RESEARCH CENTRE

Inria Saclay Centre at Institut Polytechnique de Paris

IN PARTNERSHIP WITH:

Institut Polytechnique de Paris, CNRS

2024 ACTIVITY REPORT

Project-Team MERGE

Mathematics for Evolution, Reproduction, Growth and Emergence

IN COLLABORATION WITH: Centre de Mathématiques Appliquées (CMAP)

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Biology

Inria

Contents

Project-Team MERGE

Creation of the Project-Team: 2023 March 01

Keywords

Computer sciences and digital sciences

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

A6.1.2. – Stochastic Modeling

A6.1.4. – Multiscale modeling

A6.2.1. – Numerical analysis of PDE and ODE

A6.2.3. – Probabilistic methods

A6.2.4. – Statistical methods

A6.3.1. – Inverse problems

Other research topics and application domains

B1. – Life sciences

B1.1. – Biology

B1.1.2. – Molecular and cellular biology

B1.1.6. – Evolutionnary biology

B1.1.8. – Mathematical biology

B2. – Health

B2.2.3. – Cancer

B2.2.6. – Neurodegenerative diseases

B2.3. – Epidemiology

B2.4.2. – Drug resistance

B3. – Environment and planet

B3.6. – Ecology

B3.6.1. – Biodiversity

1 Team members, visitors, external collaborators

Research Scientists

- Marie Doumic-Jauffret [Team leader, Inria, HDR]
- Gael Raoul [CNRS, Researcher]
- Milica Tomasevic [CNRS, Researcher]

Faculty Members

- Vincent Bansaye [ECOLE POLY PALAISEAU, Professor, HDR]
- Sylvie Méléard [Ecole Polytechnique, Professor, HDR]

Post-Doctoral Fellow

- Nadia Belmabrouk [Ecole polytechnique]

PhD Students

- Maxence Baccara [ECOLE POLY PALAISEAU, from Oct 2024]
- Luce Breuil [ECOLE POLY PALAISEAU, from Apr 2024]
- Nicoleta CAZACU [ECOLE POLY PALAISEAU, from Nov 2024]
- Mateo Deangeli Bravo [ECOLE POLY PALAISEAU, from Oct 2024]
- Ana Fernandez Baranda [ECOLE POLY PALAISEAU]
- Guillaume Garnier [Sorbonne Université]
- Viviana Gavilanes [Sorbonne Université, from Nov 2024]
- Anouar Jeddi [ECOLE POLY PALAISEAU]
- Madeleine Kubasch [ECOLE POLY PALAISEAU, until Oct 2024]
- Maxime Ligonniere [Université de Tours]
- Ignacio Madrid Canales [ECOLE POLY PALAISEAU, until May 2024]
- Jules Olayé [ECOLE POLY PALAISEAU]
- Alexandre Perrin [ECOLE POLY PALAISEAU]
- Le Tuyet Nhi Pham [ECOLE POLY PALAISEAU]

Administrative Assistant

- Anna Dib [INRIA]

Visiting Scientists

- Sarah Kaakai [UNIV LE MANS, until Aug 2024, Visiting professor (délégation on the ERC SINGER)]
- Marek Kimmel [Rice University, from Sep 2024]
- Carmela Moschella [Université de Vienne, from Oct 2024 until Nov 2024]

2 Overall objectives

The wide domain of population dynamics has had many developments in recent years, in probability with the study of stochastic integro-differential equations [46] as well as in PDE analysis [118, 117]. The two approaches are combined more and more frequently, for model analysis [62, 45] as well as for estimation problems [82]. In biology, many new questions have appeared, and the very recent development, over the last decade, of the so-called "single cell" or micro-fluidic methods [135, 87, 98, 50] make these models all the more topical as they can now be quantitatively compared with the data microscopically as well as macroscopically. Many essential medical and social applications are closely related to our research, *e.g.* cancer treatment (see Section 4.1), biotechnologies (Section 4.3), antibiotic resistance (Section 4.1), species extinction (Section 4.4). Our main theoretical guideline, which can have applications in other fields (SPDE, propagation of uncertainty, PDE analysis...), is to reconcile PDE approaches with stochastic ones, in situations where the two types of dynamics play a fundamental role at different scales. Our main application guideline is to study problems directly inspired by our biologist collaborators' questions, so that even our most theoretical work could have an impact also in biology or medicine.

The applications drive our mathematical research, including the most theoretical ones. Many of our models have several possible applications so that the interests of MERGE members converge, since for instance we are interested in modelling mutations both for bacteria and for leukemic cells; emergence of survivors for senescent yeasts as well as for bacteria under antibiotic treatments; evolutionary questions for bacterial populations as well as tree populations submitted to the climate change. Moreover, most of our mathematical models have even wider applications than in biology - among many other possible examples, fragmentation processes occur in mineral crushing in the mining industry, cell division models are close to models for the TCP-IP protocol. The main application domain, shared by all team members, concerns unicellular organism populations.

Our research program is organised along three main axes. First, the study of "models through scales", *i.e.* the links between various stochastic or PDE models through convergence analysis of individual-based models towards mesoscopic or macroscopic ones, is essential for our models to have a solid foundation. The second axis is their mathematical analysis, which allows one to qualitatively compare them to biological systems and use them as predictive and exploration tools, whereas the third one develops methods for their quantitative comparison to data. For each research axis, we outline what we consider to be the major current research issues of the field, and then use a few non exhaustive examples of work in progress to give a concrete description of our work programme in the short and medium term.

To make the links between our research program and the applications more obvious, we have specified the main research axes concerned for each application.

3 Research program

Our research program is entirely devoted to the modelling and study of interacting populations. In many cases, we will also develop methods for quantitative model-data comparison through estimation methods and inverse problems.

The first research axis, "Models through scales", is devoted to mathematical problems which appear in order to obtain rigorous links between microscopic, mesoscopic and macroscopic models. These questions are closely related to the modelling work, which we have not detailed in a specific section, as it is carried out through exchanges with our medical doctors and biologists collaborators and is a direct continuation of the application questions outlined above. The second axis gathers qualitative analysis problems for the structured population models that we wrote during such modelling work, or inspired by our interdisciplinary discussions. The third axis, "Model-data comparison", goes back to the data, through inverse problems theoretical and numerical solution.

3.1 Axis 1: Models through scales

Permament members: Vincent Bansaye, Marie Doumic, Sylvie Méléard, Gaël Raoul, Milica Tomašević

When we describe non-interacting populations which undergo mutations, growth, movement, division and death, the stochastic branching process modelling each individual behaviour may be translated to a structured population equation or system in a rather direct way, by the use of random measures [82] or from the expectation of the empirical measure linked to the branching tree and so-called many-to-one formulae [68]. This is no more true once interaction between the cells or with the environment is considered: in such cases, mean-field limits have to be derived [90], by making the number of individuals in the population tend to infinity. Making such limits rigorous, and relating the asymptotic models to specific parameter regimes, is a very active research field not only for structured populations but also in physics. One faces several fundamental questions: how to describe and quantify the emergence of an initially very small number of individuals, inside multi-species interacting populations which, depending on available resources and space, will finally succeed to become dominant? How to keep track of microscopic fluctuation at the macroscopic level? How to perform a macroscopic limit when each individual interacts only with its closest neighbours rather than with the overall population? Finally, how stochasticity and heterogeneity between individuals impact macroscopic behaviours? These issues drive our work. Let us now detail some more specific problems we want to study.

From stochastic processes to constrained Hamilton-Jacobi (HJ) equations.
Permanent members: Sylvie Méléard, Gaël Raoul

Most models, for instance for the "normal" bacterial division cycle [79], consider asexual populations with clonal reproduction and vertical inheritance. We want to consider here a more general model with a transfer term, justified by biological considerations in the case of bacterial transfer [86] (see also the application section 4.1). The individual-based population process is given for any K by the jump point-measure Markov process $(\mu_t^K)_t$ on a trait subset of $\mathbb{R}^d$ weighted by $1/K$. An individual with trait x gives birth to a new individual with rate $b(x)$. With probability $1-p_K$, the new individual carries the trait x and with probability p_K, it carries a mutant trait z chosen according to the distribution $m(x,z)dz$. An individual with trait x in the population μ^K dies with death rate $d(x)+C\langle\mu^K(t),1\rangle$. Further an individual with trait x chooses a partner with trait y at rate $h_K(x,y,\mu^K)=\tau(x,y)/K\langle\mu^K,1\rangle$ and after transfer, the couple (x,y) becomes (x,x). Then for any "good" test function φ, we have

$$\begin{aligned}\langle\mu_t^K,\varphi\rangle =&\langle\mu_0^K,\varphi\rangle+\int_0^t\int_{\mathbb{R}}\Big(\big(b(x)-d(x)-C\langle\mu_s^K,1\rangle\big)\varphi(x)+p_K b(x)\int_{\mathbb{R}}\big(\varphi(z)-\varphi(x)\big)m(x,z)dz\Big)\mu_s^K(dx)ds\\&+\int_0^t\int_{\mathbb{R}}\frac{\tau(x,y)}{\langle\mu_s^K,1\rangle}\big(\varphi(x)-\varphi(y)\big)\mu_s^K(dx)\mu_s^K(dy)ds+M^{K,\varphi}(t),\end{aligned}\tag{1}$$

where $M^{K,\varphi}$ is a square integrable martingale whose quadratic variation can be easily made explicit. By letting K go to infinity, and p_K go to p, we can derive an integro-differential equation with non local non linearities due to both competition and transfer. Uniqueness of its solution is obvious but its long-time behaviour is unknown, as well as the existence of stationary solutions. Formally, applying a limiting procedure for small mutations and time rescaling usually leads to a HJ type equation with constraints, in the formalism introduced in [74], successfully developed in [52, 119, 51], and in many extensions so far. Concentrations in such equations are too fast for realistic evolution [120]. Indeed the evolutionary dynamics strongly depend on the positivity of the density although it is exponentially small for some traits. Different papers [120, 94, 110] proposed to slow down the concentration speed by the addition of artificial terms. With Nicolas Champagnat, Sylvie Méléard introduced another point of view. The rare mutation assumption introduced in [61] allowed to obtain a time scale separation between demography and mutation. Under this assumption, they were able to characterize rigorously a general evolutionary jump process describing the successive evolutionary population states [63]. This approach was very fruitful and allowed to quantify the complete scheme from individuals to macroscopic behaviors as suggested in [107] and [73]. Nevertheless, the assumptions imposed very small mutation rates considered too slow to explain evolution (especially for microorganisms), but also too slow to capture the concentration effects of the HJ equations. At this point one may recall the usual critics by some biologists [136], of unrealistic evolutionary time scale, at least for certain species.

The first task in this study is to integrate fast mutation time scales and to show how stochastic models based on logarithmic scales can capture small populations in large approximations and explain deterministic concentration phenomena. In particular we aim to obtain new singular and constrained

HJ equations taking into account the local population extinctions. We hope that these new scales will provide an intermediate approach consistent with biological observations.

The second task is to characterize the different asymptotic behaviors in the Hamilton-Jacobi equation and to understand the role of the trade-off between demography and transfer.

Space-and-trait structured models

Permanent members: Vincent Bansaye, Marie Doumic, Gaël Raoul

Effects of spatial heterogeneity on structured population dynamics need to be studied for many applications, in ecology as well as in microbiology. Here again, relating macroscopic to individual-based models is of key importance for a correct interpretation of macroscopically observed phenomena such as morphogenesis or front propagation. Let us develop two examples: size-and-space structured models and phenotypic trait-and-space structured models.

Microcolony morphogenesis. A bacterial microcolony may form out of one single cell, growing and dividing in a petri dish without movement except due to the growth. We can describe it by an individual-based model, where each cell repulses and maybe attracts its neighbours, but how do these local interaction forces influence the overall shape of the microcolony? When and how do specific patterns emerge? Do the bacteria only repulse each other or is attraction possible? Which mesoscopic or macroscopic description would be valid? These are some of the questions we want to address.

As a first step, in [81], Marie Doumic, Sophie Hecht and Diane Peurichard proposed a purely-repulsive individual-based model of rod-shaped bacteria, where growth, division and repulsion were sufficient to explain the main characteristics of microcolonies observed.

A first research direction consists in deriving rigorously a kinetic model, including both a spatial structure and a structuring trait such as size. For a model with spherical 2D-cells dividing into equally-sized daughters, with an interaction force ϕ, an example of limit model satisfied by $u(t,x,r)$ the density of cells at time t, position x and radius r is as follows

$$\frac{\partial}{\partial t}u(t,x,r)+\frac{\partial}{\partial r}\left(g(r)u\right)+\nabla\cdot(G[u]u)+\beta(r)u$$

$$=2\sqrt{2}\beta(\sqrt{2}r)\int_0^1\kappa(\theta)u(t,x+\alpha r\left(\cos(2\pi\theta),\sin(2\pi\theta)\right),\sqrt{2}r)d\theta,$$

$$u(0,x)=u_0(x),\qquad g(0)u(t,x,0)=0,$$

$$G[u]=-\int_{\Omega\times(0,\infty)}\phi(|\frac{x-x'}{r+r'}|^2)(x-x')u(dx',dr'). \quad (2)$$

This should generalize the model proposed in [112]. However, the main drawback is that to prove rigorously this limit, departing from a stochastic differential equation of the same kind as (1) when the number of cells K tends to infinity, one needs to assume a nonlocal interaction kernel G, so that at the limit each cell interacts with infinitely many others. This is false for many applications and in particular for morphogenesis. We thus want to derive, from (2), a macroscopic model where the nonlocal interaction kernel G boils down to a local one, cells interacting only with the ones at the same macroscopic position x [60]. However, even for simpler cases - for instance forgetting with the growth and division terms - many difficulties appear, since existing methods [115, 114], based on energy inequalities and compactness embeddings [97, 103], cannot apply due to the lack of compactness in the size variable.

Another research direction, for not isotropic cells but rather rod-shaped bacteria like *E. coli*, is to include a direction for each individual. In this spirit, nematic liquid crystal models [42, 102] have been proposed to describe a variety of biological active fluids, *e.g.* cellular monolayers [77, 134, 137]; though, how they may be derived from individual-based models such as the hard-rod model of [137, 81] or the models of [66, 134] remains unclear. We aim at deriving, formally and then - on simplified versions of

the model - rigorously, a continuous model of liquid crystal type.This could then be a step towards the reverse question: how to estimate the *microscopic* interaction function from a *macroscopic* picture of the colony at a given time, see Section 3.3.

Space and phenotype species models. Sexual reproductions imply the recombination of DNA during reproductions. The models describing the effect of recombinations on trait-structured species can be divided into two classes: the ones describing the dynamics of a small number of loci (typically less than 3), and the ones considering an infinite number of loci. In the latter case, the main model used is the so-called infinitesimal model, that was developed by Fisher in 1919 [88]. This model is reminiscent of collision models from statistical physics, which provides an interesting perspective to study the dynamics of these models, in particular when this phenotypic structure is coupled to a distribution of the species in space.

Our first goal will be to generalize the derivation of mascroscopic limits[111, 54] to situations where a finite (but large) number of loci are present, and/or where the reproduction is partially asexual. We would like to study the spatial dynamics of such species compare to asexual species on one side, and to the infinitesimal model case on the other side. From a ecological stand point, this would help us understand the impact of recombination on species' range.

Our second goal will be to use these macroscopic limits to build travelling waves for the structured population models. We would then take advantage of the diffusion operator that represents the effect of the spatial dispersion of individuals. The main roadblock here will be to develop a good framework for the macroscopic travelling waves [108]. This is difficult because the macroscopic equations (describing the population by its size and mean phenotypic trait in each location) involves a so-called gene flow term, that we do not fully apprehend yet. This difficulty is directly related to ecological questions: gene flow is an important effect of sexual reproduction on a species' evolutionary dynamics.

The last objective on this topic would be to develop a software able to simulate the dynamics of a species' range. Based on the travelling wave analysis we have developed [37], we believe we could use recently developed fast-marching algorithms [109] to propose a description of the effect of climate change on a given species.

From local interaction models to cross-diffusion equations. Many interactions of species and cells are local, which means that they occur when individuals are close enough, at a distance negligible for the macroscopic scale. Going from the individual level to macroscopic models raises several mathematical challenges linked in particular to the control of the non linearity in the motion component [89]. This issue is linked to the control of the limiting PDE (stability, non-explosion, invariant distribution, entropic structure) and the distance involved in the convergence of the stochastic process. Vincent Bansaye, Ayman Moussa and Felipe Munoz have developed duality estimates to prove stability of the limit and get a strong convergence of the stochastic model seen as a random perturbation [47].

Non-markovian interactions: from local interaction model to the parabolic-parabolic Keller-Segel system

Permanent members: Milica Tomašević

An important mathematical challenge is to derive mean-field limits for *non-Markovian* interaction, *i.e.,* when the past also needs to be taken into account. Such models appear for instance in neuroscience [65, 64] and chemotaxis. To model chemotaxis, the parabolic-parabolic Keller-Segel model has been stated phenomenologically, but to interpret it we need to introduce interaction memory, which provides tremendous analysis difficulties since particles are now non-markovian both in time and space. New methods have been proposed by Milica Tomašević, with a stochastic representation of the *mild* formulation of the equation and a particle approximation [125, 129, 127]. The equations obtained have been little studied before Milica Tomašević's Ph.D thesis, so that many questions remain open. Concerning the convergence of the particle systems towards the Keller-Segel model, an important problem is the obtention of explicit convergence rates, when the number of particles tends to infinity, for the

propagation of chaos of the particle system in 1D. A possible way is to extend techniques developed by Jabin and Wang [95] for the quantitative study of the mean-field boundaries of particle systems in non-regular Markovian interaction. The aim is to control the relative entropy between the joint law of the particles and the law of N independent copies of the Keller-Segel system. By exploiting the results on the Keller-Segel nonlinearity in 1 dimension and on the Sobolev type estimation on the densities of the system (chapter 4 in [128]), a regularization of the interaction kernel of the particles allows to obtain a first convergence rate for the marginal laws in time of an arbitrary particle, explicit but suboptimal (due to the regularization procedure). To obtain the optimal convergence rate, we think to develop an essentially probabilistic approach suggested by the recent works of Veretennikov [133] and Lacker [101] as well as by the partial Girsanov transformations introduced in [96].

3.2 Axis 2: Qualitative analysis of structured populations

Diffusion-growth-fragmentation processes and equations

Permanent members: Marie Doumic, Sylvie Méléard

To model the growth of a bacterial population in a chemostat, a new model of growth and fragmentation, coupled to a differential equation for the resource, was proposed by Josué Tchouanti in his thesis [126]. Using a combination of probabilistic and analytical methods, he proved the existence, uniqueness and regularity of solutions, as well as the convergence in large populations of the individual-based model. This model also present similiarities with the proliferation of parasites in dividing cells studied by Vincent Bansaye [49, 44].

One of the very interesting novelties of this model is to consider the growth not as a purely deterministic process, leading to a transport term in the size structured equation $\frac{\partial}{\partial x}(\tau(x)u(t,x))$, but to take into account the intrinsic stochasticity in growth, so that a diffusion-type term $\frac{\partial^2}{\partial x^2}(D(x)u(t,x))$ is added, which degenerates at the boundary $x = 0$. We thus want to study further this equation, its long-time dynamics with and without interaction (*i.e.* in the linear case as well as with nonlinear couplings), how it differs from the much more studied growth-fragmentation equation, and which model seems more relevant in which applicative case. We also want to adapt the model to metabolic heterogeneity cases, *i.e.* when we model the capacity for bacteria to feed on two distinct nutrients, which leads to distinguish two populations competing for two resources.

Ergodicity analysis and exponential convergence for multi-dimensional growth-fragmentation processes and equations

Permanent members: Vincent Bansaye, Sylvie Méléard, Milica Tomašević

Based on data from the Edinburgh's lab of Meriem El Karoui, Ignacio Madrid Canales introduced during his thesis an adder growth-fragmentation stochastic process modelling the growth of bacteria. He studied its long time behaviour and proved that conveniently renormalized, the associated semigroup converges exponentially to a well defined measure. The aim is now to generalize this result in higher dimensions, motivated by the different growth strategies that bacteria can have under stress. Mathematically the question is also largely open.

Understanding the links between genealogical and population behaviours

Permanent members: Vincent Bansaye, Marie Doumic and Sylvie Méléard

Microfluidic experiments allow one to follow a genealogical lineage of cells, whereas most previous experiments as well as "natural" conditions consist in observing a full population dynamics. The natural question then comes to relate the two models, and to understand how certain phenomena may be observed in one setting but not in the other - for instance, how a few individuals may finally invade the whole population; how survivor cells may emerge from a senescent population; or yet, how to find the "signature" of a phenomenon that happened in the past from the observation of a population at a fixed time.

Differential influence of the initial condition Time to extinction in the case of genealogical data differs drastically from time to extinction for a dividing whole population, so that observing the first occurs at a much faster timescale than the second. Relating the two in simple models like the Galton-Watson tree is straightforward, but much more involved in more complex cases [46], especially if rare mutation events occur (see Section 3.1). With a view towards telomere shortening models and the interpretation of experiments carried out by Teresa Teixeira's lab, we want to assess rigorously the relations between these two observation cases in increasingly complex models. Reversing time in population models which are in a stationary regime has been well developed during the past decades, using coalescent and duality theories, in particular in the case of fixed population size. Understanding the genealogical structure in transitory regime (such as growth), keeping track of the initial conditions (in particular in finite window size of experiments or cancer treatment or epidemics) or capturing the effect of variations of the populations raise new and fundamental mathematical issues. For that purpose, we aim at developing spinal approaches, which consist in a forward construction distinguishing an individual bound to be the sample at a future time.

Time reversed trajectories. A natural question is to get information on individuals from observation on the whole population at a given time. More precisely, given a finite sample of living individuals, we aim first, to find their genealogical and trait's history and second, to find the explicit time reversed path from a sampled individual to its ancestor. A particularly interesting case is the one when the initial density of the whole stochastic process is close to a Dirac measure. This question motivated an abundant literature in population genetics with the so-called Kingman coalescent (see [99], [55] and references therein), or lookdown processes [76], [85] in a context of fixed and small population size, almost neutrality and individuals independence. Genealogy of branching processes models have also been introduced, allowing demographic structure but no interactions (cf. [104]). Our framework is different: we focus on bacteria or cells which form large populations and for which assumptions of neutrality, extrinsic control of population size or non-interacting individuals are violated. Developing methods which relax such hypotheses is a contemporary challenge, which could be used in different contexts (see below how this point of view can be of particular relevance to study the individuals responsible of the population survival in case of environmental changes). Inspired by Perkins [116], Sylvie Méléard and Viet Chi Tran constructed in [106] a nonlinear historical super-process with values in a paths measure space, capturing the history of a large population. It is a heavy object which might not be tractable for our goal.

Our purpose is to introduce more tractable tools, exploiting the large population assumption ($K \to \infty$) and the spinal techniques developed for branching processes (cf [93, 92], [104] and references therein). We have seen that the stochastic process (1) is close to the solution of an integro-differential equation. Therefore, we can construct for large K a coupling between the stochastic process and a non-homogeneous structured branching process where the interaction terms have been replaced by their deterministic approximation. We should obtain some non-homogeneous biased Markov process by giving its associated infinitesimal generator. The next step would consist in finding the time reversed trajectory of a sample individual. This will be done using time reversal theory for non-homogeneous Markov processes, see [67, 113]. This program has already been developed in the Gaussian case [59] and lead to a precise quantitative description of the reverse trajectories explaining the genetic or phenotypic characteristics of a living individual.

3.3 Axis 3: Model-data comparison

Permanent members: Marie Doumic, Sylvie Méléard, Milica Tomašević

Comparing models to data, either qualitatively or quantitatively, is an essential step for all the previously seen tasks, especially the asymptotic studies through scales. It is often done in a purely informal way, by recursive discussions with our biologists collaborators and qualitative comparison, see Section 4 and for examples of models we design in such interdisciplinary work [40, 56, 57, 80]. It may also be carried out with the use of theoretical analysis as in Axis 2, or by sensitivity analysis on the parameters (as for instance in [43, 91, 131]), or by relatively standard data analysis tools , as has been done for instance in [53, 58, 105] by various members of the team; our added value then lies in the biological conclusions and models conception rather than in methodological novelties. In other cases however, no standard

method is available, or yet, we are led by experimentalists to formulate new inverse problem questions, see for instance [82] for a review of the estimation of the division rate in structured population equations, or yet [39, 83] for the study of inverse problems formulated with biologists.

In this section, we thus explain some of the methodological developments that will be carried out in MERGE in this field of ("deterministic" or "statistical") inverse problems. The underlying question, throughout the section, is to estimate growth and division functional parameters of the individuals. Though we work with external collaborators who are experts in statistics, our team would greatly benefit from the recruitment of a statistician, in order to stay at the cutting edge of new methods like bayesian approaches or machine learning.

Estimate growth, division, interaction features in structured populations

The estimation of the division rate in non-interacting populations has been developed in a series of papers over the last decade [82]. The question we want to address now is whether growth and division rates are modified by cell-to-cell interaction (or yet by antibiotic resistance or by competition), and reciprocally, how distributed growth and division rates may have an influence on the morphogenesis of the bacterial microcolony. In this task, we aim to provide answers based on more realistic individual-based models. We plan the following steps:

- Develop parametric and non-parametric inference of the interaction function from single individual tracking. A similar study has been carried out by Laetitia Della Maestra and Marc Hoffmann [72] for Mc-Kean-Vlasov equation; we would like to add a size structure and a non-constant number of individuals. We will first assume that the growth and division rates do *not* depend on the interaction between cells, so that prior to this step we have used the methods already developed to infer these functional parameters. We may also build upon biophysical studies such as in [138].

- Develop statistical hypothesis testing to accept or reject the assumption made in the previous step that division and growth are not influenced by the interaction inferred. Reciprocally, test whether different division or growth rates would give rise to different morphogenesis.

- Generalise the methods and adapt them to new problems, in particular the mycelial networks [75].

Estimate mutation or fragmentation kernel density

The question of estimating the fragmentation kernel in polymer breakage experiments [78] surprisingly rejoins the question of estimating the so-called *Distribution of Fitness Effects* (DFE) which characterizes the accumulation of mutations in bacteria [122]. As shown in [78], these are so-called *severely ill-posed* inverse problems, for which we aim at developing new approaches, two in particular: rely on short-time instead of long-term behaviour, adapt statistical methods developed for decoumpounding Poisson processes and deconvolution [84].

State estimation and observation inequalities for depolymerisation models

In depolymerisation experiments, prior to parameter estimation, we began to address the question of state estimation, *i.e.* how to infer the initial condition out of measurements of moments time dynamics. Whereas it is relatively straightforward if we approximate the discrete system by a backward transport equation [39], we address the question of estimating it from the next order approximation, namely a transport-diffusion equation; this new problem is closer to the experimental system but gives rise to a severely ill-posed inverse problem, for which we want to find an observation inequality thanks to Carleman estimates [70, 69].

Calibrating the mycelial network model

The model developed in [130] paves the way to new parametric calibration methods that we wish to confront with the real observations made by mycological colleagues of the LIED laboratory (Paris Diderot University), as well as with their empirical results.

The parametric calibration based on the solutions of the spectral problem can lead to new simple descriptors that characterize the growth of the fungus.

The first objective is to see how values obtained in [75] for the exponential growth rates compare with the one obtained in [130] as a solution of the spectral problem related to the corresponding growth and fragmentation equation. For the latter, there is an interpretation through the main characteristics of the network (ratio between the number of external nodes and the total length of the network at a sufficiently large time t).

Then, we could test how these descriptors change in different growth environments. This will allow us to quantify the impact of various forms of stress (nutrient depletion, pH, ...).

From a theoretical point of view, we would have to justify this empirical approach and demonstrate a "many to one" formula to be able to correctly sample our model. It should also be proved that the estimators thus constructed are consistent and converge, when $t \to \infty$, to the quantities they are supposed to approximate.

3.4 Software development and dissemination

Permanent members: Marie Doumic, Milica Tomašević

3.5 CellDiv: a platform for biologists to estimate cell division rates

The CellDiv plateform has been developed by Cédric Doucet and Adeline Fermanian and is already available at . It allows a biologist to upload experimental data of dividing cells, either along a genealogical lineage (microfluidic experiments) or inside an exponentially growing culture (petri dish case), and to get the best-fit estimation of the division rate, according to estimation methods combining statistics and PDE analysis [82].

This plateform will be maintained and completed, to accept other types of data (for instance cells dividing into unequal daughters or with heterogeneous growth rates), estimate the division in more general structured population models, and add statistical tests to select the best-fit model. To date, only Marie Doumic being involved in this project, we need to hire an engineer to continue to develop it - a short term goal being to write a proposal for the help of an engineer from SED.

4 Application domains

Unicellular organisms population models are a transversal application of our work, in various aspects and with different biologists collaborators that we detail below. There are many fascinating issues raised by the understanding of their growth and evolutionary mechanisms, which have prominent societal and health impact - cancer treatment, prevention of antibiotic resistance, aging diseases, control and evolution of epidemics, population viability analysis.

4.1 Bacterial growth

Permanent members: Vincent Bansaye, Marie Doumic, Sylvie Méléard, Gaël Raoul

Biologists collaborators: Meriem El Karoui (Ecole polytechnique and University of Edinburgh), Lydia Robert (INRAe), Charles Baroud (Institut Pasteur and Ecole polytechnique)

Possible new collaborations (first contacts made): Nicolas Desprat (ENS Paris), Claude Loverdo (Sorbonne University)

Bacteria are ubiquitous unicellular organisms, present in most parts of earth, and among the first living beings in evolution. Most animals carry millions of bacteria- one human possesses as many bacteria as one's own cells. They are vital, for instance the ones of the gut for facilitating digestion, and very useful in industry (biofilms, sewage treatment, cheese production...) as well as potentially pathogenic, causing infectious diseases, increasingly more difficult to treat due to their high capacity of developing resistance to antibiotics. Here are some of the questions we want to tackle concerning bacterial growth.

The bacterial cell cycle Coordination between cell growth and division is often carried out by 'size control' mechanisms, where the cell size has to reach a certain threshold to trigger some event of the cell cycle, such as DNA replication or cell division. Concerning bacteria, recent articles [38, 124] stated the excellent adequacy of the so-called "incremental model", where the structuring variable which triggers division is the size increase of the bacteria since birth, to experimental data. This opens up new questions to refine and analyse this model, test its validity in extreme growth conditions such as antibiotic treatments, and understand its links with intracellular mechanisms. *Main research axis: 3, and the CellDiv platform.*

Antibiotic response and resistance emergence To address the emergence of antibiotic-resistant strains of bacteria, it is essential to understand quantitatively the response of bacteria to antibiotic treatments. Under the action of an antibiotic that causes damage to cellular DNA, bacteria change their growth strategy and do not respond homogeneously to this stress. Of particular importance is the so-called SOS response: in response to DNA damage induced by antibiotic treatments, the cell cycle is arrested and DNA repair and mutagenesis are induced (cf. [41]). Cells with high SOS response will grow for an abnormal duration, producing long filaments that are impervious to antibiotics. Understanding the distribution of sizes in the population of bacteria will allow a better quanitfication of antibiotics effects. On this subject, we work with Meriem El Karoui who carries out microfluidic experiments in Edinburg university. *Main research axis: 2.*

Microcolony morphogenesis When bacterial microcolonies grow, they can aggregate to one another and form a biofilm. How do they interact? How do their growth and division characteristics translate into the shape of the colony? Inside the gut, it has been proved that the immune response acts not by killing bacteria but by making them aggregate after division; how do these aggregates form and break is another question tackled by Claude Loverdo at Lab. Jean Perrin (Sorbonne). *Main research axis: 1 (short term in collaboration with Diane Peurichard and Sophie Hecht).*

Bacterial growth in a chemostat; the gut as a chemostat A chemostat is a specific experiment, where the number of bacteria is let constant by a permanent influx and outflux. The functional mechanism of the very gut could be modeled as a chemostat. *Main research axis: 2 (mid to long term / only first contacts made).*

Mutations The pace of evolution and possible trajectories depend on the dynamics of mutation incidence and the effects of mutations on fitness. Mutation dynamics has been for the first time analyzed directly by Lydia Robert and co-authors [122], using two different microfluidic experiments which led them to the conclusion of a Poissonnian appearance of bacterial mutations, and to a first parametric estimation of the so-called "distribution of fitness effects" (DFE) of mutations. How to assess better the shape of the DFE, and apply the method not only to deleterious or neutral but also to possibly beneficial mutations, is one of our goals. *Main research axis: 3, short term (Guillaume Garnier's ongoing Ph.D).*

Horizontal gene transfer Microorganisms such as bacteria tend to exhibit a relatively large "evolution speed". They have also the particularity to exchange genes by direct cell-to-cell contact. We are particularly interested in plasmids horizontal gene transfer (HGT): plasmids carry pathogens or genes coding for antibiotics resistances, and plasmid exchange is considered by biologists as the primary reason for antibiotics resistance. *Main research axis: 1, both short and long-term research, included in the ERC project SINGER.*

4.2 Cancer and aging

MERGE members involved: Vincent Bansaye, Marie Doumic, Sylvie Méléard

Medical doctors and biologists collaborators: Stéphane Giraudier and Raphael tzykson (St Louis hospital), Teresa Teixeira (IBPC), Zhou Xu (Sorbonne University), Michael Rera (CRI)

Cell division dynamics combine several fundamental processes that are involved in aging and cancers, such as replication and mutation, differentiation and proliferation, quiescence. The main research axis concerned by these applications is axis 2, together with an important modelling work performed through interdisciplinary discussions with MD and biologists.

Leukemic mutations and hematopoeisis Hematopoiesis is the process of producing blood cells from stem cells and progenitors. These highly regulated mechanisms keep at equilibrium the number of blood cells such as red blood cells, white blood cells and platelets (mature cells). We want to understand the emergence of leukaemia or resistance to chemotherapy through the mechanisms of erythropoiesis (production of red blood cells) and leukopoiesis (white blood cell formation). *This application also rejoins the application 3.1.*

Senescence by telomere shortening Telomeres cap the ends of linear chromosomes, and help maintain genome integrity by preventing the ends being recognized and processed as accidental chromosomal breaks. When telomeres fall below a critical length, cells enter replicative senescence. However, the exact structure(s) of the short or dysfunctional telomeres either triggering permanent replicative senescence or promoting genome instability remains to be defined; this is the main focus of Teresa Teixeira's lab at IBPC, which has developed microfluidic as well as population experiments to follow senescence triggering in yeast cells. *Main research axis: 1 and 2. This application is both a long-term goal, in a long-lasting collaboration with Teresa Teixeira and Zhou Xu, and has short and mid-terms objectives, through Anaïs Rat's finishing Ph.D and Jules Olayé forthcoming Ph.D (co-supervised by Milica Tomašević and Marie Doumic).*

Ageing in drosophyla Ageing's sensitivity to natural selection has long been discussed because of its apparent negative effect on an individual's fitness. In the recent years, a new 2-phases model of ageing has been proposed by Hervé Tricoire and Michael Rera [71, 132], describing the ageing process not as being continuous but as made of at least 2 consecutive phases separated by a dramatic transition. It was first observed in drosophila, and then shown to be evolutionary conserved; this raises the question of an active selection of the underlying mechanisms throughout evolution. *Main research axis: 2 and 3.*

4.3 Fragmentation, aggregation, filamentation phenomena

Permanent members: Vincent Bansaye, Marie Doumic, Milica Tomašević

Biologist collaborators: Human Rezaei (INRAe), Florence Chapeland-Leclerc and Eric Herbert (LIED, Univ. Paris Diderot), Sascha Martens (Vienna University), Wei-Feng Xue (Univ. of Kent)

Protein polymerisation: amyloid formation and autophagy

Protein polymerisation occurs in many different situations, from functional situations (actin filaments, autophagy) to toxic ones (amyloid diseases). It involves complex reaction networks, making it a challenge to identify the key mechanisms, for instance which mechanisms lead to the initial formation of polymers during the first reaction steps (nucleation), how and where the polymers break, or yet the aggregates formation, out of (at least) two different proteins, in autophagy. With our biologist collaborators, our aim in these applications is to isolate the most meaningful reactions, study their behaviour *(Research axis 2)*, and compare them - qualitatively and, if possible, quantitatively - with experimental data.

Mycelial network

Filamentous fungi are complex expanding organisms that are omnipresent in nature. They form filamentous structures, growing and branching to create huge networks called *mycelia*. We aim at modelling, understanding and estimating the main mechanisms of mycelial formation. We have already studied a first model without interactions and we will now study the impact of fusion of filaments on the growth of the network. *Main research axes: 2 and 3.*

4.4 Evolutionary epidemiology and ecology

Permanent members: Vincent Bansaye, Gaël Raoul

Biologists collaborators: Sylvain Billiard, Nicolas Lœuille (Institute of Ecology and Environmental Sciences, Paris), François Massol (Center for Infection and Immunity of Lille), Ophélie Ronce (ISEM, Montpellier), François Deslandes (INRAe), Sylvain Gandon (CEFE Montpellier), Elisabeta Vergu (INRAe)

In ecology, the influence of a spatially heterogeneous environment and of different contact structures is at the heart of current problems (biological invasions, epidemiology, etc.), as well as the interaction between different species. The questions we look at concern how a species can invade the range of another one, leading to its extinction; how an epidemics spreading is influenced by contact structures; resilience and tipping points in ecosystems. Applications are as varied as the links between light and plankton species evolution in shallow water lakes, the replacement of red squirrels by grey squirrels, or the current pandemics. *Main research axis: 1.*

Emergence of bacterial resistance in heterogeneous environments

When an antibiotic treatment is applied to a population, bacteria resistant to the treatment have an opportunity to develop. If several treatments are used, life threatening multi-resistant bacteria can appear. Understand the dynamics of bacterial populations in such heterogeneous environments would provide interesting perspectives to improve treatments and keep antibiotic resistance in control. On this topic, we will collaborate with S. Gandon lab at CEFE, that tackles this problem with a combination of theory and experiments. *This also rejoins the application domain 3.1., and the main research axis is axis 2.*

Dynamics of species submitted to climate change

The impact of climate change on natural species is a complicated matter. An important research effort has been made on the modification of species' niche in coming years, but this is only a partial clue for the future of species. In collaboration with Ophélie Ronce at ISEM, we will investigate how the local adaptation of species will is shook by global changes. With François Massol in CIIL and Nicolas Loeuille in IEES, we will focus on the impact of interspecies effects: predation, parasitism, cooperation, etc. *Main research axis: 1.*

Contacts structured by graphs

In the context of spatial ecology and epidemiology, the contacts between individuals leading to predation or transmission of a desease are often modeled by graph. It may represent the connected sites (metapopulations) or the nature of the contacts (multilevel contact structure) between individuals. The description of the population dynamics is important for prediction : stability, explosion, coexistence... The macroscopic approximation when the population and the graph are large is a key question for model reduction and analysis of these models. The mathematical challenges raised are linked to homogeneisation and spatial random graphs, multiscale modelling and local interactions. Collaborations with Sylvain Billiard (Lille, biologist) and Elisebeta Vergu (INRAe, epidemiologist) and Michele Salvi (Roma, mathematician) and Ayman Moussa (Paris Sorbonne, mathematician). *Main research axis: 1.*

5 Social and environmental responsibility

The MERGE project-team brings together mathematicians with complementary competences and interests, in order to integrate at a high level different areas of mathematical analysis (multiscale stochastic processes, partial or integro-differential equations) and microbiology, ecology, cancer medicine. If successful, this research can have fundamental impacts in these fields. General mathematical frameworks unifying different biological questions from single cell to ecological problems not only can improve modelling and simulations but also create a considerable synergy in all these scientific communities. It will also create collaborations between mathematicians (the links between models through scales, taking

into account varying environment, interaction between cells...) which could have potential applications in other domains, beyond biology and ecology. In Mathematics, this research tackles fundamental problems from the representation of stochastic microscopic effects in large approximations to macroscopic representations. Successful results would open a new area of research at the interface of probability and analysis, tracking the rare but fundamental effects.

In Biology, this research addresses fundamental questions of growth, mutation and resistance. Successful results will offer interesting opportunities for medical innovations based on evolutionary or adaptive strategies.

6 Highlights of the year

6.1 Visiting professors

Our team welcome Prof. Marek Kimmel from Rice University, specialist of stochastic models applied to biology, from Sep. 15 to December 15. He gave a very appreciated series of five research courses.

Our team welcome Prof. Sarah Kaakai, assistant professor at Le Mans University, till August 31, thanks to Sylvie Méléard's ERC advanced grant. She has now moved to Paris 13 university.

6.2 Awards

Sylvie Méléard, Professor at the École polytechnique and member of our Inria MERGE project team, has been awarded the Irène Joliot-Curie - Woman Scientist of the Year prize, awarded by the Académie des sciences and created by the French Ministry of Higher Education and Research. The prize is awarded to a woman who has made an outstanding contribution to research in all the sciences. The prize recognises Sylvie Méléard's pioneering role and innovative work in the field of probability, modelling and mathematical analysis for ecology and biology.

Madeleine Kubasch received the L'Oréal-Unesco Jeunes Talents prize for women in science for her doctoral work on mathematical models of epidemic propagation at our Inria project-team MERGE (Mathematics for Evolution, Reproduction, Growth and Emergence), at the Center for Applied Mathematics (CMAP) and INRAE's Mathematics and Informatics Applied from the Genome to the Environment (MaIAGE) unit, under the supervision of Vincent Bansaye and Elisabeta Vergu (+).

7 New software, platforms, open data

7.1 New software

7.1.1 telomeres

Name: Simulation of cell populations and lineages during replicative senescence.

Keywords: Stochastic models, Statistical inference, Monte-Carlo methods, Branching system, Population approach, Computational biology

Functional Description: Code associated with "Mathematical model linking telomeres to senescence in Saccharomyces cerevisiae reveals cell lineage versus population dynamics".

Preprint version of the associated article: https://www.biorxiv.orgcontent/10.1101/2023.11.22.568287v1
See also Chapter 3 of the PhD thesis: https://theses.hal.science/tel-04250492

The telomeres package contains all the necessary auxiliary code. This is where the mathematical model is encoded, with its default parameters (parameters.py). More generally, it contains all the functions allowing to

Posttreat the raw data (make_*.py) Simulate the model (simulation.py) Plot the simulated and experimental data, the laws of the model... (plot.py)

The scripts in this folder are not intended to be modified (unless you find errors, in which case please let me know) or used directly to run simulations.

The makeFiles folder contains scripts to run to generate the data/processed directory, that contains the posstreated data.

The main folder contains the scripts that should be run to perform the simulations and plot their results.

URL: https://zenodo.org/records/14525443

Contact: Anais Rat

8 New results

8.1 Axis 1: Models through scales

We refer to 3.1 for a presentation of the research program in this direction.

8.1.1 Chemotaxis models

Participants: Charles Bertucci, Mathias Rakotomalala, Milica Tomasevic, Guillaume Woessner.

Curvature in chemotaxis: A model for ant trail pattern formation

In [21], we propose a new model of chemotaxis motivated by ant trail pattern formation, formulated as a coupled parabolic-parabolic local PDE system, for the population density and the chemical field. The main novelty lies in the transport term of the population density, which depends on the second-order derivatives of the chemical field. This term is derived as an anticipation-reaction steering mechanism of an infinitesimally small ant as its size approaches zero. We establish global-in-time existence and uniqueness for the model, and the propagation of regularity from the initial data. Then, we build a numerical scheme and present various examples that provide hints of trail formation.

On a multi-dimensional McKean-Vlasov SDE with memorial and singular interaction associated to the parabolic-parabolic Keller-Segel model

In the article [16], we firstly prove the well-posedness of the non-linear martingale problem related to a McKean-Vlasov stochastic differential equation with singular interaction kernel in $\mathbb{R}^D$ for $d \geq 3$. The particularity of our setting is that the McKean-Vlasov process we study interacts at each time with all its past time marginal laws by means of a singular space-time kernel. Secondly, we prove that our stochastic process is a probabilistic interpretation for the parabolic-parabolic Keller-Segel system in $\mathbb{R}^d$. We thus obtain a well-posedness result to the latter under explicit smallness condition on the parameters of the model.

8.1.2 Limits of large populations with local or nonlocal interaction and heterogeneity

Participants: Vincent Bansaye, Marie Doumic, Sophie Hecht, Marc Hoffmann, Ayman Moussa, Felipe Munoz, Benoit Perthame, Diane Peurichard.

For the study of large populations with local interaction, Vincent Bansaye, together with Felipe Munoz and Ayman Moussa, developed approaches in a discrete space that grows simultaneously with the local size of the population [48]. We introduced duality techniques to handle the convergence of the stochastic process to a cross-diffusion and the stability of the limiting PDE. Ayman Moussa and Vincent Bansaye are currently supervising a pre-thesis student, Alexandre Bertoloni, who is extending these resu lts by incorporating births and deaths with local density dependence, along with a reaction term.

Originally motivated by the morphogenesis of bacterial microcolonies, the aim of a series of articles, in a collaboration between Marie Doumic, members of the Inria project-team MUSCLEES and Marc Hoffmann, is to explore models through different scales for a spatial population of interacting, growing

and dividing particles. After the modelling and simulation article [81], we studied the rigorous limits through scales of a model including growth, division and interaction.

In [26], we start from a microscopic stochastic model, write the corresponding stochastic differential equation satisfied by the empirical measure, and rigorously derive its mesoscopic (mean-field) limit. Under smoothness and symmetry assumptions for the interaction kernel, we then obtain entropy estimates, which provide us with a localization limit at the macroscopic level. Finally, we perform a thorough numerical study in order to compare the three modeling scales. An important difficulty of this work is to take into account the continuous size structure, which leads to a lack of compactness for the localisation limit.

In the article [12], we study a multi-species system, which may be seen as a discrete counterpart of the size-structured one [26]. At the mesoscopic level, the system is quadratic, written under the form of transport equations with a nonlocal self-generated drift. We establish the localisation limit, that is the convergence of nonlocal to local systems, when the range of interaction tends to 0. These theoretical results are sustained by numerical simulations. The major new feature in this analysis is that we do not need diffusion to gain compactness, at odd with the existing literature. The central compactness result is provided by a full rank assumption on the interaction kernels. In turn, we prove existence of weak solutions for the resulting system, a cross-diffusion system of quadratic type.

8.1.3 A scenario for an evolutionary selection of ageing

Participants: Tristan Roget, Sylvie Méléard, Michael Rera.

Signs of ageing become apparent only late in life, after organismal development is finalized. Ageing, most notably, decreases an individual's fitness. As such, it is most commonly perceived as a non-adaptive force of evolution and considered a by-product of natural selection. Building upon the evolutionarily conserved age-related Smurf phenotype, we propose a simple mathematical life-history trait model in which an organism is characterized by two core abilities: reproduction and homeostasis [15]. Through the simulation of this model, we observe 1) the convergence of fertility's end with the onset of senescence, 2) the relative success of ageing populations, as compared to non-ageing populations, and 3) the enhanced evolvability (i.e. the generation of genetic variability) of ageing populations. In addition, we formally demonstrate the mathematical convergence observed in 1). We thus theorize that mechanisms that link the timing of fertility and ageing have been selected and fixed over evolutionary history, which, in turn, explains why ageing populations are more evolvable and therefore more successful. Broadly speaking, our work suggests that ageing is an adaptive force of evolution.

8.1.4 Phenotypic plasticity trade-offs in an age-structured model of bacterial growth under stress

Participants: Meriem El Karoui, Ignacio Madrid, Sylvie Méléard.

Under low concentrations of antibiotics causing DNA damage, *Escherichia coli* bacteria can trigger stochastically a stress response known as the SOS response. While the expression of this stress response can make individual cells transiently able to overcome antibiotic treatment, it can also delay cell division, thus impacting the whole population's ability to grow and survive. In order to study the trade-offs that emerge from this phenomenon, we propose a bi-type age-structured population model that captures the phenotypic plasticity observed in the stress response [2, 3] . Individuals can belong to two types: either a fast-dividing but prone to death "vulnerable" type, or a slow-dividing but "tolerant" type. We study the survival probability of the population issued from a single cell as well as the population growth rate in constant and periodic environments. We show that the sensitivity of these two different notions of fitness with respect to the parameters describing the phenotypic plasticity differs between the stochastic approach (survival probability) and the deterministic approach (population growth rate). Moreover, under a more realistic configuration of periodic stress, our results indicate that optimal population growth

can only be achieved through fine-tuning simultaneously both the induction of the stress response and the repair efficiency of the damage caused by the antibiotic.

8.1.5 Dynamics of a kinetic model describing protein transfers in a cell population

Participants: Pierre Magal†, Gaël Raoul.

We consider a cell population structured by a positive real number which represents the number of P-glycoproteins carried by the cell. In this article, we introduce a kinetic model to describe the dynamics of the cell population, and consider an asymptotic limit of this equation: if transfers are frequent, the population can be described through a system of two coupled ordinary differential equations. The main idea of this manuscript is to combine Wasserstein distance estimates on the kinetic operator to more classical estimates on the macroscopic quantities.

8.1.6 Macroscopic limit from a structured population model to the Kirkpatrick-Barton model

Participants: Gaël Raoul.

We consider an ecology model in which the population is structured by a spatial variable and a phenotypic trait. The model combines a parabolic operator on the spatial variable with a kinetic operator on the trait variable. We combine a contraction argument based on Wasserstein estimates on the phenotypic variable with parabolic estimates controlling the spatial regularity of solutions to prove the convergence of the population size and the mean phenotypic trait to solutions of the Kirkpatrick-Barton model, which is a well-established model in evolutionary ecology.

8.2 Axis 2: qualitative analysis of structured populations

We refer to 3.2 for a presentation of the research program in this direction.

8.2.1 Long-time behaviours

Participants: Pierre Collet, Claire Ecotière, Jules Olayé, Sylvie Méléard, Milica Tomasevic.

Long-time behaviour of a multidimensional age-dependent branching process with a singular jump kernel.

In the article [4] , we investigate the ergodic behaviour of a multidimensional age-dependent branching process with a singular jump kernel, motivated by studying the phenomenon of telomere shortening in cell populations. Our model tracks individuals evolving within a continuous-time framework indexed by a binary tree, characterised by age and a multidimensional trait. Branching events occur with rates dependent on age, where offspring inherit traits from their parent with random increase or decrease in some coordinates, while the most of them are left unchanged. Exponential ergodicity is obtained at the cost of an exponential normalisation, despite the fact that we have an unbounded age-dependent birth rate that may depend on the multidimensional trait, and a non-compact transition kernel. These two difficulties are respectively treated by stochastically comparing our model to Bellman-Harris processes, and by using a weak form of a Harnack inequality. We conclude this study by giving examples where the assumptions of our main result are verified.

Long-time behaviour of a degenerate stochastic system modeling the response of a population to its environmental perception.

In [23], accepted for publication in Electronic Communications in Probability, we study the asymptotics of a two-dimensional stochastic differential system with a degenerate diffusion matrix. This system describes the dynamics of a population where individuals contribute to the degradation of their environment through two differentbehaviors, responding more or less intensively to their environmental perception. We exploit the almost one-dimensional form of the dynamical system to compute explicitly the Freidlin-Wentzell action functional. This allows us to give conditions under which the small noise regime of the invariant measure is concentrated around the equilibria of the dynamical system having the smallest diffusion coefficient.

8.2.2 Time reversal and ancestral lineages

Participants: Vincent Bansaye, Pierre Collet, Jaime San Martin, Sylvie Méléard.

Ancestral lineage for interacting populations.
In [6], we consider Markov jump processes describing structured populations with interactions via density dependance. We propose a Markov construction with a distinguished individual which allows to describe the random tree and random sample at a given time via a change of probability. This spine construction involves the extension of type space of individuals to include the state of the population. The jump rates outside the spine are also modified. We apply this approach to some issues concerning evolution of populations and competition. For single type populations, we derive the diagram phase of a growth fragmentation model with competition and the growth of the size of birth and death processes with multiple births. We also describe the ancestral lineages of a uniform sample in multitype populations.

Branching diffusion processes and spectral properties of Feynman Kac semigroup
The article [24] is motivated by the study of the long time behavior of linear functionals of birth and death diffusion processes as well as the time reversal of the spinal process by means of spectral properties of the associated Feynman-Kac semigroup. We generalize for this non Markovian semigroup the theory of quasi-stationary distribution (q.s.d.) and Q-process. We consider a situation where the underlying diffusion process doesn't come down rapidly from infinity but the compactness properties follow from the divergence of the death rate at infinity. We establish the complete spectral decomposition for the Feynman-Kac semigroup. An interesting consequence is the identification of the law of the reversal time spinal process issued from q.s.d. with the Q-process of the Feynman-Kac semigroup.

8.2.3 Evolutionary dynamics - stochastic and deterministic mutation models

Participants: Matthieu Alfaro, Vincent Bansaye, Sirine Boucenna, Vasilis Dakos, Marie Doumic, Xavier Erny, Quentin Griette, Anouar Jeddi, Sylvain Gandon, Sylvie Méléard, Sepideh Mirrahimi, Gaël Raoul, Anaïs Rat, Magali Tournus.

Sharp approximation and hitting times for stochastic invasion processes We are interested in the invasion phase for stochastic processes with interactions. A single mutant with positive fitness arrives in a large resident population at equilibrium. By a now classical approach, the first stage of the invasion is well approximated by a branching process. The macroscopic phase, when the mutant population is of the same order as the resident population, is described by the limiting dynamical system. We capture the intermediate mesoscopic phase for the invasive population and obtain sharp approximations. It allows us to describe the fluctuations of the hitting times of thresholds, which inherit a large variance from the first stage. We apply our results to two models which are first motivations. In particular, we quantify the hitting times of critical values in cancer emergence and epidemics [8].

Convergence of a discrete selection-mutation model with exponentially decaying mutation kernel to a Hamilton-Jacobi equation

In the preprint [32], Anouar Jeddi (Ph.D student supervised by Sylvie Méléard and Sepideh Mirrahimi) derives a Hamilton-Jacobi equation with obstacle from a discrete linear integro-differential model in population dynamics, with exponentially decaying mutation kernel. The fact that the kernel has exponential decay leads to a modification of the classical Hamilton-Jacobi equation obtained previously from continuous models as in Barles-Mirrahimi-Perthame. We consider a population composed of individuals characterized by a quantitative trait, subject to selection and mutation. In the regime of large population, small mutations and large time, we prove that the WKB transformation of the density converges to the unique viscosity solution of a Hamilton-Jacobi equation with obstacle.

The article [13] has been published in Evolution Letters. In this article, we have analysed the evolutionary dynamics of pathogens spreading in a heterogeneous host population where selection varies periodically in space. We study both the transient dynamics taking place at the front of the epidemic and the long-term evolution far behind the front. In particular, we identify the conditions where a generalist pathogen carrying multiple adaptations can outrace a coalition of specialist pathogens. We also show that finite host populations promote the spread of generalist pathogens because demographic stochasticity enhances the extinction of locally maladapted pathogens.

The article [123] is submitted to the Journal of Theoretical Biology. Shallow lakes ecosystems may experience abrupt shifts (ie tipping points) from one state to a contrasting degraded alternative state as a result of gradual environmental changes. It is crucial to elucidate how eco-evolutionary feedbacks affect abrupt ecological transitions in shallow lakes. We explore the eco-evolutionary dynamics of submerged and floating macrophytes in a shallow lake ecosystem under asymmetric competition for nutrients and light. We show how rapid trait evolution can result in complex dynamics including evolutionary oscillations, extensive diversification and evolutionary suicide. Overall, this study shows that evolution can have strong effects in the ecological dynamics of bistable ecosystems.

Exponential convergence to a steady-state for a population genetics model with sexual reproduction and selection.

We are interested in the dynamics of a population structured by a phenotypic trait. Individuals reproduce sexually, which is represented by a non-linear integral operator. This operator is combined to a multiplicative operator representing selection. When the strength of selection is small, we show that the dynamics of the population is governed by a simple macroscopic differential equation, and that solutions converge exponentially to steady-states that are locally unique. The analysis is based on Wasserstein distance inequalities using a uniform lower bound on distributions. These inequalities are coupled to tail estimates to show the stability of the steady-states.

Is there an advantage of displaying heterogeneity in a population where the individuals grow and divide by fission? This is a wide-ranging question, for which a universal answer cannot be easily provided. In [28], we aim at providing a quantitative answer in the specific context of growth rate heterogeneity by comparing the fitness of homogeneous versus heterogeneous populations. We focus on a size-structured population, where an individual's growth rate is chosen at its birth through heredity and/or random mutations. We use the long-term behaviour to define the Malthus parameter of such a population, and compare it to the ones of averaged homogeneous populations. We obtain analytical formulae in two paradigmatic cases: first, constant rates for growth and division, second, linear growth rates and uniform fragmentation. Surprisingly, these two cases happen to display similar analytical formulae linking effective and individual fitness. They allow us to investigate quantitatively the crossed influence of heredity and heterogeneity, and revisit previous results stating that heterogeneity is beneficial in the case of strong heredity.

8.2.4 The epidemiological footprint of contact structures in models with two levels of mixing

Participants: Vincent Bansaye, François Deslandes, Madeleine Kubasch, Elisabeta Vergu†.

In human contact networks, individuals often belong to several contact structures, such as a home and a workplace or school. This social organization is relevant to study in an epidemic context, as it is the subject of control measures such as telecommuting or school closures. However, the influence of these structures on the epidemic is not yet well understood. We are therefore investigating a model

with two levels of mixing, namely a uniformly mixing global level, and a local level divided into two layers of contacts within households and workplaces, respectively. We are seeking to develop reduced models that closely approximate these epidemic dynamics, while being more manageable for numerical and/or theoretical analysis. In [1] , a simulation study compares several telecommuting strategies, and shows that there are more effective strategies than the most naive strategy of allowing only a number of workers in the workplace proportional to the size of the workplace. Next, we highlight two indicators of the epidemic impact of the location size distribution, namely the variance and the exponential growth rate observed at the start of an epidemic. In addition, we calibrate a uniformly mixing epidemic model to provide a good approximation of the home-work model, as shown by the numerical exploration. This reduced model thus provides an easily parameterizable and numerically satisfactory approximation. Finally, in [100, Chapter 4], a sensitivity study enables us to understand the impact of model parameters on the performance of this reduced model, by quantifying the impact of epidemic parameters on its ability to predict key features of the epidemic.

8.2.5

Participants: Marie Doumic, Klemens Fellner, Mathieu Mezache, Juan Velazquez.

To provide a mechanistic explanation of sustained then damped oscillations observed in a depolymerisation experiment, a bi-monomeric variant of the seminal Becker-Döring system has been proposed in (Doumic, Fellner, Mezache, Rezaei, J. of Theor. Biol., 2019). When all reaction rates are constant, the equations are the following:

$$\frac{dv}{dt} = -vw + v\sum_{j=2}^{\infty} c_j, \qquad \frac{dw}{dt} = vw - w\sum_{j=1}^{\infty} c_j,$$
$$\frac{dc_j}{dt} = J_{j-1} - J_j \ , \ j \geq 1 \ , \quad J_j = wc_j - vc_{j+1} \ , \ j \geq 1 \ , \ J_0 = 0,$$

where u and w are two distinct unit species, and c_i represents the concentration of clusters containing i units. We study in detail the mechanisms leading to such oscillations and characterise the different phases of the dynamics, from the initial high-amplitude oscillations to the progressive damping leading to the convergence towards the unique positive stationary solution. We give quantitative approximations for the main quantities of interest: period of the oscillations, size of the damping (corresponding to a loss of energy), number of oscillations characterising each phase. We illustrate these results by numerical simulation, in line with the theoretical results, and provide numerical methods to solve the system.

8.2.6 Ongoing PhD theses

Participants: Ana Fernandez Baranda, Mateo Deangelo Bravo, Jules Olayé, Alexandre Perrin.

Following [19], the second Ana Fernandez Baranda's work is to model hematopoiesis (formation of blood cells) as a continuum process. Until now, the modeling of this phenomenon has assumed a hierarchical structure where, at the moment of differentiation, a cell transitions into a new type of cell. However, recent biological studies suggest that differentiation is instead a continuous process, where the phenotype of cells varies widely and does not allow for a clear separation of cells into distinct categories. Starting from a stochastic model with a finite number, N, of compartments, where each compartment corresponds to a stage in the cell's maturation, the idea is to determine the dynamics as the number of compartments approaches infinity, which represents continuous differentiation, as opposed to stepwise differentiation. To study this, we consider a measure that aggregates the compartments of immature cells, from 2 to $N-1$. This results in three coupled processes: one describing the stem cells, another for the immature cells, and a third for the red blood cells.

Mateo Deangelo Bravo has begun his Ph.D in September 2024. He models the evolution of a population of bacteria (through a measure-valued process) characterized by real values (possibly representing a genetic trait, the number of plasmids or an adaptability to the environment). This population is subject to the dynamics of births, deaths, competition, mutation and horizontal transfer (such as conjugation, plasmid transfer). The aim is the study of the ancestral lines, i.e. to trace the evolution of genetic traits in a lineage back to the initial time, starting with an individual sampled at a fixed time $T > 0$.

After a 6-month pre-doc, supervised by Sarah Kaakai, Marie Doumic and Michael Rera, Luce Breuil has begun her Ph.D in September 2024. She worked on a 2-phase mathematical model of aging, based on the biological discovery by Michaël Rera [121, 132] of two consecutive phases in the aging of drosophila. With non-parametric kernel estimation and parametric estimation, we estimated the rates of transition from each phase to the next and the potential dependence between both phases through a thorough statistical study of in-vitro drosophila data. She also worked on proving the convergence of the hazard rate kernel estimator for a very general class of kernels, much less restrictive than what is usually found in the literature. Finally, she also derived a stochastic model for 2-phase aging in the wild, adding competition and birth, and studied its convergence to a deterministic model in large population.

Maxime Ligonnière, co-supervised by Vincent Bansaye and Marc Peigné, works on the study of multitype Galton-Watson processes in random environment (MGWREs), with infinitely many types. He also studied some associated products of random operators. MGWREs are a class of stochastic, individual based population models, with a structuration according to a type or trait. The offpsring of an individual is random and depends both on the type or trait of this individual and on the state of the environment at the time of the reproduction. The environment evolves through time according to a random stationary process. We are particularly interested in the so called supercritical regime, where the population survives with positive probability. We prove the mathusian growth of the population, as well as the convergence of the distribution of types at large time to a trajectory determined by the environmental sequence. We particularly introduce an example of a process modelling a population with a discrete age structure, with infinitely many age classes. In this context, we provide more tractable criterions which guarantee our various assumptions are met. A prerequisite for this work was to obtain ergodicity results for some products of random operators which act on some infinite dimensional measure spaces. To establish these ergodicity properties, we used a Doeblin-type hypothesis which assumes the existence of a special type produced in the offpsring of individuals of all types. These generalizes previously known results for $d \times d$ matrices with positive entries. Once again we focused particularly on the case of operators modelling a age structured population, called infinite Leslie matrices which are an infinite dimensional extension of the famous Leslie matrices commounly used in demographic studies and matrix population models.

Jules Olayé's Ph.D focuses on the study of mathematical models in relation to the biological phenomenon of telomere degradation, under the supervision of Marie Doumic and Milica Tomašević. His collaborative projects are described in Section 8.3.5, 8.2.1. A second work, supervised by Marie Doumic, involves solving an inverse problem related to biological phenomena. We assume that we are observing the times at which cells enter a cemetery state, called the "senescence state", and we wish to recover the initial telomere size distribution that existed at the start of the dynamics. This work was completed during 2024, and has resulted in a pre-publication [34]. In parallel with these two works, he has been working on a stochastic modeling project supervised by Frédérique Clément. They modeled the phenomenon of neurogenesis with compound Poisson processes, implemented it, and studied its moments in detail [10].

Alexandre Perrin has begun his Ph.D, funded by the ERC Advanced Grant SINGER, in September 2023, and is supervised by Sylvie Méléard, Meriem El Karoui and Marie Doumic. While significant efforts have been made to model bacterial cell division, few models have incorporated DNA replication into the control of this process. To date, models that attempt to capture the coordination between replication and division cycles are based on fundamentally different assumptions, and yet no study provide a rigorous quantitative comparaison. As a result, key questions regarding how replication quantitatively controls cell division remain unresolved. To address this, we have developed a robust mathematical framework to compare models of coordination of replication and division cycles proposed in the literature. Through theoretical analysis, we identified necessary and sufficient conditions for these

models to exhibit physiological behaviour in cell cycles, and tested whether these conditions accords with experimental data. Additionally, a comprehensive statistical analysis allowed us to assess the models' ability to reproduce the joint distributions of cell cycles related quantities. This in-depth analysis led to the development of a novel model for the coordination of replication and division cycles, which provides an accurate fit to the data across a wider range of growth conditions than previous models.

Guillaume Garnier's Ph.D, co-supervised by Lydia Robert, Marc Hoffmann and Marie Doumic, is devoted to the study of the effects of mutations on the fitness of the bacteria E. coli. He has developed a non-parametric statistical method based on Fourier estimators that can be used to reconstruct the Distribution of Fitness Effects (DFE) from microfluidic data of "Mother Machine", see [122] and also Sections 8.3.3, 8.3.4, 8.3.5. This work has enabled us to explore various methods and construct a statistical estimator of this density. Extensive analytical work was carried out to formally demonstrate their convergence property, which was illustrated using numerical simulations [30].

In collaboration with Marie Doumic and Miguel Escobedo, Guillaume Garnier is also currently working on an integro-PDE, satisfied in expectation by the empirical measure inferred above. This work is an in-depth theoretical analysis of the long-time evolution of the fitness distribution.

8.3 Axis 3: Model-data comparison

We refer to 3.3 for a presentation of the research program in this direction.

8.3.1 Telomere shortening, a unifying model

Participants: Anaïs Rat, Marie Doumic, Teresa Teixeira, Zhou Xu.

Progressive shortening of telomeres ultimately causes replicative senescence and is linked with aging and tumor suppression. Studying the intricate link between telomere shortening and senescence at the molecular level and its population-scale effects over time is challenging with current approaches but crucial for understanding behavior at the organ or tissue level. In the article [5] , accepted for publication in Nature Communications, we developed a mathematical model for telomere shortening and the onset of replicative senescence using data from Saccharomyces cerevisiae without telomerase. Our model tracks individual cell states, their telomere length dynamics, and lifespan over time, revealing selection forces within a population. We discovered that both cell genealogy and global telomere length distribution are key to determine the population proliferation capacity. We also discovered that cell growth defects unrelated to telomeres also affect subsequent proliferation and may act as confounding variables in replicative senescence assays. Overall, while there is a deterministic limit for the shortest telomere length, the stochastic occurrence of non-terminal arrests drive cells into a totally different regime, which may promote genome instability and senescence escape. Our results offer a comprehensive framework for investigating the implications of telomere length on human diseases. Our model has also been used further in another experimental device, where one telomere is cut at a given very short length thanks to CrisPr-Cas9 technique [20]. Alongside this modelling and simulation approach, Jules Olayé's Ph.D work focused on several interesting problems raised by this collaboration, see Sections 8.2.1, 8.2.6 and [34], [4] .

8.3.2 Classical Myelo-Proliferative Neoplasms emergence and development in patients based on real-life incidence and mathematical modeling

Participants: Ana Fernandez Baranda, Vincent Bansaye, Emelyne Lauret, M Mounier, Sylvie Méléard, Stéphane Giraudier.

Mathematical modeling offers the opportunity to test hypothesis concerning Myeloproliferative emergence and development. In [19], we tested different mathematical models based on a training cohort (n = 264 patients) (Registre de la côte d'Or) to determine the emergence and evolution times

before JAK2V617F classical Myeloproliferative disorders (respectively Polycythemia Vera and Essential Thrombocytemia) are diagnosed. We dissected the time before diagnosis as two main periods: the time from embryonic development for the JAK2V617F mutation to occur, not disappear and enter in proliferation, and a second time corresponding to the expansion of the clonal population until diagnosis. We demonstrate using progressively complexified models that the rate of active mutation occurrence is not constant and doesn't just rely on individual variability, but rather increases with age and takes a median time of $63.1 +/- 13$ years. A contrario, the expansion time can be considered as constant: 8.8 years once the mutation has emerged. Results were validated in an external cohort (national FIMBANK Cohort, $n = 1248$ patients). Analyzing JAK2V617F Essential Thrombocytema versus Polycythemia Vera, we noticed that the first period of time (rate of active homozygous mutation occurrence) for PV takes approximatively 1.5 years more than for ET to develop when the expansion time was quasi-similar. In conclusion, our multi-step approach and the ultimate time-dependent model of MPN emergence and development demonstrates that the emergence of a JAK2V617F mutation should be linked to an aging mechanism, and indicates a 8-9 years period of time to develop a full MPN.

8.3.3 Quantitative effects of the stress response to DNA damage in the cell size control of Escherichia coli

Participants: Ignacio Madrid Canales, James Broughton, Sylvie Méléard, Meriem El Karoui.

In Escherichia coli the response to DNA damage shows strong cell-to-cell-heterogenity. This results in a random delay in cell division and asymmetrical binary fission of single cells, which can compromise the size homeostasis of the population. To quantify the effect of the heterogeneous response to genotoxic stress (called SOS response in E. coli) on the growth of the bacterial population, we propose a flexible time-continuous parametric model of individual-based population dynamics [22]. We construct a stochastic model based on the "adder" size-control mechanism, extended to incorporate the dynamics of the SOS response and its effect on cell division. The model is fitted to individual lineage data obtained in a 'mother machine' microfluidic device. We show that the heterogeneity of the SOS response can bias the observed division rate. In particular, we show that the adder division rate is decreased by SOS induction and that this perturbative effect is stronger in fast-growing conditions.

8.3.4 A unifying mathematical approach for the coordination of DNA replication and cell division in E. coli

Participants: Alexandre Perrin, Marie Doumic, Meriem El Karoui, Sylvie Méléard.

While significant efforts have been made to model bacterial cell division, few models have incorporated DNA replication into the control of this process. To date, models that attempt to capture the coordination between replication and division cycles are based on fundamentally different assumptions, and yet no study provide a rigorous quantitative comparaison. As a result, key questions regarding how replication quantitatively controls cell division remain unresolved. To address this, we have developed a robust mathematical framework to compare models of coordination of replication and division cycles proposed in the literature. Through theoretical analysis, we identified necessary and sufficient conditions for these models to exhibit physiological behaviour in cell cycles, and tested whether these conditions accords with experimental data. Additionally, a comprehensive statistical analysis allowed us to assess the models' ability to reproduce the joint distributions of cell cycles related quantities. This in-depth analysis led to the development of a novel model for the coordination of replication and division cycles, which provides an accurate fit to the data across a wider range of growth conditions than previous models.

8.3.5 Exploitation of microfluidic data

Participants: Vincent Bansaye, Charles Baroud, Jules Olayé, Guillaume Garnier.

In [35], we describe fluctuations in population sizes of Bellman-Harris processes to estimate lifetime distributions from temporal population size tracking. This involves determining two fluctuation regimes, leveraging recent results for Crump-Mode-Jagers processes, and applying these findings to microfluidic data.

8.3.6 Asymptotic inverse problems for fragmentation and depolymerisation models

Participants: Marie Doumic, Miguel Escobedo, Philippe Moireau, Magali Tournus.

Given a phenomenon described by a self-similar fragmentation equation, how to infer the fragmentation kernel from experimental measurements of the solution ? To answer this question at the basis of our work, a formal asymptotic expansion suggested us that using short-time observations and initial data close to a Dirac measure should be a well-adapted strategy. We prove error estimates in Total Variation and Bounded Lipshitz norms; this gives a quantitative meaning to what a "short" time observation is. Our analysis is complemented by a numerical investigation [11].

In another study, we focused on depolymerisation reactions, which constitute frequent experiments, for instance in biochemistry for the study of amyloid fibrils. The quantities experimentally observed are related to the time dynamics of a quantity averaged over all polymer sizes, such as the total polymerised mass or the mean size of particles. The question analysed here is to link this measurement to the initial size distribution. To do so, we first derive, from the initial reaction system two asymptotic models: at first order, a backward transport equation, and at second order, an advection-diffusion/Fokker-Planck equation complemented with a mixed boundary condition at $x = 0$. We estimate their distance to the original system solution. We then turn to the inverse problem, i.e., how to estimate the initial size distribution from the time measurement of an average quantity, given by a moment of the solution. This question has been already studied for the first order asymptotic model, and we analyse here the second order asymptotic. Thanks to Carleman inequalities and to log-convexity estimates, we prove observability results and error estimates for a Tikhonov regularization. We then develop a Kalman-based observer approach, and implement it on simulated observations. Despite its severely ill-posed character, the second order approach appears numerically more accurate than the first-order one [27].

9 Partnerships and cooperations

Participants: All team members.

9.1 International research visitors

9.1.1 Visits of international scientists

Marek Kimmel

Status Full Professor

Institution of origin: Rice University

Country: USA

Dates: September-December 2024

Context of the visit: Telomeres project with Marie Doumic, Jules Olayé, Teresa Teixeira

Mobility program/type of mobility: sabbatical stay, 5 mini-courses on stochastic modelling of biological dynamics. Inria program for invited professors

Carmella Moschella

Status Ph.D student (advisor: Christian Schmeiser and Sara Merino)

Institution of origin: University of Vienna

Country: Austria

Dates: June 2024 and October-November 2024

Context of the visit: collaboration on coagulation-transport equations for modelling autophagy, in collaboration with Marie Doumic and Christian Schmeiser

Mobility program/type of mobility: grant for Ph.D students' mobility of the university of Vienna

Sarah Kaakai

Status Associate Professor

Institution of origin: Université du Mans

Country: France

Dates: September 2023 to August 2024

Context of the visit: sabbatical stay and collaboration with Sylvie Méléard, Marie Doumic and Michael Rera on mathematical models for ageing. Sarah Kaakai's stay was the occasion of a new collaboration around Luce Breuil's pre-doctoral internship, now giving rise to a co-supervised Ph.D thesis.

Mobility program/type of mobility: ERC SINGER funding of a "délégation" from Le Mans.

Jaime San Martin

Status Professor

Institution of origin: Universidad de Chile

Country: Chile

Dates: June 2024

Context of the visit: long-standing collaboration with Sylvie Méléard

Mobility program/type of mobility: ERC SINGER

9.1.2 Visits to international teams

Gaël Raoul has a regular collaboration and long-term visits every year with research groups in Vietnam:

- with Marc Choisy and Pham Thanh Duy, Oxford Clinical Research Unit, Ho Chi Minh city, Vietnam. They work on the multi-drug resistance of Klebsiella pneumoniae.
- with Vo Hoang Hung, Saigon University, Ho Chi Minh city, Vietnam. They work on the effect of an age structure on the propagation of population in the context of climate change.

Research stays abroad In 2024, Gaël Raoul has visited Vietnam from August 1st to September 22nd. On August 26-28, he visited the Hanoi branch of OUCRU toi discuss with biologist Tung Trinh Son and medical doctor Thomas Kesterman, to discuss the clinical aspects of antibiotic resistance. He returned to Ho Chi Minh City for September 30th-October 11th to give a lecture "Theoretical Partial Differential Equations" at the University of Sciences of Ho Chi Minh, for the franco-Vietnamese master of Mathematics .

Sylvie Méléard visited Chile, Valparaiso for 2 weeks, at the occasion of the 3rd International Biostochastic Workshop and the launching of Inria Chile institute.

9.2 European initiatives

9.2.1 Other european programs/initiatives

M. Tomasevic is the PI in the project IEA - International Emerging Actions of CNRS with University of Bath, Title: Chemotaxis in random environments: from microscopic to macroscopic viewpoints. Funding 4K 2025, 4K 2024.

9.3 National initiatives

- The MMB Chaire, *Modélisation Mathématique et Biodiversité*, headed by Sylvie Méléard since 2009, has been renewed till 2027. It funds PhD and post-doctoral grants, a yearly summer school and scientific meetings every two month. This has a great role in uniting our community and Vincent Bansaye and Marie Doumic participate in the steering committee.
- Our research on telomere shortening modelling is structured around several fundings:
  - The INCa Projet *TheFinalCut*, headed by Teresa Teixeira (total: 0,78 M€), 2020–2024
  - Following the funding of the PEPR MathVives, a project on telomere shortening modelling, DyLT (approx. 1MEuro), *Influence of telomere length dynamics and environmental conditions on biological and clinical aspects of aging*, has been accepted. Headed by Nicolas Champagnat (Inria project-team TOSCA), and Marie Doumic being the head of Axis 2 of the project, it will be a meeting place for mathematicians and biologists in this field and will be an important opportunity for the pooling of forces on this important topic.
  - Jules Olayé's Ph.D, co-supervised by Milica Tomašević and Marie Doumic, has been funded by the EDMH.
- We are part of many ANR projects: Marie Doumic participates to the ANR GITTE (Genome Instability Triggered by Telomere Erosion) 2025-2028 (800 k€,) and to the ANR project ENERGENCE (433 k€), 2022–2026, *ENERgy driven modelling of tissue architecture emerGENCE and homeorhesis*, headed by Diane Peurichard. Milica Tomašević participates to the ANR project NEMATIC (367 k€), 2021–2025 on *Analyse Modelisation et Simulation Multi-échelle*, headed by Eric Herbert.
- Sylvie Méléard is the P.I. of a Aviesan-Inserm ITMO Cancer project (261 k€), 2022–2026 on *Mathématiques pour une meilleure compréhension des néoplasmes myélo-prolifératifs et leurs thérapeutiques*.

10 Dissemination

Participants: all team members.

10.1 Promoting scientific activities

Sylvie Méléard is the head of the MMB chair: organisation of workshops and a research school in June 2024 , together with fundings of Ph.D and post-doctoral grants.

10.1.1 Scientific events: organisation

The team organised, on April 3rd, a kick-off meeting for the launching of the team (50 participants, and a series of four "twin talks" with a biologist and a mathematician speaking together on a given interdisciplinary project).

Sylvie Méléard organised, as every year, the summer school of the MMB Chaire in Aussois, 10-14 June, 2024 (70 participants, including many members of MERGE - Vincent Bansaye, Luce Breuil, Marie Doumic, Alexandre Perrin, Ana Fernandez Baranda, Anouar Jeddi, Milica Tomasevic - and many collaborators of our team).

Sylvie Méléard also organised a retreat of her ERC SINGER, on December 2-4, to which many members of MERGE participated.

We organise local seminars, called "MERGE aperitif", where our students or invited students give talks. Luce Breuil, Jules Olayé, Alexandre Perrin, Ana Baranda, as well as Claudia Fonte Sanchez and Manuel Esser gave talks in 2024.

M. Tomasevic co-organized two research schools at CIRM in 2024 : Stochastic and Deterministic Analysis for Irregular Models (8-12 jan) and Collective behavior and Pattern formation (1-5 july). The second one obtained the MJC funding of Inria.

M. Tomasevic co-organized the Annual research school of the Chaire MMB at Aussois (juin 2024). She also co-organized an invited session on the Journée MAS entitled Mean field limits and control (Poitiers, Aug 2024) and the Conference 50 ans CMAP at Ecole polytechnique (sept 2024).

M. Tomasevic co-organizes the probability seminar of CMAP.

M. Tomasevic is co-responsable of the thematic group MABIOME of SMAI and a member of the Scientific council of the RT Maths bio santé.

Marie Doumic organised a mini-symposium at the ECMTB Conference in Toledo, Spain, on Telomere dynamics modelling, where Jules Olayé, Anaïs Rat and Marek Kimmel gave talks.

Sylvie Méléard co-organised the conference *A lifelong journey in stochastic analysis: from branching processes to statistical mechanics*, IHP Paris 2024.

10.1.2 Scientific events and invited talks

Vincent Bansaye participated in:

- Meeting « Probability, Ecology and Evolution » in Besancon, 10/12/2024, talk on branching processes and networks
- Conference « Ecological networks, complex systems, stability » , 28/10/2024, talk on Stochastic functional responses in ecology
- Conference « Non local branching Markov process », in CIRM , 20th September 2024, talk on Branching processes for growing, living network;
- Meeting Inov3PT, Paris, 9 janvier 2024, talk on invasive stochastic process and applications

Marie Doumic gave

- a talk in the TeloEMBO meeting, April 6-10 2024, Rome
- a 3-hour minicourse at the Mittag-Leffler Institute for the "Kinetic Theory arising from mathematical biology" conference, Stockholm, Sweden, July 1-5 2024
- several seminars: Toulouse (September 30th), Brest (September 9th), Versailles (December 16th), CMAP.

Madeleine Kubasch gave talks in

- Dec 2024 — « Besançon meeting on Probability, Ecology and Evolution », Université Bourgogne Franche-Comté, Besançon.
- August 2024 — 11th Bernoulli-IMS World Congress in Probability and Statistics, Organized Contributed Paper Session « Stochastic Epidemic Models », Bochum (Germany).

- May 2024 — Workshop « Spatial Epidemic Models (Including Graphs and Graphons) », Rice Global Paris Center, Paris.

Maxime Ligonnière gave talks in

- Séminaire de Probabilités de l'Institut Fourier, Grenoble, November 2023
- Workshop of the ANR RAWABRANCH, Angers, March 2024
- Séminaire de probabilités LMBA, Brest, April 2024
- Séminaire de Probabilités, LPSM, Sorbonne université, Paris, May 2024
- Workshop Produits de matrices et branchement, ESAIP, Angers, June 2024
- Workshop on branching processes and products of random matrices, LMBA, UBS, Vannes, July 2024

Sylvie Méléard gave talks in:

- Valparaiso 2024, Biostochastic
- HKIAS International Conference on Mathematical Analysis and its Applications, City University of Hong Kong, 2024
- 30 ans du Laboratoire Manceau de Mathématiques : Probabilités - Statistique - Risque, 2024
- Non-local branching processes, CIRM 2024
- Seminaries: Inria Dyogene Seminar, February 2024 ; Rennes 2024, Séminaire MoVi.

Jules Olayé

- gave talks at the kick-off meeting of MERGE and of the PEPR Maths VivES DyLT project
- gave a talk at the 13th ECMTB (European Conference on Mathematical and Theoretical Biology), Toledo, Spain
- presented posters at the "Mathematical Biology: Collective Behavior and Pattern Formation", CIRM, Marseille, and at the 50th anniversary of the CMAP

Gaël Raoul gave talks in

- several seminars: Chaire MMB seminar (May 6th 2024), Seoul National University (October 18th 2024), online seminar of the National Center for Theoretical Sciences in Taiwan (0ctober 25th 2024).
- the ReaDiNet conférence in Jeju, Korea (October 23th 2024).

Milica Tomasevic gave talks at the following conferences and seminars:

- Conference PDE and Probability in interaction: functional inequalities, optimal transport and particle systems, jan 2024 CIRM
- French Japanese Conference on Probability & Interactions, Mar 2024, IHES
- Non-local operators, probability and singularities, May 2024, online seminar
- Frontiers in Interacting Particle Systems, Aggregation-Diffusion Equations and Collective Behavior, june 2024 CIRM
- Colloquium de laboratoire de Maths, Créteil, déc 2024.

10.1.3 Journal

Marie Doumic is editor in Chief of ESAIM Proceedings and Surveys.

Marie Doumic and Gaël Raoul are editors of the Journal of Mathematical Biology.

Marie Doumic is associate editor for Kinetic and Related Models and the Bulletin des Sciences Mathématiques.

Sylvie Méléard is associate editor for the Comptes-Rendus de l'Académie des Sciences (CRAS).

10.1.4 Research administration

Vincent Bansaye is vice-president of the Applied Math Department of Ecole Polytechnique and of Fondation Mathématique Jacques Hadamard (FMJH).

Marie Doumic, Sylvie Méléard and Vincent Bansaye are members of the steering committee of the MMB chair.

Marie Doumic is a member of the board of the ESMTB (European Society for Mathematical and Theoretical Biology).

Sylvie Méléard is a member of the Scientific Advertisory Board of HIM (Hausdorff Research Institute for Mathematics, Bonn, Germany), CMM (Center for Mathematical Modeling, Santiago, Chili) and of CRM (Centre de recherches mathématiques, Montréal, Canada).

10.2 Teaching - Supervision - Juries

10.2.1 Teaching

Vincent Bansaye gave 3 courses.

Sylvie Méléard is the head of the master "Mathematics for living sciences" and gave a course on Stochastic Processes in the master.

M. Tomasevic is a part time professor at DMAP, Ecole polytechnique with 64h of service. In addition, she gives an M2 course (24h) at M2 in probability at Jussieu.

Luce Breuil gave probability tutorials for Bachelor 2 students of Ecole Polytechnique as well as linear algebra classes for the Master X-HEC.

10.2.2 Supervision

Several students are co-supervised by two permanent members of MERGE:

- Alexandre Perrin is co-supervised by Marie Doumic and Sylvie Méléard
- Ana Fernandez Baranda is co-supervised by Vincent Bansaye and Sylvie Méléard
- Jules Olayé is co-supervised by Marie Doumic and Milica Tomasevic
- Nadia Belmabrouk's post-doctoral studies are in collaboration with Vincent Bansaye and Sylvie Méléard.

Vincent Bansaye also supervised Maxence Baccara (with Sylvain Billiard and Jean-René Chazottes) and Alexandre Bertolino (with Ayman Moussa).

Marie Doumic also co-supervised Guillaume Garnier (with Marc Hoffmann and the biologist Lydia Robert, funded by Inria-INRAE grants), Luce Breuil (with Sarah Kaakai and the biologist Michael Rera, funding AMX) and Viviana Gavilanes (with the biologist Zhou Xu, funded by MITI of CNRS).

Sylvie Méléard also supervised Ignacio Madrid Canales (Co direction with the biologist M. El Karoui), Defense in February 2024 and co-Supervised (50%) Anouar Jeddi (with Nicolas Champagnat) and Mateo Deangelo Bravo (with Viet Chi Tran).

Gaël Raoul co-advises the PhD thesis of Le Tuyet Nhi Pham with Giovanni Conforti, University of Padova, Italy. The PhD thesis is devoted to the development of new entropic optimal transport methods inspired by biological problems. Sirine Boucenna defended her Ph.D on September 26th, 2024, on the eco-evolutive dynamics of ecosystems under stress, under the supervision of Vasilis Dakos and Gaël Raoul.

Mililca Tomasevic also co-supervises N. Cazacu's Ph.D since 2024 with A. Richard (CentraleSupelec) and the postdoctoral project of Hadamard Lecturer T. Cavalazzi since 2023 with A. Richard. M. Tomasevic co-supervised two internships of level M2.

10.2.3 Juries

Vincent Bansaye participated in 4 juries (3 Ph.D, 1 Habilitation thesis). Sylvie Méléard participated in 5 juries (3 PhD thesis: Ignacio Madrid Canales, Laurent Freoa, Louis-Pierre Chaintron) and 2 habilitation thesis (Boris Nectoux and Clément Foucart).

M. Tomasevic was a vice president of the recruting jury of an assistant professor position at Ecole polytechnique.

Marie Doumic participated to the selection committee of a full professor at INSA Toulouse (May 2024) and to the admission jury of DR Inria. She reviewed the PhD thesis of Nathan Quiblier and Nga Nguyen, chaired Lucie Laurence's defence, and was a member of the habilitation thesis committee of Mélanie Prague.

10.3 Popularization

10.3.1 Specific official responsibilities in science outreach structures

Sylvie Méléard is now member of the Organisation Committee of the SMF-BNF cycle "un texte, une aventure mathématique" : The lecturer chooses a mathematical text dating back several decades, or even much longer, which has particularly influenced him. Based on this text, its author and its history, the lecturer will show how an ancient mathematical problem leads to current questions and ongoing mathematical research. Combining history and mathematics, the conferences enable a wide audience to discover contemporary mathematics.

10.3.2 Productions (articles, videos, podcasts, serious games, ...)

For Sylvie Méléard's Irène Joliot-Curie price, there have been several articles: , .

For Madeleine Kubasch's L'Oréal-Unesco price, there also have been several articles , , , , .

Marie Doumic has been interviewed for "l'oreille mathématique" , a podcast produced by IHP.

For the kick-off day of MERGE, on April 3rd, Marie Doumic, Sylvie Méléard and Gaël Raoul have been interviewed for the Ecole Polytechnique website and Inria website .

Guillaume Garnier participated to "ma thèse en 180 secondes" .

10.3.3 Participation in Live events

Sylvie Méléard gave a conference at the Institut Montaigne with title "Mathématiques et biodiversité".

Madeleine Kubasch gave a large audience presentation in the framework of « Entretiens de l'Excellence » at École polytechnique, presenting her work and career for 700 middle-schoolers . She also participated to the Fête de la Science and presented her research work at the Cité des Sciences et de l'Industrie, in the framework of the price "Young Talents France L'Oréal-Unesco For Women and Science".

Marie Doumic participated to middle school's career mornings.

10.3.4 Others science outreach relevant activities

Vincent Bansaye participated in the setting up and took part in the math club at Gérard Philippe secondary school, Massy.

11 Scientific production

11.1 Major publications

[1] ***Best Paper***
V. Bansaye, F. Deslandes, M. Kubasch and E. Vergu. 'The epidemiological footprint of contact structures in models with two levels of mixing'. In: *Journal of Mathematical Biology* (30th Sept. 2024). DOI: 10.1007/s00285-024-02147-z. URL: https://hal.science/hal-04012906 (cit. on p. 20).

[2] ***Best Paper***
I. M. Canales, J. Broughton, S. Méléard and M. El Karoui. *Quantitative effects of the stress response to DNA damage in the cell size control of Escherichia coli*. 11th Sept. 2024. URL: https://hal.science/hal-04694122 (cit. on p. 16).

[3] ***Best Paper***
M. El Karoui, I. Madrid and S. Méléard. *Phenotypic plasticity trade-offs in an age-structured model of bacterial growth under stress*. 19th Mar. 2024. URL: https://polytechnique.hal.science/hal-04511813 (cit. on p. 16).

[4] ***Best Paper***
J. Olayé and M. Tomasevic. *Long-time behaviour of a multidimensional age-dependent branching process with a singular jump kernel*. 5th Aug. 2024. URL: https://hal.science/hal-04667551 (cit. on pp. 17, 22).

[5] ***Best Paper***
A. Rat, V. Martinez Fernandez, M. Doumic, M. T. Teixeira and Z. Xu. 'Individual cell fate and population dynamics revealed by a mathematical model linking telomere length and replicative senescence'. In: *Nature Communications* 16.1 (25th Jan. 2025), p. 1024. DOI: 10.1101/2023.11.22.568287. URL: https://hal.science/hal-04305005 (cit. on p. 22).

11.2 Publications of the year

International journals

[6] V. Bansaye. 'Spine for interacting populations and sampling'. In: *Bernoulli* 30.2 (1st May 2024). DOI: 10.3150/23-BEJ1645. URL: https://hal.science/hal-03219097 (cit. on p. 18).

[7] V. Bansaye, F. Deslandes, M. Kubasch and E. Vergu. 'The epidemiological footprint of contact structures in models with two levels of mixing'. In: *Journal of Mathematical Biology* (30th Sept. 2024). DOI: 10.1007/s00285-024-02147-z. URL: https://hal.science/hal-04012906.

[8] V. Bansaye, X. Erny and S. Méléard. 'Sharp approximation and hitting times for stochastic invasion processes'. In: *Stochastic Processes and their Applications* 178 (Dec. 2024), p. 104458. DOI: 10.1016/j.spa.2024.104458. URL: https://hal.science/hal-03915479 (cit. on p. 18).

[9] 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.

[10] F. Clément and J. Olayé. 'A stochastic model for neural progenitor dynamics in the mouse cerebral cortex'. In: *Mathematical Biosciences* 372 (June 2024), p. 109185. DOI: 10.1016/j.mbs.2024.109185. URL: https://inria.hal.science/hal-04351283 (cit. on p. 21).

[11] M. Doumic, M. Escobedo and M. Tournus. 'An inverse problem: recovering the fragmentation kernel from the short-time behaviour of the fragmentation equation'. In: *Annales Henri Lebesgue* 7 (5th Sept. 2024), pp. 621–671. DOI: 10.5802/ahl.207. URL: https://hal.science/hal-03494439 (cit. on p. 24).

[12] M. Doumic, S. Hecht, B. Perthame and D. Peurichard. 'Multispecies cross-diffusions: from a nonlocal mean-field to a porous medium system without self-diffusion'. In: *Journal of Differential Equations* 389 (25th Apr. 2024), pp. 228–256. DOI: 10.1016/j.jde.2024.01.017. URL: https://hal.science/hal-04108050. In press (cit. on p. 16).

[13] Q. Griette, M. Alfaro, G. Raoul and S. Gandon. 'Evolution and spread of multiadapted pathogens in a spatially heterogeneous environment'. In: *Evolution Letters* 8.3 (1st June 2024), pp. 427–436. DOI: 10.1093/evlett/qrad073. URL: https://hal.science/hal-04693075 (cit. on p. 19).

[14] A. Rat, V. Martinez Fernandez, M. Doumic, M. T. Teixeira and Z. Xu. 'Individual cell fate and population dynamics revealed by a mathematical model linking telomere length and replicative senescence'. In: *Nature Communications* 16.1 (25th Jan. 2025), p. 1024. DOI: 10.1101/2023.11.22.568287. URL: https://hal.science/hal-04305005.

[15] T. Roget, C. Macmurray, P. Jolivet, S. Meleard and M. Rera. 'A scenario for an evolutionary selection of ageing'. In: *eLife* 13 (1st Nov. 2024), RP92914. DOI: 10.7554/eLife.92914.3. URL: https://hal.science/hal-04780157 (cit. on p. 16).

[16] M. Tomašević and G. Woessner. 'On a multi-dimensional McKean-Vlasov SDE with memorial and singular interaction associated to the parabolic-parabolic Keller-Segel model'. In: *Stochastic Analysis and Applications* 42.4 (18th Aug. 2024), pp. 767–796. DOI: 10.1080/07362994.2024.2381768. URL: https://inria.hal.science/hal-04191117 (cit. on p. 15).

International peer-reviewed conferences

[17] M. Doumic. 'Moments approaches for asymptotic inverse problems of depolymerisation and fragmentation systems'. In: *Journées Equations aux dérivées partielles*. Journées Equations aux Dérivées Partielles. Aussois, France, 2024. URL: https://hal.science/hal-04632888.

Reports & preprints

[18] V. Bansaye, P.-Y. Boëlle, S. Cauchemez, B. Cazelles, P. Crepey, L. Cristancho-Fajardo, J.-S. Dhersin, S. Dumitrescu, P. Ezanno, A. Flahault, J.-L. Golmard, P. Hoscheit, H. Mermoz Kouye, M. Kubasch, C. Laredo, A. Mallet, L. Opatowski, C. Prieur and A. Véber. *Hommage à Elisabeta Vergu*. 2024. URL: https://hal.science/hal-04230307.

[19] A. F. Baranda, V. Bansaye, E. Lauret, M. Mounier, V. Ugo, S. Méléard and S. Giraudier. *Classical Myelo-Proliferative Neoplasms emergence and development based on real life incidence and mathematical modeling*. 2024. DOI: 10.48550/arXiv.2406.06765. URL: https://hal.science/hal-04926537 (cit. on pp. 20, 22).

[20] P. Berardi, V. Martinez Fernandez, A. Rat, F. Rosas Bringas, P. Jolivet, R. Langston, S. Mattarocci, A. Maes, T. Aspert, B. Zeinoun, K. Casier, H. Kazemier, G. Charvin, M. Doumic, M. Chang and M. T. Teixeira. *The shortest telomere in telomerase-negative cells triggers replicative senescence at a critical threshold length and also fuels genomic instability*. 29th Jan. 2025. DOI: 10.1101/2025.01.27.635053. URL: https://hal.science/hal-04926171 (cit. on p. 22).

[21] C. Bertucci, M. Rakotomalala and M. Tomasevic. *Curvature in chemotaxis: A model for ant trail pattern formation*. 30th Sept. 2024. URL: https://hal.science/hal-04676778 (cit. on p. 15).

[22] I. M. Canales, J. Broughton, S. Méléard and M. El Karoui. *Quantitative effects of the stress response to DNA damage in the cell size control of Escherichia coli*. 11th Sept. 2024. URL: https://hal.science/hal-04694122 (cit. on p. 23).

[23] P. Collet, C. Ecotière and S. Méléard. *Long time behavior of a degenerate stochastic system modeling the response of a population face to environmental impacts*. 2nd May 2024. URL: https://hal.science/hal-04566978 (cit. on p. 18).

[24] P. Collet, S. Méléard and J. San MARTIN. *Branching diffusion processes and spectral properties of Feynman-Kac semigroup*. 12th Apr. 2024. URL: https://hal.science/hal-04544252 (cit. on p. 18).

[25] M. Doumic, K. Fellner, M. Mezache and J. J. L. Velázquez. *Asymptotic Analysis of a bi-monomeric nonlinear Becker-Döring system*. 4th July 2024. URL: https://hal.science/hal-04635659.

[26] M. Doumic, S. Hecht, M. Hoffmann and D. Peurichard. *Scaling limits for a population model with growth, division and cross-diffusion*. 16th Oct. 2024. URL: https://hal.science/hal-04740457 (cit. on p. 16).

[27] M. Doumic and P. Moireau. *Asymptotic approaches in inverse problems for depolymerization estimation*. 29th Sept. 2024. URL: https://hal.science/hal-04713806 (cit. on p. 24).

[28] M. Doumic, A. Rat and M. Tournus. *Comparison Between Effective and Individual Fitness in a Heterogeneous Population*. 20th Dec. 2024. URL: https://cnrs.hal.science/hal-04852370 (cit. on p. 19).

[29] M. El Karoui, I. Madrid and S. Méléard. *Phenotypic plasticity trade-offs in an age-structured model of bacterial growth under stress*. 19th Mar. 2024. URL: https://polytechnique.hal.science/hal-04511813.

[30] G. Garnier. *Decompounding with unknown noise through several independents channels*. 17th May 2024. URL: https://hal.science/hal-04460693 (cit. on p. 22).

[31] G. Guo and M. Tomasevic. *Mean-field limit of particle systems with absorption*. 25th July 2024. URL: https://hal.science/hal-04584980.

[32] A. Jeddi. *Convergence of a discrete selection-mutation model with exponentially decaying mutation kernel to a Hamilton-Jacobi equation*. 2024. DOI: 10.48550/arXiv.2412.06657. URL: https://hal.science/hal-04927829 (cit. on p. 19).

[33] M. Ligonnière. *A Kesten Stigum theorem for Galton-Watson processes with infinitely many types in a random environment*. 14th Nov. 2024. URL: https://hal.science/hal-04784393.

[34] J. Olayé. *An inverse problem in cell dynamics: Recovering an initial distribution of telomere lengths from measurements of senescence times*. 20th Jan. 2025. URL: https://hal.science/hal-04901291 (cit. on pp. 21, 22).

[35] J. Olayé, H. Bouzidi, A. Aristov, S. G. Ramos, C. Baroud and V. Bansaye. *Estimation of the lifetime distribution from fluctuations in Bellman-Harris processes*. 6th Feb. 2024. URL: https://hal.science/hal-04437341 (cit. on p. 24).

[36] J. Olayé and M. Tomasevic. *Long-time behaviour of a multidimensional age-dependent branching process with a singular jump kernel*. 5th Aug. 2024. URL: https://hal.science/hal-04667551.

11.3 Cited publications

[37] M. Alfaro, J. Coville and G. Raoul. 'Travelling waves in a nonlocal reaction-diffusion equation as a model for a population structured by a space variable and a phenotypic trait'. In: *Communications in Partial Differential Equations* 38.12 (2013), pp. 2126–2154 (cit. on p. 6).

[38] A. Amir. 'Cell size regulation in bacteria'. In: *Physical Review Letters* 112.20 (2014), p. 208102 (cit. on p. 11).

[39] A. Armiento, M. Doumic, P. Moireau and H. Rezaei. 'Estimation from Moments Measurements for Amyloid Depolymerisation'. In: *Journal of Theoretical Biology* 397 (Mar. 2016), pp. 68–88. DOI: 10.1016/j.jtbi.2016.02.037. URL: https://hal.archives-ouvertes.fr/hal-01248255 (cit. on p. 9).

[40] A. Armiento, P. Moireau, D. Martin, N. Lepejova, M. Doumic and H. Rezaei. 'The mechanism of monomer transfer between two structurally distinct PrP oligomers'. In: *PLOS ONE* 12.7 (July 2017). DOI: 10.1371/journal.pone.0180538. URL: https://hal.archives-ouvertes.fr/hal-01574346 (cit. on p. 8).

[41] Z. Baharoglu and D. Mazel. 'SOS, the formidable strategy of bacteria against aggressions'. In: *FEMS Microbiology Reviews* 38.6 (Nov. 2014), pp. 1126–1145. DOI: 10.1111/1574-6976.12077 (cit. on p. 11).

[42] J. M. Ball and A. Majumdar. 'Nematic liquid crystals: from Maier-Saupe to a continuum theory'. In: *Molecular crystals and liquid crystals* 525.1 (2010), pp. 1–11 (cit. on p. 5).

[43] H. T. Banks, M. Doumic, C. Kruse, S. Prigent and H. Rezaei. 'Information content in data sets for a nucleated-polymerization model'. In: *Journal of biological dynamics* 9.1 (2015), pp. 172–197 (cit. on p. 8).

[44] V. Bansaye. 'Proliferating parasites in dividing cells: Kimmel's branching model revisited'. In: *The Annals of Applied Probability* 18.3 (2008), pp. 967–996 (cit. on p. 7).

[45] V. Bansaye, B. Cloez and P. Gabriel. 'Ergodic behavior of non-conservative semigroups via generalized Doeblin conditions'. In: *Acta Applicandae Mathematicae* (2019), pp. 1–44 (cit. on p. 3).

[46] V. Bansaye and S. Méléard. *Stochastic Models for Structured Populations*. Vol. 16. Springer, 2015 (cit. on pp. 3, 8).

[47] V. Bansaye, A. Moussa and F. Muñoz-Hernández. 'Stability of a cross-diffusion system and approximation by repulsive random walks: a duality approach'. In: *arXiv preprint arXiv:2109.07146* (2021) (cit. on p. 6).

[48] V. Bansaye, A. Moussa and F. Muñoz-Hernández. 'Stability of a cross-diffusion system and approximation by repulsive random walks: a duality approach'. In: *J. Eur. Math. Soc.* (2024). 41 pages. URL: https://hal.science/hal-03344301 (cit. on p. 15).

[49] V. Bansaye and V. C. Tran. 'Branching Feller diffusion for cell division with parasite infection'. In: *ALEA: Latin American Journal of Probability and Mathematical Statistics* 8 (2011), pp. 95–127 (cit. on p. 7).

[50] A. Barizien, M. Suryateja Jammalamadaka, G. Amselem and C. N. Baroud. 'Growing from a few cells: combined effects of initial stochasticity and cell-to-cell variability'. In: *Journal of the Royal Society Interface* 16.153 (2019), p. 20180935 (cit. on p. 3).

[51] G. Barles, S. Mirrahimi and B. Perthame. 'Concentration in Lotka-Volterra parabolic or integral equations: a general convergence result'. In: *Methods and Applications of Analysis* 16.3 (2009), pp. 321–340 (cit. on p. 4).

[52] G. Barles and B. Perthame. 'Concentrations and constrained Hamilton-Jacobi equations arising in adaptive dynamics'. In: *Contemporary Mathematics* 439 (2007), pp. 57–68 (cit. on p. 4).

[53] M. Barthe, J. Tchouanti, P. H. Gomes, C. Bideaux, D. Lestrade, C. Graham, J.-P. Steyer, S. Méléard, J. Harmand and N. Gorret. 'Availability of the Molecular Switch XylR Controls Phenotypic Heterogeneity and Lag Duration during Escherichia coli Adaptation from Glucose to Xylose'. In: *Mbio* 11.6 (2020), e02938–20 (cit. on p. 8).

[54] N. Barton. 'Adaptation at the edge of a species' range'. In: *Integrating ecology and evolution in a spatial context*. 2001 (cit. on p. 6).

[55] N. Berestycki. 'Recent progress in coalescent theory'. In: *ENSAIOS MATEMÁTICOS* 16 (2009), pp. 1–193 (cit. on p. 8).

[56] C. Bonnet, P. Gou, V. Bansaye, C. Lacout, K. Bailly, M.-h. Schlagetter, E. Lauret, S. Meleard and S. Giraudier. *Modeling the behavior of hematopoietic compartments from stem to red cells in murine steady state and stress hematopoiesis*. 2019 (cit. on p. 8).

[57] C. Bonnet, P. Gou, S. Girel, V. Bansaye, C. Lacout, K. Bailly, M.-H. Schlagetter, E. Lauret, S. Méléard and S. Giraudier. 'Multistage hematopoietic stem cell regulation in the mouse: a combined biological and mathematical approach'. In: *iScience* (2021), p. 103399 (cit. on p. 8).

[58] T. Bourgeron, Z. Xu, M. Doumic and M. T. Teixeira. 'The asymmetry of telomere replication contributes to replicative senescence heterogeneity'. In: *Scientific Reports* 5 (Oct. 2015), p. 15326. DOI: 10.1038/srep15326. URL: https://hal.sorbonne-universite.fr/hal-01272075 (cit. on p. 8).

[59] V. Calvez, B. Henry, S. Méléard and V. C. Tran. 'Dynamics of lineages in adaptation to a gradual environmental change'. In: *Annales Henri Lebesgue, to appear* (2021) (cit. on p. 8).

[60] J. A. Carrillo, K. Craig and Y. Yao. 'Aggregation-diffusion equations: dynamics, asymptotics, and singular limits'. In: *Active Particles, Volume 2*. Springer, 2019, pp. 65–108 (cit. on p. 5).

[61] N. Champagnat. 'A microscopic interpretation for adaptive dynamics trait substitution sequence models'. In: *Stochastic processes and their applications* 116.8 (2006), pp. 1127–1160 (cit. on p. 4).

[62] N. Champagnat, R. Ferrière and S. Méléard. 'Unifying evolutionary dynamics: from individual stochastic processes to macroscopic models'. In: *Theoretical Population Biology* 69.3 (2006), pp. 297–321 (cit. on p. 3).

[63] N. Champagnat and S. Méléard. 'Polymorphic evolution sequence and evolutionary branching'. In: *Probability Theory and Related Fields* 151.1-2 (2011), pp. 45–94 (cit. on p. 4).

[64] J. Chevallier. 'Mean-field limit of generalized Hawkes processes'. In: *Stochastic Processes and their Applications* 127.12 (2017), pp. 3870–3912 (cit. on p. 6).

[65] J. Chevallier, M. J. Cacéres, M. Doumic and P. Reynaud-Bouret. 'Microscopic approach of a time elapsed neural model'. In: *Mathematical Models and Methods in Applied Sciences* (Dec. 2015), http://www.worldscientific.com/doi/10.1142/S021820251550058X. DOI: 10.1142/S0218202515500 58X. URL: http://hal.upmc.fr/hal-01159215 (cit. on p. 6).

[66] H. Cho, H. Jönsson, K. Campbell, P. Melke, J. W. Williams, B. Jedynak, A. M. Stevens, A. Groisman and A. Levchenko. 'Self-organization in high-density bacterial colonies: efficient crowd control'. In: *PLOS Biology* 5.11 (2007), e302 (cit. on p. 5).

[67] K. L. Chung and J. B. Walsh. 'To reverse a Markov process'. In: *Acta Mathematica* 123 (1969), pp. 225–251 (cit. on p. 8).

[68] B. Cloez. 'Limit theorems for some branching measure-valued processes'. In: *Advances in Applied Probability* 49.2 (2017), pp. 549–580 (cit. on p. 4).

[69] P. Cornilleau and S. Guerrero. 'Controllability and observability of an artificial advection–diffusion problem'. In: *Mathematics of Control, Signals, and Systems* 24.3 (2012), pp. 265–294 (cit. on p. 9).

[70] J.-M. Coron and S. Guerrero. 'Singular optimal control: a linear 1-D parabolic–hyperbolic example'. In: *Asymptotic Analysis* 44.3, 4 (2005), pp. 237–257 (cit. on p. 9).

[71] E. Dambroise, L. Monnier, L. Ruisheng, H. Aguilaniu, J.-S. Joly, H. Tricoire and M. Rera. 'Two phases of aging separated by the Smurf transition as a public path to death'. In: *Scientific Reports* 6.1 (2016), pp. 1–7 (cit. on p. 12).

[72] L. Della Maestra and M. Hoffmann. 'Nonparametric estimation for interacting particle systems: McKean–Vlasov models'. In: *Probability Theory and Related Fields* (2021), pp. 1–63 (cit. on p. 9).

[73] U. Dieckmann and R. Law. 'The dynamical theory of coevolution: a derivation from stochastic ecological processes'. In: *Journal of mathematical biology* 34.5 (1996), pp. 579–612 (cit. on p. 4).

[74] O. Diekmann, P.-E. Jabin, S. Mischler and B. Perthame. 'The dynamics of adaptation: an illuminating example and a Hamilton–Jacobi approach'. In: *Theoretical Population Biology* 67.4 (2005), pp. 257–271 (cit. on p. 4).

[75] J. Dikec, A. Olivier, C. Bobée, Y. D'angelo, R. Catellier, P. David, F. Filaine, S. Herbert, C. Lalanne and H. Lalucque. 'Hyphal network whole field imaging allows for accurate estimation of anastomosis rates and branching dynamics of the filamentous fungus *Podospora anserina*'. In: *Scientific Reports* 10.1 (2020), pp. 1–16 (cit. on pp. 9, 10).

[76] P. Donnelly and T. G. Kurtz. 'Genealogical processes for Fleming-Viot models with selection and recombination'. In: *Annals of Applied Probability* (1999), pp. 1091–1148 (cit. on p. 8).

[77] A. Doostmohammadi, S. P. Thampi, T. B. Saw, C. T. Lim, B. Ladoux and J. M. Yeomans. 'Celebrating Soft Matter's 10th Anniversary: Cell division: a source of active stress in cellular monolayers'. In: *Soft Matter* 11.37 (2015), pp. 7328–7336 (cit. on p. 5).

[78] M. Doumic, M. Escobedo and M. Tournus. 'Estimating the division rate and kernel in the fragmentation equation'. In: *Ann. Inst. H. Poincaré Anal. Non Linéaire* 35.7 (2018), pp. 1847–1884. DOI: 10.1016/j.anihpc.2018.03.004. URL: https://doi.org/10.1016/j.anihpc.2018.03.004 (cit. on p. 9).

[79] M. Doumic, M. Hoffmann, N. Krell and L. Robert. 'Statistical estimation of a growth-fragmentation model observed on a genealogical tree'. In: *Bernoulli* 21.3 (2015), pp. 1760–1799 (cit. on p. 4).

[80] M. Doumic, K. Fellner, M. Mezache and H. Rezaei. 'A bi-monomeric, nonlinear Becker–Döring-type system to capture oscillatory aggregation kinetics in prion dynamics'. In: *Journal of Theoretical Biology* 480 (2019), pp. 241–261 (cit. on p. 8).

[81] M. Doumic, S. Hecht and D. Peurichard. 'A purely mechanical model with asymmetric features for early morphogenesis of rod-shaped bacteria micro-colony'. In: *Mathematical Biosciences and Engineering* 17.6 (2020), pp. 6873–6908 (cit. on pp. 5, 16).

[82] M. Doumic and M. Hoffmann. 'Individual and population approaches for calibrating division rates in population dynamics: Application to the bacterial cell cycle'. In: *Modeling and Simulation for Collective Dynamics*. Vol. 40. Lecture Notes Series, Institute for Mathematical Sciences, National University of Singapore. WORLD SCIENTIFIC, Feb. 2023, pp. 1–81. DOI: 10.1142/9789811266140_0001. URL: https://hal.science/hal-03328781 (cit. on pp. 3, 4, 9, 10).

[83] M. Doumic, A. Olivier and L. Robert. 'Estimating the division rate from indirect measurements of single cells.' In: *Discrete and Continuous Dynamical Systems-Series B* 25.10 (2020) (cit. on p. 9).

[84] C. Duval and J. Kappus. 'Adaptive procedure for Fourier estimators: application to deconvolution and decompounding'. In: *Electronic Journal of Statistics* 13.2 (2019), pp. 3424–3452 (cit. on p. 9).

[85] A. M. Etheridge and T. G. Kurtz. 'Genealogical constructions of population models'. In: *The Annals of Probability* 47.4 (2019), pp. 1827–1910 (cit. on p. 8).

[86] D. R. Evans, M. P. Griffith, A. J. Sundermann, K. A. Shutt, M. I. Saul, M. M. Mustapha, J. W. Marsh, V. S. Cooper, L. H. Harrison and D. Van Tyne. 'Systematic detection of horizontal gene transfer across genera among multidrug-resistant bacteria in a single hospital'. In: *Elife* 9 (2020), e53886 (cit. on p. 4).

[87] A. Fievet, A. Ducret, T. Mignot, O. Valette, L. Robert, R. Pardoux, A. R. Dolla and C. Aubert. 'Single-Cell Analysis of Growth and Cell Division of the Anaerobe *Desulfovibrio vulgaris Hildenborough*'. In: *Frontiers in Microbiology* 6 (2015), p. 1378 (cit. on p. 3).

[88] R. A. Fisher. 'XV.—The correlation between relatives on the supposition of Mendelian inheritance.' In: *Earth and Environmental Science Transactions of the Royal Society of Edinburgh* 52.2 (1919), pp. 399–433 (cit. on p. 6).

[89] J. Fontbona and S. Méléard. 'Non local Lotka-Volterra system with cross-diffusion in an heterogeneous medium'. In: *Journal of Mathematical Biology* 70.4 (2015), pp. 829–854 (cit. on p. 6).

[90] N. Fournier and S. Méléard. 'A microscopic probabilistic description of a locally regulated population and macroscopic approximations'. In: *The Annals of Applied Probability* 14.4 (2004), pp. 1880–1919 (cit. on p. 4).

[91] C. Graham, J. Harmand, S. Méléard and J. Tchouanti. 'Bacterial metabolic heterogeneity: from stochastic to deterministic models'. In: *Mathematical Biosciences and Engineering* 17.5 (2020), pp. 5120–5133 (cit. on p. 8).

[92] S. C. Harris, S. G. Johnston and M. I. Roberts. 'The coalescent structure of continuous-time Galton–Watson trees'. In: *The Annals of Applied Probability* 30.3 (2020), pp. 1368–1414 (cit. on p. 8).

[93] S. C. Harris and M. I. Roberts. 'The many-to-few lemma and multiple spines'. In: *Annales de l'Institut Henri Poincaré, Probabilités et Statistiques* 53.1 (2017), pp. 226–242 (cit. on p. 8).

[94] P.-E. Jabin. 'Small populations corrections for selection-mutation models'. In: *Networks & Heterogeneous Media* 7.4 (2012), p. 805 (cit. on p. 4).

[95] P.-E. Jabin and Z. Wang. 'Quantitative estimates of propagation of chaos for stochastic systems with $W^{-1,\infty}$ kernels'. In: *Inventiones mathematicae* 214.1 (2018), pp. 523–591 (cit. on p. 7).

[96] J.-F. Jabir, D. Talay and M. Tomašević. 'Mean-field limit of a particle approximation of the one-dimensional parabolic-parabolic Keller-Segel model without smoothing'. In: *Electronic Communications in Probability* 23 (2018), pp. 1–14 (cit. on p. 7).

[97] A. Jüngel, S. Portisch and A. Zurek. 'Nonlocal cross-diffusion systems for multi-species populations and networks'. In: *arXiv preprint arXiv:2104.06292* (2021) (cit. on p. 5).

[98] A. N. Kapanidis, A. Lepore and M. El Karoui. 'Rediscovering bacteria through single-molecule imaging in living cells'. In: *Biophysical Journal* 115.2 (2018), pp. 190–202 (cit. on p. 3).

[99] J. F. C. Kingman. 'The coalescent'. In: *Stochastic processes and their applications* 13.3 (1982), pp. 235–248 (cit. on p. 8).

[100] M. Kubasch. 'Approximation of stochastic models for epidemics on large multi-level graphs'. Theses. Institut Polytechnique de Paris, July 2024. URL: https://theses.hal.science/tel-04717689 (cit. on p. 20).

[101] D. Lacker. 'On a strong form of propagation of chaos for McKean-Vlasov equations'. In: *Electronic Communications in Probability* 23 (2018), pp. 1–11 (cit. on p. 7).

[102] F. Lin and C. Wang. 'Recent developments of analysis for hydrodynamic flow of nematic liquid crystals'. In: *Phil. Trans. R. Soc. A* 372.2029 (2014), p. 20130361 (cit. on p. 5).

[103] P.-L. Lions and S. Mas-Gallic. 'Une méthode particulaire déterministe pour des équations diffusives non linéaires'. In: *Comptes Rendus de l'Académie des Sciences-Series I-Mathematics* 332.4 (2001), pp. 369–376 (cit. on p. 5).

[104] A. Marguet. 'Uniform sampling in a structured branching population'. In: *Bernoulli* 25.4A (2019), pp. 2649–2695 (cit. on p. 8).

[105] H. Martin, M. Doumic, M. T. Teixeira and Z. Xu. 'Telomere shortening causes distinct cell division regimes during replicative senescence in Saccharomyces cerevisiae'. In: *bioRxiv* (2021) (cit. on p. 8).

[106] S. Méléard and V. C. Tran. 'Nonlinear historical superprocess approximations for population models with past dependence'. In: *Electronic Journal of Probability* 17 (2012), pp. 1–32 (cit. on p. 8).

[107] J. Metz, S. A. Geritz, G. Meszéna, F. Jacobs and J. Van Heerwaarden. 'Adaptive dynamics: a Geometrical Study of the Consequences of Nearly Faithful Reproduction'. In: *Stochastic and Spatial Structures of Dynamical Systems*. North-Holland, 1996, pp. 183–231 (cit. on p. 4).

[108] J. R. Miller. 'Invasion waves and pinning in the Kirkpatrick–Barton model of evolutionary range dynamics'. In: *Journal of mathematical biology* 78.1 (2019), pp. 257–292 (cit. on p. 6).

[109] J.-M. Mirebeau and J. Portegies. 'Hamiltonian fast marching: A numerical solver for anisotropic and non-holonomic eikonal PDEs'. In: *Image Processing On Line* 9 (2019), pp. 47–93 (cit. on p. 6).

[110] S. Mirrahimi, G. Barles, B. Perthame and P. E. Souganidis. 'A Singular Hamilton–Jacobi Equation Modeling the Tail Problem'. In: *SIAM Journal on Mathematical Analysis* 44.6 (2012), pp. 4297–4319 (cit. on p. 4).

[111] S. Mirrahimi and G. Raoul. 'Dynamics of sexual populations structured by a space variable and a phenotypical trait'. In: *Theoretical Population Biology* 84 (2013), pp. 87–103 (cit. on p. 6).

[112] S. Motsch and D. Peurichard. 'From short-range repulsion to Hele-Shaw problem in a model of tumor growth'. In: *Journal of mathematical biology* 76.1-2 (2018), pp. 205–234 (cit. on p. 5).

[113] M. Nagasawa. 'Time reversions of Markov processes'. In: *Nagoya Mathematical Journal* 24 (1964), pp. 177–204 (cit. on p. 8).

[114] K. Oelschläger. 'Large systems of interacting particles and the porous medium equation'. In: *Journal of Differential Equations* 88.2 (1990), pp. 294–346 (cit. on p. 5).

[115] K. Oelschläger. 'On the derivation of reaction-diffusion equations as limit dynamics of systems of moderately interacting stochastic processes'. In: *Probability Theory and Related Fields* 82.4 (1989), pp. 565–586 (cit. on p. 5).

[116] E. A. Perkins. *On the martingale problem for interactive measure-valued branching diffusions*. Vol. 549. American Mathematical Soc., 1995 (cit. on p. 8).

[117] B. Perthame. *Parabolic equations in biology*. Lecture Notes on Mathematical Modelling in the Life Sciences. Springer, Cham, 2015, pp. xii+199. DOI: 10.1007/978-3-319-19500-1. URL: http://dx.doi.org/10.1007/978-3-319-19500-1 (cit. on p. 3).

[118] B. Perthame. *Transport equations in biology*. Frontiers in Mathematics. Basel: Birkhäuser Verlag, 2007, pp. x+198 (cit. on p. 3).

[119] B. Perthame and G. Barles. 'Dirac concentrations in Lotka-Volterra parabolic PDEs'. In: *Indiana University Mathematics Journal* (2008), pp. 3275–3301 (cit. on p. 4).

[120] B. Perthame and M. Gauduchon. 'Survival thresholds and mortality rates in adaptive dynamics: conciliating deterministic and stochastic simulations'. In: *Mathematical Medicine and Biology: a journal of the IMA* 27.3 (2010), pp. 195–210 (cit. on p. 4).

[121] M. Rera, R. I. Clark and D. W. Walker. 'Intestinal barrier dysfunction links metabolic and inflammatory markers of aging to death in *Drosophila*'. In: *Proceedings of the National Academy of Sciences* 109 (Dec. 2012), pp. 21528–21533 (cit. on p. 21).

[122] L. Robert, J. Ollion, J. Robert, X. Song, I. Matic and M. Elez. 'Mutation dynamics and fitness effects followed in single cells'. In: *Science* 359.6381 (2018), pp. 1283–1286 (cit. on pp. 9, 11, 22).

[123] G. R. S. Boucenna and V. Dakos. 'Evolutionary outcomes arising from bistability in ecosystem dynamics'. 2023 (cit. on p. 19).

[124] S. Taheri-Araghi, S. Bradde, J. T. Sauls, N. S. Hill, P. A. Levin, J. Paulsson, M. Vergassola and S. Jun. 'Cell-Size Control and Homeostasis in Bacteria'. In: *Current Biology* 11679.1-7 (2015) (cit. on p. 11).

[125] D. Talay and M. Tomašević. 'A new McKean–Vlasov stochastic interpretation of the parabolic–parabolic Keller–Segel model: The one-dimensional case'. In: *Bernoulli* 26.2 (2020), pp. 1323–1353 (cit. on p. 6).

[126] J. Tchouanti. 'Well posedness and stochastic derivation of a diffusion-growth-fragmentation equation in a chemostat'. preprint. 2021 (cit. on p. 7).

[127] M. Tomasevic. 'A new McKean–Vlasov stochastic interpretation of the parabolic-parabolic Keller–Segel model: The two-dimensional case'. In: *The Annals of Applied Probability* 31.1 (2021), pp. 432–459 (cit. on p. 6).

[128] M. Tomasevic. 'On a probabilistic interpretation of the Keller-Segel parabolic-parabolic equations'. Theses. Université Côte d'Azur, Nov. 2018. URL: https://tel.archives-ouvertes.fr/tel-01932777 (cit. on p. 7).

[129] M. Tomasevic. 'Propagation of chaos for stochastic particle systems with singular mean-field interaction of $L^q - L^p$ type'. preprint. 2020 (cit. on p. 6).

[130] M. Tomasevic, A. Véber and V. Bansaye. 'Ergodic behaviour of a multi-type growth-fragmentation process modelling the mycelial network of a filamentous fungus'. preprint. 2020 (cit. on pp. 9, 10).

[131] M. Tournus and Xue. 'Insights into the dynamic trajectories of protein filament division revealed by numerical investigation into the mathematical model of pure fragmentation'. In: *PLOS Computational Biology* 17.9 (Sept. 2021), pp. 1–21. DOI: 10.1371/journal.pcbi.1008964. URL: https://doi.org/10.1371/journal.pcbi.1008964 (cit. on p. 8).

[132] H. Tricoire and M. Rera. 'A new, discontinuous 2 phases of aging model: Lessons from Drosophila melanogaster'. In: *PLOS One* 10.11 (2015), e0141920 (cit. on pp. 12, 21).

[133] A. Y. Veretennikov. 'On mean-field (GI/GI/1) queueing model: existence and uniqueness'. In: *Queueing Systems* 94.3 (2020), pp. 243–255 (cit. on p. 7).

[134] D. Volfson, S. Cookson, J. Hasty and L. S. Tsimring. 'Biomechanical ordering of dense cell populations'. In: *Proceedings of the National Academy of Sciences* 105.40 (2008), pp. 15346–15351 (cit. on p. 5).

[135] P. Wang, L. Robert, J. Pelletier, W. L. Dang, F. Taddei, A. Wright and S. Jun. 'Robust Growth of *Escherichia coli*'. In: *Current Biology* 20.12 (2010), pp. 1099–103 (cit. on p. 3).

[136] D. Waxman and S. Gavrilets. '20 questions on adaptive dynamics'. In: *Journal of evolutionary biology* 18.5 (2005), pp. 1139–1154 (cit. on p. 4).

[137] Z. You, D. J. Pearce, A. Sengupta and L. Giomi. 'Geometry and mechanics of microdomains in growing bacterial colonies'. In: *Physical Review X* 8.3 (2018), p. 031065 (cit. on p. 5).

[138] H.-P. Zhang, A. Be'er, E.-L. Florin and H. L. Swinney. 'Collective motion and density fluctuations in bacterial colonies'. In: *Proceedings of the National Academy of Sciences* 107.31 (2010), pp. 13626–13630 (cit. on p. 9).