2nd INTERNATIONAL WORKSHOP IN NEURODYNAMICS (NDY'18)

A workshop on Neuroscience and Dynamical systems

Castro Urdiales, Cantabria, Spain
September 26-29, 2018

Scientific committee

- Serafim Rodrigues
- Toni Guillamon
- Peter Ashwin
- Mathieu Desroches
- Silvia Daun
- Roberto Barrio

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Contents

1 INTRODUCTION

Neuroscience is nowadays one of the most collaborative and active scientific research fields as it has been increasingly involving the participation of experts from other disciplines. In particular, computational and mathematical aspects of neuroscience are currently playing an important role both in modeling and replicating experimental findings and in explaining the underlying mechanisms of neurophysiological or cognitive processes. Differential equations are ubiquitous in the modeling of such phenomena and, consequently, nonlinear dynamics and dynamical systems techniques become fundamental sources of new mathematical and computational tools to study neuroscience models.

The aim of this Second Workshop on Neurodynamics, NDy'18 (first edition was NDy'14) is to present an overview of successful achievements in this rapidly developing collaborative field by putting together different types of applications of nonlinear dynamics (geometrical tools in dynamical systems, numerical methods, computational schemes, dynamical measures,...) to different problems in neuroscience (mononeuronal dynamics, network activity, cognitive problems,...). Additional emphasis will be put on experimental findings seeking for theoretical explanations, and therefore this meeting is focussed on using mathematics as the primary tool for elucidating the fundamental mechanisms responsible for experimentally observed behavior in the applied neurosciences. Importantly, it will draw attention to those pieces of mathematical theory which are likely to be relevant to future studies of the brain. The final goal is spreading together mathematical methodology and neuroscience challenges and stimulating future cross-collaborations among participants, being Mathematical Neuroscience the generic topic for NDy'18.

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2 PROGRAMME

	Wednesday	Thursday	Friday	Saturday
9:30-10:00		S. Daun	J. Rubin	H. Osinga
10:00-10:30		C. Gros	J.J. Torres	D. Pazó
10:30-11:00		S. Farjami	J. Creaser	H. Meijer
11:00-11:30		*Coffee break*	*Coffee break*	*Coffee break*
11:30-12:00		A. Guillamon	P. Varona	R. Barrio
12:00-12:30		R. Guevara	A. Lozano	V.A. Makarov
12:30-13:00	Reception	C. Masoller	G. Huguet	E. Köksal Ersöz
13:00-13:30				
13:30	LUNCH	LUNCH	LUNCH	LUNCH
15:45	Opening			
16:00-16:30	J.M. Delgado	P. Kloeden	A. Roxin	
16:30-17:00	G. Capo	J.M. Kroos	L.H. Duc	
17:00-17:30	D. Zakharov	B. Gutkin	C. Vich	

19:30	OPEN DISCLOSURE CONFERENCE: J.M. Delgado		
21:00			SOCIAL DINNER

All the talks will be placed at the CIEM center, 4th Maria Aburto street (see the map at the end of the program).

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3 COMMITTEES

3.1 Scientific Committee

Peter Ashwin
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Universidad de Zaragoza, Spain.

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Mathieu Desroches
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3.2 Organizing Committee

Computational Dynamics Group (CoDy)
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Alvaro Lozano, Centro Universitario de la Defensa.
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Lucía Pérez, Universidad de Oviedo.
Marcos Rodríguez, Universidad de Zaragoza.
Sergio Serrano, Universidad de Zaragoza.

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4 ABSTRACTS

Homoclinic dissection of fold/hom neuron bursting models: the Hindmarsh-Rose model

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Abstract

The wide-range assessment of brain and behaviors is one of the pivotal challenges of this century. To understand how an incredibly sophisticated system such as the brain *per se* functions dynamically, it is imperative to study the dynamics of its constitutive elements – neurons. Fold/hom bursting phenomena is found in numerous fast-slow models, and specially in neuron models [5, 6]. The existence of an homoclinic bifurcation curve is a requirement to its appearance, but the real structure of the homoclinic bifurcations in the global parametric space of fold/hom neuron models is not known. Here we provide a global analysis of the organization of the homoclinic bifurcation manifolds in the parametric phase space [2, 3] and how topologically different 2D manifolds are present. The detailed numerical analysis and continuation curves give results that lead us to conjecture the theoretical organization of these systems (exemplified in the canonical Hindmarsh-Rose neuron model). All the different homoclinic bifurcation manifolds are classified and several codimension-2 homoclinic bifurcation curves are shown (like Orbit-flip, Inclination-flip and Belyakov points). The global picture reveals several codimension-3 points that are detailed. Besides, due to the structure of the homoclinic manifolds as tubular-like shapes with very sharp folds, isolas [1] of homoclinic bifurcation curves are shown once the small parameter is fixed on the model. Moreover, isolas of codimension-2 homoclinic curves are detected, like isolas of Belyakov points. All these bifurcations are connected with the spike-adding process and canards in fast-slow models as each spike-adding bifurcation is related with the existence of one homoclinic bifurcation manifold that is exponentially close to the rest of homoclinic bifurcation manifolds, giving rise to a homoclinic structure that we call "Homoclinic mille-feuille" [3].

References

[1] Avitabile, D., Desroches, M., Rodrigues, S.: On the numerical continuation of isolas of equilibria, *International Journal of Bifurcation and Chaos*, 22 (11), 1250277, (2012).

[2] Barrio, R., Ibáñez, S., Pérez, L.: Hindmarsh-Rose model: Close and far to the singular limit, *Physics Letters A*, 381 (6), pp. 597-603, (2017).

[3] Barrio, R., Ibáñez, S., Pérez, L.: Homoclinic organization in fold/hom bursters: the Hindmarsh-Rose model. *Preprint*, (2018).

[4] Barrio, R., Martínez, M. A., Serrano, S., Shilnikov, A.: Macro and micro-chaotic structures in the Hindmarsh-Rose model of bursting neurons, *Chaos*, 24 (2), 023128, (2014).

[5] Barrio, R., Shilnikov, A.: Parameter-sweeping techniques for temporal dynamics of neuronal systems: case study of the Hindmarsh-Rose model, *J Mathematical Neuroscience* 1 (6), 1-22, (2011).

[6] Linaro, D., Champneys, A., Desroches, M., Storace, M.: Codimension-two homoclinic bifurcations underlying spike adding in the Hindmarsh-Rose burster, *SIAM J. Appl. Dyn. Syst.*, 11 (3), pp. 939962, (2012).

A computational model integrating brain electrophysiology, metabolism and hemodynamics

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Abstract

Several mathematical models have been developed in the recent years to describe the brain activity. The latter is a complex interaction between several dynamics that coexist in a working brain. In particular, we highlight the electrophysiological activity of the neurons, the metabolic cycle of the neuron-astrocyte complex that provides the neurons with the energy needed to produce action potentials, the nutrient supply through the Brain Blood Barrier from the capillaries that irrigate the cerebral tissue, and the blood flow in the circulatory system. Building on the electro-metabolic double-feedback model introduced in [1], we include hemodynamic processes in the brain by considering a neurovascular unit comprising of arteries, veins and capillaries. The hemodynamic model employed estimates the blood vessel compliance and the corresponding blood flow changes during neuronal activation. Aiming at providing a deeper understanding of the mechanisms through which the brain regulates cerebral blood flow and metabolism in order to produce the required amount of energy for the neuronal activation, we analyze the changes in membrane potential and ionic concentrations, the metabolite concentrations and the blood flow in response to a vasodilatory stimulus. The proposed integrated model presents nontrivial computational challenges stemming from the dramatically different time scales of the dynamics at play: milliseconds for the electrophysiology, minutes for the metabolism and seconds for the blood.

References

[1] Calvetti, D., Capo Rangel, G., Gerardo-Giorda, L., Somersalo, E.: A computational model integrating brain electrophysiology and metabolism highlights the key role of extracellular potassium and oxygen, *J. Theor. Biol.* **446** (2018), 238–258.

A novel network modelling approach for EEG-microstates

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Abstract

Altered brain dynamics are observed with different levels of consciousness. Here we analyse brain activity recorded using an electroencephalogram (EEG) to identify changes in the intrinsic temporal organisation of the brain dynamics during pharmacologically induced loss of consciousness. We convert the EEG data into sequences of EEG-microstates, epochs with variable durations (typically 80-120ms long) in which the topography of the scalp electric field is fixed but the polarity can invert. Each microstate provides a measure of overall momentary brain activity as a spatial summation of all concurrently active intracranial sources. In healthy resting state data, brain activity has been consistently shown to visit four different microstates, with characteristic patterns of transition between each. The fast switching between microstates is indicative of rapid sequential activation of different underlying brain networks. Changes in microstate sequences have been observed under anaesthesia, as well as in a variety of neurological disorders. Analysis of the timings and properties of these transitions is a potentially powerful method of identifying resting state network changes and abnormalities. Here, we examine the effect of anaesthetic on microstate sequences and propose a novel modelling approach. The residence times of each of the four microstates have heavy tailed distributions that change as the level of awareness decreases, along with the transition probabilities and measure of long range temporal correlations. We construct noisy network attractor models in which each node is one of the microstates and show how the models capture the observed statistical properties of the sequences.

Mathematical modeling of the neural control of insect locomotion

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Abstract

The mechanism underlying the generation of stepping has been the object of intensive studies. Stepping involves the coordinated movement of different leg joints and is, in the case of insects, produced by antagonistic muscle pairs. In the stick insect, the coordinated actions of three such antagonistic muscle pairs produce leg movements and determine the stepping pattern of the limb. The activity of the muscles is controlled by the nervous system as a whole and more specifically by local neuronal networks for each muscle pair. While many basic properties of these control mechanisms have been uncovered, some important details of their interactions in various physiological conditions have so far remained unknown.

We have created a neuro-mechanical model of the coupled three joint control system of the stick insects middle leg to unravel details of the neuronal and mechanical mechanisms driving a stepping single leg in situations other than forward walking. The model can generate forward, backward, or sideward stepping as well as searching movements. Using the model, it is, because of it's detailed biological description, possible to make detailed suggestions as to how rhythmic stepping might be generated by the central pattern generators of the local neuronal networks, how this activity might be transmitted to the corresponding motoneurons, and how the latter might control the activity of the related muscles. The entirety of these processes yields the coordinated interaction between neuronal and mechanical parts of the system. Moreover, based on experimental findings which state that only the activity of the muscles which move the leg forward and backward is reversed during backwards walking, we hypothesize and verify a mechanism by which motoneuron activity is modified by a premotor network and therefore suggest that this mechanism might serve as a basis for fast adaptive behaviour, like switches between forward and backward stepping, which occur, for example, during curve walking, and especially sharp turning, of insects.

This neuro-mechanical model of the middle leg has been adapted to describe stepping of the front and the hind leg and all six leg controllers have been coupled to describe coordination (walking) patterns typically observed in the stick insect.

Learning as a functional state of the brain: studies in wild-type and transgenic animals

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Abstract

While contemporary Neuroscience is paying increasing attention to subcellular and molecular events and other intracellular phenomena underlying the acquisition, storage, and retrieval of newly acquired motor and cognitive abilities, similar attention should be paid to the study of the electrophysiological phenomena taking place at cortical and subcortical neuronal and synaptic sites during the precise moment of learning acquisition, extinction, and recall [1-7]. These in vivo approaches to the study of learning and memory processes will allow the proper integration of the important information collected from in vitro and delayed molecular studies. During the presentation, I will summarize studies in behaving mammals carried out in our laboratory during the past ten years on the relationships between experimentally evoked LTP and LTD and activity-dependent changes in synaptic strength taking place in hippocampal, prefrontal and related cortical and subcortical circuits during the acquisition of classical and operant conditioning tasks [2,6]. These studies suggest that different hippocampal synapses are selectively modified in strength during the acquisition of classical, but not instrumental, conditioning paradigms. In contrast, selected prefrontal and striatum synapses are more directly modified by instrumental learning. These studies also show that besides NMDA receptors, many other neurotransmitter, intracellular mediating, and transcription factors participate in these two types of associative learning. Although experimentally evoked LTP seems to prevent the acquisition of classical eyeblink conditioning when induced at selected hippocampal synapses, it proved to be ineffective in preventing the acquisition of operant conditioned tasks when induced at numerous hippocampal, prefrontal, and striatal sites. The differential roles of these cortical structures during these two types of associative learning will be described and the distributed and timed nature of associative learning abilities will be stressed [5,8,9].

References

[1] Delgado-Garcia JM & Gruart A. TINS, 29: 330, 2006.
[2] Gruart A, Muñoz MD & Delgado-García JM. J Neurosci, 26: 1077, 2006.

[3] Leal-Campanario R, Fairén A, Delgado-García JM & Gruart A. PNAS USA, 104:11459, 2007.
[4] Clarke JR, Cammarota M, Gruart A, Izquierdo I & Delgado-García JM. PNAS USA, 107: 2652, 2010.
[5] Hasan MT, Hernández-González S, Dogbevia G, Treviño M, Bertocchi I, Gruart A & Delgado-García JM. Nature Comm, 4:2258, 2013. doi:10.1038/ncomms3258.
[6] Gruart A, Sánchez-Campusano R, Fernández-Guizán A & Delgado-García JM. A Cerebral Cortex, 25: 2542, 2015.
[7] Madroal N, Delgado-García JM, Fernández-Guizán A, Chatterjee J, Khn M, Mattucci C, Jain A, Tsetsenis T, Illarionova A, Grinevich V, Gross CT & Gruart A. Nature Comm, 7:10923, 2016. doi: 10.1038/ncomms10923.
[8] Ammann C, Márquez-Ruiz J, Gómez-Climent MA, Delgado-García JM & Gruart A. J Neurosci, 36: 6988, 2016.
[9] Fernández-Lamo I, Delgado-García JM & Gruart A. Cerebral Cortex, 14: 1, 2017.

Stochastic Fitzhugh-Nagumo neuron model in excitable regime embeds a leaky integrate-and-fire model.

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Abstract

In this talk, I am going to present a complete mathematical construction for a stochastic leaky-integrate-and-fire model (LIF) mimicking the inter-spike interval (ISI) statistics of a stochastic FitzHugh-Nagumo neuron model (FHN) in the excitable regime, where the unique fixed point is stable. Under specific types of noises, there exists a global random attractor for the stochastic FHN system. The linearization method is then applied to estimate the firing time and to derive the associate radial equation representing a LIF equation. This result confirms the previous prediction by Ditlevsen and Greenwood (2012) for Morris-Lecar neuron model in the bistability regime consisting of a stable fixed point and a stable limit cycle.

This is joint work with Marius Yamakou, Tat Dat Tran and Juergen Jost.

Dual Role of Inhibitory Pre-synaptic Inputs in Stellate Cell Model: A Dynamical System Perspective

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Abstract

The inhibitory activities of cerebellar stellate cells can affect the response of Purkinje cells, the sole output of the cerebellum involved in motor control. These inhibitory interneurons appear to exhibit biphasic first spike latency with respect to the holding potential and to increase their excitability over time. When these neurons are stimulated with a pair of inhibitory and excitatory pre-synaptic inputs, they can fire action potential for a fixed excitatory input if the magnitude of the inhibition is below or above a specific range. We previously used a modified HodgkinHuxley type model, consisting of six ionic currents (including $I_{Na}, I_K, I_L, I_A and I_T$), to study the increase in excitability over time and the biphasic latency profile in stellate cells. We recently devised the same model to investigate how increasing the amplitude of pre-synaptic inhibitory input while keeping the amplitude of excitation the same can switch the system from being responsive to non-responsive and back to responsive again. This was done by first performing times-scale separation and reducing the model from 6 to 3 dimensions. A comparison between the full and reduced models was also conducted to show that they are both type 1 oscillators possessing a saddle-node on an invariant circle (SNIC) bifurcation. Applying slow-fast analysis on the two models revealed that they possess three steady states formed by the intersection of the critical manifold with the nullcline of the slowest variable. We showed that the middle steady state is a saddle fixed point whose stable manifold (computed from the reduced model) acts as a separatrix that determines the switching behaviour in response to pre-synaptic inhibitory-excitatory inputs. It also provides further explanation as to how the ghost of the SNIC acts to generate the biphasic latency profile. In this talk, I will present an overview of these results and the implications of this on excitability in stellate cells.

May Hebbian learning induce balanced chaos in adapting and autonomously active networks?

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Abstract

Neural information processing includes the extraction of information present in the statistics of afferent signals. For this, the afferent synaptic weights w_j are continuously adapted, changing in turn the distribution $p_\theta(y)$ of the post- synaptic neural activity y, which is in turn dependent on parameters θ of the processing neuron. The functional form of $p_{theta}(y)$ will hence continue to evolve as long as learning is ongoing, becoming stationary only when learning is completed. This stationarity principle can be captured by the Fisher information

$$F_\theta = \int p_\theta(y) \left(\frac{\partial}{\partial \theta} ln(p_\theta(y)) \right)^2 dy, \qquad \frac{\partial}{\partial \theta} \to \sum_j w_j \frac{\delta}{\delta w_j}$$

of the neural activity with respect to the afferent synaptic weights w_j . The learn- ing rules derived from the stationarity principle are self-limiting [1], performing a standard principal component analysis with a bias towards a negative excess Kurtosis [2].

For large autonomous networks of continuous-time rate-enconding neurons, respecting Dales law and whose synapses evolve under these plasticity rules, plus synaptic pruning, we find [3]: (a) The continuously ongoing adaption of all synaptic weights leads to a homeostatic self-regulation of the typical magnitude of the synaptic weights and of the neural activities. (b) The system settles into autonomously ongoing chaotic neural activity (the usual starting point for learning of coherent patterns of activity) in which the excitatory and inhibitory inputs tend to balance each other. (c) Short-term synaptic plasticity stabilizes the balanced state.

References

[1] R. Echeveste and C. Gros. Generating Functionals for Computational Intelligence: The Fisher Information as an Objective Function for Self-Limiting Hebbian Learning Rules. Frontiers in Robotics and AI, 1:1, 2014.

[2] R. Echeveste, S. Eckmann and C. Gros. The Fisher information as a neural guiding principle for independent component analysis. Entropy, 17:38383856, 2015.
[3] P. Trapp, R. Echeveste and C. Gros. E-I balance: necessary or inevitable? (to be published).

Information content in functional networks of synchronized neural activity: implications for the pathological and normal brain.

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Abstract

It is said that complexity lies between order and disorder. In physiology, complexity issues are being considered with increased emphasis. Of crucial importance in the medical setting, pathological activity has been associated with low variability/complexity. In the case of the nervous system, it is well known that excessive synchronization is connected with pathologies such as epilepsy and Parkinson disease. However, brain rhythms and neural synchronization are also crucial for perception and cognition, so it is clear that either too much or not enough synchronization can lead to dysfunctional brain states. Here, we investigate the connection between synchronization and complexity in brain dynamics. We have first shown in vivo in a rat model of absence seizures, that the epileptic thalamocortical system can be considered as a self-sustained macroscopic oscillator, and also modeled it as a system of two Kuramoto oscillators. This confirms that large-scale low-complexity dynamics can emerge in pathological brain states. We have then investigated global synchronization in human brain dynamics following a statistical mechanics approach, to identify features of brain organization that are optimal for sensory processing, and that may guide the emergence of cognition. We applied this method to datasets comprising electrophysiological recordings of epileptic patients and also normal subjects during different sleep stages. We found that the information content of functional networks correlates with the state of consciousness/functionality: normal wakeful states are characterized by the greatest number of possible configurations of interactions between brain networks, representing highest entropy and intermediate synchrony values. These findings help to guide in a more formal sense inquiry into how conscious awareness arises from brain dynamics and it has important consequences for the control and monitoring of pathological synchronization.

Estimation of synaptic conductances in the spiking regime

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Abstract

To understand the flow of information in the brain, some computational strategies have been developed in order to estimate the synaptic conductances impinging on a single neuron directly from its membrane potential. However, despite these existent strategies that give circumstantial solutions, they all present the inconvenience that the estimation can only be done when the neuron is not spiking. The main constraint to provide strategies for the oscillatory regimes is related to the nonlinearity of the input-output curve since most of the methods rely on an a priori linear relationship, which is no longer true in spiking regimes.

In this talk, we present a first proof of concept to address the estimation of synaptic conductances when the neuron is spiking, using a simplified spiking neuronal model, called the McKean model [1], which is given by a slow-fast piecewise linear system. Under suitable conditions, that ensure the existence of a periodic orbit in the model, we are able to find out an improved approximated function for the period T depending on the I_{ext} and g_{syn}, that is $T(I_{ext}, C, g_{syn})$. This function results to be monotone with respect to g_{syn} allowing us to infer a steady synaptic conductance from the cell's oscillatory activity with relative errors of order C.

Finally, we extend the results to a computational approach to estimate the conductances in more realistic models.

References

[1] Coombes S.: Neuronal networks with gap junctions: A study of piecewise linear planar neuron models. *SIAM Journal of Applied Dynamical Systems* **7**(3) (2008) 1101–1129.

Development of inhibitory synaptic delay drives maturation of thalamocortical network dynamics

A. Romagnoni [1], **M.T. Colonnese** [2], **J. D. Touboul** [3], **B. Gutkin** [1]

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Abstract

Nervous system maturation occurs at multiple levelssynaptic, circuit, and networkthe timescales es of which are quite divergent. For example, many synaptic properties mature gradually, while emergent network dynamics change abruptly. In this talk, we will present recent work combining experimental and theoretical approaches to investigate a sudden transition in spontaneous thalamocortical activity necessary for the development of vision. Inspired by in vivo measurement of synaptic currents, we will present an extension of the Wilson and Cowan model to take into account the relative onset timing and amplitudes of inhibitory and excitatory population responses. We show that a gradual change in the ratio of inhibitory to excitatory onset times drives a bifurcation of network activity, from high-amplitude oscillations to a non-oscillatory active state, similar to that observed in vivo. Our results show that abrupt changes in network responses do not require similarly dramatic changes in the underlying circuits, and implicate inhibitory timing as a critical determinant of thalamocortical activity maturation.

Neuroprotective role of gap junctions in a neuron-astrocyte network model.

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Abstract

I will present a detailed biophysical model for a neuron/astrocyte network in order to explore mechanisms responsible for the initiation and propagation of cortical spreading depolarizations (slowly propagating waves of rapid, near-complete depolarization of brain cells that may last for about a minute) and the role of astrocytes in preventing these pathological waves. Simulations of the model illustrate how properties of spreading depolarizations, such as wave-speed and duration of depolarization, depend on several factors, including the neuron and astrocyte pump strengths. In particular, we consider the neuroprotective role of astrocyte gap junction coupling. The model demonstrates that a syncytium of electrically coupled astrocytes can maintain a physiological membrane potential in the presence of an elevated extracellular potassium concentration and efficiently distribute the excess potassium across the syncytium. This provides an effective neuroprotective mechanism for delaying or preventing the initiation of spreading depolarizations.

Joint work with A. Joglekar, L. M. Messi, R. Buckalew, S. Wong, D. Terman (OSU)

Asymptotic behaviour of a neural field lattice model with a Heaviside operator

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Abstract

A neural field lattice system motivated by the Amari neural field model is studied. It is formulated as an infinite-dimensional ordinary differential inclusion on a weighted space of infinite sequences. The existence of solutions is proved via a sequence finite-dimensional approximations and the solutions are shown to generate a nonautonomous set-valued dynamical system which possesses a nonautonomous pullback attractor. Forward omega limit sets for the set-valued dynamical system are also discussed.

Canard mediated mixed-mode bursting oscillations in a rate model

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Abstract

The term mixed-mode oscillations (MMOs) is used to describe the dynamics that combine small-amplitude oscillations and large-amplitude oscillations. MMOs arise in multiple-timescale systems with at least two slow variables and a folded critical manifold. The pivotal role of the folded singularities and associated canard structures in shaping these complex dynamics has been identified in many models of biological rhythms. Mixed-mode bursting oscillations (MMBOs) can appear in four-dimensional (4D) systems with two slow and two fast variables as a combination of folded-node type dynamics following fast oscillations of bursting type [1].

In this work we focus on a rate model that accounts for the spontaneous activity in the developing spinal cord of the chicken embryo [2]. The dynamics is that of a classical square-wave burster, with alternation of silent and active phases. Tabak et al. [2] have proposed two different three-dimensional (3D) models with variables representing average population activity, fast activity-dependent synaptic depression and slow activity-dependent depression of two forms. In [3] various 3D combinations of these four variables have been studied further to reproduce rough experimental observations of spontaneous rhythmic activity. In this talk, we first show the spike-adding mechanism via canards in one of these 3D models from [2] where the fourth variable is treated as a control parameter. Then we discuss how a canard-mediated slow passage in the 4D model explains the sub-threshold oscillatory behavior which cannot be reproduced by any of the 3D models. We also dissect the MMBOs in the 4D model by pointing out the relation between the sub-threshold oscillations and skipe-adding mechanism to the bursts. Finally, we relate the canard-mediated slow passage to the intervals of burst and silent phase that have been linked to the blockade of glutamatergic or GABAergic/glycinergic synapses over a wide range of developmental stages.

References

[1] Desroches, M., Kaper, T.J. and Krupa, M.: Mixed-mode bursting oscillations: Dynamics created by a slow passage through spike-adding canard explosion in a square-wave burster. Chaos 23 (4) (2013) 046106.
[2] Tabak, J., Senn, W., ODonovan, M.D., and J. Rinzel.: Modeling of spontaneous activity in developing spinal cord using activity-dependent depression in an excitatory network. J. Neurosci. 20 (8) (2000) 30413056.
[3] Tabak, J., ODonovan, M.D., and J. Rinzel.: Differential control of active

and silent phases in relaxation models of neuronal rhythms. J Comput. Neurosci. 21 (3) (2006) 307328.

Patient-specific modeling of cortical spreading depression

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Abstract

Migraine is a common disease in present day population and a third of the migraine patients suffers from migraine aura, perceptual disturbances preceding the typical headache. Cortical Spreading Depression (CSD), a depolarisation wave that originates in the visual cortex and propagates across the cortex to the peripheral areas, has been suggested as a correlate of visual aura. Until now little is known about the origin of this phenomenon and possible curative treatments. However, the complex and highly individual characteristics of the brain cortex suggest that the geometry might have a significant impact in supporting or contrasting the propagation of CSD. Accurate patient-specific computational models are thus fundamental to cope with the high variability in cortical geometries among individuals, but also with the conduction anisotropy induced in a given cortex by the complex neuronal organisation in the grey matter.

In order to study the role the geometry has in shaping the CSD, we introduce a reaction-diffusion model for extracellular potassium concentration on a personalized brain geometry obtained from MRI imaging. Patient-specific conductivity tensors are derived locally from Diffusion Tensor Imaging (DTI) data and provide detailed information about the anisotropy and the electrical conductivity properties of the cortical tissue. Additionally, we introduce a multiscale PDE-ODE model that couples the propagation of the depolarisation wave associated to CSD with a detailed electrophysiological model for the neuronal activity to capture both macroscopic and microscopic dynamics.

Insect moving gaits, pattern bifurcations and basic neuron models

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Abstract

The last few years a large number of studies has focus their attention to understand the mechanisms that govern the insect movement in order to apply them to autonomous robot movement. Small networks of neurons model central pattern generators (CPG) that control insect locomotion [1, 5]. In this work, we study small CPGs (6-neuron model) for insect locomotion where each neuron follows the same neuron model. Among others, we will use the Hodgkin-Huxley like model of Ghigliazza-Holmes [5].

A first key point is the development of a detailed "roadmap" that provides an exhaustive information [3] about the dynamics of a single neuron. Such information shades light on the effect of varying a parameter. This helps us to identify locomotive properties determined by individual neurons or by whole network. By using suitable symmetry reductions, the basic 6-neuron model can be reduced to a 3-cell model [1, 5, 8]. Therefore, a detailed bifurcation analysis of a 3-neuron model [7] is also relevant. With a suitable combination of short and weak global inhibitory and excitatory stimuli over the network, we can switch between different stable patterns in small neuron networks (in our case a 3-neuron network). We develop a systematic study [6] showing and explaining the effects of applying the pulses at different moments. Moreover, we apply the technique on a completely symmetric network and on a slightly perturbed one (a more realistic situation). The approach of using global stimuli, as in the case of applying a current or a chemical substance to all the network, allows one to avoid undesirable synchronization patterns with nonaggressive stimuli. Also, the use of the roadmaps reveals [3, 4] the existence of heteroclinic cycles between saddle fixed points (FP) and invariant circles (IC) in a 3-cell CPG network. Such a cycle underlies a robust jiggling behavior in bursting synchronization [4].

Finally a detailed analysis of the complete 6-neuron model is performed [2], showing the transitions from the different insect moving gaits, and in particular the tripod or tetrapod coordination patterns. The study of the complete model permits to link with previous results using other 3-cell models [7] (leech CPG) or reduced insect moving 3-oscillator models [1, 5, 8].

References

[1] Aminzare., Z, Srivastava, V., Holmes., P.: Gait transitions in a phase oscillator model of an insect central pattern generator, *SIAM J. on Dynamical Systems*, 17 (1), 626-671, (2018).

[2] Barrio, R., Lozano, Á., Rodríguez, M., Serrano, S.: Patterns in disgusting cockroaches, Preprint, 2018.

[3] Barrio, R., Martínez, M. A., Serrano, S. ,Shilnikov, A.: Macro and micro-chaotic structures in the Hindmarsh-Rose model of bursting neurons, *Chaos*, 24 (2), 023128, (2014).

[4] Barrio, R., Rodríguez, M., Serrano, S. ,Shilnikov, A.: Mechanism of quasi-periodic lag jitter in bursting rhythms by a neuronal network, *EPL*, 112 (3), 38002, (2015).

[5] Ghigliazza, R., Holmes.,P.: A minimal model of a central pattern generator and motoneurons for insect locomotion, *SIAM J. on Dynamical Systems* 3 (4), pp. 671-700, (2004).

[6] Lozano, Á., Rodríguez, M., Barrio, R.: Control strategies of 3-cell Central Pattern Generator via global stimuli, *Scientific Reports* 6, 23622, (2016).

[7] Wojcik, J., Schwabedal, J., Clewley, R., Shilnikov, A.: Key bifurcations of bursting polyrhythms in 3-cell central pattern generators, *PloS ONE* 9 (4), e92918, (2014).

[8] Yeldesbay, A., Tibor, T., Daun. S.: The role of phase shifts of sensory inputs in walking revealed by means of phase reduction, *Journal of Computational Neuroscience*, 44 (3), 313-339, (2018).

Encoding and acquiring memories in high-dimensional brain

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Abstract

Codifying memories is one of the fundamental problems of modern Neuroscience. The functional mechanisms behind this phenomenon remain largely unknown. Experimental evidence suggests that some of the memory functions are performed by stratified brain structures such as the hippocampus, where pyramidal neurons in the CA1 region receive a highly multidimensional input from the CA3 area. We thus assess the implication of the abundance of neuronal signaling routes converging onto single cells on the information processing. We show that single neurons can selectively detect and learn arbitrary information items if they operate in high dimensions [1]. The argument is based on stochastic separation theorems and the concentration of measure phenomena [2]. We demonstrate that a simple functional model of a neuron is capable of explaining: 1) the extreme selectivity of single neurons to the information content, 2) clustering of several even uncorrelated stimuli, and 3) learning new items by associating them with already "known" ones. These findings constitute a basis for organization of complex memories in ensembles of single neurons.

Acknowledgements. This work was supported by the Spanish Ministry of Science, Innovation, and Universities under grant FIS2017-82900-P.

References

[1] Tyukin, I., Gorban, A.N., Calvo, Carlos., Makarova, J., Makarov, V.A.: High-dimensional brain: A tool for encoding and rapid learning of memories by single neurons. *Bull. Math. Biol.* DOI: 10.1007/s11538-018-0415-5 (2018).

[2] Gorban, A.N., Makarov, V.A., Tyukin, I.Y.: The unreasonable effectiveness of small neural ensembles in high-dimensional brain. *Phys. Life Rev.* (2018).

On the encoding of weak periodic signals by coupled FitzHugh-Nagumo neurons

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Abstract

Sensory neurons encode and transmit information of external inputs in their spike sequences; however, how the information of a weak signal is encoded in the presence of noise remains poorly understood. Different encoding mechanisms can be expected to be functional under different conditions. In this talk I will focus on a conceptually simple problem: how neurons encode a subthreshold periodic input? First, I will focus in an individual neuron. I will present results of simulations of the stochastic FitzHugh-Nagumo (FHN) model that suggest that, when the neuron perceives the weak signal, it can encode the information of the period and of the amplitude of the signal in the form of more-expressed and less-expressed spike patterns, which are defined by the relative timing of the spikes and thus, are robust to the presence of noise [1]. As not individual neurons but neuronal populations are responsible for signal encoding and transmission, a relevant question is how a second neuron, which does not perceive the signal, affects the detection and the encoding of the signal, done by the first neuron. To address this issue, in the second part of the talk, I will present results of simulations of two coupled stochastic FHN neurons. Simulations show that the first neuron, which perceives the signal, fires a spike train that also has preferred and infrequent patterns carrying the signal information [2]. Therefore, signal encoding in symbolic spike patterns is robust to coupling, and thus, it can be a plausible mechanism of signal encoding. Finally, I will discuss ongoing work devoted to understand the encoding of weak signals by small ensembles of neurons, with modular coupling structure.

References

[1] J. A. Reinoso, M. C. Torrent, and C. Masoller, "Emergence of spike correlations in periodically forced excitable systems", Phys. Rev. E. 94, 032218 (2016).

[2] M. Masoliver and C. Masoller, "Subthreshold signal encoding in coupled FitzHugh-Nagumo neurons", arXiv:1711.08309 (2018).

Modelling of focal epilepsy; lessons from grid recordings

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Abstract

Grid recordings in the work-up for epilepsy surgery offer a unique opportunity to further our understanding of the dynamics during epileptic seizures. We discuss variants of neural mass models based on two types of grid recordings.

Based on Utah array recordings we show how small-scale neuronal networks may impose widespread effects on large network dynamics. Motivated by data of seizure evolutions as well as multi-unit spike activity during seizures we motivate that the typical sigmoidal activation function may need to be replaced by a Gaussian function. Next in a multiscale nonlinear model, feedforward inhibition features a dual role in seizures: while inhibition at the wavefront fails, allowing seizure propagation, feedforward inhibition of the surrounding centimeter-scale networks is activated via long-range excitatory connections.

Single Pulse Electrical Stimulation probes the network and tissue under- neath a subdural electrode grid. In response to stimulation one finds both consistent early responses (ER) ($< 100\,ms$) and random delayed responses (DR) (100-400 ms). The ERs can be used to construct patient-specific effective networks. We find that most DRs may be explained as a second order response, i.e. the initial stimulation evokes neural activity that triggers the DRs. We show that feedforward inhibition is a plausible ingredient in a coupled neural mass model to explain the stochastic nature of DRs as well as its waveform.

Bursting in the presence of a locally separating manifold

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Abstract

The mechanism underlying multi-spike bursting of neurons is typically explained with models that exhibit different time scales with a single slow variable. The bursting patterns observed in such slow-fast systems are periodic orbits that successively track different coexisting attracting states associated with the so-called fast subsystem, for which the slow variable is viewed as a parameter. In particular, the threshold that determines when bursting occurs is identified as the basin boundary between two attractors associated with the active and silent phases. In reality, however, the bursting threshold is a more complicated object. We use the numerical methods presented in [1] to compute an approximation of the bursting threshold as a locally separating stable manifold of the full slow-fast system. As a representative example, we use a three-dimensional Morris-Lecar model that has one slow and two fast variables. We compute the locally separating stable manifold and investigate how the bursting periodic orbit interacts with this manifold. We also explain how this manifold organises the number of spikes in the bursting periodic orbit and illustrate its role in a spike-adding transition as we vary a parameter.

References

[1] Farjami, S., Kirk, V, Osinga, H.M.: Computing the stable manifold of a saddle slow manifold. *SIAM Journal on Applied Dynamical Systems* **17**(1) (2018) 350–379.

Kuramoto model for excitation-inhibition-based oscillations

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Abstract

The Kuramoto model (KM) is a theoretical paradigm for investigating the emergence of rhythmic activity in large populations of oscillators [1]. A remarkable example of rhythmogenesis is the feedback loop between excitatory (E) and inhibitory (I) cells in large neuronal networks. Yet, although the EI-feedback mechanism plays a central role in the generation of brain oscillations [2], it remains unexplored whether the KM has enough biological realism to describe it. In this contribution we present a two-population KM that is analytically solvable to a large extent, and describes the main features of the EI-based rhythms [3]: (i) Oscillations set in exclusively due to the cooperative action of both E and I populations. (ii) Oscillations emerge if excitatory dynamics is faster than inhibition. (iii) Otherwise, when inhibition is faster than excitation, strong enough self-coupling is necessary for synchrony to occur. (iv) Excitation always precedes inhibition. (v) The transition between incoherence and synchronization is often hysteretic.

References

[1] Y. Kuramoto. Chemical Oscillations, Waves, and Turbulence. Springer-Verlag, Berlin, (1984).

[2] M. Whittington et al.: Inhibition-based rhythms: experimental and mathematical observations on network dynamics. Int. J. Psychophysiol. **38**, 315 (2000).

[3] E. Montbrió and D. Pazó: Kuramoto model for excitation-inhibition-based oscillations. Phys. Rev. Lett. (in press).

Network mechanisms underlying the role of oscillations in cognitive tasks

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Abstract

Oscillatory activity robustly correlates with task demands during many cognitive tasks. However, not only are the network mechanisms underlying the generation of these rhythms poorly understood, but it is also still unknown to what extent they may play a functional role, as opposed to being a mere epiphenomenon. Here we study the mechanisms underlying the influence of oscillatory drive on network dynamics related to cognitive processing in simple working memory (WM), and memory recall tasks. Specifically, we investigate how the frequency of oscillatory input interacts with the intrinsic dynamics in networks of recurrently coupled spiking neurons to cause changes of state: the neuronal correlates of the corresponding cognitive process. We find that slow oscillations, in the delta and theta band, are effective in activating network states associated with memory recall by virtue of the hysteresis in sweeping through a saddle-node bifurcation. On the other hand, faster oscillations, in the beta range, can serve to clear memory states by resonantly driving transient bouts of spike synchrony which destabilize the activity. We leverage a recently derived set of exact mean-field equations for networks of quadratic integrate-and-fire neurons [1] to systematically study the bifurcation structure in the periodically forced spiking network. Interestingly, we find that the oscillatory signals which are most effective in allowing flexible switching between network states are not smooth, pure sinusoids, but rather burst-like, with a sharp onset. We show that such periodic bursts themselves readily arise spontaneously in networks of excitatory and inhibitory neurons, and that the burst frequency can be tuned via changes in tonic drive. Finally, we show that oscillations in the gamma range can actually stabilize WM states which otherwise would not persist.

References

[1] E. Montbrió, D. Pazó and A. Roxin A macroscopic description for networks of spiking neurons, *Phys. Rev. X* 5:021028 (2015).

Getting our feet wet: rivers and other interesting orbits in neuronal models

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Abstract

In this work, we introduce a general new change of coordinates, `local orthogonal rectification` or LOR, that can be applied at any selected curve in the phase space of a dynamical system. LOR, based on the Frenet frame, yields a coordinate system, the LOR frame, which allows us to rigorously study curves in a flow typically, trajectories that exhibit whichever properties we specify, such as periodicity or certain asymptotic behaviors. We use the LOR approach to derive a novel definition for rivers, long-recognized but poorly understood trajectories that locally attract other orbits yet need not be related to invariant manifolds or other familiar phase space structures; to identify rivers within several example neuronal systems; and to analyze how these structures impact model neuronal dynamics. We also discuss extensions to arbitrary dimensions and some interesting examples involving canards.

Noise-induced spiking activity suppression in neural systems

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Abstract

The rhythmic activity of spiking neurons is known to be sensitive to noise. In such neurons, inverse stochastic resonance (ISR) in which the average activity of a neuron exhibits a pronounced minimum as noise intensity increases, can occur. Here, I report our latest results concerning the study of ISR in different neural systems. First, I will show the case of a single neuron that receives a biophysically realistic noisy current originated from uncorrelated presynaptic spikes arriving through many afferents. In the absence of short-term synaptic plasticity (STSP), such noise source can originate ISR as a function of the presynaptic firing rate. Also, the presynaptic firing rate range for ISR emergence is strongly influenced by STSP [1]. Interestingly, this fact induces a double inverse stochastic resonance (DISR), with two distinct wells centered at different presynaptic firing rates. Secondly, and motivated by the fact that emergent phenomena in the brain, such as information processing, cognition, and mental diseases occur at neural population level, and could strongly be influenced by brain structure, we studied also ISR in large populations of neurons [2]. ISR can then emerge as a consequence of channel noise, synaptic strength, the presence of excitatory and inhibitory currents, and topological features of the network as degree distribution and mean connectivity degree. Finally, we describe the dynamical mechanisms inducing ISR at the single neuron and neural population levels.

References

[1] Uzuntarla, M., Torres, J.J., So, P., Ozer, M, Barreto, E.: Double inverse stochastic resonance with dynamic synapses. Phys. Rev. E 95 (2017) 012404.

[2] Uzuntarla, M., Barreto, E., Torres, J.J.: Inverse Stochastic Resonance in Networks of Spiking Neurons. PLoS Comput. Biol. 13(7) (2017), e1005646.

Sequential neural processing: from central pattern generators to cognitive functions

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Abstract

A large variety of neural activity can be seem as robust sequential activations among subcellular processes, neurons, networks or brain regions. Sequences underlie the generation, coordination and control of multiple neuronal information processes at different levels in the organization of the nervous system. This can be observed in simple central pattern generator circuits that produce rhythmic motor sequences [1], in the sensory-motor transformation of invertebrates [2], and all the way up to human cognitive processes involving the sucesive activation of different brain regions [3]. In this talk I will argue that there are common features in the production of robust sequences at all description levels and dynamic phenomena that are typically disregarded when analyzing experimental data. I will emphasize the need for theoretical paradigms to describe multilevel and hiearchical sequence production. Finally, I will discuss how these models can also be used in bio-inspired robotics and the design of novel closed-loop experimental procotols and human-computer interactions.

References

[1] Elices, I., and Varona, P.: Asymmetry Factors Shaping Regular and Irregular Bursting Rhythms in Central Pattern Generators. *Front. Comput. Neurosci.* **11** (2017) 9.

[2] Latorre, R., Levi, R., and Varona, P.: Transformation of context-dependent sensory dynamics into motor behavior. *PLoS Comput. Biol.* **9** (2013) e1002908.

[3] Varona, P., and Rabinovich, M. I.: Hierarchical dynamics of informational patterns and decision making. *Proc. R. Soc. B* **283** (2016) 20160475.

Phasic dopamine influences on a two-alternative forced choice task

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Abstract

Mammals selecting actions in noisy contexts quickly adapt to unexpected outcomes to better exploit opportunities arising in the future. Such feedback-based changes in behavior rely on long term plasticity within cortico-basal-ganglia-thalamic (CBGT) networks, driven by dopaminergic (DA) modulation of cortical inputs to the direct (D) and indirect (I) pathways of the striatum. However, it remains unclear how changes in action value, determined by competition between the D and I pathways, influence the mechanisms of the action selection process itself.

In this talk, we focus on developing a learning network consisting of striatal neurons and their cortical inputs, with corticostriatal synaptic plasticity driven by phasic reward signals, resulting from simulated actions and their consequent dopamine release. In fact, we present a general learning rule to simulate the performance in a two-alternative forced choice task, driven by changes in dopamine signalling induced by outcomes of actions, that varies over the course of simulations.

In the model, the performance of a selected action yields a reward that triggers a phasic dopamine response. Consequently, the spiking model of the striatum is augmented with phenomenological representations of action values, updated by comparing the reward received versus the current value of that action; and dopamine release. The level of dopamine is derived from comparing the reward level r_i resulting from the performance of action i to the maximum value believed to be attainable across all actions, based on past experience. Finally, dopamine levels determine the changes in weights of cortical synaptic inputs to eligible striatal neurons that participated in the action.

Results show that the synchrony of the striatal network drives selection between two actions with distinct reward outcomes, showing a learning of the preferred action in settings with fixed reward outcomes. After the model is tuned based on fixed reward scenarios, its performance agrees with behavioral experiments with probabilistic reward paradigms.

Dynamical mechanisms of high frequency spiking of a dopamine neuron

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Abstract

Dopamine neurons located in the ventral tegmental area (VTA) play a key role in many cognitive tasks. Here we consider some dynamical mechanisms underlying synchronization properties of DA neurons. The first dynamical mechanisms concern the change of excitability (spike generation) class of the DA neuron depending on its synaptic inputs and synaptic currents. The neuronal excitability determines the neurons response to stimuli, its synchronization and resonance properties and, ultimately, the computations it performs in the brain. We investigated the dynamical mechanisms underlying the excitability type of DA neurons using both a conductance-based biophysical and a phenomenological models, and its regulation by intrinsic and synaptic currents. Calibrating the model to reproduce low-frequency tonic firing results in N-methyl-D-aspartate (NMDA) excitation balanced by GABA-mediated inhibition and leads to class I excitable behavior characterized by a continuous decrease in firing frequency in response to hyperpolarizing currents. Furthermore, we analyzed how the excitability class of the DA neuron model is influenced by changes in the intrinsic current composition. The key characteristics of synaptic conductances that are often tonically active in vivo also change the class of excitability: Depolarizing GABA receptors reversal potential or co-activating AMPA receptors leads to an abrupt frequency drop to zero, which is typical for type II excitability. Coactivation of NMDARs together with AMPARs and GABARs shifts the class I/II boundary toward more hyperpolarized GABAR reversal potentials. Collectively, these results imply that class I excitability in dopamine neurons might be important for low firing rates and fine-tuning basal dopamine levels, while switching excitability to type II during NMDAR and AMPAR activation may facilitate a transient increase in dopamine concentration, as class II neurons are more amenable to synchronization by mutual excitation.

Another dynamical mechanism allowing to "overclock" the DA neuron relates the action of the synchronized GABA neuron population (which is much faster than the DA neurons). In the framework of a circuit model of the VTA, asynchronous activity of GABA neurons provides a constant level of inhibition to the DA neuron, and, when removed, produces a classical disinhibition burst. In contrast, when GABA neurons are synchronized by a common synaptic input, they are able to

produce a moderately strong high frequency pulse train which can provide high frequency forced oscillations of a DA neuron. Such oscillations have the frequency coinciding with the frequency of the external force and amplitude that is larger than the amplitude of the intrinsic oscillations. Distinct from the previous mechanisms, the frequency growth was not based on lowered firing rate of the GABA neurons or weaker hyperpolarization by the GABAR synaptic current. We explain such dynamics in detail using the McKean oscillator for which we analytically built a map that gives an explanation of these properties. It was shown that such high frequency forced oscillations exist in the large region of the external force parameters (pulse amplitude and frequency). Interestingly, in application to neuroscience, both excitatory and inhibitory inputs can force the high-frequency oscillations.

This work was partially supported by the Russian Foundation for Basic Research (grants 17-02-00874 and 18-41-520001). Denis Zakharov acknowledges support of Russian Science Foundation grant 18-11-00294 (numerical simulations). Alexey Kuznetsov was supported by NIH NIAAA grant R01AA022821. Boris Gutkin was supported by the LABEX ANR-10-LABX-0087 IEC and IDEX ANR-10-IDEX-0001-02 PSL* and also acknowledges the RF academic excellence Program 5-100.

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6 OTHER INFORMATION

All the talks will be placed at the CIEM center, 4th Maria Aburto street.

Lunches

Lunches will be served at Hotel Las Rocas (Calle Flaviobriga, 1) at 13:30.

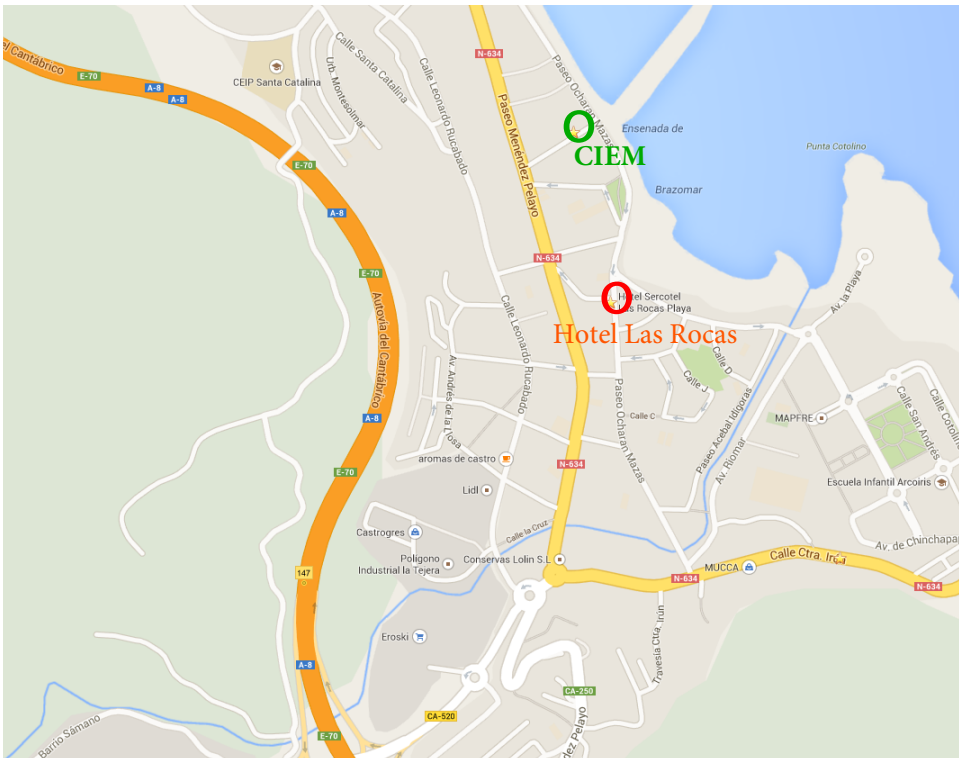

Figure 1: Location of the CIEM and Hotel Las Rocas.

Workshop Dinner

The Workshop Dinner will be on Friday 28th at 21:00 at Hotel Las Rocas.

Open Disclosure Conference

On Wednesday 26th José María Delgado will offer an open conference entitled : 'Hablando de lo que entiende: el cerebro en vivo y en directo' at the CIEM center at 19:30.