symmetric exclusion processes in weak contact with reservoirs . . . 9
7.10 Hydrodynamics of active matter models on a lattice . . . 9
7.11 Hydrodynamic behavior near dynamical criticality of a facilitated conservative lattice gas . . . 9
7.12 Mapping hydrodynamics for the facilitated exclusion and zero-range processes . . . 10
7.13 Stationary Fluctuations For The Facilitated Exclusion Process . . . 10
7.14 Hydrodynamic limit for a boundary-driven facilitated exclusion process . . . 10
7.15 Cutoff for the transience and mixing time of a SSEP with traps and consequences on the FEP 11
7.16 Simuscale: A Modular Framework for Multiscale Single-Cell Modelling . . . 11
7.17 Effect of Alcohol and Cocaine Abuse on Neuronal and Non-Neuronal Cell Turnover in the Adult Human Hippocampus . . . 11

8 Partnerships and cooperations 12
8.1 International initiatives . . . 12
8.1.1 Associate Teams in the framework of an Inria International Lab or in the framework of an Inria International Program . . . 12
8.1.2 Inria associate team not involved in an IIL or an international program . . . 12
8.1.3 STIC/MATH/CLIMAT AmSud projects . . . 13
8.1.4 Participation in other International Programs . . . 13
8.2 International research visitors . . . 13
8.2.1 Visits of international scientists . . . 13
8.3 National initiatives . . . 14
8.4 Regional initiatives . . . 15
8.4.1 IXXI project on cell migration . . . 15
8.4.2 SHAPEMED Structuring project on Alzheimer . . . 15

9 Dissemination **16**
9.1 Promoting scientific activities . . . 16
9.1.1 Scientific events: organisation . . . 16
9.1.2 Scientific events: selection . . . 16
9.1.3 Journal . . . 17
9.1.4 Invited talks . . . 17
9.1.5 Research administration . . . 17
9.2 Teaching - Supervision - Juries . . . 17
9.2.1 Teaching . . . 17
9.2.2 Supervision . . . 18
9.2.3 Juries . . . 19
9.3 Popularization . . . 19

10 Scientific production **20**
10.1 Publications of the year . . . 20
10.2 Cited publications . . . 22

Project-Team MUSICS

Creation of the Project-Team: 2024 July 01

Keywords

Computer sciences and digital sciences

A6. – Modeling, simulation and control

A6.1. – Methods in mathematical modeling

A6.1.1. – Continuous Modeling (PDE, ODE)

A6.1.2. – Stochastic Modeling

A6.1.3. – Discrete Modeling (multi-agent, people centered)

A6.1.4. – Multiscale modeling

A6.2. – Scientific computing, Numerical Analysis & Optimization

A6.2.1. – Numerical analysis of PDE and ODE

A6.2.3. – Probabilistic methods

A6.2.4. – Statistical methods

A6.3.1. – Inverse problems

A6.3.3. – Data processing

A8.12. – Optimal transport

Other research topics and application domains

B1. – Life sciences

B1.1. – Biology

B1.1.3. – Developmental biology

B1.1.4. – Genetics and genomics

B1.1.5. – Immunology

B1.1.7. – Bioinformatics

B1.1.8. – Mathematical biology

B1.1.10. – Systems and synthetic biology

B2.2.3. – Cancer

B2.2.4. – Infectious diseases, Virology

B2.2.6. – Neurodegenerative diseases

B2.3. – Epidemiology

1 Team members, visitors, external collaborators

Research Scientists

- Thomas Lepoutre [Team leader, INRIA, Researcher, from Jul 2024]
- Mostafa Adimy [INRIA, Senior Researcher, from Jul 2024]
- Aymeric Baradat [CNRS, Researcher, from Jul 2024]
- Samuel Bernard [CNRS, Researcher, from Jul 2024]
- Clément Erignoux [INRIA, ISFP, from Jul 2024]
- Olivier Gandrillon [CNRS, Senior Researcher, from Jul 2024]
- Michèle Romanos [CNRS, from Jul 2024]

Faculty Members

- Thibault Espinasse [UNIV LYON I, Associate Professor, from Jul 2024]
- Laurent Pujo-Menjouet [UNIV LYON I, Associate Professor, from Jul 2024]
- Léon Tine [UNIV LYON I, Associate Professor, from Jul 2024, HDR]

Post-Doctoral Fellows

- Mohammed Elghandouri [INRIA, Post-Doctoral Fellow, from Nov 2024]
- Thi Nhu Thao Nguyen [CNRS, Post-Doctoral Fellow, from Jul 2024]

PhD Students

- Charlotte Camus [INRIA, from Jul 2024]
- Maxime Estavoyer [INRIA, from Jul 2024]
- Clemence Fournie [CNRS, from Jul 2024]
- Grégoire Ranson [UNIV YORK, from Jul 2024]

Administrative Assistants

- Claire Alexandre [INRIA]
- Sylvie Boyer [INRIA]

Visiting Scientists

- Pablo Amster [Univ Buenos Aires , from Sep 2024 until Nov 2024]
- Claudia Pio Ferreira [GOUV BRESIL, from Sep 2024 until Oct 2024]

2 Overall objectives

MUltiScale Interacting Cell Systems, or MUSICS, is an newly created Inria team at the Centre Inria de Lyon devoted to the multiscale modelling and analysis of cellular dynamics. It is jointly supported by members of the ICJ (Institut Camille Jordan, University Lyon 1, CNRS and Inria), and the LBMC (ENS Lyon, CNRS) under the leadership of Thomas Lepoutre (Inria and ICJ). MUSICS inherits in part the staff and the research topics of the late Inria team Dracula, headed by Mostafa Adimy, that was set up in 2011.

3 Research program

Biological systems can be described at many organization scales, starting from the molecular level, to cellular, whole body, and all the way up to the population level. Each scale is rich and complex in its own right, but also interact with other scales and this is a crucial feature.

Yet it contains a much higher level of complexity, both in terms of computations and modelling. The historical, reductionist approach that has been used in molecular biology for the past 30 years consists in inferring the biological function, often at the tissue or whole body level, from molecular observations. There are several areas where this approach does not work so well. If the average cellular phenotype is not representative of the whole population phenotype, no matter how finely individual cells will be characterised, there will be a mismatch between the prediction and the observation. For the reductionist approach to work, it must take into account what happens when cells are brought together, that is, the tissue ecology. Cell population dynamics, in a broad sense, is the study of the phenomena that occur when many cells are brought in together, interact, proliferate, differentiate and die. One major difficulty that arises when analyzing such systems stems from the fact that those different scales do not behave independently but display strong, constant and dynamic interactions. In this context, the idea of a privileged level of causation loses its meaning, calling for new formal tools and approaches that aim at capturing the so-called "circular causality", where causation moves both upward and downward [40]. Upward causation is the set of processes by which the elements at lower levels interact and produce changes at higher levels. For example, a modification in the function of a gene product will alter the proliferation capacity of a cell that will alter the tissue composition. Downward causation is the set of constraints imposed by the higher levels on the dynamics at lower levels. For example, the generation at the tissue level of a gradient of a morphogen will result in a change in gene expression in individual cells. The gradient is a property of the tissue, not individual cells. Despite the variety of existing techniques to handle causality, this complexity of living systems poses new challenges and calls for the development of new tools. The MUSICS project is devoted to the development of tools and methods to study **multiscale processes in biology with potential applications in medicine**.

MUSICS will mainly focus on the **cellular level**, taking into account interactions at smaller spatial (and faster) scales (e.g. cellular content, gene expression), or at larger spatial scales (e.g. tissue, organism). The **cell**, as the structural unit of living organisms, has always played a key role in biology. With the rise of molecular biology and genomics, the role of the cell had been somewhat relegated to the background, in favour of molecular data acquired on large numbers of cells. The existence, extent and role of intercellular diversity was largely underestimated. Molecular biology was until recently based upon the assumption (or approximation) of the existence of an "average cell" that could be characterised from population measurements. This view proved to be not only wrong, but irrelevant [39]. **Rather, cellular diversity seems to be a key feature to understand biological systems and dynamics**.

What has dramatically changed in the last decade is the access to this diversity, notably through the revolution of **single cell data**. We now have access to gene expression at the resolution of the (single) cell for a large number of genes (thousands) in a large number of (individual) cells (up to millions) [43]. The recent years have witnessed an explosion in both the amount and the diversity of single-cell omics data. This has led to new opportunities to develop computationally efficient and statistically sound models and methods, with many challenges ahead [37].

One of the main drivers for cellular variability lies within the **gene expression** process that is intrinsically stochastic [36]. Notably, the observable regime for gene expression, when analysed at the single cell level, can be characterised as bursty [42]. This means that mRNA production occurs in brief episodes (bursts), generating a characteristic gamma distribution of mRNA transcripts when analysed over a sufficiently large amount of individual cells [38]. Such variability is often not taken into account at all in current modelling schemes. For example in a recent paper which developed a model of multicellular gene expression that accounts for intra- and intercellular gene regulation [41], gene expression is reduced to a binary variable.

It is therefore critical to develop new modelling approaches in which the molecular-based variability is correctly taken into account at the molecular level, so that its impact at higher levels (cellular and tissular) can be analysed.

Similarly, the way such molecular variability is constrained by higher levels should also be incorporated into the modelling process. Finally, we will build on our expertise in developing population models

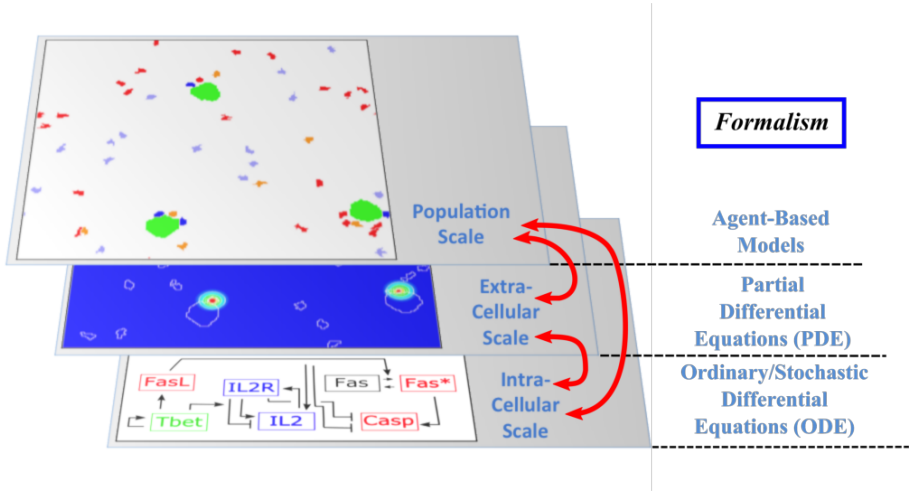

Figure 1: Non-exhaustive view of interacting scales.

that can be analysed mathematically in order to be able to derive relevant predictions in simplified situations (corresponding to mean-field limits, for instance). This leads to a structure of the project into three thematic axes of different size (more members in the first one, and fewer in the two others).

Axis 1 **Modelling and theoretical analysis in population dynamics.** This methodological axis concerns population dynamics in general. This leads to the study of questions related to existence, uniqueness and asymptotic behaviour for population models, described in terms of **partial differential equations** (PDEs), **integro-differential equations**, or **delay differential equations**. Moreover, we have a strong focus on an intermediate description: structured population dynamics. This is the biggest axis and concerns most members of the teams.

Axis 2 **Simulate efficiently large populations** of individuals with internal dynamics influenced by the population (chemical signalling, overcrowding ...). This approach is not only adapted when the coupling of scales is strong but can also be used to test the validity approximation of weak coupling used in population models. This can also guide the construction of new simplified models (based on numerical observations). Moreover, internal dynamics assessed on the data will be encoded in the simulation tool with the addition of nonlinear feedback loops. The axis is notably computational but contains also the analysis of large population limit.

Axis 3 Understand, analyse and **infer the internal dynamics from data with a mechanistic description**. This challenge is more related to statistical inference (mechanistic description has consequences on the structure of the noise) and leads to difficult questions linked to large deviations and optimal transportation. Axis 3 mixes some deep theoretical questions related to stochastic hybrid models with direct confrontations to data.

Only such multiscale modelling approaches will allow to investigate one of the most challenging characteristics of living systems, namely the circular causality that drives them [40].

4 Application domains

Detailed in the research program

5 Highlights of the year

The team was created in July 2024!

5.1 Awards

Léon Tine was awarded the Maurice Audin mathematics prize for his research into the mathematical modelling of mechanisms linked to physics and biology. link

6 New software, platforms, open data

6.1 New software

6.1.1 Simuscale

Name: Multiscale simulation of cell populations

Keywords: Ode, Simulation, Multiscale, Multi-agent

Scientific Description: SiMuScale is a C++ simulation framework that models both intra- and extra-cellular processes at different time scales. Its decoupled architecture allows for an easy and parsimonious extension of the model with e.g. a new kind of intra-cellular formalism.

Functional Description: Simuscale is a multiscale, individual-based modelling platform written in C++ for performing numerical simulations of heterogeneous populations of individual cells evolving in time and interacting physically and biochemically. Models are described at two levels: cellular level and population level. The cellular level describes the dynamics of single cells, as defined by the modeller. Cells have an internal state that includes default properties such as cell size and position, and may also include any other cell-specific state, such as gene or protein expression. The population level describes the mechanical constraints and biochemical interactions between cells. Cells evolve in bounded 3D domain, and can divide or die. Simuscale implements the physical simulator that manages the simulations at the population level. It delegates the details of cellular dynamics to each cell. This makes Simuscale modular, as it can accommodate any number of cell models with the same simulation, including models with different modelling formalisms. Biochemical interactions occur between cells that are in contact with each other, through intercellular signals. Intercellular signals can be known to all or to a subset of the cells only. Simuscale expects an input file describing the initial cell population and numerical options, it runs a simulation over a specified time interval, updating the cell population at given time steps, and generates an output file containing the state of each cell at each time step, and the tree of cell divisions and deaths.

Release Contributions: Includes diffusive signals (nonlocal) across the whole simulation domain

URL: `https://gitlab.inria.fr/bernard1/simuscale`

Publications: hal-04489553, hal-04400510

Contact: Samuel Bernard

Participants: Carole Knibbe, David Parsons, Fabien Crauste, Olivier Gandrillon, Raphael Bournhonesque, Samuel Bernard

Partners: CNRS, UCBL Lyon 1

7 New results

Preliminary remarks: some results of the year have been obtained within the Dracula Inria Team.

7.1 Mathematical modelling of the motility regime switching in Myxobacteria

Participants: Maxime Estavoyer, Thomas Lepoutre.

Maxime Estavoyer has studied in [5] the modelling of motility regime switching in Myxobacteria. This has taken the form of accurate numerical simulations in particular shed light on the fact that the existence of a faster group speed may not always results in an acceleration of the invasion. In an asymptotic (scalar and not anymore a system) limit of fast exchange Maxime Estavoyer and Thomas Lepoutre have established the existence of a threshold for such an advantage. Namely, there exists a θ^* such that for a speed advantage smaller that θ^* the invasion is not accelerated whereas it is accelerated above the threshold. This corrresponds to a transition between pulled and pushed fronts [16].

7.2 Results on stability for HIV

Participants: Mostafa Adimy, Laurent Pujo-Menjouet.

In [2], an examination is conducted on a model derived from the inquiry into the efficacy of HIV Pre-Exposure Prophylaxis (PrEP) within high-risk populations. To achieve this objective, we employ an SI model coupled with an age-structured equation to delineate the dynamics of individuals under PrEP protection, incorporating an infected-dependent rate of new users recruited from the susceptible population. This nonlinear term is contingent upon a factor dedicated to the political or economic context of a government. Local asymptotic stability for both disease-free and endemic equilibria is established, and global asymptotic stability for the disease-free steady-state is demonstrated. To address the system's behavior, a reduction of the partial differential equation is undertaken, presenting it as a coupled system of differential equations and a delayed difference equation. Lastly, persistence is substantiated when the endemic equilibrium is realized.

7.3 Modelling the antigen–antibody complex activity

Participants: Mostafa Adimy, Charlotte Dugourd-Camus.

Using the laws of chemical reactions, we propose in [10] a new approach to modelling the antigen–antibody complex activity. The resulting expression covers not only purely competitive or purely independent binding but also synergistic binding which, depending on the antibodies, can promote either neutralization or enhancement of viral activity. The results indicate that efficient viral neutralization is associated with purely independent antibody binding, whereas strong viral activity enhancement is expected in the case of purely competitive antibody binding. Finally, data collected during a secondary dengue infection were used to validate the model. The dataset includes sequential measurements of virus and antibody titres during viremia in patients. Data fitting shows that the two antibodies are in strong competition, as the synergistic binding is low. This contributes to the high levels of virus titres and may explain the antibody-dependent enhancement phenomenon. Besides, the mortality of infected cells is almost twice as high as that of susceptible cells, and the heterogeneity of viral kinetics in patients is associated with variability in antibody responses between individuals. Other applications of the model may be considered, such as the efficacy of vaccines and antibody-based therapies.

7.4 Mathematical modelling of dialog between yeast cells

Participants: Thomas Lepoutre.

In [6] with Vincent Calvez, Nicolas Meunier and Nicolas Muller, we develop a model to describe some aspects of communication between yeast cells. It consists in a coupled system of two one-dimensional non-linear advection-diffusion equations in which the advective field is given by the Hilbert transform. We give some sufficient condition for the blow-up in finite time of the coupled system (formation of a singularity). We provide a biological interpretation of these mathematical results.

7.5 Modelling prion and Alzheimer

7.5.1 Alzheimer and inflammation

Participants: Laurent Pujo-Menjouet, Léon Tine.

In [9], we introduce and study a new model for the progression of Alzheimer's disease incorporating the interactions of Aβ-monomers, oligomers, microglial cells and interleukins with neurons through different mechanisms such as protein polymerization, inflammation processes and neural stress reactions. In order to understand the complete interactions between these elements, we study a spatially-homogeneous simplified model that allows to determine the effect of key parameters such as degradation rates in the asymptotic behavior of the system and the stability of equilibriums. We observe that inflammation appears to be a crucial factor in the initiation and progression of Alzheimer's disease through a phenomenon of hysteresis, which means that there exists a critical threshold of initial concentration of interleukins that determines if the disease persists or not in the long term. These results give perspectives on possible anti-inflammatory treatments that could be applied to mitigate the progression of Alzheimer's disease. We also present numerical simulations that allow to observe the effect of initial inflammation and concentration of monomers in our model.

7.5.2 Prion replication

Participants: Laurent Pujo-Menjouet.

Prion diseases, or transmissible spongiform encephalopathies (TSEs), are neurodegenerative disorders caused by the accumulation of misfolded conformers (PrPSc) of the cellular prion protein (PrPC). During the pathogenesis, the PrPSc seeds disseminate in the central nervous system and convert PrPC leading to the formation of insoluble assemblies. As for conventional infectious diseases, variations in the clinical manifestation define a specific prion strain which correspond to different PrPSc structures. In [17], we implemented the recent developments on PrPSc structural diversity and tissue response to prion replication into a stochastic reaction-diffusion model using an application of the Gillespie algorithm. We showed that this combination of non-linearities can lead prion propagation to behave as a complex system, providing an alternative to the current paradigm to explain strain-specific phenotypes, tissue tropisms, and strain co-propagation while also clarifying the role of the connectome in the neuro-invasion process.

7.5.3 Estimation of nucleation

Participants: Léon Tine.

In [20], we are interested in the modeling of Alzheimer's disease from the angle of the amyloid cascade hypothesis, where the pathogenic agent is the Aβ protein in its oligomeric form. The formation dynamics of this pathogenic form is modeled by a Becker–Doring type model where APP (Amyloid Precursor Protein) protein, after cleavage by specific enzymes, forms monomeric Aβ proteins, which, by polymerization and/or nucleation, lead to the formation of oligomeric Aβ. We propose an optimal control problem to estimate the rate of nucleation which seems to be at the base of this amyloid cascade hypothesis and for which no (experimental) measurement exists for the moment.

7.6 In silico modelling of CD8 T cell immune response

Participants: Samuel Bernard, Olivier Gandrillon, Thi Nhu Thao Nguyen.

The CD8 T cell immune response operates at multiple temporal and spatial scales, including all the early complex biochemical and biomechanical processes, up to long term cell population behavior. In order to model this response, we devised in [21] a multiscale agent-based approach using Simuscale software. Within each agent (cell) of our model, we introduced a gene regulatory network (GRN) based upon a piecewise deterministic Markov process formalism. Cell fate – differentiation, proliferation, death – was coupled to the state of the GRN through rule-based mechanisms. Cells interact in a 3D computational domain and signal to each other via cell–cell contacts, influencing the GRN behavior. Results show the ability of the model to correctly capture both population behavior and molecular timedependent evolution. We examined the impact of several parameters on molecular and population dynamics, and demonstrated the add-on value of using a multiscale approach by showing the influence of molecular parameters, particularly protein degradation rates, on the outcome of the response, such as effector and memory cell counts.

7.7 Selection and refinement in ensembles of executable gene regulatory networks

Participants: Olivier Gandrillon.

In [4], we present a Design of Experiment strategy to use as a second stage after the inference process. It is specifically fitted for identifying the next most informative experiment to perform for deciding between multiple network topologies, in the case where proposed GRNs are executable models. This strategy first performs a topological analysis to reduce the number of perturbations that need to be tested, then predicts the outcome of the retained perturbations by simulation of the GRNs and finally compares predictions with novel experimental data. Results: We apply this method to the results of our divide-and-conquer algorithm called WASABI, adapt its gene expression model to produce perturbations and compare our predictions with experimental results. We show that our networks were able to produce in silico predictions on the outcome of a gene knock-out, which were qualitatively validated for 48 out of 49 genes. Finally, we eliminate as many as two thirds of the candidate networks for which we could identify an incorrect topology, thus greatly improving the accuracy of our predictions. Conclusion: These results both confirm the inference accuracy of WASABI and show how executable gene expression models can be leveraged to further refine the topology of inferred GRNs. We hope this strategy will help systems biologists further explore their data and encourage the development of more executable GRN models

7.8 A new collision avoidance model with semi implicit random batch resolution

Participants: Léon Tine.

Research on crowd simulation has important and wide range of applications. The main difficulty is how to lead all particles with a same and simple rule, especially when particles are numerous. In [8], we firstly propose a two dimensional agent-based collision avoidance model, which is a N-particles Newtonian system. The collision interaction force, imminent interaction force and following interaction force are designed, so that particles can be guided to their respective destinations without collisions. The proposed agent-based model is then extended to the corresponding mean field limit model as N→∞. Secondly, notice that direct simulation of the N-particles Newtonian system is very time-consuming, since the computational complexity is of order O(N2). In contrast, we propose an efficient hybrid resolution strategy to reduce the computational complexity. It is a combination of the Random Batch method (Shi Jin, Lei Li, and Jian-Guo Liu. Random batch methods (RBM) for interacting particle systems. Journal of Computational Physics, 400:108877, 2020.) and the method based on local particles Newtonian system. Thanks to this hybrid resolution strategy, the computational complexity is reduced to O(N). Finally, various tests are presented to show robustness and efficiency of our collision avoidance model and the hybrid resolution strategy.

7.9 Steady state large deviations for one-dimensional, symmetric exclusion processes in weak contact with reservoirs

Participants: Clément Erignoux.

Consider the symmetric exclusion process evolving on an interval and weakly interacting at the end-points with reservoirs. Denote by $I_{[0,T]}(\cdot)$ its dynamical large deviations functional and by $V(\cdot)$ the associated quasi- potential, defined as $V(\gamma) = inf_{T>0} inf_u I_{[0,T]}(u)$, where the infimum is carried over all trajectories u such that $u(0) = \bar{\rho}$, $u(T) = \gamma$, and $\bar{\rho}$ is the stationary density profile. We derive in [3] the partial differential equation which describes the evolution of the optimal trajectory, and deduce from this result the formula obtained by Derrida, Hirschberg and Sadhu for the quasi-potential through the representation of the steady state as a product of matrices.

7.10 Hydrodynamics of active matter models on a lattice

Participants: Clément Erignoux.

Active matter has been widely studied in recent years because of its rich phenomenology, whose mathematical understanding is still partial. We present some results in [12], linking microscopic lattice gases to their macroscopic limit, and explore how the mathematical state of the art allows to derive from various types of microscopic dynamics their hydrodynamic limit. We present some of the crucial aspects of this theory when applied to weakly asymmetric active models. We comment on the specific challenges one should consider when designing an active lattice gas, and in particular underline mathematical and phenomenological differences between gradient and non-gradient models. Our purpose is to provide the physics community, as well as member of the mathematical community not specialized in the mathematical derivation of scaling limits of lattice gases, some key elements in defining microscopic models and deriving their hydrodynamic limit.

7.11 Hydrodynamic behavior near dynamical criticality of a facilitated conservative lattice gas

Participants: Clément Erignoux.

We investigate in [13] a $2d$-conservative lattice gas exhibiting a dynamical active-absorbing phase tran- sition with critical density ρc. We derive the hydrodynamic equation for this model, showing that all critical exponents governing the large scale behavior near criticality can be obtained from two independent ones. We show that as the supercritical density approaches criticality, distinct length scales naturally appear. Remarkably, this behavior is different from the subcritical one. Numerical simulations support the critical relations and the scale separation.

7.12 Mapping hydrodynamics for the facilitated exclusion and zero-range processes

Participants: Clément Erignoux.

We derive in [14] the hydrodynamic limit for two degenerate lattice gases, the facilitated ex- clusion process (FEP) and the facilitated zero-range process (FZRP), both in the symmetric and the asymmetric case. For both processes, the hydrodynamic limit in the symmetric case takes the form of a diffusive Stefan problem, whereas the asymmetric case is characterized by a hyperbolic Stefan problem. Although the FZRP is attractive, a property that we extensively use to derive its hydrodynamic limits in both cases, the FEP is not. To derive the hydrodynamic limit for the latter, we exploit that of the zero-range process, together with a classical mapping between exclusion and zero-range processes, both at the microscopic and macroscopic level. Due to the degeneracy of both processes, the asymmetric case is a new result, but our work also provides a simpler proof than the one that was previously proposed for the FEP in the symmetric case.

7.13 Stationary Fluctuations For The Facilitated Exclusion Process

Participants: Clément Erignoux.

We derive in [15] the stationary fluctuations for the Facilitated Exclusion Process (FEP) in one dimension in the symmetric, weakly asymmetric and asymmetric cases. Our proof relies on the mapping between the FEP and the zero-range process used in previous work, where hydrodynamic limits were derived for the FEP, to its stationary fluctuations. Our results thus exploit works on the zero-range process's fluctuations, but we also provide a direct proof in the symmetric case, for which we derive a sharp estimate on the equivalence of ensembles for the FEP's stationary states.

7.14 Hydrodynamic limit for a boundary-driven facilitated exclusion process

Participants: Clément Erignoux.

We study in [29] the symmetric facilitated exclusion process (FEP) on the finite one- dimensional lattice $\{1,\dots,N-1\}$ when put in contact with boundary reservoirs, whose action is subject to an additional kinetic constraint in order to enforce ergodicity. We study in details its stationary states in various settings, and use them in order to derive its hydrodynamic limit as $N \to \infty$, in the diffusive space-time scaling, when the initial density profile is supercritical. More precisely, the macroscopic density of particles evolves in the bulk according to a fast diffusion equation as in the periodic case, and besides, we show that the boundary-driven FEP exhibits a very peculiar behaviour: unlike for the classical SSEP, and due to the two- phased nature of the FEP, the reservoirs impose Dirichlet boundary conditions which do not coincide with their equilibrium densities. The proof is based on the classical entropy method, but requires significant adaptations to account for the FEP's non-product stationary states and to deal with the non-equilibrium setting

7.15 Cutoff for the transience and mixing time of a SSEP with traps and consequences on the FEP

Participants: Clément Erignoux.

Motivated by the study of the Facilitated Exclusion Process (FEP), which has attracted significant scrutiny in recent years, we introduce in [30] a new particle system that we call the SSEP with traps. It is nonreversible, attractive, and has a transient regime, which makes its study more challenging than that of the classical SSEP. We study its transience time, meaning the time after which the system is no longer in a transient state with high probability. We show that both the transience and the mixing time exhibit a cutoff at time $\frac{1}{\pi^2} K^2 \log K$ for a system of size K. We further define a new mapping between the SSEP with traps and the FEP. We expect that this mapping will be a very useful tool to study the FEP's microscopic and macroscopic behaviour. In particular, it enables us to show that the FEP's transience time undergoes a cutoff at time $\frac{1}{4\pi^2} N^2 \log N$. Notably, our results show that for a FEP with particle density $\rho > 1/2$, the transient component is exited in a diffusive time. This allows to extend to any initial configuration the upper-bound from Ayre and Chleboun for the mixing time of the FEP.

7.16 Simuscale: A Modular Framework for Multiscale Single-Cell Modelling

Participants: Samuel Bernard, Olivier Gandrillon.

Simuscale is a multiscale, individual-based modelling platform for performing numerical simulations of heterogeneous populations of individual cells evolving in time and interacting physically and biochemically [28]. Models are described at two levels: cellular level and population level. The cellular level describes the dynamics of single cells, as defined by the modeller. Cells have an internal state that includes default properties such as cell size and position, and may also include any other cell-specific state, such as gene or protein expression. The population level describes the mechanical constraints and biochemical interactions between cells. Cells evolve in bounded 3D domain, and can divide or die. Simuscale implements the physical simulator that manages the simulations at the population level. It delegates the details of cellular dynamics to each cell. This makes Simuscale modular, as it can accommodate any number of cell models with the same simulation, including models with different modelling formalisms. Biochemical interactions occur between cells that are in contact with each other, through intercellular signals. Intercellular signals can be known to all or to a subset of the cells only. Simuscale expects an input file describing the initial cell population and numerical options, it runs a simulation over a specified time interval, updating the cell population at given time steps, and generates an output file containing the state of each cell at each time step, and the tree of cell divisions and deaths.

7.17 Effect of Alcohol and Cocaine Abuse on Neuronal and Non-Neuronal Cell Turnover in the Adult Human Hippocampus

Participants: Samuel Bernard.

Clinical studies on humans with a history of chronic abuse of alcohol or cocaine show cognitive impairments associated with hippocampal atrophy. Adult hippocampal neurogenesis is a process important for memory formation and has been shown to be impaired by alcohol and cocaine in rodent models. It has thus been suggested that a reduction in adult neurogenesis may contribute to cognitive dysfunctions seen in patients with abuse. In addition, reduced adult neurogenesis has been suggested to play a role in the pathology of addiction vulnerability. We have previously demonstrated persistent adult hippocampal neurogenesis throughout life by measuring 14C concentrations in genomic DNA, incorporated during

cell division, in a mixed cohort of subjects. In this study, we use the same strategy to assess the extent of cell turnover of neuronal and nonneuronal cells in the hippocampus of humans with known history of alcohol and cocaine abuse and compare these with healthy controls [27]. We find that there is significant neuronal and nonneuronal turnover in healthy controls, as well as in individuals with long term alcohol use or cocaine use. Using mathematical modelling, we compare the extent of cell turnover of neurons and non-neuronal cells and did not find any significant difference between healthy controls and the two addiction groups. While we cannot exclude scenarios of altered adult neurogenesis over shorter periods of time, our data does not support the theory of low neurogenesis as a mechanism of addiction vulnerability.

8 Partnerships and cooperations

8.1 International initiatives

8.1.1 Associate Teams in the framework of an Inria International Lab or in the framework of an Inria International Program

Participants: Mostafa Adimy, Charlotte Camus, Grégoire Ranson, Laurent Pujo-Menjouet, Léon Tine.

Title: Associated team DIFAIRE “Infectious disease prevention: a multi-scale approach combining crowd dynamics and immuno-epidemiology”,

Partner Institution(s):
- Partner Institution(s): Centre de Recherche Systèmes Complexes et Interactions de Ecole Centrale de Casablanca (A. Jebrane [Coordinator])
- Laboratoire d’Étude et de Recherche en Mathématiques Appliquées (LEREMA), École Mohammedia d’Ingénieurs, Université Mohammed V, Rabat.

Date/Duration: 2024-2026.

Additionnal info/keywords: The aim is to use a crowd movement model adapted to each social context to simulate contact dynamics (contact matrices) and evaluate the risk of pathogen transmission. This approach takes into account the behavioral, demographic and environmental characteristics of populations, as well as the different transmission routes (direct and indirect contact). The process involves simulating activity locations separately, initially focusing on residential areas as a case study. Expected results include the reproduction of population interactions and the generation of contact matrices to provide information for the macroscopic epidemiological model.

8.1.2 Inria associate team not involved in an IIL or an international program

Participants: Mostafa Adimy, Charlotte Dugourd-Camus.

Title: Associated team MoCoVec "Modelling and Biological Control of Vector-Borne Diseases: the case of Malaria and Dengue"

Partner Institution(s):
- MAMBA Inria, Paris (P.A. Bliman [Coordinator])
- FAPESP São Paulo, Brazil.

Date/Duration: 2022-2025.

Additionnal info/keywords: Focusing on dengue and malaria, two diseases transmitted by vector mosquito and which cause high morbidity and mortality around the world, this project aims to model disease transmission, its spread and control, in a context of climatic and environmental change.

For this, the main drives of disease transmission will be addressed to understand which factors modulate the spatio-temporal patterns observed, especially in Brazil

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8.1.3 STIC/MATH/CLIMAT AmSud projects

Participants: Mostafa Adimy.

Title: MATH AmSud project TOMENADE "Topological methods and non autonomous dynamics for delay differential equations"

Partner Institution(s):
- Laboratoire des Signaux et Systèmes (L2S), CNRS, Centrale Supelec
- Argentina (P. Amster [Coordinator]) - Chile - Brazil.

Date/Duration: , 2022-2024. :

Additionnal info/keywords: This project addresses open problems about non autonomous systems of delay differential equations modeling some phenomena from life sciences, namely, a meta-populations version of the Nicholson equations and models of competition in a stirred chemostat. Nevertheless, the ideas and methods could be certainly extended in several ways, and we also expect to make progress in topics as the (non autonomous) topological linearization problem and the possibility of converse results for persistence.

8.1.4 Participation in other International Programs

Participants: Léon Tine, Samuel Bernard.

Title: PHC-Maghreb “Mathematical modeling and control of the spread of infectious diseases in the Mediterranean area”

Partner Institution(s):
- Inria, ICJ (Université Lyon 1),
- Mohammed V University of Rabat,
- Ecole Nationale d’Ingénieurs de Tunis,
- Université Tlemcen

Date/Duration: 2022-2024

Additionnal info/keywords: This research project aims to contribute to the development of some decision-making tools in the context of major global public health challenges: namely the modelling, monitoring and control of the spread of infectious diseases in the socio-economic current context. To do this, it is a question of contributing to: 1) improving mathematical representations of the human immune system, 2) construction of compartmental epidemiological models in which susceptible individuals are divided into several classes according to their immunity (vaccinated or not, age, infection with or without provisional immunity, infection with or without recurrence, etc.).

8.2 International research visitors

8.2.1 Visits of international scientists

Other international visits to the team

Pablo Amster

Status (Professor)

Institution of origin: University of Buenos Aires

Country: Argentina

Dates: september October 2024

Context of the visit: Collaboration with Mostafa Adimy

Mobility program/type of mobility: (sabbatical, internship, research stay, lecture...)Invitation by the center.

8.3 National initiatives

ANR Prio Diff

Participants: Laurent Pujo-Menjouet, Léon Tine.

Title: Impact of replication and structural diversification of prions on their cerebral dissemination

Partner Institution(s):
- Inrae Jouy-en-Josas, France
- Inrae Toulouse, France
- CEA, Fontenay aux Roses, France
- Institut Camille Jordan, France

Date/Duration: July 2021-June 2025

Additionnal info/keywords: Prions are lethal proteinaceous pathogens with major public-health risks due to their zoonotic and iatrogenic potential. They are composed of aggregated, misfolded conformers of the host-encoded prion protein that progressively deposit in the brain by a self-perpetuating reaction. The underlying molecular mechanisms of replication and tissue dissemination remain mostly elusive. Our objective is to model these processes entirely based on recent advances that prion aggregates are conformationally heterogeneous and dynamic rather than uniform and static. To achieve this, we will map in prion-infected brain the structural diversification-to-bioactivity/neurotoxicity landscape of prion assemblies in a spatiotemporal manner and mathematically build a multiscale model of diversification and lesion spreading. The goal is to generate an open access model capable of predicting the disease progression and identify key elementary process for therapeutics intervention and early diagnostics. / Keywords: interactions hôtes pathogènes, infectiologie, modélisation prion, tissue diffusion, neurotropism.

ANR PLUME

Participants: Thomas Lepoutre, Maxime Estavoyer.

Title: Molecular and morphogenetic control of feather pattern formation

Partner Institution(s):
- Centre interdisciplinaire de recherche en biologie (M. Manceau [Coordinator])
- Institut de Biologie du Développement de Marseille
- Brandeis University.

Date/Duration:2021-2025

Additionnal info/keywords: The objectives are to identify the hierarchy of pattern forming mechanisms establishing initial patterning spaces, characterise material properties and mechanical stresses controlling primordia self-organisation, and uncover how how cell and mechanical dynamics control the timely wave of primordia production. This work will shed light on the mechanisms governing pattern variation and fidelity in nature.

Participants: Olivier Gandrillon, Thi Nhu Thao Nguyen, Thomas Lepoutre.

Title: PEPR Santé Numérique , project AI4scMed (Multiscale AI for single-cell-based precision medicine)

Partner Institution(s):
- Inria
- Inserm
- CNRS

Date/Duration: since 2023

Additionnal info/keywords: We are concerned by WP4: "Towards multiscale mechanistic models for innovative treatments" in collaboration with CNRS (F. Crauste) and Inria team MUSCA (F. Clément). Coordinator: F. Picard (CNRS, ENS Lyon).

8.4 Regional initiatives

8.4.1 IXXI project on cell migration

Participants: Thomas Lepoutre, Michèle Romanos.

Title: Modeling and characterizing migration in glioblastoma, modeling sensitive and resistant cells in interaction

Partner Institution(s):
- Centre de recherche en Cancérologie de Lyon (CRCL, Erika Cosset).

Date/Duration:2021-2025

Additionnal info/keywords: The aim of this project is to develop a simple model of cell migration that can be parameterized with respect to homogeneous data. Once such a model has been characterized, we'll be able to build a strain-mixing model to propose a description of the effect of resistant cells on susceptible cells (which can become resistant in the presence of stress and resistant cells).

8.4.2 SHAPEMED Structuring project on Alzheimer

Participants: Laurent Pujo-Menjouet.

Title: MAHATMA

Partner Institution(s):
- RDSE - UMR1296 Inserm (Nicolas Foray).
- U1314 INSERM UMR 5284 CNRS MELIS (Desestret Virginie).
- Centre de Recherche CliniqueVieillissement-Cerveau-Fragilité, Hôpital des Charpennes (Garnier-Crussard Antoine).

- UMRS1028 INSERM UMR 5292 (CRNL), LYON1 (Quadrio Isabelle).

Date/Duration:36 months

Additionnal info/keywords: Multidisciplinary approach applied to clinical, biological and mathematical modeling of Alzheimer's disease. Alzheimer's disease (AD) is the most common cause of dementia whose diagnosis is based on clinical history, brain imaging and pathophysiological biomarkers like β-amyloid deposits and tau aggregates. Despite considerable efforts, therapeutic approaches related to these biomarkers have failed to provide efficient AD treatment. Recently, the UMR 1296 (team 1) has published evidence that skin fibroblasts from AD patients specifically show that the ATM protein, a major actor of the DNA damage signaling, progressively agglutinates around the nucleus by interacting with and phosphorylating the perinuclear APOE protein by forming perinuclear ATM crowns, quantifiable by immunofluorescence. The formation of these ATM crowns is a major step of a general model involving DNA breaks in AD process. These findings have been published and consolidated by a first mathematical modelling of the formation of the ATM crowns and protected by a patent deposed in January 2023. However, these findings obtained from 10 early AD donors need to be more documented. The goal of this study is to consolidate and validate the breakthrough hypotheses of the perinuclear ATM crowns as specific actors of the involvement of DNA breaks in the AD process through an integrated multidisciplinary approach involving physicians, neurologists, and geriatricians (HCL), biologists (INSERM) and mathematicians (LYON 1) from Lyon institutions. The MAHATMA project is made of 5 workpackages (WP) including 2 consolidation WPs to consolidate the mechanistic model with 40 additional sporadic AD donors and 40 controls, and to develop 2D/3D mathematical models of the formation of the ATM crowns in response to different exogenous stress. Two valorization WPs will permit to secure the plus- value at the clinical scale (novel clinical studies) and the industrial scale (novel predictive and diagnosis assays).Kewords: Alzheimer's disease, ATM, biomarkers, DNA repair, oxidative stress, mathematical modelling, pluridisciplinarity.

9 Dissemination

9.1 Promoting scientific activities

Participants: Thomas Lepoutre.

Participation to MathaLyon (intervention in highschools for mathematical experiments)

9.1.1 Scientific events: organisation

General chair, scientific chair

- Olivier Gandrillon co-organized the conference entitled Like a rolling marble

Member of the organizing committees

- Laurent Pujo-Menjouet co-organized the BONITOS (Bone and Orthopedics Interdisciplinary Symposium) 2024 at CUNY, New-York, MAY, 2024
- Laurent Pujo-Menjouet co-organized the Modeling of Neurodegenerative Diseases minisymposium at the SMB Annual meeting, Seoul, South Korea July, 2024

9.1.2 Scientific events: selection

Member of the conference program committees

- Thomas Lepoutre Member of the scientific comittee of JMBS24 (session of the thematic network Math-Bio-Santé)
- Clément Erignoux Member of the scientific comittee of CJC-MA24

9.1.3 Journal

Member of the editorial boards

- Laurent Pujo-Menjouet is member of the editorial board of:
  - Journal of Theoretical Biology,
  - Mathematical Modelling of Natural Phenomena
  - Plos One

Reviewer - reviewing activities All the member of the team are involed in reviewing processes.

9.1.4 Invited talks

- Thomas Lepoutre, Mathematical Biology: Collective Behavior and Pattern Formation CIRM, Marseille

9.1.5 Research administration

- Thomas Lepoutre is member of the board of Insitut Camille Jordan
- Thomas Lepoutre is member of the scientific council of Insitut Camille Jordan
- Olivier Gandrillon is member of comité de direction de l'IXXI

9.2 Teaching - Supervision - Juries

9.2.1 Teaching

- Mostafa Adimy , 20.0 h, Delay Differential Equations in Population Dynamics and Epidemiology Postgraduate students UNESP, Botucatu, São Paulo, Brazil
- Thomas Lepoutre , 27.0 h, EDP in life sciences M2 Mathématiques avancées UCBL
- Samuel Bernard , 18.0 h, UE MAT2555M Dynamique celluliare et systèmes complexes M2 Math en Action UCBL
- Michèle Romanos , 4.0 h, UE SysBiol 2024 M2 (UCBL) CNRS
- Thibault Espinasse , 9.0 h, MAT2559M Graphes et réseaux en écologie M2 UCBL
- Thibault Espinasse , 18.0 h, MAT2574M Méthodes en apprentissage statistique M2 UCBL
- Thibault Espinasse , 24.0 h, MAT2565M Remise à niveau en statistique M2 UCBL
- Laurent Pujo-Menjouet , 18.0 h, Mathématiques et statistique pour la santé M2 UCBL
- Laurent Pujo-Menjouet , 9.0 h, Modeling in biology and medicine M2 UCBL
- Laurent Pujo-Menjouet , 3.0 h, Approfondissement didactique et expérimentation M2 UCBL
- Laurent Pujo-Menjouet , 3.0 h, Du modèle biologique au modèle statistique M2 UCBL
- Samuel Bernard , 15.0 h, BMMATH5 Processus stochastiques M1 (cycle ingénieur) INSA Lyon
- Samuel Bernard , 18.0 h, BMMATH4 ED-EDP M1 (cycle ingénieur) INSA Lyon

- Laurent Pujo-Menjouet , 18.0 h, BMMATH4 ED-EDP M1 (cycle ingénieur) INSA Lyon
- Thibault Espinasse , 10.0 h, MAT1325M Cas pratiques M1 UCBL
- Thibault Espinasse , 18.0 h, MAT1345M Classification et réseaux de neurones M1 UCBL
- Thibault Espinasse , 36.0 h, MAT1350M Statistique bayesienne M1 UCBL
- Laurent Pujo-Menjouet , 48.0 h, Systèmes dynamiques M1 UCBL
- Samuel Bernard , 12.0 h, BMMATH3 EDO avancées L3 (cycle ingénieur) INSA Lyon
- Laurent Pujo-Menjouet , 12.0 h, BMMATH3 EDO avancées L3 (cycle ingénieur) INSA Lyon
- Samuel Bernard , 15.0 h, BMMATH2 Algèbre linéaire et analyse de données L3 (cycle ingénieur) INSA Lyon
- Thibault Espinasse , 19.0 h, MAT3166L Analyse des données L3 UCBL
- Laurent Pujo-Menjouet , 12.0 h, Biomathématiques et modélisation L3 UCBL
- Laurent Pujo-Menjouet , 19.0 h, Mathématiques et statistique appliquées à la santé 2 L3 UCBL
- Thomas Lepoutre , 40.0 h, UE RB35 (parcours médecine sciences) L2 UCBL
- Charlotte Camus , 9.0 h, MAT2091L Algèbre 3 L2 UCBL
- Thibault Espinasse , 43.0 h, MAT2075L Probabilités-statistiques 2 L2 UCBL
- Laurent Pujo-Menjouet , 33.0 h, Mathématiques et statistique appliquées à la santé 2 L2 UCBL
- Léon Tine , 196.0 h, MAT2012L; MAT1074L; MAT1056L; MAT2027L; MAT2096L; MAT2013L L1, L2,L3 UCBL
- Charlotte Camus , 36.0 h, MAT1054L Algèbre 2 L1 UCBL
- Charlotte Camus , 8.0 h, MAT1059L Khôles L1 UCBL
- Laurent Pujo-Menjouet , 50.0 h, Fondamentaux des maths pour la santé - mineure disciplinaire maths pour les PASS L1 UCBL
- Laurent Pujo-Menjouet , 7.5 h, MD Sciences pour la santé L1 UCBL
- Laurent Pujo-Menjouet , 36.0 h, Mathématiques et statistique appliquées à la santé 1 L1 UCBL

9.2.2 Supervision

- PhD of Cheikh Gueye on Inverse problem and application to Alzheimer's disease modeling, defended in April 2024, co-supervisor: Léon Tine (with Laurent Pujo Menjouet and Ionel Sorin ciuperca)
- PhD of Maxime Estavoyer on Propagation and pattern formation in biology, defended in November 2024, [26] supervisor: Thomas Lepoutre
- PhD of Baptiste Maucourt on Contrôle agro-écologique d'un système parasite-hôte spatio-temporel. Prévention de la propagation et optimisation de la récolte, defended in July 2024, co-supervisor: Thomas Lepoutre (with Léo Girardin and Batien Boussau)
- PhD in Progress: Charlotte Dugourd, "Nested Immuno-epidemiological modeling of the dynamics of intra- and inter-host infections", Université Lyon 1, since October 01, 2022, supervisor: Mostafa Adimy.
- PhD in progress: Arsène Marzorati, University Lyon 1, since October 01, 2022, supervisors: Samuel Bernard and Jonathan Rouzaud-Cornabas.

- PhD in progress: Basile Fornara, "Mécanismes de dissémination des prions dans les tissus cérébraux : une approche synthétique",Université Paris Cité, since October 21, 2022, supervisors: Human Rezaei and Laurent Pujo-Menjouet.
- PhD in progress: Grégoire Ranson, "Mathematical modeling of epidemics spreading dealing with temporary treatment efficiency" , since January 1st, 2022, supervisors Mostafa Adimy, Laurent Pujo-Menjouet, Jianhonw Wu (York university)
- PhD in progress: Théo Loureaux, "Contribution to the study of neurodegenerative diseases", since January 1st, 2023, supervisors Laurent Pujo-Menjouet, Suzanne Sindi (UC Merced)
- PhD of Ruben Taieb, supervisor Mostafa Adimy (with Arnaud Ducrot, Le Havre)
- PhD in progress : Clemence Fournie, supervisor Olivier Gandrillon (co-supervision with Fabien Crauste, Paris)
- Post-doc: Thao Nguyen Thi Nhu, supervisors: Olivier Gandrillon
- Post-doc: Mohammed Elghandouri,supervisor Mostafa Adimy
- Post-doc: Mathieu Calero,supervisor Laurent Pujo-Menjouet
- PhD in progress: Arsène Marzorati, "Mixed floating precision schemes for ODEs in large dimensions", supervisors Samuel Bernard (co-supervisor Jonathan Rouzaud-Cornabas)
- PhD in progress: Clémence Métayer, "Machine learning for the dynamics of interactions between the NLRP3 immune receptor, DNA repair and the circadian clock for lung cancer treatment optimisation", co-supervisor Samuel Bernard (supervisor A Ballesta)
- PhD defended: Embla Steiner (September 6th, 2024, Karolinska Institute), co-supervisor Samuel Bernard (supervisor Jonas Frisén)
- PhD in progress : Brune Massoulié, "Macroscopic behavior and timescales for kinetically constrained lattice gases", supervisor Clément Erignoux (co-supervision with Cristina Toninelli, Paris)
- PhD in progress : Hugo Da Cunha, "Macroscopic behavior of non-equilibrium facilitated exclusion processes", supervisor Clément Erignoux (co-supervision with Marielle Simon, Lyon)

9.2.3 Juries

- Sirine Boucenna ISEM Montpellier Dynamiques éco-évolutives dans les écosystèmes soumis à un stress Rapporteur Thomas Lepoutre
- Adli El Abdouni Univ. Versailles Études d'équations à noyaux non-locaux périodiques en temps et d'ondes progressives Examinateur Thomas Lepoutre
- Enguerrand Petit, Univ. Paris Dauphine, Temps de mélange pour des processus de Markov à espaces d'états continus. Examinateur Clément Erignoux

9.3 Popularization

Participants: Laurent Pujo-Menjouet.

Popularizing talks: Nuit de la lecture (January 2024), table-ronde Musée des Confluences - A nos amours (February 2024), Pint of Science (May 2024), Conference BU-INSA (December 2024)

10 Scientific production

10.1 Publications of the year

International journals

[1] M. Adimy, A. Chekroun and C. Dugourd-Camus. 'Is it more effective to protect susceptible individuals or isolate infected people to prevent the spread of a SIR-type epidemic?' In: *Discrete and Continuous Dynamical Systems - Series B* (Nov. 2024). URL: https://inria.hal.science/hal-04847754.

[2] M. Adimy, A. Chekroun, G. Ranson and L. Pujo-Menjouet. 'Stability Analysis of a New Differential-Difference Model Applied to the Pre-exposure Prophylaxis (PrEP) Effect on the Spread of HIV'. In: *Qualitative Theory of Dynamical Systems* 23.5 (238) (11th July 2024). DOI: 10.1007/s12346-024-01093-x. URL: https://inria.hal.science/hal-04777788 (cit. on p. 6).

[3] A. Bouley, C. Erignoux and C. Landim. 'Steady state large deviations for one-dimensional, symmetric exclusion processes in weak contact with reservoirs'. In: *Annales de l'Institut Henri Poincaré (B) Probabilités et Statistiques* (2024). URL: https://hal.science/hal-03897408. In press (cit. on p. 9).

[4] M. Bouvier, S. Zreika, E. Vallin, C. Fourneaux, S. Gonin-Giraud, A. Bonnaffoux and O. Gandrillon. 'TopoDoE: a design of experiment strategy for selection and refinement in ensembles of executable gene regulatory networks'. In: *BMC Bioinformatics* 25.1 (2024), p. 245. DOI: 10.1186/s12859-024-05855-x. URL: https://hal.science/hal-04678148 (cit. on p. 8).

[5] V. Calvez, A. El Abdouni, M. Estavoyer, I. Madrid, J. Olivier and M. Tournus. 'Regime switching on the propagation speed of travelling waves of some size-structured Myxobacteria population models'. In: *ESAIM: Proceedings and Surveys* 77 (18th Nov. 2024), pp. 195–212. DOI: 10.1051/proc/202477195. URL: https://hal.science/hal-04532644 (cit. on p. 6).

[6] V. Calvez, T. Lepoutre and N. Meunier. 'A nonlinear system to model communication between yeast cells during their mating process'. In: *Nonlinearity* 37.4 (12th Mar. 2024), p. 045013. DOI: 10.1088/1361-6544/ad247b. URL: https://inria.hal.science/hal-04798913 (cit. on p. 7).

[7] V. Calvez, T. Lepoutre and D. Poyato. 'Ergodicity of the Fisher infinitesimal model with quadratic selection'. In: *Nonlinear Analysis: Theory, Methods and Applications* 238 (1st Jan. 2024), p. 113392. DOI: 10.1016/j.na.2023.113392. URL: https://hal.science/hal-03274734.

[8] T. Chen, C. Yang, L. M. Tine and Z. Guo. 'A new collision avoidance model with semi implicit random batch resolution'. In: *Communications in Mathematical Sciences* (26th Apr. 2024). URL: https://hal.science/hal-04797608 (cit. on p. 9).

[9] I. S. Ciuperca, L. Pujo-Menjouet, L. M. Tine, N. Torres and V. Volpert. 'A qualitative analysis of an Aβ-monomer model with inflammation processes for Alzheimer's disease'. In: *Royal Society Open Science* (15th May 2024). URL: https://hal.science/hal-03877951 (cit. on p. 7).

[10] C. Dugourd-Camus, C. Ferreira and M. Adimy. 'Modelling the mechanisms of antibody mixtures in viral infections: the cases of sequential homologous and heterologous dengue infections'. In: *Journal of the Royal Society Interface* 21.219 (16th Oct. 2024), p. 20240182. DOI: 10.1098/rsif.2024.0182. URL: https://inria.hal.science/hal-04777129 (cit. on p. 6).

[11] L. El Nachef, L. Bodgi, M. Estavoyer, S. Buré, A.-C. Jallas, A. Granzotto, J. Restier-Verlet, L. Sonzogni, J. Al-Choboq, M. Bourguignon, L. Pujo-Menjouet and N. Foray. 'Prediction of Cancer Proneness under Influence of X-rays with Four DNA Mutability and/or Three Cellular Proliferation Assays'. In: *Cancers* 16.18 (18th Sept. 2024), p. 3188. DOI: 10.3390/cancers16183188. URL: https://inria.hal.science/hal-04722189.

[12] C. Erignoux. 'On the hydrodynamics of active matter models on a lattice'. In: *Markov Processes And Related Fields* 30.1 (27th May 2024), pp. 57–80. DOI: 10.61102/1024-2953-mprf.2024.30.1.002. URL: https://hal.science/hal-03431146 (cit. on p. 9).

[13] C. Erignoux, A. Roget, A. Shapira and M. Simon. 'Hydrodynamic behavior near dynamical criticality of a facilitated conservative lattice gas'. In: *Physical Review E* 110.3 (3rd Sept. 2024), p. L032101. DOI: 10.1103/PhysRevE.110.L032101. URL: https://hal.science/hal-04742490 (cit. on p. 10).

[14] C. Erignoux, M. Simon and L. Zhao. 'Mapping hydrodynamics for the facilitated exclusion and zero-range processes'. In: *The Annals of Applied Probability* (2024). URL: https://hal.science/hal-03889620. In press (cit. on p. 10).

[15] C. Erignoux and L. Zhao. 'Stationary fluctuations for the facilitated exclusion process'. In: *Electronic Journal of Probability* 29 (2024), pp. 1–41. DOI: 10.1214/24-EJP1208. URL: https://hal.science/hal-04379637 (cit. on p. 10).

[16] M. Estavoyer and T. Lepoutre. 'Travelling waves for a fast reaction limit of a discrete coagulation-fragmentation model with diffusion and proliferation'. In: *Journal of Mathematical Biology* 89.1 (13th May 2024), p. 2. DOI: 10.1007/s00285-024-02099-4. URL: https://hal.science/hal-04516285 (cit. on p. 6).

[17] B. Fornara, A. Igel, V. Béringue, D. Martin, P. Sibille, H. Rezaei and L. Pujo-Menjouet. 'The dynamics of prion spreading is governed by the interplay between the non-linearities of tissue response and replication kinetics'. In: *iScience* 27.12 (2024). DOI: 10.1016/j.isci.2024.111381. URL: https://hal.science/hal-04836040 (cit. on p. 7).

[18] C. Fourneaux, L. Racine, C. Koering, S. Dussurgey, E. Vallin, A. Moussy, R. Parmentier, F. Brunard, D. Stockholm, L. Modolo, F. Picard, O. Gandrillon, A. Paldi and S. Gonin-Giraud. 'Differentiation is accompanied by a progressive loss in transcriptional memory'. In: *BMC Biology* 22.1 (12th Mar. 2024), p. 58. DOI: 10.1186/s12915-024-01846-9. URL: https://hal.science/hal-04734188.

[19] C. Gueye, S. I. Ciuperca, L. Pujo-Menjouet and L. M. TINE. 'Q-well-posedness of an Aβ-protein polymerization model'. In: *Mathematical Modelling of Natural Phenomena* 19 (7th Sept. 2023), p. 19. DOI: 10.1051/mmnp/2023028. URL: https://hal.science/hal-04381804.

[20] C. Ionel, M. Mahjoub and L. Matar Tine. 'Aβ -protein polymerization in Alzheimer disease: Optimal control for nucleation parameter estimation'. In: *Journal of Theoretical Biology* 589 (July 2024), p. 111814. DOI: 10.1016/j.jtbi.2024.111814. URL: https://hal.science/hal-04797725 (cit. on p. 8).

[21] T. N. T. Nguyen, M. Martin, C. Arpin, S. Bernard, O. Gandrillon and F. Crauste. 'In silico modelling of CD8 T cell immune response links genetic regulation to population dynamics'. In: *ImmunoInformatics* 15 (4th Sept. 2024), p. 100043. DOI: 10.1016/j.immuno.2024.100043. URL: https://hal.science/hal-04489553 (cit. on p. 8).

[22] K. I. Ouyoussef, J. El Karkri, L. M. Tine and R. Aboulaich. 'Physics-informed neural networks for parameter estimation and simulation of a two-group epidemiological model'. In: *International Journal of Modeling, Simulation, and Scientific Computing* 15.03 (19th July 2024). DOI: 10.1142/S1793962324500429. URL: https://hal.science/hal-04798230.

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