INDAM Meeting

NeuroMath, Mathematical and Computational Neuroscience: cell, network and data analysis

Cortona (Italy), September 12-16, 2016

Istituto Nazionale di Alta Matematica “F. Severi”

Dipartimento di Matematica “F. Enriques” . UniMI

Centro ADAMSS – UniMI

ABSTRACTS

INVITED SPEAKERS

Giorgio Ascoli (Krasnow Institute, George Mason University, USA)

In and out of the Matrix: from neuron types to associative learning

According to leading theories of memory formation, storage, and retrieval, the brain represents information in the form of network connectivity. In this context, neural circuits can be described to a first approximation as (very large) directed graphs. I will describe three related lines of research spanning the range of theoretical, empirical, and computational neuroscience, in which data transformations using matrix notation offer simple mathematical solutions to open problems. The first “matrix neuroscience” application uses stochastic block modeling to define neuronal classification directly from network connectivity. The underlying idea is that, although no two neurons synapse exactly with the same partners, neurons can be grouped according to the relative similarity of their input and output patterns. The second study, starting from a large-scale literature-derived knowledge-base of synaptic biophysics (amplitude, kinetics, and plasticity), demonstrates that unknown parameters can be confidently imputed based on sparse measurements with basic matrix-completion techniques. This approach can be extended to non-square matrices for extracting putative genetic expression data in identified neuron types from incomplete experimental records. Lastly, we derived an analytic formulation linking prior neural connections (background knowledge) to possible new synapses (learning potential) based on the assumption of efficient (quasi-minimal) wiring. Computer simulations showed that the resulting connectionist rule boosts the one-trial acquisition of real associations relative to spurious (random) co-occurrences. These examples suggest that greater involvements of mathematicians could be tremendously helpful in advancing neuroscience.

Borghese N. Alberto (Università degli studi di Milano, I)

Exergaming for autonomous rehabilitation

A key factor in neurorehabilitation is intensive training. This, given the costs of classical rehabilitation, can be obtained only if patient is enabled to train, at least partially, by himself. Exergames have been largely explored for this aim: the patient is prompted to perform specific movements (those required by rehabilitation) by a videogame; his movement is picked-up by cameras or other instruments and applied to his/her avatar performing the same movement inside the videogame. However, most of exergames are not designed with a clear focus on rehabilitation requirements and constraints, and this limits their use. Even worse, they lack any supervision, typical of a real therapist; this can easily make exercising alone dangerous. We show here how designing an adequate virtual therapist (VT) endowed with artificial intelligence and inserting it inside the game engine, autonomous rehabilitation at home may become effective and safe. Safety is a major concern: to avoid incorrect postures and movements, the clinician can teach to the VT the correct movement. Fuzzy systems, combined with a graphical interface, allow using a simple and intuitive way to transfer such knowledge from real therapist to the VT. The VT provides also a real-time feed-back to the patient on the quality of his motion through an informative color coding scheme applied to the patient's avatar body segments. This feedback is complemented with a VT avatar that, in the extreme situations, pauses the game and explains the correct way to do the movement. Role of the avatar is also to welcome the patient and summarize the therapy results to him/her to increase compliance; text to speech and simple animation are aimed at improving engagement. Personalization and adaptation are also important. We identify a key parameter for each game associated to the dimension on which patient is currently being trained (range of motion, speed, accuracy) and allow the clinician to set this value according to the patient. Mechanisms of Dynamic Difficult Adaptation in real-time are implemented to tune this value to the actual patient status. An approach based on Bayesian on-line optimization will be presented. Quantitative data can then be reviewed by the clinician inside the hospital. He/she can program patients follow-up visits and help. The Game Engine is complemented with a middle-ware to accommodate different tracking devices, depending on the rehabilitation requirements. Preliminary results on the extension of this platform for hand/finger rehabilitation by using custom designed sensorized objects will also be reported. The resulting two-level platform (hospital/home) is becoming a general framework in the health domain in general, where some services are being moved through the web and could be delivered, in the next future, also through intelligent machines. The platform Preliminary results on usability with patients and therapists suggest that the approach can maintain a proper challenge level while keeping the patient motivated, safe, and supervised for a long time.

Stephen Coombes (School of Mathematical Sciences Nottingham, UK)

Next generation neural field modelling

Neural mass models have been actively used since the 1970s to model the coarse grained activity of large populations of neurons and synapses. They have proven especially fruitful for understanding brain rhythms. However, although motivated by neurobiological considerations they are phenomenological in nature, and cannot hope to recreate some of the rich repertoire of responses seen in real neuronal tissue. In this talk I will first discuss a theta-neuron network model that has recently been shown to admit to an exact mean-field description for instantaneous pulsatile interactions. I will then show that the inclusion of a more realistic synapse model leads to a mean-field model that has many of the features of a neural mass model coupled to an additional dynamical equation that describes the evolution of network synchrony. I will further show that this next generation neural mass model is ideally suited to understanding beta-rebound. This is readily observed in MEG recordings whereby hand movement causes a drop in the beta power band attributed to a loss of network synchrony. Existing neural mass models are unable to capture this phenomenon since they do not track any notion of network coherence (only firing rate). I will finish my talk by presenting some preliminary results for the spatio-temporal pattern formation properties of a neural field version of this model.

Egidio D’Angelo (Università di Pavia - BCC, I)

New perspectives for neuron and brain modeliing: the Human Brain Project approach

Paolo Del Giudice (Italian National Institute of Health, I)

Density-based clustering of parallel spike trains allows for efficient use of pairwise correlations for inference

The old idea, that pairwise correlations between neural activities can be informative of the synaptic efficacies, has been revived thanks to the increasing availability of multiple simultaneous electrophysiological recordings, and to theoretical advance on using such large matrices of (individually small) correlations for reliable inference of effective synaptic efficacies. For approaches to inference based on pairwise equilibrium Ising-like models, Boltzmann learning in principle can return maximum likelihood estimate of couplings.

Many efforts were devoted to either circumvent computational load of Boltzmann learning through various mean-field approximations, or to approximate the equilibrium distribution in the neighborhood of the data points. On the other hand, the same abundance of parallel neural recordings motivated efforts to develop compact representations of multi-dimensional neural data, e.g. using dimensional reduction techniques like PCA. We propose here that density-based clustering in the space of neural activity configurations provides both an alternative to dimensional reduction for compact representation of the data, and an interesting option to significantly improve inference of effective synaptic couplings. Density-based clustering is based on the frequency of visit of discrete neighborhoods in the neural configuration space, and implicitly defines an energy landscape' whose local maxima are the centroids of the clusters. For the purpose of inference it allows to define equilibrium models in terms of the pairwise correlations between the centroids of the identified clusters, analogously to the way the Hopfield model is formulated in terms of the correlations between the memory patterns; we show that such reduced models, by effectively averaging out noise in the pairwise correlations of the single recorded activity configurations, allow for better inference of the synaptic couplings. To this end we first apply the density-based clustering and the clustering-aided inference procedures to the Hopfield model.

Based on theoretical motivations and electrophysiological evidence, we then consider a multi-modular network of spiking and adapting neurons, with approximately bistable modules. To the extent that the single modules are bistable, the multi-modular network can be roughly viewed as a network of binary, Hopfield-like units for which pairwise correlations and mean activities would completely define an energy landscape. In reality, even with approximately bistable neural modules, and even neglecting adaptation, the correspondence between the multi-modular spiking network and the corresponding Hopfield model? is only a convenient metaphor; constructing a multi-modular network with a prescribed pattern of spatial correlations required us to develop an ad-hoc method (a pseudo-Boltzmann learning), which may have an independent and general interest.The procedure of density-based clustering is, by construction, blind to the dynamics of the underlying trajectories in the neural state space. However, we show that it provides a convenient way to expose features of complexity of the dynamics, by first converting the original multi-dimensional time series of the neural activities into the discrete symbolic sequence of centroids, and then measuring the corresponding relative Lempel-Ziv compressibility; we illustrate the method by showing the modulation of the complexity of the reduced dynamics determined by different strengths of spike-frequency adaptation.

Wulfram Gerstner (LCN - EPFL, CH)

Derivation of population dynamics from spiking single-neuron models

Can we replace a standard leaky integrate-and-fire model by something that is at the same level of complexity, but well-grounded on experimental data? Can we replace standard Wilson-Cown type rate equations (or field equations) by other equations that are at the same level of complexity, but directly derivable from models of single neurons? In this talk, I will present a processing chain from experimental somatic single-electrode recordings to generalized integrate-and-fire models and from these to population rate equations. The parameters of the neuron models are directly extracted from experimental data, using ideas from Generalized Linear Models. Groups of similar neurons are arranged in populations with random connectivity. The population equations are derived using mean-field methods and can be interpreted as a generalized renewal process with adaptation and finite-size fluctuations.

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Michele Giugliano (University of Antwerp, B)

The Dynamical Response Properties of Cortical Neurons

Earlier theoretical studies on simplified neuronal models suggested that the joint firing activity of ensembles of cortical neurons may relay downstream rapidly varying components of their synaptic inputs, with no attenuation. Information transmission in networks of weakly-coupled model neurons may in fact overcome the limits imposed by the spike refractoriness and the slow integration of individual cells, effectively extending their input-output bandwidth.

My lab has been the first to experimentally explore and test such a hypothesis. We designed a stimulation protocol to directly probe the (dynamical) response properties of pyramidal cells of the rat neocortex in vitro, by means of patch-clamp recordings. This identifies the linear transfer function of neurons, linking (recreated) synaptic inputs to the firing probability. In the Fourier domain, this correspond to magnitude and phase of the response for progressively more rapid oscillating inputs. Interestingly, such a novel characterisation offers a deeper access to the biophysics of information processing (e.g. relevant to predict correlations) than (stationary) frequency-current curves, which are widely used to classify neuronal phenotypes.

To our surprise, not only we confirmed that pyramidal neurons can track and relay inputs varying in time faster the cut-off imposed by membrane electrical passive properties (~50 cycles/s), but we found that they do it substantially faster (up to ~200 cycles/s) than explained by their ensemble mean firing rates (~10 spikes/s). In addition, above 200 cycles/s neurons attenuate their response with a power-law relationship and a linear phase lag.

Such an unexpectedly broad bandwidth of neuronal dynamics could be qualitatively related to the dynamics of the initiation of the action potential. Interested to explore and test such a possibility, we found a first indirect confirmation of it in terms of correlation between the action potentials rapidness at onset and the neuronal bandwidth, over a large set of experiments.

A second more direct confirmation - which will conclude the presentation - came from our recent study where we applied the same protocols to in vitro human cortical (healthy) tissue, exceptionally obtained from therapeutic resective brain surgery. We found that human L2/3 cortical neurons fire much “steeper” action potentials than in rodent neurons of the same layer, and have a much more extended bandwidth reaching 1000 cycles/s, violating the predictions of existing models and opening intriguing new directions for the phylogenetics of neuronal dynamics.

Alberto Mazzoni (The Bio Robotics Institute –SSA, I)

Modeling Local Field Potential

Extracellular recordings include low-frequency fluctuations, called Local Field Potential (LFP), superimposed to action potentials shapes. LFP has been filtered out for decades until it was found that it was somehow correlated with the global synaptic input of the local network and could then carry information complementary to the one of the spikes regarding the output of single neurons. While now neurophysiologists commonly use LFP as a tool to study cortical dynamics, the biophysics underlying the signal is still far from being completely understood. Here, I will discuss how computational neuroscience in the past ten years helped clarifying the different components contributing to the LFP and hence the physiological interpretation of the signal. The level of detail of the simulations has been fruitfully modulated depending on the phenomena under investigation: a simple ball-and stick model was sufficient to capture the onset of LFP oscillations due to image contrast observed in the primary visual cortex, while a multi-compartmental model was needed to explain the observed frequency-dependence of the LFP. These two approaches were bridged in a recent work. I will finally present how such studies made possible to analytically reconstruct population firing rates from acquired LFP in the cortex and a striking application of peripheral LFP modeling to neuro-engineering. LFP modeling is then a particularly bright case of mathematical neuroscience empowering neurophysiology.

Michele Migliore (Institute of Biophysics – CNR, I)

Self-organization of microcircuits in a brain system

The functional operations of neuron microcircuits, involved with higher brain functions, require a continuous self-organization of the underlying synaptic network that is extremely difficult to explore experimentally. In the olfactory bulb system, recent experimental evidence suggests that odor processing before cortical action is organized in well-defined, sparse, and segregated synaptic clusters. The observed columnar organization of these clusters can emerge from the interaction among odor inputs, action potential backpropagation in the mitral cell lateral dendrites, and dendrodendritic mitral-granule cell synapses. In this talk, I will first discuss how the feedback and lateral inhibitory action at the cellular level can explain the experimentally-observed firing dynamics of mitral cells during sniffs of different odors. Then, I will introduce, discuss, and analyze the results obtained with a large-scale 3D model of the olfactory bulb microcircuit and a novel theoretical approach. I will show the mechanisms and requirements for forming one or more glomerular units in response to a given odor; how and to what extent the glomerular units interfere or interact with each other during learning; their computational role within the olfactory bulb microcircuit; and how their action can be formalized into a theoretical framework in which the olfactory bulb can be considered to contain “odor operators” unique to each individual. The results provide new and specific theoretical and experimentally testable predictions.

Gianluigi Mongillo (CNRS - Université Paris Descartes, F)

Inhibitory connectivity defines the realm of excitatory plasticity

Information to be preserved over intermediate (days) to long (months and years) time periods is thought to be encoded by synaptic modifications in the relevant brain regions. Consistently with this notion, experiments have exposed significant re-organization of the excitatory connectivity in cortical networks upon learning. Experiments, however, also show that excitatory connectivity is volatile in the absence of learning, raising the question of how information is maintained in such unstable synaptic architecture. Using a biologically-constrained model of cortical network, we show that the patterns of firing rates in the network are primarily determined by the inhibitory sub-network, despite the fact that the majority of neurons and of synapses are excitatory. This is a direct consequence of the differences in the distributions of the firing rates of excitatory and inhibitory neurons. Thus, the patterns of firing rates are robust against the substantial remodeling of the excitatory connectivity, which preserves the overall distribution of connections. By contrast, transient changes in the distribution of excitatory connections, which have been associated with learning-induced plasticity, can have a substantial effect on the pattern of network activity.These results have important implications for the roles of the excitatory and inhibitory networks in learning and memory processes. The inhibitory sub-network, rather than providing “blanket inhibition”, maintains the memory patterns for long periods of time in the volatile cortex. Learning-related excitatory plasticity directs the necessary changes in the inhibitory sub-network by transiently breaking the balance between excitation and inhibition.

Daniele Orlandi (LANE - IRCCS Institute - The Saint John of God Clinical Research Centre, Brescia, I)

E-infrastructures for neuroscientists: the neuGRID & GAAIN examples

Background: The Global Alzheimer's Association Interactive Network (GAAIN - https://www.gaain.org) is an e-infrastructure aiming to federate worldwide datasets of the brain. The European side of the GAAIN initiative (EU-GAAIN) exposes 5 datasets (4’051 subjects) currently hosted on the distributed neuGRID e-infrastructures (www.neugrid4you.eu). The GAAIN’s main objective is to build up the technology for understanding the underlying mechanism of Alzheimer’s disease and other forms of dementia through a big-data-driven approach.

Methods: EU-GAAIN data hosted in the neuGRID platform are federated through the Data Partner Clients (DPC) and mapped to a common data schema12. A distributed pipeline execution system allows a user-friendly pipeline execution relying on an innovative virtualized solution (i.e.: Docker and VirtualBox) hosted in the neuGRID3 platform.

Results: The EU-GAAIN provides 5 (E-ADNI/PharmaCOG, I-ADNI, ARWIBO, EDSD, OASIS) out of the 24 datasets actually exposed through the GAAIN Interrogator. The EU-GAAIN feeds the GAAIN cohort with a significant number of morphological and functional scans, surrogate imaging biomarkers (i.e.: 4’653 cortical and subcortical volumes), cognitive assessments, biochemical markers (i.e.: 286 CSF values, 235 APOE genotype). Through the GAAIN portal the aforementioned results of data queries are displayed in graphs and summary tables (fig.1) providing sufficient information to view trends in aggregated data and to discover new evidences.

Conclusions: The EU-GAAIN through the grid/cloud neuGRID platform is currently in an expanding phase recruiting new European data partners. Research efficiency can be increased if neuroscientists can access secure federated platforms with half a million of subjects’ data from a single-entry point. That creates an efficient connection among scientists worldwide. Global Alzheimer's Association Interactive Network (003278) (GAAIN) initiative is founded by the Alzheimer's Association and by National Institutes of Health grants 5P41 EB015922-16 and 1U54EB020406-01.

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Stefano Panzeri (IIT - Rovereto, I)

The contribution of millisecond spike timing of cortical neurons to sensory coding and perceptual decisions

When a neuron responds to a sensory stimulus, two fundamental codes may transmit the information specifying stimulus identity—spike rate (the total number of spikes in the sequence, normalized by time) and spike timing (the detailed millisecond-scale temporal structure of the response). Previous studies reported that millisecond-precise spike times of cortical neurons carry sensory information that cannot be extracted from spike rates defined over tens of milliseconds. However, it has remained unclear whether the extra information available in spike timing is actually used by the brain. To address this issue, we developed a mathematical approach based on information theory to relate sensory information content of spike rates and spike times to the behavioral outcome in the same trial of a perceptual discrimination task. Using this formalism to analyze neuronal responses in primary (S1) and secondary (S2) somatosensory cortex performing a whisker-based somatosensory discrimination task, we found that spike timing makes crucial contributions to tactile perception, complementing and surpassing those made by rate. The language by which somatosensory cortical neurons transmit information, and the readout mechanism used to produce behavior, appears to rely on multiplexed signals from spike rate and timing. This is joint work with the group of M.E. Diamond at SISSA.

Michele Piana (MIDA – Università di Genova, I)

Inverse problems in neurophysiology

This talk will illustrate some inverse problems concerning the analysis of neurophysiological data recorded by electro- and magnetoencephalography (EEG/MEG), electrocorticography (ECoG) and stereo EEG (SEEG). Both Bayesian and deterministic regularization methods will be used to solve such inverse problems and infer spatio-temporal information on the stream evoked by visual stimulation.

Eero Räisänen (Institute for complex systems - CNR, I)

Leaders and followers: Quantifying consistency in spatio-temporal propagation patterns

In the first part of the talk we will discuss the concept of spike train metrics and go more into details with the time scale independent ISI-distance, the SPIKE-distance and SPIKE-synchronization. We introduce a new adaptive extension that is applied to all three methods allowing for a better similarity description with some types of data. We also introduce a new rate-independent extension for SPIKE-distance, which considers only spike timing and ignores rate difference between the spike trains. In the second part we propose an algorithm that evaluates the similarity of any given set of spike trains to a synfire pattern, a perfectly consistent repetitions of the same global propagation pattern. We introduce two new indicators (termed SPIKE-Order and Spike Train Order) that allow to sort multiple spike trains from leader to follower and to quantify the consistency of the leader-follower relationships for both the original and the optimized sorting. The new algorithm is distinguished by conceptual simplicity, flexibility, low computational cost, and universality (parameter-free and time-scale adaptive). While here we focus on an application to neuronal spike trains (Giant Depolarized Potentials), the algorithm is very generic and applicable to any kind of discrete data. Together with the other measures ISI-distance, SPIKE- distance and SPIKE Synchronization, SPIKE-Order is implemented in both the Matlab-based graphical user interface SPIKY

(http://www.fi.isc.cnr.it/users/thomas.kreuz/sourcecode.html) and the Python library PySpike (https://github.com/mariomulansky/PySpike).

Collaboration with Nebojsa Bozanic, Martin Pofahl, Mario Mulansky, and Thomas Kreuz.

Laura Sacerdote (University of Torino, I)

Stochastic Integrate and Fire Models for single Neuron Activity

In 1964, Gernstein and Mandelbrot1 proposed the Integrate and Fire model to account for the observed stable behavior of the Interspikes Intervals (ISIs) distribution. Their study of histograms of ISIs revealed the stable property and they suggested modeling the membrane potential through a Wiener process in order to get the inverse Gaussian as first passage time distribution, i.e. a stable distribution. Later many variants of the original model were suggested with the aim to improve the model realism. In that framework, appeared models including the membrane potential spontaneous decay (Leaky Integrate and Fire model) as well as the presence of reversal potentials or dependences between successive spikes (Multi-compartment models). However, researches forgot the initial clue for the model while they were working on the realism of their model: the Interspikes Intervals of the Leaky Integrate and Fire model have not the stable First Passage Time distribution observed by Gernstein and Mandelbrot. The same holds for many other variants of this model.

Holden (1975) observed that stable distributions determine a simple transmission pathway while different ISIs distributions would determine an incredible variety of firing distributions as the information progresses in the network. Signals from different neurons are summed up during the elaboration and the presence of stable distributions simplifies the final code thanks to suitable limit theorems. Furthermore, the stable ISIs paradigm gives rise to a more robust transmission algorithm since a possible lack of detection of some spike from the surrounding neurons does not change the nature of the final distribution.

Here we start with a short review on Integrate and Fire models. Then we rethink to these models, taking advantage of the mathematical progresses on Levy processes3. Hence, we propose to start the model formulation from the main property, i.e. the stable nature of the ISIs distribution.

This is a preliminary contribution in this direction and we limit ourselves to some aspects of the modelling proposal but we are conscious that these will be simplified examples and some further mathematical study will be necessary to make realistic some of our assumptions. In this framework we plan to present a model that exhibits tempered stable distributed ISIs, that is stable behavior with finite moments. We will model the supremum of the membrane potential through an inverse tempered stable subordinator, and the ISIs according with the Integrate and Fire paradigm. Special cases include Gamma or Inverse Gaussian distributed ISIs.

Keywords: Stable Distribution; Integrate and Fire Model; ISIs distribution

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Shyam Diwakar (Amrita School of Biotechnology, Amrita University, India)

Computations in the cerebellar granular layer microcircuit: from Population responses to robotic abstractions

Information transmission at the Mossy Fiber (MF) - Granule cell (GrC) synaptic relay is crucial to understand mechanisms of signal coding in the cerebellum. The cerebellum input stage has been known to perform combinatorial operations on input signals. Using detailed multi-compartmental models of neurons, a network model was employed to study information transmission and signal recoding in the cerebellar granular layer and to test observations like center-surround organization and population roles of single granule neurons. Modeling population activity such as local field potentials and clinically relevant fMRI-Blood Oxygen Level Dependent signals allow comparing population roles of spiking patterns. Understanding population activities of underlying neurons reveal emergent behavior as patterns of information flow in neural circuits. Local field potentials (LFPs) arise from complex interactions of spatial distribution of current sources, time dynamics, and spatial distribution of dipoles apart underlying conductive properties of the extracellular medium. We reconstructed LFP to test and parameterize the molecular mechanisms of cellular function with network properties. Recent algorithms developed for reconstructing LFP signals allow implicating the nature of interactions in cerebellar microcircuitry. An abstraction of the cerebellar dynamics also allows to implicate spiking neurons based architecture to implicitly represent forward and inverse kinematics of a simple robotic articulator.

Keywords : Cerebellum; network; LFP; mathematical modeling; BOLD, computational neuroscience; robotics

SHORT TALK - POSTER TALK

Luisa Andreis (Università degli Studi di Padova, I)

Simultaneous jumps in interacting particle systems and McKean-Vlasov limits

We consider systems of N weakly interacting diffusions with jumps, having the peculiar feature that the jump of one component may induce simultaneous jumps of all others. Models belonging to this class have been proposed for the dynamics of neuronal systems, and their limiting ($N\to\infty$) behavior has been studied for some special cases. We aim to study this model in a generalvd-dimensional framework, to prove propagation of chaos and derive the corresponding McKean-vVlasov equation. We mainly use a coupling technique, to underline the role of the simultaneousvjumps in the rate of convergence for the size of the system going to infinity.

Anna Cattani (IIT-Rovereto, I)

The complexity of dynamics in small neural circuits

Brain networks are characterized by different spatial scales, which strongly determine the techniques that are used for studying the network organization and dynamics. Mean-field approximations [1,2] are a powerful tool for studying large neural networks with a number of neurons spanning from 103 to 1011 cells (comprising both the upper limit of the mesoscopic scale and the macroscopic scale), but they do not describe well the behavior of networks composed of a smaller numbers of neurons spanning up to hundreds of cells (this comprises both the microscopic scale and the lower limit of the mesoscopic scale). Even though understanding the dynamics of small networks is important for both studying invertebrate circuits [3] and for studying very local cortical circuits such as microcolumns [4] or the interactions between specific components of other cortical microcircuits [5,6,7], mathematical methods that correctly describe small networks are still rare [8].

Here we present our recent progress [9] that led to a novel systematic analysis of the dynamics of an arbitrary-size network composed of homogeneous populations of excitatory and inhibitory firing-rate neurons. Specifically, we studied the local bifurcations of its neural activity with an approach that is largely analytically tractable, and we numerically determined the global bifurcations. We found that in the regime of strong inhibition the network gives rise to very complex dynamics, caused by the formation of multiple branching solutions of the neural dynamics equations that emerge through spontaneous symmetry-breaking. This qualitative change of the neural dynamics is a finite-size effect of the network, which is not predicted by the mean-field approximation. For this reason, our study advances the tools available for the comprehension of finite-size neural circuits, going beyond the insights provided by the mean-field approximation and the current techniques for the quantification of finite-size effects.

A most prominent important consequence of local bifurcations is the ability of mesoscopic networks to regulate dynamically their correlation structure [10].

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A hybrid model for the computationally-efficient simulation of the cerebellar granular layer

Interesting phenomena in the brain often involve complex networks with an extremely large number of neurons. The description of the whole network at the microscopic level, i.e., the modeling of each single neuron and synapse, may lead to numerical models demanding a tremendous computational cost, even on the most advanced computers. The difficulties of such a description may be alleviated to some extent by identifying a hierarchy among interacting populations of neurons, and by using models with different spatial resolutions and costs for simulating the behavior of different populations.

Here we present our recent work [1] whose aim was to efficiently describe the membrane potential dynamics of neural populations formed by species having a high density difference in specific brain areas. In more detail, we proposed a hybrid model whose main ingredients are a conductance-based model (ODE system) and its continuous counterpart (PDE system) obtained through a limit process in which the number of neurons confined in a bounded region of the brain tissue is sent to infinity. Specifically, in the discrete model, each cell is described by a set of time-dependent variables [2], whereas in the continuum model cells are grouped into populations whose spatiotemporal evolutions is described by a set of continuous variables [3]. Communications between populations, which translate into interactions among the discrete and the continuous models, are the essence of our hybrid model.

The cerebellum and cerebellum-like structures [4] show in their granular layer a large difference in the relative density of neuronal species making them a natural testing ground for our hybrid model. By reconstructing the ensemble activity of the cerebellar granular layer network and by comparing our results to a more realistic computational network [5,6], we demonstrated that our description of the network activity, even though it is not biophysically detailed, is still capable of reproducing salient features of neural network dynamics. Specifically, the hybrid model reproduces interesting dynamics such as local microcircuit synchronization, traveling waves, center-surround, and time-windowing. Finally, our modeling approach yields a significant computational cost reduction by increasing the simulation speed at least 270 times.

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Linear and Nonlinear Analysis of Neural Signals

The extraction of the hidden information contained in the neurophysiological recordings is a crucial point to understand how the brain work in normal or pathological conditions. There are several techniques that can be used, each spanning different spatial and temporal time scales. Among them Local Field Recordings (LFP) is now largely employed to investigate the dynamic of local population of neurons (about 104) . In this contribution are presented some results obtained by analyzing with linear and nonlinear methods LFP signals from free moving mice. Moreover, new method to detect linear and nonlinear correlations between bivariate time series is proposed and described. This method, called the Boolean Slope Coherence (BSC), was tested using time series generated with different models and the corresponding results were compared with those obtained with other known coupling measures. Moreover, the BSC algorithm also works for signals contaminated by noise. The results indicate that the BSC method can be employed to quantify the coupling level between biological signals, like LFP or EEG. In addition, the BSC method can be used to establish the prevalence of the coupling directionality between two coupled biological systems. Examples of its application to neurophysiological recordings will be presented too.

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Methodologies for the analysis of Intracranial Pressure and Heart Rate data in traumatic brain injuries patients

Intracranial pressure (ICP) after severe brain injuries or similar life threatening conditions can be continuously monitored [1]. The ICP signal contains useful information to predict life threatening conditions such as intracranial hypertension. So far, monitoring approaches are focusing mainly on the relationship between arterial blood pressure and intracranial pressure. Own observation in pediatric patients however, showed that changes in heart rate have direct influence on the ICP.Our hypothesis therefore is that the HR-ICP relationship can be quantified via complex event processing methods. A few works concentrate on the capability of identifying a model describing the intracranial system behaviour. For example in [2] the authors present an estimation algorithm based on hidden state estimation approach and non linear Kalman filters to estimate unobserved variable given some measurements such as ICP and cerebral blood flow velocity (CBFV). What might be interesting is understanding the interelationship between ICP and other measures of the monitored patients. For example in [3] the authors present ApEN an algorithm based on the adaptive calculation of approximate entropy, integrated with a causal coherence analysis that is able to exploit the potential interaction between ICP and R wave intervals [3]. Interesting in this sense is also [4] where the authors extract indeces from beat to beat mean intracranial pressure measurements and intervals between consecutive normal sinus heart beats (ICP and RR intervals). Starting from the visual observation that heart rate and ICP present peaks at similar points, we applied several statistical methodologies to identify such co-occurences of peaks and the relationships existing between the two time series. Moreover we are currently investigating the relationship existing also with the other variables monitored. This preliminary analysis performed appear to be promising and we are now extending our work to perform online peaks detection of ICP peaks considering the relationship between the ICP and HR.

The dataset we are working on is composed by 38 pediatric patients with traumatic brain injury. For all of the patients, we have the following parameters:abp mean arterial pressure (mmHg),HR heart (rate /min), ICP inracranial pressure (mmHg), AMP intracranial pulse pressure amplitudes ,HRVLFHF heart rate variability (ratio lowfrequency power / high frequency power, HRhfRel percentage of high frequency power ,CPP cerebral perfusion pressure (mmHg). The time series are sampled at a rate of 1.2E-05/second.

We used the techniques of recurrence plots (RP) to further analyse our time series, considering the presence of similarity in their dynamics, shown from the time plot. RP is a statistical analysis technique used for nonlinear data. The data are visualized through a graph in a square matrix (column and rows represents a pair of times), where the elements are representation of the times at which a state of the dynamical system recurred [5]. Mathematically RP represents the time stamps in which the phase space trajectory of the system that we are considering, passes through the same area in the phase space [5] [6].

In signal theory the cross correlation represents the similarity between two signals, as a function of the shift or temporal translation applied to one of the two signals [7] [8]. We performed the cross correlation function between the two time series ICP and HR to further analyse the values of the correlation between them.

A further analysis we performed for understanding the relationship between two time series is the Wavelet Coherence, that is a method able to determine and to visualize areas with high common power (i.e. high common correlation) between two time series [9]. Before performing such test, we checked for the normality of the two time series considering the Shapiro-Wilcox Test for normality. Since the test showed normality in the data proposed, we performed the Wavelet Coherence between the two time series. The resulting plot shows particularly interesting characteristics. In fact it identifies regions (in red) where the two signals are highly correlated and it also tells us in which time instants such correlation happens. This is particularly useful for our analysis, considering the fact that we are looking for correlation in particular time instances (i.e. when peaks occur). Therefore such time instances could be revealed by the Wavelet Coherence graphs. Moreover we performed two additional analysis with wavelets, involving the wavelets correlations and the wavelet clustering.

In the first case, the wavelet correlation showed a high correlation between the ICP and HR. In the case of clustering, so far we have analysed the wavelet power clustering considering three time series HR, ICP and HRVLFHF. The ICP and HR are clustered together and further from the time series of HRVLFHF supporting even more our hypothesis about similarity between HR and ICP behaviours.

In addition to these analysis, we implemented a peak detection algorithm, following the first algorithm suggested in [10]. In this way we could try to find correlations between peaks happening in the ICP and in the HR series, seeing the possible temporal correlation between them. This is the first step for a further implementation of peaks prediction algorithm that will be the next step in our study.

We performed preliminary analysis on peaks detection in HR and ICP and we obtained a significant overlap in the peaks detected in the ICP and HR, suggesting the validation of our initial intuition regarding the possibility of crosstalks events between ICP and HR as well as the possibility for a future utilization of HR information to predict ICP peaks.

The preliminary analysis performed on a subset of 3 patients from the cohort of 38 patients, suggests that our initial visual intuition is confirmed from a preliminary statistical analysis of the dataset. The Wavelet Coherence, as well as the peaks detection algorithm and the recurrence plots, confirmed our preliminary hypothesis. We are now further analysing the time series using the Granger Causality method, trying to understand the causality correlations existing between the various time series as well as further develop our methodology to implement an online ICP peaks detection algorithm.

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Transitions between Asynchronous and Synchronous States: A Theory of Correlations in Small Neural Circuits

The study of correlations in neural circuits is a topic of central importance to systems neuroscience [1,2]. Notwithstanding, a theory is still to be formulated that could explain how the parameters of small networks composed of a few tens of neurons affect their correlation structure. In this work we introduce a mathematical formalism for studying correlations which is not based on statistical averaging and which can be applied to networks of arbitrary size [3]. We study the correlation structure in different regimes, showing that external stimuli cause the network to switch from asynchronous states characterized by weak correlation and low variability, to synchronous states characterized by strong correlations and wide temporal fluctuations. Asynchronous states are generated by strong stimuli, while synchronous states occur through critical slowing down when the stimulus moves the network close to a local bifurcation. In particular, strongly positive correlations occur at the saddle-node and Andronov-Hopf bifurcations of the network, while strongly negative correlations occur when the network undergoes a spontaneous symmetry-breaking at the branching-point bifurcations. Branching points describe the spontaneous formation of heterogeneous activity in populations of homogeneous neurons [4], and they are not predicted by large-scale theories such as the mean-field approximation. They quantify the network's ability to regulate its degree of functional heterogeneity, which is thought to help reducing the detrimental effect of noise correlations on cortical information processing [5,6,7]. Moreover, the branching points may explain the still poorly understood origin and functional role of negative correlations observed in experimental recordings of cortical activity [8,9].

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Formal models of visual perception based on cortical architectures

In presence of an Input stimuli, the visual cortex codifies the features of position and orientation. Considering the geometry of the cortex generated by the vector fields X_1 and X_2 defined in [3]:

$$\vec{X}_1 = (\cos\theta, \sin\theta, 0), \quad \vec{X}_2 = (0, 0, 1), \tag{1}$$

we can model the cortical connectivity with different stochastic kernels. These kernels are fundamental solutions of suitable operators, functions of the vectors X_1 and X_2. If we describe the long range propagation with a deterministic component in direction X_1 (which describes the long range connectivity) and stochastic component along X_2 (the direction of intracolumnar connectivity) we obtain that the associated probability density is the fundamental solution of Fokker Planck equation. This operator has a fundamental solution $\Gamma 1$ that satisfies:

$$X_1\Gamma_1((x,y,\theta),(x',y',\theta')) + \sigma^2 X_{22}\Gamma_1((x,y,\theta),(x',y',\theta')) = \delta(x,y,\theta). \quad (2)$$

If we assume that intracolumnar and long range connections have comparable strength, we have to modify the equation of long range propagation, since the coefficients of propagation in both directions X_1 and X_2 are stochastics. The operator reduces to the Sub-Riemannian Laplacian that satisfies:

$$X_{11}\Gamma_2((x,y,\theta),(x',y',\theta')) + \sigma^2 X_{22}\Gamma_2((x,y,\theta),(x',y',\theta')) = \delta(x,y,\theta). \quad (3)$$

Both these kernels are in good agreement with the connectivity measured by Bosking in tree shrew [2]. Starting from these kernels, the problem of grouping has been faced by means of spectral analysis of suitable affinity matrices [6,7]. Considering the set of points (x_i; y_i) in which the gradient results sufficiently high with directions θi and called ω the symmetrization of Γ, we have evaluated the affinity matrix:

$$A \in R_{nxn} \quad where \quad A_{i,j} = \omega((x_i,y_i,\theta_i),(x_j,y_j,\theta_j)) \quad with \quad i,j = 1,...,n \quad (4)$$

$$Au_m = \lambda_m u_m. \quad (5)$$

Following this model, the eigenvectors u_m of the affinity matrix represent the perceptual units and the salient objects in the scene corresponds to eigenvectors with highest eigenvalues. In [7] it has been observed that this spectral analysis can be produced by the neural activity in the primary visual cortex, by means of symmetry breaking of solutions of mean field equation. For the numerical simulations, I have considered particularly Kanizsa figures as clear examples of problems of visual perception [4].

The model of cortical connectivity obtained as fundamental solution of the Fokker Planck equation has been applied to the analysis of retinal images [1,5], to afford problems of grouping during the tracking of blood vessels. Combining spectral analysis and spectral clustering algorithm [8] it has been possible to group different perceptual units in these images.

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A neuro-mathematical model for geometrical optical illusions

Geometrical optical illusion (GOIs) have been of great interest due to the possibility to understand, through the effect they produce on neural connections, the behaviour of low-level visual processing. They have been defined in the XIX century by German psycologists (Oppel 1854 [4], Hering, 1878, [3]) in terms of phenomenology of vision, as situations in which there is an awareness of a mismatch of geometrical properties between an item in object space and its associated percept (Westheimer 2008, [5]). As pointed out by Eagleman (Nature,2001 [2]) the study of these systematic misperceptions combined with recent techniques for brain's activity recording provides a brilliant insight to lead new experiments and hypothesis on receptive fields of V1 and feedback mechanisms.

In this framework, starting from the geometrical model introduced by Citti and Sarti in 2003 [1], we provide an efficient mathematical model which allows to interpret these phenomena and to measure the perceived misperception, involving image-processing techniques and expressing the displacement through PDEs. We expect this to be the starting point of new considerations about feedback mechanism between V1 and the retina and the study of lateral inhibition.

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Reduced dynamics of pattern formation in a mean-field cortical model

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An improved Perona-Malik edge-enhancing denoising algorithm to efficiently detect neural events

Denoising is a fundamental step in signal analysis. In particular, we are interested in smoothing signals where mainly noise is present, while preserving or enhancing 'edges' and features related to the recorded activity. An important class of denoising techniques is based on diffusion and consists in solving PDEs with the noisy signal as initial data and suitable boundary conditions.

A widely-used filter with these properties was presented by Perona and Malik. They proposed to regulate the diffusion using the magnitude of the gradient of the signal. In the algorithm, when the gradient increases the diffusion is initially reduced then stopped. The diffusion can also be inverted to highlight some features of the signal.

We present a modification of the Perona-Malik filter. Instead of using the magnitude of the gradient to identify 'edges' we introduce an alternative local quantity, based on the variation of the signal, to regulate the diffusion. We demonstrate that the introduced equation is well-posed and admits a unique solution.

In conclusion we apply the classical Perona-Malik filter and the new designed filter to simulated membrane potential signals and to calcium imaging data from cell culture networks. We compare the obtained results and discuss the advantages of the introduced approach.

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e-infrastructures for neuroscientists: the neuGRID & GAAIN examples

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The ERP study to measure inhibition task in central executive function of working memory with neuronal correlation

Working Memory (WM) is short term memory which is responsible to process the information for limited time period. Broadly it involves two parts one is temporary storage system and another is information processing system. The temporary storage system is divided into small chunks and information processing system is further divided in three subsystem phonological loop, visual sketch pad and central executive function (CEF). CEF is responsible to play several important roles during performing cognitive task. In the CEF inhibition process refers to the ability to consciously inhibit dominant, automatic and proponent response when necessary. In this study our objective to examine the role of central executive function during inhibition process. We measured the activity of fronto-parietal lobe in form of Event-Related Potential (ERP) with the help of Neuroscan, EEGLab, sLORETA tools. A paradigm design of inhibition task was conducted by providing a set of visual stimuli to the subject and responses were recorded in specific period of time. The measurement of activation of brain areas in individuals were analyzed by gender discriminative comparison of positive and negative amplitude peaks of ERP. The cognitive experiment was performed on thirty healthy control subjects with certain parametric constraints to judge behavior based on average responses in order to establish relationship between ERP and local area of brain activation.

We found that numbers of correct responses were higher in males in comparison to females. We also found that lower peak amplitude activity of brain area in males than females which reveals that males utilize less activation of brain areas to perform inhibition task better than females corresponding to their same brain areas. Findings from this study will give a better understanding of CEF and brain activity in males and females. It will also help us to understand the concept of CEF in general. In addition, it might also help to understand the neural correlates of inhibition process.

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Comparing Bayesian Data Assimilation methods for Parameter Estimation in a Neuron Model

Data assimilation (DA) has proved to be an efficient framework for estimation problems in real-world complex dynamical systems arising in geoscience, and it has also begun to show its power in computational neuroscience. The ensemble Kalman filter (EnKF) is believed to be a powerful tool of DA in practice. In comparison to the other filtering methods of DA, such as the bootstrap filter (BF) and optimal sequential importance re-sampling (OPT-SIRS), it is considered more convenient in many applications, but with the theoretical flaw of Gaussian assumption.

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Ito excursion theory: an application to the firing paradigm in stochastic neuronal models

Integrate and Fire (IF) models are among the most used descriptions of the single neuron membrane potential dynamics. However, in many instances, data are not consistent with a relevant feature of such models. We refer to the absorbing assumption imposed to the membrane potential at the threshold level, i.e. the firing condition. The presence of the absorbing boundary is often disregarded, introducing important errors in the estimation procedure [1, 2].

Mainly motivated by statistical purposes, we propose here a new definition of the firing time of a neuron. The new model relaxes the absorption condition and allows crossing of the threshold without firing. We assume that a spike is generated as the membrane potential reaches a fixed threshold level and remains above it for a sufficiently long time interval. The firing time is defined as

$$H = \inf\{t \geq 0 | (t - g_t) \cdot 1_{v_t \geq S} \geq \Delta\}$$

where Vt is the neuron membrane potential, $1A$ is the is the indicator function of the set A, Δ is the time window that the process has to spend above the threshold S and ∀ t,

$$g_t = \sup\{ s \leq t, V_s = S \}$$

In order to derive the Laplace transform of H for a general diffusion process Vt, we study H in the framework of Ito excursion theory [3]. In particular, we review the question of the first excursion of a diffusion process Vt above a certain level S with length strictly greater than Δ. Main references related to this problem are [4] and [5].

Finally, we specialize our results for the three diffusion processes thst appear in (Leaky) Integrate and Fire neuronal models: Wiener, Ornstein-Uhlenbeck and Feller processes.

The results discussed in this paper are seminal to approach the estimation of the parameters for this new familiy of neural models.

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Different levels of computaional neurostimulation