Modeling of life in Toulouse: from the atom to the animal

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Toulouse

Programme Scientifique

Tutorial on mathematical models

Manon Costa (IMT)

Tutorial on mathematical models for the evolution of populations

In this talk I will present how to model the evolution of a natural population using different random or deterministic processes, as well as the links between the models. The aim is to make this talk as accessible as possible.

Protein conformation and dynamics

Juan Cortés (LAAS-CNRS)

Generative models and analysis tools for investigating highly-flexible (intrinsically disordered) proteins

Proteins can have very different architectures, generally involving a concatenation of relatively rigid domains and flexible regions. Indeed, many proteins in eukaryotes, prokaryotes and viruses are composed of several domains connected by linkers, and flexible tails are also frequently found at the termini of rigid domains. Besides, flexible loops connecting secondary structure elements within domains are omnipresent in proteins. All these types of flexible regions (linkers, tails and loops), in addition to fully flexible, intrinsically disordered proteins, play key functional roles, usually related to inter- or intramolecular interactions.

While the structure of rigid domains can be accurately determined using experimental methods or predictors such as AlphaFold2, the structural study of flexible regions remains a challenge. It requires computational methods for the generation of conformational ensemble models that are fitted or refined on the basis of experimental measurements. In recent years, we have developed several algorithms, based on fragment databases and robotics-inspired techniques, for the conformational sampling of flexible loops and intrinsically disordered regions. Building on this work, we propose a unified approach to sample conformations of proteins with complex architectures composed of rigid and flexible regions. Our approach integrates a multi-agent reinforcement learning technique to improve sampling performance while taking into account the specificities of each flexible/disoriented region of the protein. In addition to these generative models, we have developed statistical tools for the analysis and comparison of conformational ensembles of highly-flexible proteins.

Matthieu Chavent (CBI - LMGM)

MD simulations to decipher membrane protein assemblies from the nano- to the meso-scale

Membrane proteins play pivotal roles in cellular functions, and understanding their intricate assemblies is crucial for unraveling cellular processes. This talk delves into the world of Molecular Dynamics (MD) simulations, a powerful computational tool to explore the dynamics of biological systems. Focusing on membrane protein assemblies, we embark on a journey from the nano- to the

meso-scale, leveraging MD simulations to decipher the complex interplay of these proteins within lipid bilayers. The presentation will highlight key insights from my team to understand membrane protein assemblies from eukaryotic to bacterial cells. I will also quickly discuss challenges, and advancements in utilizing MD simulations as a virtual microscope to unravel the structural intricacies and dynamic behaviors of membrane protein assemblies.

Olivier Gadal (CBI- LMGM)

Modelling chromosome structure in vivo

Spatial organisation of chromosomes is a key feature for genome stability, transcription and is required for proper mitotic segregation. Using a large panel of technics, ranging from imaging chromatin position and motion in living cells to chromosome capture technologies, underlying mechanisms responsible of genome organization are now actively explored. In model organism such as Saccharomyces cerevisiae, in silico models of the entire genome have been developed. A model based on passively moving polymer chains and local tethering accounted for a large amount of experimental data. In my presentation, I will discuss success and limit of ability of in silico model to predict global organisation of chromatin fibers observed by microscopic technics.

Catherine Tardin (IPBS)

Deciphering DNA conformational changes with physics modeling

Despite the enormous amount of work performed since the discovery of the B-form of DNA 70 years ago, the conformational dynamics of the nucleic acids within cells remains a complex system to investigate. To delineate the relative importance of different physico-chemical parameters of the DNA molecule and its environment on the DNA conformation, several theoretical tools based on statistical physics can be used.

In this talk, I will present how we are able to obtain details on local defects or global changes in DNA by carrying out in vitro single-DNA experiments and jointly developing relevant physics-based tools for the prediction of DNA conformations, in the course of a long-term collaboration with Nicolas Destainville and Manoel, Manghi (IRSAMC-LPT, Toulouse).

Flashtalks and grant possibilities

Tutorial on artificial intelligence

Rufin Van Rullen (CERCO)

Brain-inspired multimodal deep learning.

I will describe our recent efforts to design novel deep neural network architectures drawing inspiration from cognitive neuroscience. One example is the addition of feedback connections implementing "predictive coding" principles into standard convolutional neural networks: this makes the systems more robust to noise or adversarial perturbations, and can also render them susceptible to perceptual illusions--just like real brains. Another example is the design of multimodal

(e.g. text+image) architectures following the "Global Workspace" theory of cognitive science. The independent modalities converge onto a common representation space (the global workspace), and the shared information is then broadcast back towards the entire system. Such an architecture provides a form of referential meaning or "grounding" to each unimodal system. In addition, the broadcast mechanism can be trained with unsupervised cycle-consistency objectives, which makes such systems particularly attractive compared with state-of-the-art models trained on billions of paired data samples (e.g. text+image).

Cellular Dynamics

Denis Krndija (CBI - MCD)

Modelling Gut Homeostasis: Decoding the Critical Role of Active Cell Migration

The homeostatic turnover of epithelial tissues, driven by stem cell division, is a fundamental aspect of adult life. The intestinal epithelium is the fastest self-renewing tissue in mammals, renewing itself every 3-5 days. This renewal process begins in crypts, small stromal invaginations containing dividing stem cells. After leaving the crypts, the cells migrate upwards along the villi, finger-like projections into the intestinal lumen, and are eventually extruded at the tips of the villi. Precise coordination of cell proliferation, migration and extrusion is essential to maintain homeostatic cell numbers in this dynamic epithelial
renewal.

Despite its physiological and clinical importance, the mechanisms that control the turnover of intestinal epithelial cells remain largely unknown. Using a combination of biophysical modeling, 4D ex vivo imaging, novel mouse models, pharmacological perturbations and biomechanical measurements, we investigated the biophysical mechanisms underlying
epithelial migration on intestinal villi during homeostasis. Our quantitative analyses, including cell density and velocity profiles, coupled with laser ablation experiments in mice, revealed that previously unidentified active migratory forces play a critical role in epithelial turnover.

Consistently, we found that epithelial migration depends on actin cytoskeletal dynamics and polarized basal processes of enterocytes. By combining experiment and theory, we unraveled the spatial interplay between the forces driving intestinal epithelial turnover and proposed a two-tier biophysical mechanism involving the complementary actions of mitotic pressure and active cell migration.

In summary, our findings challenge the concept of passive tissue renewal and introduce active migratory forces as a fundamental component of homeostatic renewal of the adult gut epithelium.

Michèle Romanos (Camille Jordan, Lyon)

Mathematical tools in action: exploring their application in cellular dynamics

In this talk, we will explore a fundamental question in developmental biology: How do embryonic cells self organize to shape the future adult ? To address this question, we use an interdisciplinary approach involving a combination of biological techniques alongside image analysis, trajectory tracking, mathematical modeling, and numerical simulations. The talk particularly addresses the following questions: 1) why and when do we use mathematical modeling ? 2) what are the most

suitable mathematical tools to effectively answer this biological question? 3) how do we apply them practically in our context ? 4) what mutual benefits arise from the dynamic interaction between mathematical modeling and biological experiments ?

Population dynamics: behavior and evolution

Alfonso Perez Escudero (CBI - CRCA)

Understanding the constraints to Optimal Foraging: Looking outside evolution's training set.

Optimality principles offer a powerful way of understanding biological systems, because evolutionary adaptation is akin to an imperfect optimization process. In principle, predictions based on optimization principles will only be accurate in the natural conditions to which the animal is adapted. Different conditions (such as a laboratory) may elicit a behavior that is extremely suboptimal, and which may be very hard to predict. A similar phenomenon occurs with artificial neural networks, whose behavior becomes highly unpredictable when facing inputs that differ significantly from those that existed in their training set. However, we found that application of Optimal Foraging to the nematode Caenorhabditis elegans, taking into account its sensory constraints, predicts a conspicuous switch between two foraging states (called "roaming" and "dwelling"), which have been observed in unnatural laboratory conditions. We hypothesize that this behavior is maladaptive and has never been selected by evolution, yet it can be predicted by Optimal Foraging Theory.

Robin Aguilée (LEDB)

The legacy of archipelago structure and history on species communities in volcanic islands

Coauthors : Amandine Vidal-Hosteng, Félix Pellerin, Maxence Soubeyrand,
Jeremy Choin, Rampal Etienne and Christophe Thébaud.

Volcanic archipelagos are dynamic environments: volcanic eruptions, subsidence, erosion and sea level fluctuations continuously change the number, size and connectivity of islands coexisting in an archipelago. We examine how such geo-environmental dynamics affects the ecological and evolutionary processes and we determine the resulting biodiversity dynamics. We used an individual-based model, ecologically neutral within the archipelago. Several islands emerge in succession with a typical volcanic ontogeny. We considered both mainland and inter-island dispersal. Geographically isolated populations diverged over time, possibly leading to new species. We track the genealogy of individuals and reconstruct the genealogy of species. We found that in an archipelago, islands hosted more diversity and more endemic species, at both island and archipelago levels, than an equivalently-sized single isolated island. This was due to an "archipelago effect": inter-island dispersal increased within-island diversity through species occurrence on multiple islands; species may undergo divergence on the colonised islands, eventually becoming new species, thereby increasing archipelago diversity. Biodiversity dynamics of different islands may differ even on islands with identical geo-environmental dynamics because the archipelago effect varied over time and affected each island differently, which we called the "history effect". We showed that these archipelago and history effects leave detectable signatures on the genealogy of species: they determine the speed at which species are formed and how clustered the species are in the genealogy. These results demonstrate how the geo-environmental dynamics in volcanic
archipelagos may explain the contrasted biodiversity patterns observed in different archipelagos.

Snacks, drinks, discussions