<u>Workshop ANR ChaMaNe</u>
<u>Challenges in Mathematical Neuroscience</u>

February 20 – 23, 2024

Salle de conférence, Dieudonné building, Université Côte d'Azur,
Parc Valrose, 06000 Nice, France

Tuesday February 20th

10h-10h30	Welcome - coffee
10h30-11h30	[Bio] Michele Bertacchi (iBV, Nice) *Cortical neurogenesis: experimental observation and possible mathematical modeling*
11h30-12h30	[Bio] Pierre-Yves Jacob (LNC, Marseille) *Entorhinal grid cell activity during a goal directed navigation task.*
12h30-13h30	Lunch break (Rest. Admin. des impôts, rue Cadéi Nice)
13h30- 15h30	Long break to work (and/or collaborate on the biological open questions presented on Tuesday morning)
15h30-16h30	Delphine Salort (LCQB, Sorbonne Université) *Some PDE models from neurosciences with partial diffusion*
16h30-17h30	Eric Luçon (MAP5, Paris Cité) *Hawkes processes and the Neural Field Equation on the real line*

Wednesday February 21st

9h30-10h30	Olivier Faugeras (Inria, Université Côte d'Azur) *A new twist on the large size limit behaviour of networks of Hopfield-like neurons*
10h30-11h15	coffee break
11h15-12h15	Nicolas Torres (IMAG, Granada) *Analysis of an elapsed time model with discrete and distributed delays. New insights and theory.*
12h15-13h30	Lunch break (Rest. Admin. des impôts, rue Cadéi Nice)
13h30- 15h30	Long break to work (and/or collaborate on the biological open questions presented on Tuesday morning)

Change of room Wednesday afternoon: Fizeau 5th floor

15h30-16h30 Fizeau 5	Zoé Agathe-Nerine (MAP5, Paris Cité) *Long-term stability of interacting Hawkes processes*
16h30-17h30 Fizeau 5	Kadmo de Souza Laxa (NeuroMat, Sao Paulo) *Metastability in a Stochastic System of Spiking Neurons with Leakage*

Thursday February 22nd

9h30-10h30	Susanne Solem (Dpt Math., Norwegian University of Life Science) *A stochastic neural field in the form of a PDE with a tricky boundary condition*
10h30-11h15	coffee-break
11h15-12h15	Emre Baspinar (Inria, Université Côte d'Azur) *A biologically plausible decision-making model based on interacting cortical columns*
12h15-13h30	Lunch break (Rest. Admin. des impôts, rue Cadéi Nice)
13h30- 15h30	Long break to work (and/or collaborate on the biological open questions presented on Tuesday morning)
15h30-16h30	Anna Melnykova (Avignon) *Granger Causal Inference in Multivariate Hawkes Processes by Minimum Message Length*
16h30-17h30	Francis Filbet (IMT, Toulouse) *Asymptotic analysis and numerical schemes for the FitzHugh-Nagumo transport equation with strong local interactions*
19h30	Fancy dinner at restaurant

Friday February 23rd

9h00-9h45	Sophie Jaffard (LJAD, Nice) *Provable local learning rule for a Hawkes network*
9h45-10h30	Qingyou He (LCQB, Sorbonne Université) *Exponential time decay rate for a weakly nonlinear Fokker-Planck Equation with partial diffusion.*
10h30-11h15	coffee break
11h15-12h15	Samuel Deslauriers-Gauthier (Inria, Université Côte d'Azur) *Identifying and correcting cross-subject atlas variability using graph alignment*
12h15-13h30	Lunch break (Rest. Admin. des impôts, rue Cadéi Nice)

THE END

ABSTRACTS

[Bio] Michele Bertacchi (iBV, Nice)

Cortical neurogenesis: experimental observation and possible mathematical modeling

The cerebral cortex is a highly complex structure responsible for various cognitive functions, and understanding how corticogenesis progresses during embryonic development is crucial for unraveling brain development and function. At early phases of neural development, self-renewing symmetric divisions increase the number of progenitor cells, while later steps of neurogenesis are characterized by asymmetric differentiative divisions that generate neurons. These two opposite processes need to be tightly controlled in time and space. While the general structure of progenitor and neuronal layers is maintained in different regions along the antero-posterior axis of the neocortex, the neuronal output (*i.e.* the number of neurons locally produced) can greatly vary, as the progenitors in each region of the cortex can behave differently.
Some determining factors that need to be considered for a mathematical model are the size and type of the founder population (apical vs basal), the duration of cortical neurogenesis, the proportion of different progenitor types, their spatial arrangement, and the fine-tuned balance between self-renewing and differentiative divisions (symmetric vs asymmetric). Our team is in particular interested by the role of the expression of a particular gene: the Nr2f1. We previously unraveled the role of the Nr2f1 gene to fine-tune the cell cycle dynamics and to control the neuronal output in the posterior-most cortex, but its role in other areas is still unknown. On the experimental side, Nr2f1 mutant mice can be used to take into account this regionalized aspect of neurogenesis, by measuring distinct rates of corticogenesis along the antero-posterior axis.
Existing models or simulations are based on ODE or agent-based simulation but do not take into account the spatial aspect, that is the regionalized aspect of corticogenesis. Our goal is to collaborate to integrate mathematical modelling and experimental observations to highlight the different strategies and factors that can explain regional diversity along the antero-posterior axis of the mammalian neocortex in terms of number of locally produced neurons.

[Bio] Pierre-Yves Jacob (LNC, Marseille)

Entorhinal grid cell activity during a goal directed navigation task.

Spatial navigation relies on a mental representation of space supported by the activity of space-coding neurons including place cells and grid cells. The activity of these cells has been mostly exclusively described in animals navigating in simple environments, in which they freely move. However, rodents or humans navigation does not resemble to freely moving behaviour but is used to reach goals.
This presentation will show recent unpublished data of a project aimed to characterize how grid cells and place cells code spatial information during goal-directed navigation. Previous

studies on the effect of goal on grid cells activity merged goal location with reward, making difficult to conclude about the nature of the information (i.e. location or reward) integrated by the grid cells network. We used a continuous-goal directed navigation task which allows separating spatial goal from the reward. We found a local distortion of the grid map around the goal that only emerges when a halt inside the goal zone is required to obtain the reward. This indicates that the grid map distortion does not simply reflect a goal coding but also integrates temporal constraints of the task. This parallels previous results demonstrating that in the same task the hippocampal place cells code for goal location through a local out-of-field activity. Our results strengthen the view that neuronal activity on the entorhinal-hippocampal network does not simply map the environment in a pure spatial representation but instead provides a complex representation of external events within their spatio-temporal context.
By describing new properties of place cells and grid cells in complex spaces, our team tries to understand the neurobiological bases of the cognitive map in more ecologically relevant environments than the ones traditionally used in laboratory settings.

Zoé Agathe-Nerine (MAP5, Paris Cité)

Long-term stability of interacting Hawkes processes

We consider a multivariate Hawkes process modeling the activity of N interacting neurons, regularly positioned on a bounded space. We study the model and its large population limit, that can be described by the neural field equation (NFE). We study the long-time stability of the synaptic current of the population, as $N \to \infty$, in case the synaptic memory kernel is exponential, up to time horizons that are polynomial in N in two different cases: one where there is a unique stationary solution to the NFE, and one where the NFE admits a locally stable manifold of stationary solutions. For the latter case, we show in particular that the phase of the voltage along this manifold converges towards a Brownian motion on a time scale of order N.

Emre Baspinar (Inria, Université Côte d'Azur)

A biologically plausible decision-making model based on interacting cortical columns

The Adaptive Exponential (AdEx) mean-field framework [1] describes the averaged neuronal population dynamics modeled by the AdEx network. In the case of cerebral cortex, AdEx networks are used to model two cell types: Regular Spiking (RS) neurons, displaying spike-frequency adaptation as observed in excitatory pyramidal neurons, and Fast Spiking (FS) neurons, with no adaptation, as observed in inhibitory interneurons. AdEx networks are high dimensional, complex and difficult to analyze. AdEx mean-field models are low dimensional, simpler and easier to analyze compared to networks, yet they approximate closely the network dynamics, motivating our choice of model. Here, we extend the AdEx mean-field framework to model two networks of excitatory-inhibitory neurons, representing two different cortical columns [2, 3] . The model is biophysically plausible since it is based on intercolumnar excitation modeling the long-range connections and intracolumnar excitation-inhibition modeling the short-range connections. This connection scheme introduces bicolumnar competition, sufficient for choosing between two alternatives. Each column represents a pool of neurons voting for one of the two alternatives indicated by two stimuli presented on a monitor. We endow the model with a reward- driven learning mechanism which captures the optimal strategy maximizing the cumulative reward, as well as to model the exploratory behavior of the participant. The model has been tested on behavioral results obtained from human and macaque experiments and it provides promising performance. This model contributes to a biophysical ground for simpler phenomenological models proposed for similar decision-making tasks and it can be applied to neurophysiological data. Finally, it can be embedded in whole-brain simulators, such as The Virtual Brain (TVB), to study decision-making in terms of large-scale brain dynamics [4]. This is a joint work with Gloria Cecchini, Michael DePass, Marta Andujar, Pierpaolo Pani, Stefano Ferraina, Rubén Moreno-Bote, Ignasi Cos and Alain Destexhe.

References

[1] Di Volo M., Romagnoni A., Capone C., Destexhe A. (2019) Biologically realistic mean-field models of conductance-based networks of spiking neurons with adaptation. Neural Computation 31(5):653-680.

[2] Baspinar E., Cecchini G., DePass M., Andujar M., Pani P., Ferraina S., Moreno-Bote R., Cos I., Destexhe A. (2023) A biologically plausible decision-making model based on interacting cortical columns. bioRxiv 530384. Available from https://doi.org/10.1101/2023.02.28.530384.

[3] Baspinar E., Cecchini G., Moreno-Bote R., Cos I., Destexhe A. (2022) Jupyter notebook of a biophysically plausible decision-making model based on interacting cortical columns (v1.0.0) [Python source code]. Available from https://github.com/emrebasp/Jupyter-notebook- A-biophysically-plausible-decision-making-model-based-on-interacting-cortical-co.

[4] Turan A., Baspinar E., Destexhe A. (2023) A whole-brain model of auditory discrimination. bioRxiv 559095. Available from https://doi.org/10.1101/2023.09.23.559095.

Samuel Deslauriers-Gauthier (Inria, Université Côte d’Azur)

Identifying and correcting cross-subject atlas variability using graph alignment.

Every brain is unique, having its structural and functional organisation shaped by both genetic and environmental factors over the course of its development. Brain imaging studies produce results by averaging across a group of subjects, under the assumption that it is possible to subdivide the cortex into homogeneous areas. However, it is not obvious that the structural and functional properties of a specific region of an atlas can be assumed match across subjects. We investigate this hypothesis via a network representation of the brain, with nodes corresponding to brain regions and edges to their structural relationships. We perform graph matching on these networks to estimate, and possibly correct, the misalignment between regions across subjects.

Olivier Faugeras (Inria, Université Côte d’Azur)

A new twist on the large size limit behaviour of networks of Hopfield-like neurons

We revisit the problem of characterising the thermodynamic limit of a fully connected network of Hopfield-like neurons. Our contributions are that we provide a) a complete description of the mean-field equations as a set of stochastic differential equations depending on a mean (m(t)) and covariance (K(t, s)) functions, b) a provably convergent method for estimating these functions, and c) numerical results of this estimation as well as examples of the resulting dynamics. The mathematical tools are the theory of Large Deviations, Itô stochastic calculus, and the theory of Volterra equations.
We have generalized and set on a firm mathematical basis the work of Sompolinsky et al., e.g. [2], Helias et al., e.g. [4]. We have also extended the work of Ben Arous and Guionnet, e.g. [1], and clarified and complemented the work of Faugeras et al., e.g. [3].

Joint work with Etienne Tanré.

<u>References</u>

[1]Gérard Ben Arous and Alice Guionnet. Large deviations for Langevin spinglass dynamics. Probability Theory and RelatedFields,102(4):455– 509, 1995.

[2] A. Crisanti and H. Sompolinsky. Path integral approach to random neural networks. Physical Review E, 98(6):062120, December 2018.

[3] Olivier Faugeras,Jonathan Touboul,and Bruno Cessac.A. constructive mean-field analysis of multipopulation neural networks with random synaptic weights and stochastic inputs. Frontiers in Computational Neuroscience, 3, 2009.

[4] Alexander van Meegen, Tobias Kühn, and Moritz Helias. Large-Deviation Approach to Random Recurrent Neuronal Networks: Parameter
Inference and Fluctuation-Induced Transitions. Physical Review Letters, 127(15):158302, October 2021.

Francis Filbet (IMT, Toulouse)

Asymptotic analysis and numerical schemes for the FitzHugh-Nagumo transport equation with strong local interactions

This talk is devoted to the analysis and numerical approximation of the spatially-extended FitzHugh-Nagumo transport equation with strong local interactions. The first part will concern a review of the asymptotic analysis leading to reaction/diffusion system. In this regime, the time step can be subject to stability constraints related to the interaction kernel. To avoid this limitation, our approach is based on higher-order implicit-explicit numerical schemes. Thus, when the magnitude of the interactions becomes large, this method provides a consistent discretization of the macroscopic reaction-diffusion FitzHugh-Nagumo system. We carry out some theoretical proofs and perform several numerical experiments that establish a solid validation of the method and its underlying concepts.

Qingyou He (LCQB, Sorbonne Université)

Exponential time decay rate for a weakly nonlinear Fokker-Planck Equation with partial diffusion.

We consider the initial boundary value problem for the Fokker-Planck equation with partial diffusion and Dirac's type source term arising in neuroscience. We prove that, for the weakly nonlinear equation, the solution converges exponentially fast to the unique stationary state. The proof is based on the use of Doeblin-Harris method for a linear equation with a time dependent drift, combining with entropy estimates, in order to control the non linear term. This work is jointed with Elena Ambrogi and Delphine Salort.

Sophie Jaffard (LJAD, Nice)

Provable local learning rule for a Hawkes network

Recordings of human brain suggest that concepts are represented through sparse set of neurons that fire when the concept is activated. Neuroscientists have identified local learning rules to adjust synaptic weights, but to our knowledge there is no mathematical proof that such local rules enable to learn. We use Hawkes networks as a model for a cognitive network that can learn categories by updating synaptic weights with a local learning rule. In this network, output nodes are post-synaptic neurons that produce spikes as a discrete-time Hawkes process, whose spiking probability is a function of the weighted sum of the activity of the pre-synaptic neurons at the previous time step. Kalikow decomposition allows us to interpret these synaptic weights in the previous sum as a probability distribution. This interpretation of the synaptic weights leads to the following local vision: for a postsynaptic neuron, its presynaptic neurons can be seen as so many experts and the distribution, given by the weights, can be related to an expert aggregation problem. This is why we use at this stage an expert aggregation algorithm to update the weights, which provides a local learning rule. The resulting algorithm is called HAN (Hawkes Aggregation of Neurons) and is general enough for any expert aggregation algorithm. We were able to prove mathematically that HAN is able to learn. To the best of our knowledge, the present work mathematically proves for the first time that such local learning rules make a very simple network learn.

Eric Luçon (MAP5, Paris Cité)

Hawkes processes and the Neural Field Equation on the real line

This is an ongoing work with C. Poquet. The Neural Field Equation (NFE) was introduced by Wilson, Cowan and Amari to model mesoscopic activity of neural networks. It has particularly proven to exhibit nontrivial dynamical structures such as traveling waves. Recently, Chevallier, Duarte, Löcherbach and Ost have given a microscopic interpretation of the NFE in terms of the limit of the potential of spatially organized Hawkes processes. Whereas the previous work essentially restricts to bounded spatial domains, the aim of the talk is to discuss a similar approximation on the real line. We will give arguments in favor of the stability of such particle system w.r.t. traveling waves, on a time scale of order the size of the population.

Anna Melnykova (Avignon)

Granger Causal Inference in Multivariate Hawkes Processes by Minimum Message Length

Multivariate Hawkes processes (MHPs) are versatile probabilistic tools used to model various real-life phenomena: earthquakes, operations on stock markets, neuronal activity, virus propagation and many others. In this work, we focus on MHPs with exponential decay kernels and estimate connectivity graphs, which represent the Granger causal relations between their components. We approach this inference problem by proposing an optimization criterion and model selection algorithm based on the minimum message length (MML) principle. While most of the state-of-art methods using lasso-type penalization tend to overfitting in scenarios with short time horizons, the proposed MML-based method achieves high F1 scores in these settings. We conduct a numerical study comparing the proposed algorithm to other related classical and state-of-art methods, where we achieve the highest F1 scores in specific sparse graph settings. We illustrate the proposed method also on G7 sovereign bond data and obtain causal connections. It is a joint work with Irene Tubikanec (Klagenfurt University) and Katerina Hlavackova-Schindler (University of Vienna).

Delphine Salort (LCQB, Sorbonne Université)

Some PDE models from neurosciences with partial diffusion

In this talk, we consider different class of PDE models with partial diffusion and complex source terms. Those particular structures induce new challenges, because classical methods as entropy methods fail, even in the linear case. We explain how Doeblin-Harris type methods can be useful in this context, at least for the linear case, and give an example of application with a toy model. We then explain the difficulty to deal with the non linear case.

Susanne Solem (Dpt Math., Norwegian University of Life Science)

A stochastic neural field in the form of a PDE with a tricky boundary condition

A Fokker--Planck-like partial differential equation was recently proposed to represent stochastic neural fields with the aim of better understanding the impact of noise on grid cells. This representation allows a study of noise-induced behaviors in a deterministic framework. However, the nonlinear and non-local nature of the PDE combined with a no-flux boundary condition prevents a direct application of methods used to study properties of more classical neural field models, such as pattern formation and stability of stationary states. In this talk I will present recent results for this model, and discuss some challenges related to it. The talk is based on works with Jose A. Carrillo, Helge Holden, and Pierre Roux.

Kadmo de Souza Laxa (NeuroMat, Sao Paulo)

Metastability in a Stochastic System of Spiking Neurons with Leakage

We consider a finite system of interacting point processes with memory of variable length modeling a finite but large network of spiking neurons with two different leakage mechanisms. Associated to each neuron there are two point processes, describing its successive spiking and leakage times. For each neuron, the rate of the spiking point process is an exponential function of its membrane potential, with the restriction that the rate takes the value 0 when the membrane potential is 0. At each spiking time, the membrane potential of the neuron resets to 0, and simultaneously, the membrane potentials of the other neurons increase by one unit. The leakage can be modeled in two different ways. In the first way, at each occurrence time of the leakage point process associated to a neuron, the membrane potential of that neuron is reset to 0, with no effect on the other neurons. In the second way, if the membrane potential of the neuron is strictly positive, at each occurrence time of the leakage point process associated to that neuron, its membrane potential decreases by one unit, with no effect on the other neurons. In both cases, the leakage point process of the neurons has constant rate. For both models, we prove that the system has a metastable behavior as the population size diverges. This means that the time at which the system gets trapped by the list of null membrane potentials suitably re-scaled converges to a mean one exponential random time.

Nicolas Torres (IMAG, Granada)

Analysis of an elapsed time model with discrete and distributed delays. New insights and theory.

The elapsed time equation is an age-structured model that describes dynamics of interconnected spiking neurons through the elapsed time since the last discharge, leading to many interesting questions on the evolution of the system from a mathematical and biological point of view. In this talk, we first deal with the case when transmission after a spike is instantaneous and the case when there exists a distributed delay that depends on previous history of the system, which is a more realistic assumption. Then we study the well-posedness and the numerical analysis of these elapsed time models. For existence and uniqueness we improve the previous works by relaxing some hypothesis on the non-linearity, including the strongly excitatory case, while for the numerical analysis we prove that the approximation given by the explicit upwind scheme converges to the solution of the non-linear problem. We show some numerical simulations to compare the behavior of the system under different parameters, leading to solutions with different asymptotic profiles. Moreover, we present some new perspectives that are interesting to determine the asymptotic behavior of the system.