Book of Abstracts

Paris Biological Physics Community Day (PBPCD) 2025

7 Nov 2025

Keynote A / **Fernanda Pinheiro** (Human Technopole, Milan, Italy)

Microbial Behavior in Context

Predicting microbial responses to antibiotics, nutrient shifts, or invading species requires models grounded in measurable observables. In this talk, I will survey descriptions of microbial growth — from classic nutrient-limitation curves to contemporary growth laws — showing how growth parameters link to resource allocation and how growth perturbations reveal successive layers of physiology, ecology, and evolution.

Talk A.1 / **Marian Huot** (ENS)

Biophysics-aware prediction and rapid discovery of high-fitness SARS-CoV-2 variants

SARS-CoV-2 fitness emerges from a trade-off: immune escape versus preserved receptor engagement. In this talk, I present two complementary advances that quantify and exploit this trade-off for forecasting variant risk. First, I introduce a biophysical, statistically-mechanical model that maps molecular phenotype to epidemiological fitness: dissociation constants of the RBD to ACE2 and therapeutic antibodies (LY-CoV016, LY-CoV555, REGN10987, S309) define an explicitly epistatic fitness landscape. Validated with measured plus population infectivity data, the model predicts fitness for unseen RBD variants and explains epistatic interactions. Second, I present VIRAL, an active-learning framework that integrates protein language model priors, Gaussian processes with calibrated uncertainty, and the biophysical fitness map to triage experiments under few-shot constraints. Retrospective benchmarks show up to fivefold acceleration over random sampling while characterizing under 1% of candidates, early identification of frequently mutating sites with up to two-year lead time, and targeted discovery of antibody-escape variants that retain ACE2 binding.

Talk A.2 / **Lisa Gennai** (EPFL)

Partner determination in chaperone systems

Protein-protein interactions are crucial in nearly all cellular processes. Given the recent rapid expansion of genomic data, sequence-based computational methods stand out as a promising solution to determine interactions between proteins, assisting experimental approaches that can be inaccessibly time-consuming and resource-intensive. Paralogs of interacting proteins typically evolve to play different although possibly overlapping functions. Experimental evidence indicates that there are often preferred or obligatory partners, making the reconstruction of their interaction networks crucial for the understanding of many biological processes. We propose a technique based on protein language models and optimization algorithms to match paralogs. We complement it with coevolution-based methods and apply it to families of chaperones and co-chaperones for which interactions are still largely unknown. Chaperones play a central role in protein homeostasis, helping other proteins fold correctly, and avoiding or reverting noxious protein aggregation. They are thus an important line of defense against diseases associated with protein misfolding and aggregation such as Alzheimer's and Parkinson's, among others. We focus on the Hsp70 chaperone family and on their co-chaperones, J-domain containing proteins (JDPs). Hsp70 and JDPs interact transiently, allowing JDPs to regulate the activity of multiple Hsp70s. The dynamic nature of their interactions makes the determination of the chaperone and co-chaperone partners an especially challenging task, that could not be solved with recent state-of-the-art

computational approaches. We find that our methods are able to accurately identify protein interaction partners for bacteria with distinct chaperone machines and few J-domain proteins and Hsp70 paralogs.

Talk A.3 / **María Li López Bautista** (EPFL)

Non-equilibrium stabilization of proteins by chaperones

Within living organisms, proteins are essential components. They are responsible for carrying out almost every function in the cell. Proteins must fold into a specific three-dimensional shape to perform their diverse roles effectively. Indeed, improper folding is the root cause of many diseases [1]. Not surprisingly, there is a specific group of proteins whose function is to assist and safeguard the folding process of other proteins. These are known as molecular chaperones. Here, we focus on the 70 kiloDalton heat shock protein, Hsp70, a molecular chaperone that has been under the spotlight of scientists for decades due to its ubiquitous presence across all living systems and its assistance in a wide range of cellular processes. It is well accepted that the mechanism of action of Hsp70 chaperones consists of a biochemical energy-consuming cycle, which allows them to drive the system out-of-equilibrium and escape the inherent limitations of equilibrium thermodynamics to perform their functions efficiently [2,3]. While Hsp70s have been proven to protect cells from the accumulation of misfolded proteins, how the underlying molecular processes work remains unclear. Considering both the molecular details of chaperones and their client protein, along with a correct inclusion of the energy consumed in each step of the cycle and all relevant conformational transitions, we present a kinetic rate model for the description of the functional cycle of Hsp70 chaperones in protein folding that aims to elucidate the fundamental principles that govern their complex behavior. References: [1] Louros, N. et al. (2023). Nat. Rev. Mol. Cell Biol., 24 [2] Assenza, S. et al. (2019). eLife, 8. [3] De Los Rios, P., Barducci, A. (2014). eLife, 3.

Keynote B / **Daniel Busiello** (University of Padova, Milan, Italy)

Interactions across timescales shape information propagation and encoding in stochastic systems

The presence of interconnected fluctuating processes occurring across multiple temporal scales is a fundamental characteristic of neural networks, ecological communities, biochemical architectures, and many other complex systems. A key feature of these systems is that such processes can interact both directly and indirectly, with interactions across timescales often exhibiting intricate internal properties. This complexity makes understanding the relationships between their components a formidable challenge. In this talk, I will elucidate how the distinct timescales associated with each process influence their effective couplings. By examining the probabilistic structure of a general multiscale system, I will uncover the underlying principles that govern information propagation across different timescales. In doing so, I will clarify the interplay between mutual information and coupling structure, revealing the origin of the critical distinction between causal and functional interactions in complex stochastic systems. I will then demonstrate how this emerging information structure can be harnessed to study encoding features of stochastic neural populations with both fast and slow plasticity-induced modulations, and the performance of different nonlinear processing operations. The ideas presented in this talk provide novel insights into the processing capabilities of complex multiscale systems.

Talk B.1 / **Marie Sellier-Prono** (ENS)

Models of oscillators to study frequency parcellation in the intestine and the brain

Oscillatory spatially extended systems are often the place of synchronization phenomena: fireflies will flash in synchrony, circadian rythms of people will adapt to the day/night cycle of their region, etc. Of particular interest to us is the phenomenon of frequency parcellation: the division of the system in multiple regions of different oscillatory frequencies. It has been observed and studied in the electrical activity of smooth muscles around the small intestine, and, more recently, in the network of arteries on top of the brain (pial network). We focus on the case of the intestine, capturing the main experimental

observations in a Ginzburg Landau equation with a linear gradient in natural frequencies. We further study the solutions of the equation, characterizing its behaviour in the whole parameter space, and understanding the appearance of space-time defects. Reference: Sellier-Prono, Cencini, Kleinfeld, Vergassola, Defects, Parcellation, and Renormalized Negative Diffusivities in Nonhomogeneous Oscillatory Media, PRL 2025.

Talk B.2 / **Barnabé Ledoux** (ESPCI)

Compositional memory matters for early molecular systems.

The error catastrophe refers to the proliferation of non-functional molecules in conditions where molecular replication has low accuracy, which is likely to correspond to conditions present at the Origin of Life. This error catastrophe can be avoided thanks to transient compartmentalization, provided that the compartments are themselves functional. Usually, transient compartmentalization models assume that the content of the compartments is completely pooled at the end of a cycle, resulting in the complete loss of the compositional memory of the compartment. Here, we test this assumption by assessing the level of mixing in experiments with compartmentalized RNAs using a mixture of fluorescent dyes. We find mixing to be incomplete, in other words, compartments do not completely lose their content despite the continuous stirring, and there is therefore a certain level of compositional memory. Then, we develop a specific framework to account for this compositional memory, and we explore its role in the emergence of complexity in early molecular systems.

Talk B.3 / **Esther Zamora Sánchez** (SU)

Maze-solving with density-driven swarms

We propose a new kind of collective motion where swarms of simple agents are able to solve a complex task: successfully navigating a highly constrained space, a maze. The model consists of active memoryless particles interacting exclusively via short-ranged perception of local densities and orientations. This system generates traveling density waves when constrained in one dimension, and self-organized swarms exploring local branches in two-dimensional mazes. Depending on a single kinetic parameter, these swarms can develop large tails and further gain long-term persistence, which ultimately allows them to robustly solve mazes of virtually any kind and size. By systematic exploration of the parameter space, we show that there exists a fast solving regime where the resolution time is linear in number of squares, hence making it an efficient maze-solving algorithm. This model represents a new class of active systems with unprecedented contrast between the minimality of the processed information and the complexity of the resolved task, which is of prime importance for the interpretation and modeling of collective intelligence in living systems as well as for the design of future swarms of active particles.

Keynote C / **Javier Alegre-Cortéz** (Paris Brain Insitute, Paris, France)

Functional architecture of neuronal circuits

Internal states and behavior are implemented through brain-wide coordination of neuronal circuit activity. Such global transitions arise from the interplay between neuromodulatory systems, interoceptive signals, and intrinsic circuit dynamics. Neuromodulators are released from a few subcortical nuclei yet act diffusely across the brain, to reconfigure the excitability and connectivity of local networks, shaping perception, learning, and emotion. The amygdala, a key hub for emotional processing, receives convergent inputs from all major neuromodulatory systems and integrates interoceptive signals related to bodily states. To elucidate how these inputs jointly shape circuit function, we combine novel genetically encoded sensors for neuromodulator dynamics with multi-site, multi-color fiber photometry to monitor the simultaneous release of dopamine, norepinephrine, acetylcholine, and serotonin in behaving mice. These recordings reveal distinct patterns of combinatorial neuromodulator

release across behavioral states, defining unique signatures of internal state transitions. Using simultaneous large-scale electrophysiological recordings, we have uncovered corresponding motifs of neuronal population activity within the amygdala, revealing how specific neuromodulator combinations reconfigure local network states. To understand the mechanistic substrate of the neuromodulatory action on neuronal populations, we are using a range of computational modeling approaches, ranging from recurrent neural networks to mean-field and biophysical formulations, to infer the circuit-level mechanisms underlying these state-dependent dynamics and to generate testable predictions regarding the causal influence of neuromodulator interactions on network function. In parallel, we examine how respiration, a fundamental rhythmic physiological process, interacts with neuromodulation to structure brain-wide activity. Using optogenetic control of breathing in awake mice, together with multi-region electrophysiology spanning hippocampal, thalamic, and cortical circuits, we have established respiration as an interoceptive scaffold that synchronizes limbic dynamics and modulates neuromodulatory tone. The respiratory rhythm not only coordinates the temporal structure of neuronal firing but also adjusts the interoceptive gain and information flow through neuromodulator-mediated mechanisms. Together, these multimodal experimental and computational approaches outline some of the functional architecture principles through which neuromodulatory and interoceptive signals jointly organize neuronal circuits. This work provides a mechanistic framework linking bodily rhythms, neuromodulatory control, and circuit computation to advance our understanding of how global brain states emerge from distributed cellular processes.

Talk C.1 / **Sebastian Castedo** (ENS)

Energy-Efficient Neural Coding Under Food Restriction: Structure, Noise, and Resilience

Energy efficiency is a key constraint shaping the architecture and function of neural codes across the brain. While a recent study has revealed how individual neurons and behaviour adapt to energy limitations [1], it remains unclear how such constraints shape network-level coding. Here, we investigate how food restriction impacts population coding in the visual cortex of male mice. Analyzing neuronal responses to oriented bar stimuli in V1, we find that food-restricted animals exhibit elevated noise correlations [2], yet maintain decoding performance through a reorganization of the neural code that reduces alignment between signal and noise directions. To evaluate coding efficiency, we computed using linear response theory the signal to noise ratio which confirm robust information encoding under energy constraints. Additionally, we found that food-restricted mice paradoxically exhibit a higher effective dimensionality, with increased average eigenvalue magnitude and fewer noise-dominated modes. This suggests a shift toward a more structured and complex population code, even under metabolic stress. These findings suggest that neural circuits adapt to energy constraints by restructuring their correlation patterns in a way that sustains efficient coding. This highlights a broader principle: metabolic pressure can drive functional reorganization at the network level, offering a new perspective on how energy efficiency shapes neural computation. [1] Padamsey, Zahid, et al. "Neocortex saves energy by reducing coding precision during food scarcity." Neuron 110.2 (2022): 280-296. [2] Panzeri, Stefano, et al. "The structures and functions of correlations in neural population codes." Nature Reviews Neuroscience 23.9 (2022): 551-567.

Talk C.2 / **Ludwig Hruza** (ENS)

Gain-modulated linear networks: a tractable framework for context-dependent computations

Complex behavior often requires processing the same stimulus differently, depending on the sequence of preceding events. Network models of such context-dependent computations rely on non-linear interactions between the stimulus input and a contextual signal that modulates the state of the network. Theoretical analyses of trained RNNs have identified neural mechanisms of context-dependent computations by linearizing the activity within each context [Mante et al. 2013; Sussillo and Barak 2013; Pagan et al. 2025]. The non-linear mechanisms by which contextual inputs lead to suitable modulations, however, remain to be clarified because a tractable theoretical framework for non-linear computations is currently lacking. To address this issue, here we introduce a tractable class of models, gain-modulated linear recurrent networks. Specifically, a model of this type consists of a linear network, together with a set of gain patterns corresponding to a set of contexts. In each context, a gain pattern multiplicatively modulates the activity of the neurons, leading to linear computations in each context, but non-linear

computations across contexts. Crucially, we consider each gain pattern as a set of tunable parameters, and use a mean-field approach to examine how the relationship between these patterns and linear connectivity determines computations. Focusing on two classical context-dependent tasks, evidence selection and evidence integration, we show that conditions to solve each task can be reduced to a three-factor relation between gains, inputs and either readout weights (for evidence selection) or leading connectivity eigenvectors (for evidence integration). We identify a simple mechanism for shaping the correlation between the three factors, that introduces an effective population structure in the connectivity. We show that trained feed-forward networks (evidence selection), full-rank or low-rank recurrent networks (evidence integration) employ different variants of this same mechanism. Our work introduces a new framework for studying non-linear computations and highlights the importance of three-factor relations between connectivity, stimulus and contextual inputs.

Talk C.3 / **Pierre Houzelstein** (ENS)

Koopman analysis of stochastic oscillations in neuron networks

Collective rhythms and node synchrony are ubiquitous features of neural circuits, and have been linked to cognitive functions such as speech and memory. Characterizing synchrony in neuronal networks is important but challenging, notably because individual nodes are subject to intrinsic and environmental noise, which obscure deterministic notions of synchrony. Building on the results in [1], we propose that Koopman theory offers a powerful framework for analyzing networks of stochastic oscillators. Using data-driven methods, we map network dynamics onto the Q-function—the complex eigenfunction of the Koopman operator associated with the dominant metastable oscillatory mode of the dynamics. This representation linearizes the collective dynamics, reducing the network behavior to a well-understood complex oscillator. As shown in [2], the Koopman spectrum reveals whether the system exhibits stochastic synchrony, from which we can extract the collective oscillation phase [3] and the spatial distribution of synchrony across nodes. We demonstrate this approach on a network of stochastic FitzHugh–Nagumo neurons exhibiting noise-induced oscillations. [1] Pérez-Cervera et al., PNAS (2023). [2] Kreider et al., Chaos (2025) [3] Houzelstein et al., Physical Review Research (2025)

Keynote D / **Daria Bonazzi** (Insitut Pasteur, Paris, France)

How mechanical forces shape bacterial infections?

Mammalian cells sense and exert forces on their environment, and their responses to mechanical signals regulate their growth, motility, and behavior within tissues. However, little is known about the forces at play during microbial infections, and their impact on tissue homeostasis and disease progression. On the bacterial side, we investigated how mechanical constraints imposed upon confinement affect bacterial physiology using a microfluidic device ensuring nutrient access. In E. coli, we found that cells generate growth-induced pressure in the hundreds of kPa range decoupling growth and division, producing shorter bacteria due to increased cytoplasmic protein concentrations and crowding. Despite decreased protein synthesis, theoretical modeling predicts a novel regime of steady pressure increase, termed overpressurization, leading to transcriptional adaptation of the bacterial cell envelope to maintain cell shape. Finally, we highlight the relevance of these pressurized regimes during infection of uropathogenic E. coli and other bacterial pathogens. On the host side, we recently found that binding of the extracellular bacterium Neisseria meningitidis (Nm) on the endothelium leads to the generation of large traction forces on the extracellular matrix. This is due to the formation of a new actin-rich structure, called ancreopodia, linking the bacterial colony on the apical side of the host cell to the basal side and underlying substrate. Using super-resolution microscopy, we identified distinct apical, middle, and basal domains of ancreopodia, which significantly reorganize basal actin stress fibers, induce focal adhesions, and increase local traction forces. Dynamic imaging showed synchronized movements between bacterial colonies and basal mechanosensitive proteins, indicating direct mechanotransduction from apical infection sites to the extracellular matrix (ECM). Our results suggest ancreopodia cause topological defects in basal actin networks, potentially inducing long-range force transmission throughout the

infected cells, leading to alterations in tissue function. Overall, this work integrates bacterial pathogens as tools to shed light on complex feedbacks between cell architecture, mechanics, and function.

Talk D.1 / **Sara Formichetti** (Pasteur)

Modulation of mammalian embryonic growth by intracellular glycosylation

The main form of intracellular glycosylation in animals is O-GlcNAcylation, the reversible linkage of a monosaccharide (O-GlcNAc) to serine and threonine protein residues. The donor substrate for O-GlcNAc, UDP-GlcNAc, is the end product of a metabolic pathway responsive to nutrient levels. O-GlcNAc is present on thousands of mammalian proteins in all cellular compartments, especially in the nucleus and including RNA Polymerase II and developmentally relevant transcription factors such as OCT4 and SOX2. An ever-increasing number of in vitro studies report the regulation by O-GlcNAc of essential cellular functions such as cell cycle, translation, glycolysis, transcription. In spite of its pleiotropy, only one enzyme is responsible for O-GlcNAcylation, called O-GlcNAc transferase (OGT). The mammalian Ogt gene is essential for both cellular proliferation and embryonic development. Specifically, a functional maternal Ogt copy is required for the mouse embryo to pass the blastocyst stage. Because of this obstacle for genetics studies, the molecular function of O-GlcNAc in early mammalian development remains poorly understood and certainly never addressed in vivo. We addressed O-GlcNAc's role in the early mouse embryo through two parallel routes both overcoming cellular and embryonic lethality: i. We depleted the O-GlcNAc modification itself from the embryonic nuclei, by overexpressing in the zygote the enzyme catalyzing O-GlcNAc removal; ii. We created four Ogt-hypomorphic mouse models with OGT's catalytic activity reduced to a range of degrees. By analyzing the transcriptome of single embryos at key pre- and postimplantation stages upon different level of disruption of O-GlcNAc homeostasis, we discovered that nuclear O-GlcNAc is dispensable for embryonic genome activation and blastocyst differentiation, but that reducing O-GlcNAc slows down embryonic growth. Due to the location of Ogt on the X chromosome, male embryos are more susceptible to Ogt disruption. Our studies established a novel link between a maternally-transmitted intracellular protein glycosylation and developmental pace, with sexually-dimorphic penetrance.

Talk D.2 / **Sumeja Burekovic** (Saclay)

Active phase separation: from micro to macro

Active systems such as bacterial colonies convert chemical energy into mechanical work, for example through self-propulsion, keeping them far from equilibrium. The combination of activity and interactions such as bacterial quorum sensing gives rise to novel collective phenomena, including motility-induced phase separation (MIPS). Theoretical descriptions of MIPS range from microscopic models with experimentally controllable parameters to continuum field theories for coarse variables such as the density. The latter allow prediction of the phase diagram but are generally less interpretable. Connecting these two levels via coarse-graining remains challenging due to the consistent elimination of irrelevant fast degrees of freedom. Here, we develop a systematic coarse-graining procedure based on multiple-scales analysis. For quorum-sensing active particles, we demonstrate that our framework not only yields quantitative improvements within its regime of validity but also predicts anomalous phase behavior that cannot be captured by existing coarse-graining methods. Joint work with Filippo De Luca, Michael E. Cates, Ananyo Maitra and Cesare Nardini.

Talk D.3 / **Tristan Cerdin** (SU)

Qualifying Active Particles Motion by Counting them in Boxes

Quantifying particle dynamics with microscopy is a great interest of the active matter community. Indeed information on motion in complex systems is essential to better understand how active particles navigate, evolve and interact with their environment: To quantify their displacement one traditionally relies on particle trajectories. Trajectories can however be difficult to obtain, especially in the presence of large concentration heterogeneities — a generic feature of active matter, canonically illustrated by MIPS (Motility Induced Phase Separation). Recent work suggests an alternative strategy to quantify dynamics, which removes the need for obtaining trajectories, simply by counting particles in virtual observation boxes. The fluctuations of the number of particles in a box can be used to infer transport

parameters of passive particles. Here we develop a method to obtain the dynamic properties of active particles from fluctuating counts. We show, using experiments and simulations on dilute active particles systems, that fluctuating counts are sensitive to active motion features, recovering regimes of diffusive, ballistic and long-time diffusive motion. By deriving a theory based on hydrodynamic fields, we obtain analytical laws and limiting behaviour allowing us to directly extract dynamic parameters from experiments using this counting method. This method also opens the way to differentiate between the main systems of active motion, Run and Tumble and Active Brownian Particles, by looking at their macroscopic statistical properties, something that was not possible relying only on their trajectories.