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P01

Poissonian Potts models of cell sorting

Cellular Potts models provide a convenient discrete description of tissues, which is broadly applied in developmental biology and cancer research. The traditional approach, which is based on a modified Metropolis sampling reinterpreted as an ad-hoc dynamics, lacks control over kinetic properties of the system. We apply principles of stochastic thermodynamics to reformulate dynamics of cellular Potts models, which thus offer a richer description of tissue dynamics. Our approach is demonstrated in a case study of cell sorting in mouse embryo development.

P02

Target retrieval in multi-component self-assembly via kinetic encoding

In the 80s, J.J. Hopfield introduced an equilibrium model to encode patterns in a group of neurons modeled as discrete spin variables. Patterns are encoded via a set of nearest-neighbor interactions and can be retrieved in a certain regime of parameters corresponding to low noise and low number of patterns compared to the number of spins. We consider a spatial version of this model where colored tiles self-assemble on a square lattice to retrieve previously encoded spatial patterns. We then consider specific interactions between neighboring tiles in a given pattern to be either energetically favored [Sartori and Leibler, PNAS 2020] or kinetically boosted. The latter case of kinetic discrimination is supposed to perform well at fast growth, far from the equilibrium regime. We then aim at studying, e.g., whether the number of retrievable patterns increase upon the introduction of simple proofreading mechanisms.

P03

Stochastic dynamics of single molecules across phase boundaries

Biomolecular condensates provide distinct chemical environments, which can organise various cellular processes. The fluorescent labelling of molecules enables molecular tracking and provides an invaluable tool to probe key processes in cell biology. We discuss how biomolecular condensates govern the kinetics of chemical reactions and how this is reflected in the dynamics of individual labelled molecules. Our theoretical approach provides insights into how the dynamics of labelled molecules can be used to measure key physical properties of the condensates, such as diffusion coefficients, the partition coefficient, and the chemical reaction rates inside and outside bimolecular condensates.

P04

Mechanical aspects of mitochondrial transport, cellular organization and shape fluctuations in living cells

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P05

A Small Ensemble of Myosin Motors at Work: Fitting Experimental Data with a Stochastic Model

We developed a stochastic model to interpret the experimental output of a synthetic nanomachine mimicking the striated muscle. The nanomachine is constituted by the minimum number of myosin molecules needed to reproduce the collective mechanism of muscle myosin in the sarcomere. The mechanical output of the machine is measured with a Dual Laser Optical Tweezers which act as a force transducer. The small ensemble of molecular myosin motors in interaction with an actin filament is capable of performing isometric contraction in solution with physiological ATP concentration. A stochastic model that assumes one detached and two different force-generating attached states allows to predict the force distribution resulting from the cumulative action of the motors. The computed distribution can be superposed to the homologous experimental profile via a non-linear fitting procedure. The fitting scheme is first validated against synthetically generated data and then applied to the experimental distributions of the force exerted by an ensemble of myosin molecules purified from rabbit soleus. Accounting for the fluctuations of the force exerted by the ensemble of motors makes it possible to directly estimate the force exerted by individual myosin-actin interactions and to compute the associated duty ratio. This challenge cannot be successfully faced when solely relying on a mean field description of the scrutinized dynamics. Analysing the performance of the small ensemble of motors with a reverse engineering procedure made it possible to recover single motor properties and can pave the way for the study of the performance of unknown myosin isoforms.

P06

Optimal power extraction from active particles with hidden states

We identify generic protocols achieving optimal power extraction from a single active particle subject to continuous feedback control under the assumption that the instantaneous net velocity, but not the fluctuating contribution originating from the self-propulsion, is accessible to direct observation. Our Bayesian approach draws on the Onsager-Machlup path integral formalism and is exemplified in the cases of free run-and-tumble and active Ornstein-Uhlenbeck dynamics in one dimension. Such optimal protocols extract positive work even in models characterised by time-symmetric positional trajectories and thus vanishing informational entropy production rates. We argue that the theoretical bounds derived in this work are those against which the performance of realistic active matter engines should be compared.

P07

A geometric theory of nonequilibrium reaction networks

Combining tools from graph theory and linear algebra, we propose a framework to identify the thermodynamical observables in complex reaction networks. We apply the formalism to study the linear response, unveiling the Onsager symmetries between response and relaxation in arbitrarily complex networks.

P08

Performance benefit of information in chemotaxis

Living cells improve their fitness by sensing noisy environmental signals and then tuning their behavior in response in a modular fashion. Yet these two processes occur simultaneously, and behavioral response must affect future signal values in order for it to have a benefit. Cells have been previously shown to predict future signal values that are generated by their own behavioral response. However, understanding the design of sensing and response motifs, in terms of the fitness benefit of acquiring information, has so far been limited to slow, perturbative regimes without accounting for the continuous information flow and feedback between the environment and the cell. We address this gap by studying the dynamics of E. coli chemotaxis in a steady chemoattractor gradient, with a coarse-grained model for sensory receptors and run-and-tumble motion in the seconds timescale. We use analytical theory and numerical simulations to quantify information rate in terms of the transfer entropy between the cell and the environment in both directions, and chemotaxis performance in terms of the cell's drift speed. We find that total information rate is correlated with performance across both shallow and steep chemoattractor gradients due to a constrained variation in the mean and the fluctuations of the sensing and response variables. We also counterintuitively find that information feedback becomes negligible at both very low and very high gradients, with a turnover. We rationalize our findings in terms of the specific design of the sensing and response motifs in E. coli.

P09

Self-organization of bacterial mixtures interacting via quorum-sensing [1]

Alberto Dinelli

Coauthors: Jérémy O' Byrne, Agnese Curatolo, Yongfeng Zhao, Peter Sollich, Julien Tailleur

Understanding the self-organization of motile entities is a key problem in active matter, with applications ranging from pattern formation in biological systems to the engineering of soft active materials. Recently, the regulation of motility in bacteria via quorum sensing interactions (QS), i.e. by the local density of their peers, has shown to be a promising pathway to self-organization. So far, the literature has mostly focused on single-component active systems; however, heterogeneity should be accounted for if we aim at describing more complex situations, closer to natural ecosystems.
Here we present an analytical and numerical study of the self-organization of mixtures of QS run-and-tumble bacteria. We show the emergence of a rich large-scale phenomenology, including static and dynamic patterns. We note that QS interactions are always non-reciprocal at the microscopic scale. At the coarse-grained scale, however, we show that action reaction may be restored, and derive a condition on the microscopic parameters for the system to admit an effective large-scale free energy functional. The latter allows us to rationalize the static patterns observed in our simulations and to predict the corresponding phase diagram.
On the contrary, when non-reciprocal interactions survive coarse-graining, we derive a sufficient condition to observe the emergence of travelling patterns, from steady travelling waves to intermittency and band chaos.

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[1] A. Dinelli, J. O'Byrne, A. Curatolo, Y. Zhao, P. Sollich, and J. Tailleur, Non-reciprocity across scales in active mixtures (preprint), arXiv (2022).

P10

Decision making of nonequilibrium fluctuations

To make timely and effective decisions, we need o accumulate sensory evidence over time, until a certain decision criterion is reached. In studying perceptual decision making, the common neuroscientific approach is to measure behavior, its accuracy and speed, and then analyze it with mathematical models to make inference on the underlying mechanism. In this work we turn this approach around and from a model of the physical properties of a stimulus moving according to a non-equilibrium stationary stochastic process, we predict the decision time of human subjects. In a behavioral experiment, we asked 21 young healthy participants to judge the motion direction of a visual stimulus moving with a given drift velocity and diffusion coefficient. Results revealed that participants' decision times were well predicted by the model used to generate the stimuli and by an updated version of it into account subjects' variability in decision thresholds. Our study shows that providing a detailed model of the physical properties of the stimuli to judge allows a better characterization of the variables influencing perceptual decision and shows that studying human behavior can refine our understanding of the problem of time's arrow, within the framework of non-equilibrium statistical mechanics.

P11

Phase separation and critical size in molecular sorting

Molecular sorting is a fundamental process that allows eukaryotic cells to distill and concentrate specific chemical factors in appropriate cell membrane subregions, thus endowing them with different chemical identities and functional properties. A phenomenological theory of this molecular distillation process has recently been proposed [10.1103/PhysRevLett.126.088101], based on the idea that molecular sorting emerges from the combination of: a) phase-separation-driven formation of sorting domains, and b) domain-induced membrane bending, leading to the production of submicrometric lipid vesicles enriched in the sorted molecules. In this framework, a natural parameter controlling the efficiency of molecular distillation is the critical size of phase-separated domains. In the experiments, sorting domains appear to fall into two classes: unproductive domains, characterized by short lifetimes and low probability of extraction, and productive domains, that evolve into vesicles that ultimately detach from the membrane system. It is tempting to link these two classes to the different fates predicted by classical phase separation theory for subcritical and supercritical phase-separated domains. Here, we discuss the implication of this picture in the framework of the previously introduced phenomenological theory of molecular sorting. Sorting is observed to be most efficient when the number of sorting domains is close to a minimum. To help in the analysis of experimental data, an operational definition of the critical size of sorting domains is proposed. Comparison with experimental results shows that the statistical properties of productive/unproductive domains inferred from experimental data are in agreement with those predicted from numerical simulations of the model.

P12

Strong current response to slow modulation

We characterize the statistics --- mean and signal-to-noise ratio (SNR) --- of the conversion rate of substrate into product for the reversible substrate inhibition reaction under time-varying metabolic conditions, modeled by a periodic modulation of the product concentration. A regime of strong nonlinear response of this current to small driving frequencies is identified both via an analytical calculation and using the machinery of large deviation theory.

P13

Signature of (anti)cooperativity in the stochastic fluctuations of small systems: application to the bacterial flagellar motor

The cooperative binding of molecular agents onto a substrate is pervasive in living systems. To study whether a system shows cooperativity, one can rely on the fluctuation analysis of quantities such as the number of substrate-bound units and the residence time in an occupancy state. Since the relative standard deviation from the statistical mean monotonically decreases with the number of binding sites, these techniques are suitable for mesoscopic systems of finite sizes, such as those implicated in stochastic processes inside cells. In this work, we present a general-purpose grand canonical Hamiltonian description of a small one dimensional (1D) lattice gas with nearest-neighbor interactions as a prototypical example of cooperativity-influenced adsorption processes. We elucidate how the strength of the interaction potential between neighboring bound particles on the lattice determines the intensity of the fluctuations of the mean occupancy and we employ this relationship to compare the theoretical predictions of our model to data from single molecule experiments on bacterial flagellar motors (BFM). In this way, we find evidence that cooperativity controls the mechano-sensitive dynamical assembly of the torque-generating units, the so-called stators, onto the BFM.

P14

Non-monotonic Cooling of a Brownian Particle in Active Baths

We study the cooling and heating of a Brownian particle diffusing in a heat bath containing active particles. In the model of active Ornstein-Uhlenbeck process, we tested the Newton's law of cooling, which states that the rate at which an object cools is proportional to the difference in temperature between the object and its surroundings. We find that a Brownian Particle in an active bath may exhibit non-monotonic cooling behavior, which can be attributed to the "colored" noise generated by the active particles. Despite the discrepancies with the equilibrium statistical mechanics, this classic rate law, when combined with an effective potential scheme, continues to shed light on how substances relax to an equilibrium.

P15

Modulation of transcription factor dynamics allows versatile information transmission.

Cells continuously interact with their environment, detect its changes and generate responses accordingly. This requires interpreting the variations and, in many occasions, producing changes in gene expression. In this paper we use information theory and a simple transcription model to analyze the extent to which the resulting gene expression is able to identify and assess the intensity of extracellular stimuli when they are encoded in the amplitude, duration or frequency of a transcription factor's nuclear concentration. We find that the maximal information transmission is, for the three codifications, ~ 1.5 – 1.8 bits, i.e., approximately 3 ranges of input strengths can be distinguished in all cases. The types of promoters that yield maximum transmission for the three modes are all similarly fast and have a high activation threshold. The three input modulation modes differ, however, in the sensitivity to changes in the parameters that characterize the promoters, with frequency modulation being the most sensitive and duration modulation, the least. This turns out to be key for signal identification. Namely, we show that, because of this sensitivity difference, it is possible to find promoter parameters that yield an information transmission within 90% of its maximum value for duration or amplitude modulation and less than 1 bit for frequency modulation. The reverse situation cannot be found within the framework of a single promoter transcription model. This means that pulses of transcription factors in the nucleus can selectively activate the promoter that is tuned to respond to frequency modulations while prolonged nuclear accumulation.

P16

Thermodynamic modeling of synthetic enhancer reveals impact of binding affinity on transcriptional repression

It has long been a challenge in quantitative biology to use knowledge of input transcription factor patterns and the arrangement of binding sites for these transcription factors to predict the output pattern of gene expression. Previous studies elucidate the combinatorial explosion of parameters resulting from even a small number of binding sites and, therefore, demonstrate the necessity of considering simple regulatory architectures in order to incrementally develop our understanding of enhancer logic and eventually make predictions for complex endogenous enhancers. Here we build on previous work by Kim et al. in 2022 and explore whether thermodynamic models can be used to infer binding parameters for simple regulatory enhancers. We consider enhancers containing a single binding site with different affinities for the Runt transcription factor as measured by their PATSER score. By measuring the resulting transcriptional activity using live imaging, we infer the Runt dissociation constant as a function of the binding affinity and conduct parameter-free predictions of transcriptional activity driven by more complex enhancers in the early fruit fly embryo. We also propose a nonequilibrium model based on a cycle of four states to describe the binding and unbinding of Runt and polymerase as well as the resulting transcription. These results emphasize the complexity of eukaryotic transcriptional regulation and the importance of quantitatively dissecting their molecular structure.

P17

Optimal Control of the F1-ATPase Molecular Motor

F1-ATPase is a rotary molecular motor that in vivo is subject to strong nonequilibrium driving forces. There is great interest in understanding the operational principles governing its high efficiency of free-energy transduction. Here we use a near-equilibrium framework to design a nontrivial control protocol to minimize dissipation in rotating F1 to synthesize adenosine triphosphate. We find that the designed protocol requires much less work than a naive (constant-velocity) protocol across a wide range of protocol durations. Our analysis points to a possible mechanism for energetically efficient driving of F1 in vivo and provides insight into free-energy transduction for a broader class of biomolecular and synthetic machines.

P18

Rotational and Translational Diffusion of Water Molecules around POPE Lipid Bilayer

Intuon Chatratin[1], Somyot Srikongrug[2], and Chalermpol Kanchanawarin[1*]

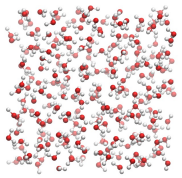
[1]Theoretical and Computational Biophysics Laboratory, Department of Physics, Faculty of Science, Kasetsart University, Bangkok, 10900, Thailand, fscicpk@ku.ac.th
[2]Department of Physics, Faculty of Science and Technology, Rambhai Barni Rajabhat University, Chanthaburi, 22000, Thailand

Abstract

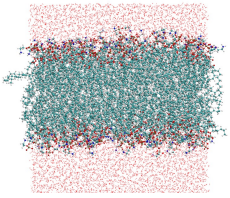
Water is an essential molecule for living systems. They form hydrogen bonded networks around biomembranes. So the structure and dynamics of water molecules near biomembrane are quite different from those that are further away (bulk water). In this study, we investigated how structural and dynamical properties of water molecules around a POPE lipid bilayer are affected using molecular dynamics method. We found that water molecules near the lipid bilayer move and rotate slower, and have less number of hydrogen bonds comparing with those much further away from it. This is due to the interactions between the charged headgroups of the lipid bilayer and the surrounding water molecules. These slow moving water molecules may form a long-lived hydrogen bonded network on the surface of the lipid bilayer that could lead to faster proton transfer between a proton source (e.g. bacteriorhodopsin; proton pump) and a proton sink (e.g. ATP synthase) along the bilayer surface.

MD Simulations of POPE Bilayer & Water Box

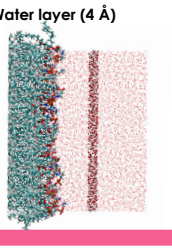
1 Water box



2 POPE bilayer



3 Water layer (4 Å)



Sytem setup

- **Water box** consists of 233 TIP3P water molecules (699 atoms)
- **POPE bilayer** consists of 144 POPE lipid molecules and 9,284 TIP3P water molecules (45,825 atoms).

MD simulations

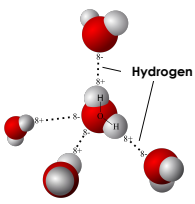
- Performed by NAMD program for 1 ns and 20 ns (Water box and POPE bilayer) using CHARMM27 force fields
- 13 Å cutoff for vdW interactions
- Langevin temperature and pressure controls at 310 K and 1 atm
- Multiple-time stepping with 2 fs per timestep
- Periodic boundary conditions
- Full electrostatic calculation using PME method

Analysis

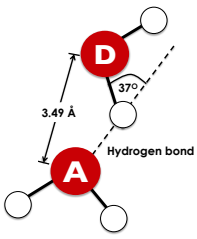
- Performed by VMD and Tcl scripting.
- Determined lipid density profile, translational and rotational diffusion coefficients and number of hydrogen bonds per water molecule.
- In POPE bilayer system, calculations were done on rectangular layers with a thickness of 4 Å along the z axis perpendicular to the membrane plane (see Figure 3). Each layer was determined by shifting the previous layer by 0.2 Å along the z-axis.

Hydrogen Bonds and Molecular Rotation

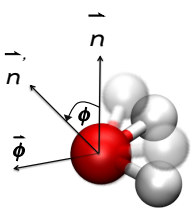
4 Four hydrogen bonds in a water molecule



5 Definition of hydrogen bond

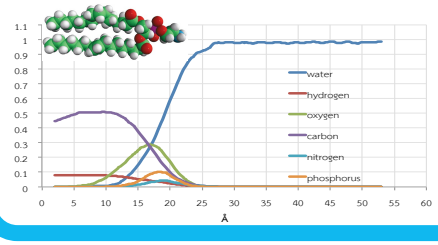


6 Rotation of water molecule

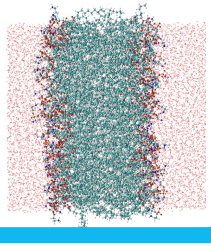


Mass Density Profile of POPE Bilayer System

7 Mass density of various atoms along the bilayer axis



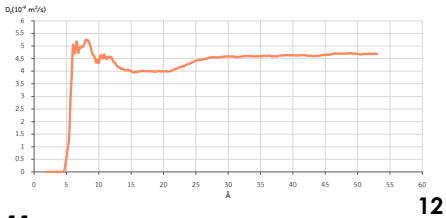
8 Lipid bilayer system



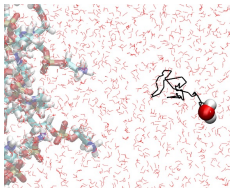
Translational and Rotational Diffusion

Diffusion	Pure Water		Water with POPE
	$r^2_{rms}(t_i)=\frac{1}{N}\sum_{j=1}^{N}\left[\vec{r}_j(t_i)-\vec{r}_j(t_o)\right]^2=6Dt_i$	$D=<\frac{displacement^2}{6t}>;t=0.2ps$	$D=<\frac{displacement^2}{6t}>;t=0.2ps$
Translation	2.87 x 10^{-5} cm^2/s	4.51 x 10^{-5} cm^2/s	4.63 x 10^{-5} cm^2/s
Rotation	0.22 rad^2/ps	0.46 rad^2/ps	0.53 rad^2/ps

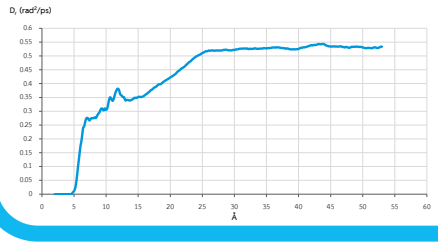
9 Translational diffusion coefficient



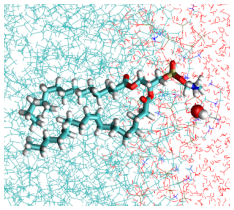
10 Trajectory of a water molecule



11 Rotational diffusion coefficient

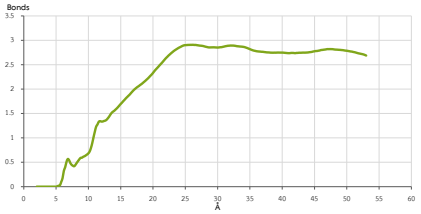


12 Orientation of a water molecule near POPE bilayer

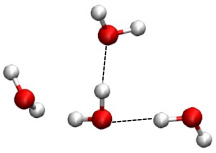


Number of Hydrogen Bonds

13 Number of H-bonds per water molecule



14 H-bonds of water in liquid phase



Conclusion

In this work, we used molecular dynamics simulation to study translational and rotational diffusion of water molecules around POPE lipid bilayer. We found that water molecules move and rotate differently from the bulk within the distance of about 5 Å away from the bilayer. In this region, the translational and rotational motions and the number of H-bonds per water molecule are reduced uniformly due to their electrostatic forces with the polar headgroups. These slowed down water molecules may form a long-lived hydrogen bonded network at the surface of the lipid bilayer. This could lead to faster proton transfer between a proton source and sink along the surface of the lipid bilayer.

Acknowledgement

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Reference

[1] Srikongrak, S., & Kanchanawarin, C. (2013). The Study of Structure and Dynamics of Water Molecules around POPE Phospholipid Bilayer using Molecular Dynamics Method. *Proceeding of Siam Physics Congress 2013*, 55-58.
[2] Xenides, D., Randolf, B. R., & Rode, B. M. (2006). Hydrogen bonding in liquid water: An ab initio QM/MM MD simulation study. *Journal of molecular liquids*, *123*(2), 61-67.
[3] Yamamoto, E., Akimoto, T., Yasui, M., & Yasuoka, K. (2014). Origin of subdiffusion of water molecules on cell membrane surfaces. *Scientific reports*, *4*.

P19

Survival and extreme statistics of entropy production

In small systems, fluctuations play a prominent role, often pushing systems far away from equilibrium. As a consequence, they are of crucial importance for the performance and robustness of both natural or synthetic microscopic motors, where work production, free energy consumption or heat dissipation become stochastic quantities describable within the framework of stochastic thermodynamics. In particular, here I will focus on universal results regarding the extreme and survival statistics of entropy production in generic steady-state processes. These results can be applied to a broad class of situations from assessing the peaks in the consumption of chemical fuel driving a molecular machine to the work extracted by microscopic photoelectric engines. In particular, I will first discuss how to derive universal inequalities for the cumulative distribution of the finite-time maximum and minimum of stochastic entropy production and their averages in generic nonequilibrium stationary states [1]. These nonequilibrium relations entail a new development of martingale theory for entropy production and substantially extend and generalize previous results on entropy production minima statistics. Then I will show how to apply these results to obtain “optimal” thresholds that guarantee, with prescribed confidence, not exceeding a maximum value of the entropy production, work, or heat, during the interval. I will illustrate the results by using a simple model for the mechanically-driven synthesis of ATP by F1-ATPase rotatory motor.

P20

Thermodynamics of growth in chemical reaction networks

Open chemical reaction networks show a variety of complex dynamical behaviour such as chemical waves, oscillations, chaotic dynamics, multistability, and so on. Progress in stochastic thermodynamics has enabled us to identify the energetic costs of these phenomena. However, very little attention has been paid to chemical growth. We identify the necessary conditions under which open homogeneous CRNs evolving with mass action kinetics show asymptotic growth. Our main results show that growth with nonequilibrium abundances requires nonlinear CRNs with the influx of at least one species from the surrounding. Linear CRNs, on the other hand, can only grow with equilibrium abundances. Our results illustrate the important interplay between topology and the chemostatting procedure in determining the asymptotic dynamics of CRNs.

P21

Entropy production of resetting processes

Stochastic systems that undergo random restarts to their initial state have been widely investigated in recent years, both theoretically and in experiments. Oftentimes, however, resetting to a fixed state is impossible due to thermal noise or other limitations. As a result, the system configuration after a resetting event is random. Here, we consider such a resetting protocol for an overdamped Brownian particle in a confining potential V(x). We assume that the position of the particle is reset at a constant rate to a random location x, drawn from a distribution p_R(x). To investigate the thermodynamic cost of resetting, we study the stochastic entropy production. We derive a general expression for the average entropy production for any V(x), and the full distribution of the entropy production for V(x)=0. We derive the large-deviation properties of the entropy production for exponential and Gaussian resetting distributions p_R(x). In the latter case, we show that the rate function has a first-order singularity at a critical value of the entropy production, corresponding to a real-space condensation transition.

P22

Taxis of cargo-carrying microswimmers in traveling activity waves

The rich phenomenology and the emergence of very fascinating collective and dynamical behaviors in active systems are attracting more and more attention in the scientific community. Active systems are widespread in nature and their theoretical modeling could complement the unprecedented recent advances in experimental techniques to get new physical insights into living matter. In particular, bacteria and eukaryotic cells typically navigate in dynamic activating media and react to time-dependent tactic stimuli of various natures, sometimes displaying unexpected migration properties. We develop a stochastic model for the motion of a self-propelled microswimmer carrying a passive cargo in an active traveling wave, and we reveal the emergence of a tactic transition from motion along the wave's propagation to motion counter the wave's propagation that is controlled by an order parameter given by the ratio between the mobility of the cargo and the mobility of the microswimmer. We verify our analytical predictions with numerical simulations and expect our results to inspire the future efficient design of bio-hybrid microswimmers.

P23

Experiment and Simulation Reveal Residual Details for How Target Binding Tunes Calmodulin's Calcium-binding Properties

We aim to elucidate the molecular mechanism of the reciprocal relation of calmodulin's (CaM) target binding and its affinity for calcium ions (Ca2+), which is central to decoding CaM-dependent Ca2+ signaling in a cell. We employed stopped-flow experiments and coarse-grained molecular simulations that learn the coordination chemistry of Ca2+ in CaM from first-principle calculations. The associative memories as part of the coarse-grained force fields built on known protein structures further influence CaM's selection of its polymorphic target peptides in the simulations. We modeled the peptides from the Ca2+/CaM-binding domain of Ca2+/CaM-dependent kinase II (CaMKII), CaMKIIp (293-310) and selected distinctive mutations at the N-terminus. Our stopped-flow experiments have shown that the CaM's affinity for Ca2+ in the bound complex of Ca2+/CaM/CaMKIIp decreased significantly when Ca2+/CaM bound to the mutant peptide (296-AAA-298) compared to that bound to the wild-type peptide (296-RRK-298). The coarse-grained molecular simulations revealed that the 296-AAA-298 mutant peptide destabilized the structures of Ca2+-binding loops at the C-domain of CaM (c-CaM) due to both loss of electrostatic interactions and differences in polymorphic structures. We provided a plausible explanation of a high Ca2+ release rate in the presence of mutant peptide in the stopped-flow experiments. We have leveraged a powerful coarse-grained approach to advance a residual understanding of the reciprocal relation in CaM, that could not be possibly achieved by other computational approaches

P24

Dynamic behaviour of microtubules around the critical temperature and effect of the electric field produced by these vibrations on its environment

In this work, we study the microtubule major cytoskeleton elements as a ferroelectric system. The behaviour of microtubules around the critical temperature was evaluated and the effect of the electric field produced by the microtubules on its environment was determined. Also, the mean-field theory approximation (MFTA) was used to evaluate the total polarization and free energy around the critical temperature. These parameters are evaluated according to the physiological and critical temperatures in the absence and the presence of the electric field produced by the vibrations of the microtubule network. Results show that the microtubule (MT) has a spontaneous polarization in the absence of an electric field which collapses above the critical temperature. Moreover, the transition from ferroelectric to paraelectric state occurs with increasing physiological temperature. The microtubule stability is observed at the minimal free energy. The free energy is higher in the paraelectric state than in the ferroelectric state and changes its behaviour at high temperatures. The electric field stabilizes and orients the microtubule in the direction of the field. The microtubule produces electric fields that strongly interact with its biological environment at a short distance while long-distance interactions are weak.

P25

Dynamical theory for evolution of the genotype-phenotype interrelationship

Theories of evolution mainly concerns with the genetic change, by assuming a given relationship from genes to the fitness. However, driving force for evolution is not directly determined by genes (genotypes), but by phenotypes, the state of organisms. The genotype-phenotype relationship that plays a crucial role in determining the function and robustness of biological systems can also change through evolution. Evolutionary theory for such relation needs to encapsulate both genetic variations and phenotypic variances by noise, rather than describing an uphill motion on a static fitness-landscape in the space of genotypes. Here we consider this relationship within the context of an evolution model that treats the nonequilibrium stochastic dynamics of both genotypes and phenotypes. In the model, adaptive changes of the gene-regulatory network that encodes genotypes are coupled to the evolution of the gene expression patterns encoding phenotypes. We studied the dynamical phase diagram of the evolved phenotypes against the noise and selection pressure, where each phase is distinguished by the temporal behaviour of the fitness, phenotypic and genetic overlaps and response to perturbations. In particular, we found a region with an enhanced robustness of the phenotypes to genetic mutations that is achieved under an intermediate level of noise, due to an emergent correlation between the dynamical response to noise and that to genetic mutations, in consistence with recent experimental observations.

P26

Universal bounds and thermodynamic tradeoffs in nonequilibrium energy harvesting

Many molecular systems operate by harvesting and storing energy from their environments. However, the maintenance of the nonequilibrium states necessary to support energy harvesting itself carries thermodynamic costs. We consider the optimal tradeoff between costs and benefits of energy harvesting in a nonequilibrium steady state, possibly in contact with a fluctuating environment. We find a universal bound on this tradeoff, which leads to closed-form expressions for optimal power output and optimal steady state distributions for three physically meaningful regimes. Our results are illustrated using a model of a unicyclic network, which is inspired by the logic of biomolecular cycles.

P27

Thermodynamic limits of sperm swimming precision

Sperm swimming is crucial to fertilise the egg, in nature and in assisted reproductive technologies. Modelling the sperm dynamics involves elasticity, hydrodynamics, internal active forces, and out-of-equilibrium noise. Here we demonstrate experimentally the relevance of energy dissipation for sperm beating fluctuations. For each motile cell, we reconstruct the time-evolution of the two main tail's spatial modes, which together trace a noisy limit cycle characterised by a maximum level of precision pmax . Our results indicate pmax ~ 10^2 s^(–1) , remarkably close to the estimated precision of a dynein molecular motor actuating the flagellum, which is bounded by its energy dissipation rate according to the Thermodynamic Uncertainty Relation. Further experiments under oxygen deprivation show that pmax decays with energy consumption, as it occurs for a single molecular motor. Both observations can be explained by conjecturing a high level of coordination among the conformational changes of dynein motors. This conjecture is supported by a theoretical model for the beating of an ideal flagellum actuated by a collection of motors, including a motor-motor nearest neighbour coupling of strength K: when K is small the precision of a large flagellum is much higher than the single motor one. On the contrary, when K is large the two become comparable.

P28

Influence of bulk crowders on the DNA target search of proteins: Theoretical Insights

The interaction of DNA-binding proteins (DBPs) with their specific target sites on the DNA initiates several important biological processes. This search process has been extensively studied in vitro. However, the presence of other proteins and macromolecules within the cellular matrix interferes with the in vivo search dynamics of DBPs by altering their diffusion. The impact of such macromolecular bulk crowders, whether static or dynamic, on the target search is explored analytically with the help of a discrete-state stochastic framework. The search is affected by the spatial positions of the bulk crowders relative to the target site as well as the mobility of the diffusing crowders. Additionally, there exits non-specific interactions between the bulk crowders and the DBPs which may also modify the entire search. The role of such (attractive) interactions is also explored theoretically using an exactly solvable discrete-state stochastic approach. Strong non-specific associations tend to accelerate the search of DBPs compared to weak interactions in the cytoplasm. Our analytical results are also supported by Monte Carlo computer simulations. We find that our predictions agree with existing experimental observations and previous simulation results which provides a physical understanding of the search process.

P29

How can we measure the dipolar interaction between domains in lipid monolayers at the air–water interface?

A great variety of biologically relevant monolayers present phase coexistence characterized by domains formed by lipids in an ordered phase state dispersed in a continuous, disordered phase. From the difference in surface densities between these phases, inter-domain dipolar interactions arise. These interactions are relevant for the determination of the spacial distribution of domains as well as their dynamics. Here, we propose a novel way of estimating the dipolar repulsion using a method based on the comparison of the pair correlation function obtained from experiments with that obtained from Brownian dynamics simulations of a model system. As an example, we determined the difference in dipolar density of a binary monolayer of DSPC/DMPC at the air-water interface from the analysis of the radial distribution of domains, and the results are compared with those obtained by surface potential determinations. A systematic analysis for the experimentally relevant parameter range is given, which may be used as a working curve for obtaining the dipolar repulsion in different systems.

P30

Decision making of non-equilibrium fluctuations

Timely effective decision-making requires gathering information based on noisy sensory evidence. This leads to the optimality problem of decision-making with respect to a speed-accuracy tradeoff. It has been revealed that the minimal time needed to decide on the direction of the arrow of time is inversely proportional to the steady-state entropy production rate of a stochastic process. In this work, we disclose the mean decision time and accuracy of individuals, exposed to a stimulus moving according to a non-equilibrium stationary stochastic process, by using mean first-passage times with fixed and fluctuating thresholds in space and time. We show that the actual mean decision time and accuracy depend on the physical properties of the stimuli, and this is sported by numerical simulations and experimental data in human behavior. Results revealed that participants' decision times were well predicted by the mathematical models that describe possible strategies implemented by the individuals. Our study shows that providing a comprehensive model of the physical properties of the stimuli to judge allows a better characterization of the variables involved in perceptual decision and shows that studying human behavior can refine the problem of time's arrow, within the framework of non-equilibrium statistical mechanics.

P31

Microscopic Theory for the Diffusion of an Active Particle in a Crowded Environment

We calculate the diffusion coefficient of an active tracer in a schematic crowded environment, represented as a lattice gas of passive particles with hardcore interactions. Starting from the master equation of the problem, we put forward a closure approximation that goes beyond trivial mean field and provides the diffusion coefficient for an arbitrary density of crowders in the system. We show that our approximation is accurate for a very wide range of parameters, and that it correctly captures numerous nonequilibrium effects, which are the signature of the activity in the system. For a certain range of parameters, when an external force is applied to the active particle, Absolute Negative Mobility can be observed in the system.

P32

A two-component EEA1-Rab5 molecular motor and its collective action

Cellular functions such as metabolism, mechanics, signal transduction, and regulation are nonequilibrium phenomena utilizing the stored energy of hydrolysis. In cells, molecular motors drive the mechanics by consuming stored energy in nucleotide phosphates while generating various types of motions. Hitherto discovered and studied motors are ATPases utilizing the energy of hydrolysis in performing cellular functions. While the functioning of individual motors is of fundamental interest, there have been attempts to understand the collective actions of these motors on force generation, step size, and processivity. Conversely, synthetic collective motors employ mechanisms such as DNA and RNA-based burnt bridge Brownian ratchets than being dependent on nucleotide phosphates. Here, we present the discovery of a new class of two-component molecular motors, which utilize the free energy of GTP hydrolysis in performing mechanical work cycles, and their collective action. The two-component molecular motor act as a polymer engine driven by reversible flexibility transitions in long tether molecule EEA1 coupled to Rab5 GTPase cycle. This identified motor does not require additional assistance and can increase its stiffness via non-specific interactions. We developed and applied biophysical tools to study the polymer fluctuations using correlation spectroscopy in combination with theoretical modelling of semi-flexible polymers undergoing flexibility switch-driven conformational changes. Furthermore, the collective action of these motors in a brush-like formation generates enhanced motion of vesicles proximal to the brushes, traversing lengths comparable to endosomes. We anticipate these findings are of great interest to biophysicists and soft-matter physicists working in the field of molecular motors and nonequilibrium dynamics.

P33

The role of asymmetric cooperativity in DNA replication

TBD

P34

Frequency response in microRNA-mediated genetic regulation

Living cells are inherently dynamic. Live-cell time-lapse microscopy and fluorescent reporter genes have allowed to track the dynamic behavior of molecules, thereby uncovering a picture where many regulatory proteins undergo pulses. Oscillatory signals can carry key biological information encoded in the shape of pulses. Specifically, some circuits have been shown to respond preferentially to certain oscillation frequencies. MicroRNAs, small RNA molecules that regulate their target messenger RNA through a post-transcriptional mechanism, have been found to be expressed in pulses. MiRNAs repress gene expression by promoting the degradation of target mRNA and/or inhibiting its translation. Regulatory circuits involving miRNAs are increasingly being uncovered acting in key biological processes, such as development and differentiation. A single miRNA regulates multiple target genes, thereby generating competition between target mRNAs. However, the interplay between competition and pulsatile signaling is poorly understood. A mRNA molecule often presents multiple binding sites relative to a specific miRNA, making the extent of repression dependent on how many sites are bound, conferring cooperative properties to the interaction. We theoretically address pulsatile signaling within miRNA-mediated regulation focusing on the role of oscillation frequency and investigating its interplay with significant features of this interaction. Our results indicate that modulation of some parameters that control competition and cooperativity could serve as a tuning mechanism: it can shift and sharpen the frequency preference response, leading to non-intuitive effects. These results can also be addressed experimentally by quantifying target fold-repression by time-lapse microscopy and using optogenetics to induce a pulsatile miRNA expression.

P35

Simulation-based inference for describing stochastic non-linear oscillations by the hair bundles of sensory cells.

Hair cells are remarkable sensors that detect sub-nanometer vibrations from sound waves and transduce them into electrical signals for neural processing. Their sensory antennas are hair-bundles that display non-linear, stochastic oscillations; for example, bistable or relaxation oscillations. Different mathematical descriptions for these oscillations have been proposed, however it is challenging to determine exact numerical values for the model parameters from stochastic trajectories. Here, we introduce a recently developed method, simulation-based inference (SBI) for determining the numerical values of parameters for a biophysical model of hair-bundle oscillations. SBI uses simulated data from the biophysical model and experimental data to infer posterior distributions of the numerical values for each model parameter. In addition, these numerical values can be used for further analyzing the biophysical model and establishing the connection from biophysical model to generic model such as the normal form of a Hopf bifurcation.

P36

Trade-offs between cost and information in cellular prediction

Living cells can leverage correlations in environmental fluctuations to predict the future environment and mount a response ahead of time. To this end, cells need to encode the past signal into the output of the intracellular network from which the future input is predicted. Yet, storing information is costly while not all features of the past signal are equally informative on the future input signal. Here, we show, for two classes of input signals, that cellular networks can reach the fundamental bound on the predictive information as set by the information extracted from the past signal: push-pull networks can reach this information bound for Markovian signals, while networks that take a temporal derivative can reach the bound for predicting the future derivative of non-Markovian signals. However, the bits of past information that are most informative about the future signal are also prohibitively costly. As a result, the optimal system that maximizes the predictive information for a given resource cost is, in general, not at the information bound. Applying our theory to the chemotaxis network of Escherichia coli reveals that its adaptive kernel is optimal for predicting future concentration changes over a broad range of background concentrations, and that the system has been tailored to predicting these changes in shallow gradients.

BRAIN CRITICALITY

SCHOOL OF PHYSICAL SCIENCES AND NANOTECHNOLOGY

P37

Griffiths phase in dynamical networks: a mechanism for emergence of consciousness?

Juan S. Rojas, Mario Cosenza

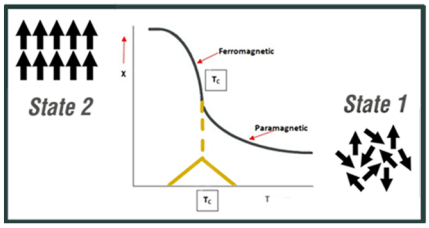
The brain spends most of its time around a region near a critical point. Then, we investigate the relation between the topology of the network and the emergence of the chaotic Griffith phase using small world network. Our work suggests a relation between neuroplasticity (conscious activity) with random connections.

Introduction

Physics

Is there any dynamical system that lives between two stable states? This has been study from some useful perspectives:

-Statistical physics. From Critical point to Griffiths Phase. (1969).



Critical Point

- Dynamical Systems. [1] We consider coupled map network:

$$x_{n+1}(i) = (1-\epsilon) f(x_n(i)) + \frac{\epsilon}{k_i} \sum_{j=1}^{N} T_{i,j} f(x_n(j))$$

$$T_{ij} = \begin{cases} 1, \text{ edge} \\ 0, \text{ other} \end{cases} \qquad f(x) = 1 - ax^2$$

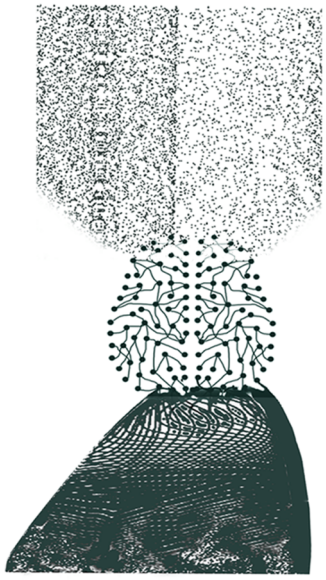
Neuroscience

-1941. Warren McCulloch. Neuronal Avalanches of activity.
-2008. Kauffman. Systems at edge of chaos are able of: "coordinate past discriminations with reliable future actions"
-2021. Consciousness is supported by near-critical slow cortical ED. **[2]**

Core Conjecture

The brain spends most of its time in a region near the critical point, not just in a critical point.

Methodology



Why we use Griffiths Phase?

Griffiths Phase represents a region in which elements repeat synchronization and desynchronization intermittently. Useful thing about studying neural dynamics in the Griffiths Phase turns around the resistance of the critical states to changes in parameters.

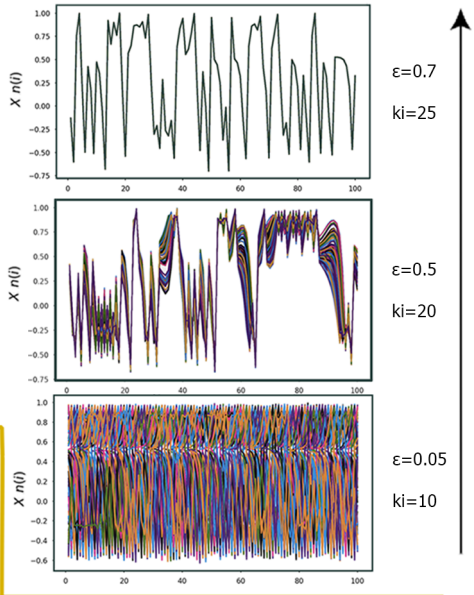
Important properties.

- Distribution of synchronized and desynchronized clusters with a power law.
- Random connections.

Why random connections?

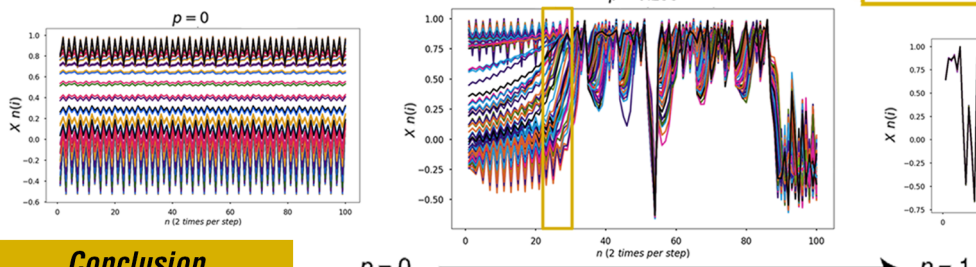
We investigate relationship between the topology of the network with emergence of the Chaotic Griffiths Phase using small world network.

Behavior of Typical Time Series
n(2 time per step)

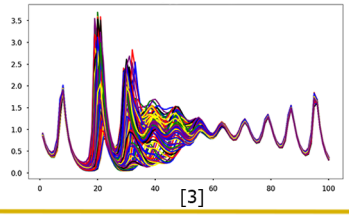


Results

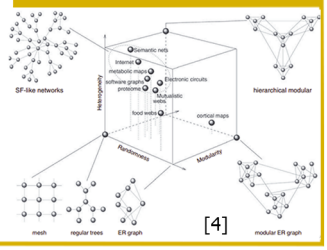
In p ≈ 0.299, we found a window that relates regular and aleatory states. This begging of Griffiths Phase does not fall into small world network with ε=0.05 and ki=20.



p = 0 → Increasing randomness → p = 1



[3]



[4]

Conclusion

We need really random connections (from p ≈ 0.299) to generate Griffiths PhaseWe suggest that "Changes in grey matter induced by training (2004)" presents an idea of random learning reconnection that could be compatible with random connection dependence.

Future Work

Acknowledgment

José Luis Herrera: Networks help.
Ivan P. Urbano: Poster edition.

[1] K. Shinoda, K. Kaneko, Physical Review Letters 117, 254101 (2016).
[2] Toker, Daniel, et al. "Consciousness is near-critical cortical ED" PNAS (2022).
[3] Chialvo, D.R. (1995). Generic excitable dynamics on a two-dimensional map.
[4] Sporns, O. (2016). Networks of the Brain. MIT press.

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