J-Biot 2025, 24-25 novembre
Les 1ères Journées de la Biologie Théorique

Jour 1 Lundi 24 novembre

8h30 Welcome-Accueil

9h Guillaume Beslon *Structural mutations set an equilibrium non-coding genome fraction*

The fraction of coding vs non-coding DNA is highly variable across the Tree of Life. Despite decades of debate, its determinants are still unknown. While some parts of the non-coding DNA arguably have a regulatory function, a large part does not seem to have a detectable impact on any phenotypic trait, the so-called Junk DNA. As such, the abundance of non-functional DNA in the vast majority of genomes throughout the Tree of Life challenges purely adaptationist explanations.

Historically, the debate on the evolutionary determinants of non-coding sequences has focused mainly on the question of selection, drift, and the balance between the two. But while these two forces are undoubtedly at the heart of evolution, evolution also requires a third force: variation. Indeed, one can state with absolute certainty that the genome architecture, and specifically the amount of non-coding sequences in a genome, can only vary through mutational events, including chromosomal rearrangements and small indels. Yet, the precise way these different types of mutations interact with the genome architecture has never been investigated in detail.

Starting from this very simple idea, we propose a mathematical model of the evolution of non-coding sequences. Assuming that the genome is partitioned into neutral and selected segments, we modeled various types of mutations susceptible to change the amount of non-coding sequences (typically chromosomal rearrangements and indels). By computing the probability for these events to be neutral or deleterious, we show that the non-coding fraction of the genome is shaped by two factors: unavoidable biases in the neutrality of the different mutation types (adding base pairs is more likely to be neutral than removing some), and strong robustness constraints imposed by the mere existence of chromosomal rearrangements. Indeed, rearrangements are more frequent and, on average, larger in larger genomes, imposing a strong second-order selection on genome size. We show that these two factors ensure the existence of an equilibrium non-coding fraction, which depends solely on the product of population size and mutation rate. Hence, by playing on these two factors – and on their product – the model is able to reproduce the full diversity of genomic architectures, from prokaryotes, for which it predicts a dense genome with a low, tightly constrained fraction of junk-DNA, to multicellular eukaryotes for which it predicts the accumulation of a substantial fraction of junk-DNA.

Reference: Luiselli, J., Banse, P., Mazet, O., Lartillot, N. and Beslon, G. (2025). Structural mutations set an equilibrium non-coding genome fraction. bioRxiv, 2025-02.

9h50 Erwan Hingant *Population model of quorum sensing.*

In 2013, Brown introduced a model for quorum sensing which exhibits bistability. We discuss two generalization to population model, the Metz and Diekmann approach and a model which keeps fluctuations in molecules transport. The second approach preserves bistability at the population level.

10h20 Aurélien Tauzin *Estimating bacterial mutation rate with simulation-based methods (ABC)*

The mutation rate is a key parameter of evolution as it defines the speed at which genetic diversity is generated de novo. It is defined as the number of mutation occurring per base pair per cell division (equal to generation for asexual organisms). A traditional approach to estimate mutation rate for bacteria is the fluctuation test, which consists in growing bacteria in a non-selective medium for then plating them in a selective environment in order to reveal the number of mutants (survivors) carrying a resistance to that stress. A mathematical model is then fitted on these experimental data to infer mutation rate. However, model makes restrictive assumptions regarding the effect of the mutations on the fitness (no effect) and the growth conditions (no death in the culture) which probably do not represent reality. The objective of my work is to develop a new simulation-based computational method for the inference of mutation rate from experimental data (fluctuation tests), taking into account non-standard demographics (death) and fitness effect of the mutation. My approach relies on Approximate Bayesian Computations: it consists in using a simulator combined with MCMC algorithms (Metropolis-Hastings) to find the parameters which best explain the experimental data. We tested it on two types of tasks: estimation of 1 parameter : mutation rate, when other parameters (death rate and fitness effect) are known, and simultaneous estimation of 2 parameters : mutation rate and fitness effect or mutation rate and death rate. This method already provides satisfying results. It competes well with the reference tools (rSalvador, which uses the Ma-Sandri-Sarkar maximum likelihood estimator, and Flan's probability generating function) in simple scenarios where these tools work. Due to its simulation-based nature, it can also generalize to more complex scenarios where these reference methods do not work.

10h35 Coffee Break Posters

11h15 Sophie Pantalacci *Serial organs as toy models to reconcile the many views on pleiotropy and its role in evolution*

Despite its significance across biology, the concept of "gene pleiotropy" remains elusive, with varied interpretations across different fields. This ambiguity, combined with challenges in direct measurement and experimental manipulation, has led to contradictory viewpoints in the literature, as well as different expectations on how pleiotropy influences adaptation and shapes evolutionary trajectories at both genetic and phenotypic levels. Our team uses the development and evolution of serial organs, in the form of the lower and upper molar, as a toy model to understand pleiotropy and its role in evolution. To achieve this goal, we marry experimental work and a new modeling framework that bridges multiple scales of biological systems, i.e. genotype, molecular activity during development, phenotype and organ function, as well as the timescales of development and evolution. We will briefly review our experimental results and present our modeling framework, where pleiotropy emerges bottom-up from these different biological scales and throughout evolutionary time as populations evolve under selection. We will review the first results obtained with this multiscale modeling framework, that reconcile observations from different fields rather than opposing them. Finally, we will open on future work towards an integrated understanding of pleiotropy.

11h45 Sergiu Ivanov *The Busy Beaver Game and Natural Selection: The Case of Rozenberg's Reaction Systems*

The busy beaver game was introduced by Tibor Radó in 1962 and consists in finding the longest halting run that can be achieved by a Turing machine with a given number of states n. The function BB(n) measuring this length is a well-studied example of an uncomputable function—a function which cannot be computed by any algorithm. In this work, we transpose the concept of the busy beaver game to reaction systems—a set rewriting-based model of computing inspired by biochemical reactions. We give a generalized framework for defining various busy beaver challenges and give concrete instantiations for longest runs, periods, preperiods, etc. We propose our busy beaver framework as a tool for metaphorically representing natural selection, since the busy beaver champions can be seen as being the most fit to a particular selection criterion. On the other hand, we follow the direction of considering reaction systems for simplified representation of individuals. We discuss the potential applications of using these theoretical tools to thinking about natural selection and the origins of Life.

12h15 Eric Fanchon *The Waddington landscape today*

The Waddington landscape, also known as the epigenetic landscape, is a metaphor for cell differentiation during development proposed in the 1940s. It has been highly influential and is still referenced today. After a brief historical overview, we will examine the limitations of this metaphor, the modeling ideas based on it, and its current applications.

12h45 Lunch Posters

14h15 Diane Peurichard *Mathematical modeling of tissue morphogenesis and regeneration*

In this talk, we investigate the mechanisms by which organs acquire their functional structure and rebuild their architecture after injury. We do this by the development of Individual Based Models (IBM) confronted to experimental data. We first propose and study a simple model for architecture emergence, featuring cells (2D spheres) appearing and growing in a dynamical network of cross-linked fibers (connected segments). Cells and fibers are supposed to interact via mechanical repulsion interactions. When applied to adipose tissues, the model produces structures that compare quantitatively well to the experimental observations and seems to indicate that cell clusters could spontaneously emerge as a result of simple mechanical interactions between cells and fibers. By suggesting that vasculature could be secondary to tissue architecture emergence, this simple model therefore proposes a new view of tissue development. In the second part of the talk, we extend the model to account for mechanisms of tissue repair after injury, and use it to explore the mechanisms responsible for adipose tissue regeneration. The model successfully generates regeneration or scar formation as functions of few key parameters, and indicates that the fate of injury outcome could be mainly due to extra-cellular (ECM) matrix rigidity. Via a combined in-vivo / in-silico approach, the model enables to identify a new in-vivo validated therapeutic target, enabling to induce regeneration in mouse adipose tissues. Altogether, these studies point to the essential role of mechanics in tissue structuring and regeneration, and bring a comprehensive view on the role of ECM crosslinking on tissue architecture emergence and reconstruction.

15h05 Olivier Ali *Hidden in plain stress: Exploring the relationship between pressure-induced stresses and geometry in plant tissues.*

Mechanical stresses play a central role during the morphogenesis of multicellular structures. Not only do they generate tissue deformations but they also provide cells with signals triggering differentiation and pacing development. This is especially true in growing plant epthelia where turgidity generates tremendous stresses within cell walls. From a systematic perspective, one can wonder what kind of signaling cues, turgor-induced stresses can provide growing cells with? In this presentation, we will see how such stresses can be related to a specific kind of geometrical descriptors of surfaces: Killing

and "pseudo"-Killing vectors fields.

15h35 Johanne Auriau *The Topological signature of the heart*

The precise arrangement of the deep cardiac myoarchitecture remains a matter of debate, as evidenced by the variety of proposed models. To provide an accurate description, our team developed a quantitative polarized light imaging (Q-PLI) macroscope that can measure the mean orientation of myofibers on a whole-organ scale with a resolution of 90 x 90 x 500 µm. In 2020, we made a breakthrough by demonstrating that the ventricular myocardium is analogous to a nematic chiral liquid crystal (NCLC). Punctual topological singularities (TSs) therefore emerged in areas where myofibers converged or changed direction abruptly. The first step consisted of a visual identification and characterisation of punctual TSs among our collection of perinatal hearts without developmental anomalies (n = 23). The second step consisted of an automated and replicable identification of TSs among the same collection using a mathematical algorithm. The number of +1/2 TSs was higher than the number of -1/2 TSs ($p<0.001$). Specific TSs were identified in distinct anatomical structures: isolated -1/2 TSs in the anterior and posterior parts of the interventricular septum (IVS); isolated +1/2 TSs at the inner extremities of ventricular trabeculations. In conclusion, this work will allow us to provide a more accurate cardiac myoarchitecture model based on biological data, while accounting for real-life heterogeneity.

15h50 Nicolas Louviaux *A biomechanical cell motility model to study long range cell communication*

Cell migration is a biological process during which cells adhere to their environment (the extra-cellular matrix) in order to drag their nucleus by contraction of their cytoskeleton. This traction effectiveness depends on the mechanical properties of the ECM that cells are able to perceive thanks to mechanosensors. This probing capacity results in cells migrating along stiffness gradients, referred to as durotaxis. The cell activity also remodel the cell environment by deforming, degrading or synthetizing it, which modifies its mechanical properties. Thus the cell-ECM interaction is bidirectional. The question I aim to study is what is the influence of the mechanical properties variations of the ECM (induced by a migrating cell) on other cells migrating in a neighborhood. Can they detect one another, what is the detection range, do they tend to gap close to finally encounter ? To study those questions, I develop a biomechanical single cell model coupled with a deformable substrate. I will present the analysis of the model on non deformable substrate to highlight the influence of the dynamic substrate on the migration patterns.

16h05 Coffee Break Posters

16h45 Maxime Renard *Viscoelastic fluid modeling for biological tissues under large deformations*

Mechanical properties of living tissues have been investigated for a few decades in the context of morphogenesis. A possible approach includes in vitro rheology experiments. The work to be presented attempts to use continuum fluid mechanics models to reproduce behaviors of F9 cells observed in a contraction geometry. Viscoelastic properties of such tissues lead to the use of Oldroyd and FENE-P models, implemented with a finite element method. Parallel computation tools and optimization techniques are used for efficiency. Good fits are obtained in some regions of the geometry. The discrepancies suggest the introduction of a yield criterion may improve comparisons.

17h Clement Moulin-Frier *Self-organization of Sensorimotor Agents and Ecosystems through Automated Discovery in the Lenia Cellular Automaton*

Continuous cellular automata, such as Lenia, enable the simulation of a large diversity of self-organized patterns (SOP) in a unified formalism. However, discovering interesting and diverse patterns capable of, for example, autopoiesis or reproduction, is a challenging problem. I will present algorithmic methods whose objective is to automate the discovery of a wide diversity of SOP in cellular automata (and more generally in any complex system). I will then show some of the discoveries made using these methods. These concern, on the one hand, the discovery of sensorimotor agents in Lenia – that is, SOP capable of self-constitution, self-maintenance and exhibiting behaviors robust to perturbations. On the other hand, I will show how proto-evolution, i.e., the formation of diverse SOP in cooperation or competition within the same simulation, can emerge in such system.

17h15 Maxime Estavoyer *Exploring morphogenetic pattern formation through a spectral approach*

Pattern formation is a fundamental process in development, arising from the combined action of cell motility, gene regulation, division dynamics, and apoptosis. However, quantifying the contribution of each of these factors to the emergence of spatial structures remains challenging. In collaboration with Matthias Merkel, we have developed a method based on a Bessel–Fourier mode decomposition to assess these contributions. Applying this approach to aggregates of stem cells expressing Brachyury, as well as to agent-based models simulating various pattern-formation scenarios, reveals a complex interplay among these processes. By linking individual trajectories to collective structures, our method provides a powerful tool for deciphering the dynamics underlying pattern formation during morphogenesis.

17h45 Mathieu Dedenon *An agent-based model for active nematics and beyond*

Biological cellular tissues often exhibit large domains of orientational order, separated by topological defects where orientation is ill-defined. This interplay of nematic order and activity has been explored based on two-dimensional continuum theory. More complex phenomena, like three-dimensional growing tissues, remain largely unexplored theoretically. We propose an agent-based model that describes cells as linear multi-particle filaments. We incorporate mechanical activity in terms of individual cell force dipoles, either contractile or extensile, giving rise to an active nematic stress. We recapitulate the active flow transition with extensile active stress and self-propulsion of +1/2-defects, in agreement with the hydrodynamic theory. In addition, we discovered unreported correlations between density and nematic orientation. With this versatile framework, we plan to explore three-dimensional geometries in the future, studying the interplay of mechanical and growth-based activity.

18h15 Assemblée Générale de la SFBT

Jour 2 Mardi 25 novembre

8h30 Welcome-Accueil

9h Olivier Gandrillon *Multiscale modeling of the spatial structure of cancer stem cells in tumoroids derived from neuroblastoma patients*

I will present the use of an original muliagent multiscale modelling approach to try to capture the specific spatial positioning of cancer stem cells with neuroblastomas patient-derived tumoroids (PDTs)—3D ex vivo structures mimicking the original tumor.

I will demonstrates the critical role of spatial stem-to-stem cell short-range signaling in PDTs organization and highlights the value of a multiscale approach to identify the minimal mechanisms required for their formation.

9h50 Martin Rosalie *Variable selection using global modelling tool: summer blooms of the algae Ostreopsis cf. ovata*

Global modelling is a tool for constructing systems of differential equations from time series. We present one use of this tool for variable selection. We study the bloom of the toxic algae (*Ostreopsis* cf. *ovata*) and look for strong relationships between the alga and its environment through the lens of dynamics. Using time series, we have highlighted the links that exist between the proliferation of this algae and salinity, oxygen, or nutrient concentrations over time.

10h20 Emma Crisci *Constraint-Driven Enumeration of Biologically relevant Elementary Flux Modes in Metabolic Networks Using Hybrid Logic-Linear Programming*

Metabolism covers all biochemical reactions sustaining life, both catabolic and anabolic, and can be modeled as oriented hypergraphs linking substrates to products. At steady state, the net production of internal metabolites is zero, ensuring balanced consumption and production. Elementary Flux Modes (EFMs) are minimal reaction sets defining feasible steady-state pathways. They describe the steady-state flux space, but their number grows combinatorially, making full enumeration impractical, and many EFMs are biologically irrelevant. We propose a method to enumerate only biologically meaningful EFMs by integrating explicit biological constraints. EFM-aspLPx combines logic programming with a linear solver through ClingoLPx, pruning non-relevant paths and reducing computation time and memory. Thermodynamic constraints, based on Gibbs free energies, restrict metabolite concentrations to realistic ranges. Applied to E. coli central metabolism, this efficiently filters EFMs and improves performance. Extensions will include enzyme cost constraints, limiting total enzyme usage.

10h35 Coffee Break Posters

10h20 Federica Padovano *Modelling the efficacy of CIK cell immunotherapy targeting MET-expressing mesothelioma cells*

Mesothelioma is a highly aggressive cancer of the mesothelial lining whose incidence continues to rise, mainly due to asbestos exposure and the long latency between exposure and disease onset. Given the limited efficacy of current treatments, novel immunotherapeutic strategies are being explored, including the use of CIK immune cells engineered with a MET-specific receptor to target MET-overexpressing tumours. We combine experimental and mathematical modelling approaches to investigate the interaction dynamics between tumour and CIK cells, focusing on the influence of tumour MET expression on CIK-mediated cytotoxicity. Ex vivo data from mesothelioma and CIK cell lines are used to inform, calibrate, and validate a mathematical model that incorporates a partial integro-differential equation describing cancer cell dynamics structured by MET expression level. The model is then employed to explore tumour–CIK combinations and predict outcomes under yet-untested experimental conditions.

11h30 Lia Sela *Modélisation mathématique des interactions entre macrophages et cellules épithéliales précancéreuses dans la cavité buccale*

Oral squamous cell carcinoma (OSCC) represents the vast majority of oral cancers and is associated with high mortality. Patients with Oral Potentially Malignant Disorders (OPMD) present a risk of developing OSCC, and identifying OPMD with a high risk of malignant transformation remains a critical clinical issue. Macrophages constitute a major immune population infiltrating the tumor microenvironment during carcinogenesis. Previous studies have reported conflicting results on the impact of M2 macrophages enrichment in the risk of OPMD malignant transformation. Foy et al. found a positive association between M2 macrophages enrichment and oral cancer-free survival in OPMD. In this work, we perform immune deconvolution and gene set enrichment analyses using OPMD gene expression data. Then we build a system of two phenotypically-structured partial differential equations comprising two cell populations : epithelial cells and macrophages. Numerical results with various parameter configurations provide biological insights into the model, with the perspective of gaining a better understanding of the drivers of malignant transformation.

11h45 Damian Bimbenet *Exploring how metabolism comes into play with radiations: an agent-based modelling approach*

The reciprocal interactions between ionising radiation (IR) and glucose metabolism in mammalian cells have gained interest over these last decades. While reactive oxygen species (ROS) and HIF-1α emerge as key mediators in these interactions, the influence of ROS on HIF-1α following irradiation is still being debated. We developed a hybrid multiscale model on Physicell that combines continuous equations for the intracellular regulation processes defining the cell metabolic state and an agent-based system to describe this metabolic state and its consequence in each individual cell in the spheroid exposed to IR. Since different intermediates between ROS and HIF-1α have been proposed by biologists, we decided to consider a generic component which influences the activity of HIF-1α and whose expression is mediated by ROS. Our model thus highlights for the first time the relative importance of the key components and intermediates in the ROS-HIF relationship in cells under irradiation.

12h Botao Dai *Response to irradiation: role of hypoxia*

More than 50% of patients with cancer receive radiotherapy to kill tumor cells. Several mathematical models predicting post-irradiation cell survival are used clinically to plan treatment; however, they often neglect the tumor microenvironment, which can modulate radiotherapy response. A key driver of radioresistance in solid tumors is hypoxia.

In this project, we focus on hypoxia-induced radioresistance. Our experiments are designed to quantify how reduced oxygen levels before and after irradiation affect survival and post-treatment dynamics. The resistance is attributed to mechanisms such as diminished oxygen fixation of radiation-induced DNA damage (lower radical yield), hypoxia-driven cell-cycle slowing or quiescence, and stress-response programs that enhance repair and persistence.

We also present a biologically motivated compartmental model describing the temporal evolution of distinct subpopulations after irradiation (e.g., repaired, senescent, and unrepaired cells). By fitting time-course data, the model estimates key transition rates and will be adapted to incorporate oxygen dependence, enabling accurate simulation of cellular responses under hypoxic conditions. This work provides insight into oxygen-dependent responses of cancer cells to radiation, informing more effective and context-aware therapeutic strategies.

12h15 Laurence Cherfils *Modèle mathématique pour la croissance tumorale et la cinétique de lactate dans les gliomes*

Gliomas are among the most prevalent and invasive forms of brain tumors. Except for grade I gliomas, which can be cured following complete surgical resection, the prognosis remains poor for grade II to IV gliomas despite radiotherapy and chemotherapy. Recent studies have highlighted the key role of lactate in tumor growth, leading to the emergence of novel therapeutic strategies targeting lactate metabolism.

In this talk, I will present mathematical models, formulated as partial differential equations, that describe the temporal evolution of tumor cell density together with lactate kinetics within the tumor microenvironment. Two therapeutic approaches are incorporated into the model: a chemotherapy treatment and a targeted therapy acting on lactate production or transport. These treatments are modeled as control functions, and our objective is to determine an optimal therapeutic strategy — that is, patient-specific dosages that minimize side effects while preserving treatment efficacy.

I will discuss analytical results related to these models and illustrate them through numerical simulations. I will conclude by presenting ongoing collaborative work with clinicians from the University Hospital of Poitiers and biologists from the IBGC laboratory in Bordeaux. This current project focuses on an “augmented” model that simultaneously describes the dynamics of glioma, lactate, and glutamate within the brain.

12h45 Lunch Posters

14h15 Annabelle Ballesta *Systems pharmacology and machine learning for optimizing treatments of brain tumors*

Glioblastoma (GBM), the most frequent and aggressive brain tumor in adults, is associated with a dismal prognostic despite intensive treatment involving surgery, radiotherapy and temozolomide (TMZ)-based chemotherapy. The initial or acquired resistance of GBM to TMZ appeals for precision medicine approaches for the design of novel efficient combination pharmacotherapies. To that end, a comprehensive approach combining quantitative systems pharmacology (QSP) and machine learning was undertaken to design TMZ-based drug combinations circumventing the initial resistance to the alkylating agent. A QSP model representing TMZ cellular pharmacokinetics-pharmacodynamics and dysregulated pathways in GBM based on ordinary differential equations was developed and validated using multi-type time- and dose-resolved datasets. In silico drug screening based on numerical optimization and subsequent experimental validation identified a strategy to re-sensitize TMZ-resistant cells consisting in combining TMZ with inhibitors of the base excision repair and of homologous recombination. Using machine learning, model parameters driving response to such optimal multi-agent therapy were derived to assist decision making in patients. Thus, we successfully demonstrated the relevance of combined QSP and machine learning to design efficient drug combinations re-sensitizing glioblastoma cells initially resistant to TMZ. The developed framework may further serve to identify personalized therapies and administration schedules by extending it to account for additional patient-specific altered pathways and whole-body features.

15h05 Jean Clairambault *The animal body plan revisited and cancer as local failure of its maintenance in tissues*

The body plan of multicellular animals is revisited as the program of construction, contained in the zygote as a self-extracting archive - and later borne in all nucleated cells of any given multicellular animal -, which is launched at fecundation. It unfolds in embryogenesis by a succession of differentiation branchings in the cellular matter produced by successive cell proliferations, leading to the different cell types a multicellular organism - in its achieved form - is made of, 20 for the sponges Porifera, 200 to 400 for Humans. The body plan, once has been physically achieved as coherent and viable the animal multicellular organism forwhich it is designed, must be maintained in the different constituting tissues and organs of the organism by local cohesion control mechanisms, some of which might be linked to the permanent action of tissue resident macrophages, already present from early embryogenesis. Cancer is a disease of animal multicellular organisms only, and its beginning always occurs in a given tissue, in which some such cohesion controls fail, firstly on differentiation, secondly on proliferation. This is a theoretical investigation of possible control mechanisms of tissue cohesion maintenance failed in cancer, attempting in particular at eliciting a role for resident macrophages in such local tissue maintenance.

15h35 Thibault Delobel *Integrating glioblastoma plasticity into combination therapy strategies to overcome therapeutic resistance: a quantitative systems pharmacology approach*

Glioblastoma (GBM) is the most aggressive primary brain tumor in adults, with a median survival below 18 months and no curative therapy available. To explore mechanisms of resistance to temozolomide (TMZ), the standard-of-care chemotherapy, we performed proteomic profiling of 12 patient-derived cell lines (PDCLs) treated or not with TMZ. Pathway enrichment and independent component analyses revealed strong inter-patient heterogeneity. Commonly deregulated proteins across PDCLs were matched to pharmacological compounds through a dedicated pipeline, and candidate molecules are now under drug screening. The next step is to build a digital twin for each PDCL, enabling personalized prediction of combination therapies. A previously developed mathematical model of TMZ pharmacokinetics-pharmacodynamics serves as a foundation. To initiate model individualization, we personalized model parameters using publicly available multi-omics and TMZ cytotoxicity data. Current work focuses on integrating proteomics-derived key species into the core model, via network reconstruction methods.

15h50 Arnaud Millet *Spatial organization of mediated-macrophage chemoprotective niches in solid tumors: A mathematical analysis*

Acquired resistance is one of the major causes of failure of standard therapies in cancer patients. Chemotherapeutic agents are still widely used and the understanding of the mechanisms leading to secondary resistance to these molecules are still puzzling. Recently, the role of the tumor immune microenvironment has been recognized. Among the cells potentially involved, macrophages seem to be the perfect culprits. In a previous work, we have shown that hypoxic macrophages are able to provide strong protection against 5-fluorouracil, a first-line chemotherapeutic agent in digestive cancers. In the present work, we use mathematical modeling to explore the spatiotemporal aspects of the treatment-induced organization of the tumor environment. Based on analytical and numerical analysis, we propose that macrophage-driven protection against chemotherapy under treatment does not rely solely on biochemical degradation, but is enhanced by the emergence of spatially structured chemotherapeutic protective niches. This work paves the way for the development of new therapeutic strategies that rely on targeting the spatial organization of tumors as a way to control treatment resistance.

16h20 Coffee Break Posters

17h Mathilde Badoual *Modeling the spatiotemporal evolution of irradiated cell populations*

More than 50% of cancer patients undergo radiotherapy. Currently, treatment plans rely on the linear-quadratic model, which predicts survival fraction but does not account for the temporal dimension. Spatiotemporal models of the effect of irradiation on tumor growth could contribute to improving radiotherapy. In this work, we combine real-time fluorescence microscopy experiments (to track the cell density of F98 glioma cells under different irradiation doses and initial cell densities) with mathematical modeling to characterize the temporal response of a cancer cell population to a single irradiation. The model very accurately reproduces all experimental data, with only three free parameters. It allows us to access and track the evolution of different cell populations after irradiation, particularly senescent and repaired cell populations. Survival fractions can also be estimated. Our model allows us to analyze and quantify the inhibitory effect (or cohort effect) of dead and senescent cell populations on the regrowth of repaired cells. The model is also used to model the evolution of cell populations subjected to spatially structured irradiation.

17h30 Tri Nguyen-Huu *Can spatial heterogeneity and connectivity improve fishery management?*

Sustainable exploitation of renewable resources requires balancing ecological integrity and production objectives. In fisheries, maximizing yield (Maximum Sustainable Yield), profit (Maximum Economic Yield), and ecosystem resilience are often conflicting goals, potentially leading to overexploitation or fish population collapses. We investigate through mathematical models (metapopulations and PDE models) how spatial heterogeneity and connectivity profoundly influence these trade-offs by shaping population dynamics and ecosystem stability. We present recent theoretical insights into how spatial structure affects catch, profit, and resilience, and how emergent spatial effects can inform optimal management strategies, including the design and placement of Marine Protected Areas.

18h00 Remise Prix Pierre Delattre

Posters

D'Urso Mariapia *State and Parameter Estimation in Bioprocess Digital Twins via Back-and-Forth Adaptive Extended Kalman Filtering*

Improving the control of bioprocesses has importance for optimizing production scale-up and enhancing both environmental and economic sustainability. Furthermore, enabling efficient testing of operational conditions helps save time and reduce costs. In the presence of precise model parametrization, digital twins of bioreactors represent a promising tool, since they allow simulations of different operational conditions without the need for additional experiments. Traditionally, non-linear observers like the adaptive Extended Kalman Filter (EKF) are used to extract unknowns in digital twins like reaction rates. In this work we compare the standard method of running the observer for a single forward pass in time, to repeatedly reversing time, running the observer back-and-forth multiple times. Benchmarks on simulated and experimental growth models show promising results, with the back-andforth method significantly improving the estimation accuracy.

Grohens Théotime *The benefits of pleiotropy for adaptive evolution in an in silico model of serial organ evolution*

Pleiotropy is often considered to act as a brake on evolution: a mutation that might have a positive effect in a given organ can be counter-selected if it is deleterious in another organ. Serial organs offer a particularly interesting model to study this hypothesis, because they share a common (pleiotropic) developmental program that is modulated by organ-specific (modular) identity genes. In theory, modular - rather than pleiotropic - mutations should therefore mainly be responsible for phenotypic variation in a given organ. However, experimental evidence from our lab has shown that pleiotropic developmental changes can support adaptive phenotypic change in one organ (upper molar), while they are compensated in another organ (lower molar), leaving its phenotype unchanged. This discrepancy suggests a previously overlooked decoupling between developmental and phenotypic pleiotropy, which we investigate in this work.

Préaubert Angélique *What does drive iterative Pattern Formation during Tooth Development ?*

Tooth morphogenesis is a complex process driven by the interplay of Mechanical Forces and molecular Signaling Pathways, particularly within specialized signaling centers called Enamel Knots (EKs). In molars, the formation of cusps involves a series of EKs that guide the iterative Epithelial-Mesenchymal interactions shaping the tooth: one for the initiation of the tooth row, one for the molar (PEK) and one for each molar cusp (SEKs). However, what does drive the transition from PEK to SEK in the developing molar remains poorly understood.

Bimbenet Damian *Exploring how metabolism comes into play with radiations: an agent-based modelling approach*
Louviaux Nicolas *A biomechanical cell motility model to study long range cell communication*
Auriau Johanne *The Topological signature of the heart*