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BOOK OF ABSTRACTS

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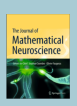

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Contents

Exit time of semi-Markov processes and neuronal models

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We characterize the distribution of the first exit time from an arbitrary open set for a class of semi-Markov processes obtained as time-changed Markov processes. For instance we estimate the asymptotic behaviour of the survival function (for large t) and of the distribution function (for small t) and we provide some conditions for absolute continuity. We have been inspired by a problem neurophyshiology and our results are particularly usefull in this field, precisely for the so-called Leacky Integrate-and-Fire (LIF) models: the use of semi-Markov processes in these models appear to be realistic under several aspects, e.g., it makes the intertimes between spikes a r.v. with infinite expectation, which is a desiderable property. Hence we provide a LIF model based on semi-Markov processes.

References

[1] G. Ascione, E. Pirozzi and B. Toaldo. On the exit time from open sets of some semi-Markov processes, *Submitted*, 2019.

This is not a bump

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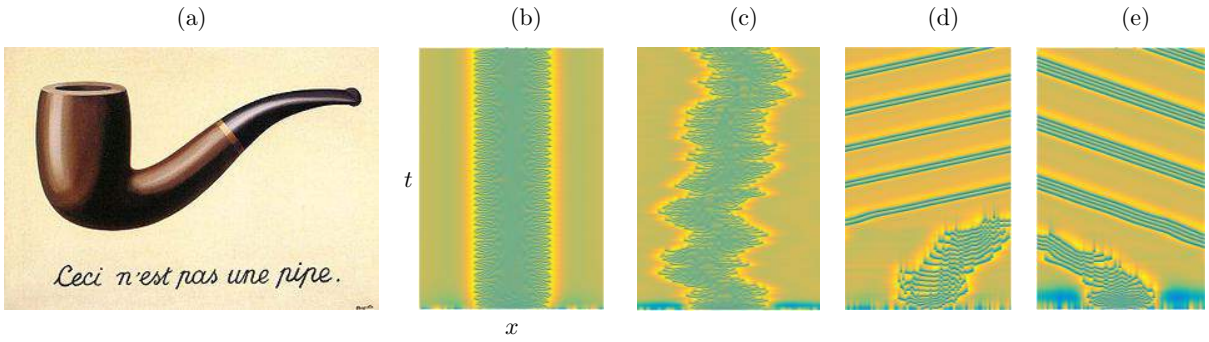

Figure 1: (a): René Magritte's painting entitled *This is not a pipe*. (b)–(d): coherent structures obtained simulating a network of leaky integrate-and-fire neurons (a discretisation of (1)) for $\beta=1$ (b), $\beta=3.5$ (c), $\beta=4.5$ (d)-(e), respectively.

The title of this talk draws inspiration from René Magritte's famous painting *This is not a pipe* (Figure (a)), which challenges the observer's perception of reality, by displaying a seemingly contradictory statement.

In particular, the talk presents analytical and numerical evidence that the coherent structures shown in Figures (b)-(c) (well known examples of *bumps* and *meandering bumps* of neuronal activity, respectively) stem from the peculiar, elusive bifurcation structure of *deterministic travelling waves*, such as the ones seen in (d)-(e).

The model simulated in Figures (b)-(e) is a spatially-extended network of leaky integrate-and-fire neurons, which are synaptically coupled via an excitatory-inhibitory kernel. The structure simulated above were found by Laing and Chow [1], and several authors have investigated spatially-continuous versions of the model [2, 3, 4].

Laing and Chow found bumps in a model with an impinging stochastic current. Other structures, also known as *bumps*, are routinely found as heterogeneous localised equilibrium solutions to neural field models which, once subjected to a stochastic forcing, display meandering bumps (see [5] and Kilpatrick's tutorial at the present conference).

However, stochasticity does not play a role in Figures (b)-(e), whose results concern a discrete version of the following (formal) *deterministic model*

$$\partial_t v(x,t) = -v(x,t) + I + \sum_{j\in\mathbb{N}} \int_{-\infty}^{\infty} w(x-y)\alpha\big(t-\tau_j(y)\big)dy - \sum_{j\in\mathbb{N}} \delta\big(t-\tau_j(x)\big), \qquad (x,t)\in\mathbb{R}\times\mathbb{R}. \tag{1}$$

where v is the voltage, w the synaptic kernel, $\alpha(t)=\beta e^{-\beta t}H(t)$ an exponential alpha function, and $\{\tau_j(x)\}$ a set of firing functions. Our results can be summarised as follows:

1. We introduce the *voltage mapping* V, that is, a functional transforming a firing set $\{\tau_j(x)\}_{j=1}^m$ into a spatiotemporal voltage profile $v(x,t)=V(\tau_1,...,\tau_m)(x,t)$ with m spikes, satisfying the evolution equation (1) in a mild sense.
2. V is used to construct travelling waves. The construction does not require a discretisation of the spatial variable x, and suggests a remarkably cheap algorithm to compute waves with arbitrary m.
3. The linearisation of V around a travelling wave is a bounded operator on a suitably-defined exponentially-weighted function space. This allows us to study asymptotic linear stability of the wave (in the sense defined by Bressloff [3]) using a parsimonious root-finding algorithm. This, together with point 2 enables us to characterise travelling waves that have not been accessible before.
4. We find that (1) supports coexisting travelling waves with an arbitrary number of spikes m, arranged on disconnected branches. All branches undergo oscillatory bifurcations and contain unstable segments; for sufficiently large m, branches are fully unstable.
5. In contrast to what has been predicted and observed for purely excitatory synaptic kernels and low m [2], the number of spikes has a dramatic impact on the wave speed and profiles: as m increases the waves have vanishingly small propagation speed, and possess a well-defined width (informally, they "converge" to a localised structure with 0 speed as $m\to\infty$).
6. We provide evidence that the *bumps* and *meandering bumps*, seen in the figure, are a form of spatiotemporal chaos, whereby the dynamics visits a large number of unstable, localised, travelling wave solutions.

References

[1] C. R. Laing and C. C. Chow, Stationary Bumps in Networks of Spiking Neurons, *Neural Computation* 13 (7), 2001.
[2] B. Ermentrout, The analysis of synaptically generated traveling waves, *J. Comput. Neurosci.* 2 (5), 1998.
[3] P. Bressloff, Traveling waves and pulses in a one-dimensional network of excitable integrate-and-fire neurons *Journal of Mathematical Biology* 40 (2), 2000.
[4] R. Oşan, R. Curtu, J. Rubin, and B. Ermentrout Multiple-spike waves in a one-dimensional integrate-and-fire neural network. *Journal of Mathematical Biology* 48 (3), 2004.
[5] Z. P. Kilpatrick and B. Ermentrout, Wandering Bumps in Stochastic Neural Fields. *SIAM J. of Applied Dynamical Systems.* 12 (1), 2013.

Circuit Polarity Effect of Cortical Connectivity, Activity and Memory

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Experimental constraints have traditionally implied separate studies of different cortical functions, such as memory and sensory-motor control. Yet, certain cortical modalities, while repeatedly observed and reported, have not been clearly identified with one cortical function or another. Specifically, while neuronal membrane and synapse polarities with respect to a certain potential value have been attracting considerable interest in recent years, the purposes of such polarities have largely remained a subject for speculation and debate. Formally identifying these polarities as on/off neuronal polarity gates, we analytically show that cortical circuit structure, behavior and memory are all governed by the combined potent effect of these gates, which we collectively term circuit polarity. Employing widely accepted, biologically validated, firing rate and plasticity paradigms, we show that circuit polarity is mathematically embedded in the corresponding models. Moreover, we show that the firing rate dynamics implied by these models are driven by on-going circuit polarity gating dynamics. Furthermore, circuit polarity is shown to segregate cortical circuits into internally-synchronous, externally-asynchronous subcircuits, defining their firing rate modes in accordance with different cortical tasks. In contrast to the Hebbian paradigm, which is shown to be susceptible to mutual neuronal interference in the face of asynchrony, circuit polarity is shown to block such interference. Noting convergence of synaptic weights, we show that circuit polarity holds the key to cortical memory, having a segregated capacity linear in the number of neurons. While memory concealment is implied by complete neuronal silencing, memory is restored by reactivating the original circuit polarity. Finally, we show that incomplete deterioration or restoration of circuit polarity result in memory modification, which may be associated with partial or false recall, or, yet, novel innovation.

Analyzing dynamic decision models using differential Chapman-Kolmogorov equations

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In a constantly changing world, decision making requires adaptive evidence accumulation. Old information becomes less relevant as the environment changes more rapidly. To understand how humans and animals make decisions in such environments we used Bayesian methods to model how an ideal observer accumulates evidence in stochastically changing environments. We focused on binary choice tasks in which an observer must report the state $s(t) \in s_\pm$ of a continuous time Markov process with switching (hazard) rate h that they observe noisily. The continuum limit of these models are nonlinear stochastic differential equations describing an *ideal observer's belief* y (log-likelihood ratio) of whether s_+ or s_- is the current state [1]:

$$\mathrm{d}y = g(t)\mathrm{d}t + \rho \mathrm{d}W - 2h\sinh(y)\mathrm{d}t,$$

where the Wiener process $\mathrm{d}W$ models observation noise, the telegraph process $g(t)$ models state switches with hazard rate h, and $2h\sinh(y)$ discounts old evidence in a fashion optimized to environmental changes. These models provide insight into how organisms can robustly discount evidence to make accurate decisions in dynamic environments [2].

To jointly characterize observation noise and stochastic switching, we derived differential Chapman-Kolmogorov (CK) equations which associate the observer's belief y (log-likelihood ratio) and the present state $s(t)$ (correct choice) with two separate random variables. Rescaling time according to the hazard rate $ht \mapsto t$ and assuming observations are Gaussian, we could map to coordinates in which the differential CK equations have a single free parameter m which corresponds to the *evidence strength* of the current trial (See Fig. 1A and [3]):

$$p_t^\pm(y,t) = \mp m p_y^\pm(y,t) + m p_{yy}^\pm(y,t) + 2\frac{\partial}{\partial y}\left(\sinh(y)p\pm(y,t)\right) + p^\mp(y,t) - p^\pm(y,t).$$

We projected this system to a jump-diffusion model for a single density $p_s(y,t)$ in which jumps from y to $-y$ correspond to state switches. The model can be integrated to determine how accurately an observer's belief represents the underlying state (Fig. 1B). We also compared the normative model to approximate models, including a model with linear leak and a leak-less model with no-flux boundaries. Both models can be tuned to have accuracy nearly identical to the ideal observer model, but they are more sensitive to changes in their evidence discounting parameters. Such heuristics may thus approximate the evidence accumulation strategies biological organisms employ in dynamic environments, as they manage a trade-off between accuracy and complexity, as well as between variability and bias.

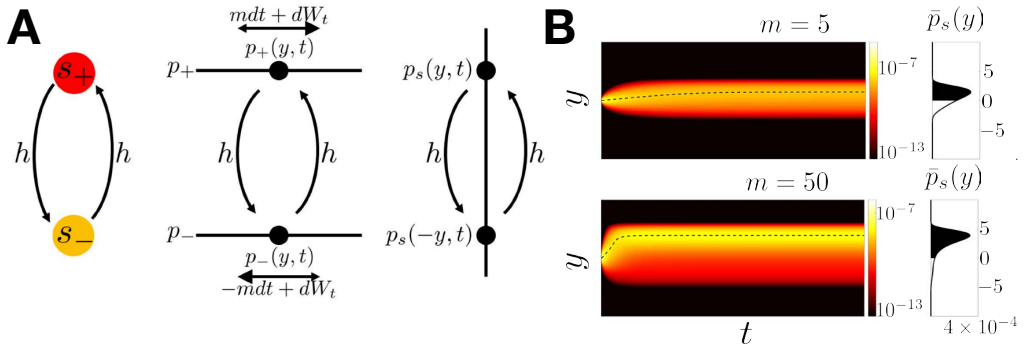

Figure 1: **A:** Schematic of differential CK equations. We define joint densities $p_\pm := p(y, s = s_\pm, t)$, where transitions of the two-state continuous time Markov process $s(t)$ transfer probability between densities. Changing variables, we define $p_s(y,t)$, so state changes transfer probability from y to $-y$. **B:** Colormap represents evolution of densities $p_s(y,t)$ for $m = 5, 50$. Right plots show stationary densities that are integrated (shading) to find response accuracy.

References: [1] A Veliz-Cuba, ZP Kilpatrick, and K Josić. SIAM Review 58 (2016) pp. 264-289; [2] CM Glaze, JW Kable, and JI Gold. Elife 4 (2015) e08825; [3] NW Barendregt, K Josić, and ZP Kilpatrick. (2019) in prep.

A sub-Riemannian model of the visual cortex based on frequency-phase and its applications

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Our objective is to develop a geometrical model of vision consistent with the neural characteristics of the visual cortex and construct orientation maps by using the relevant model geometry. Our departure point is the visual cortex model of the orientation selective neurons in the cortex, which was introduced by Citti and Sarti [1]. We extend this model and provide a novel sub-Riemannian model of the primary visual cortex which models orientation-frequency selective, phase shifted cortex cell behavior and the associated neural connectivity. We employ the model framework in order to provide a geometric procedure for multi-feature orientation map construction.

References

[1] G. Citti and A. Sarti, A cortical based model of perceptual completion in the roto-translation space, *Journal of Mathematical Imaging and Vision*, 24, (3), pp. 307-326, 2006.

Insect movement gaits: neuron model, CPG and pattern bifurcations

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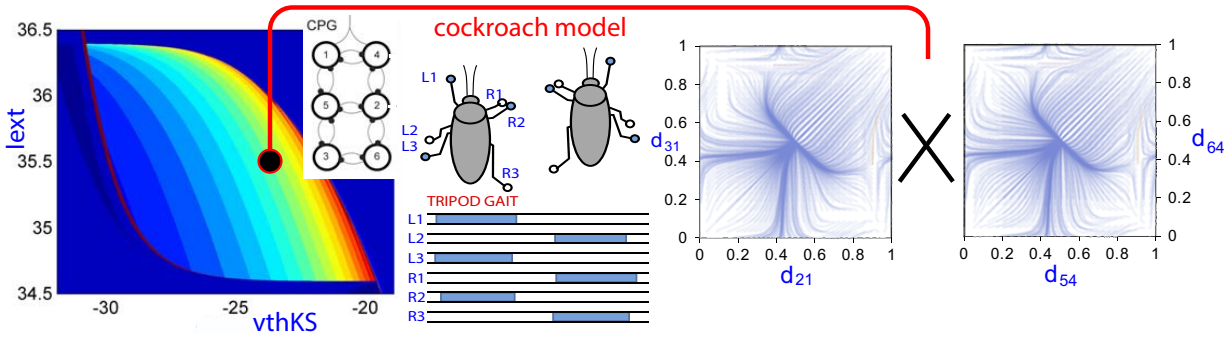
The study of the synchronization patterns that control biological processes has become a growing discipline [6]. Small networks of neurons model central pattern generators (CPG) that control insect locomotion [1, 4]. In this work, we study small CPGs (6-neuron model) for insect locomotion where each neuron follows the Hodgkin-Huxley like model of Ghigliazza-Holmes [4]. A first key point is the development of a detailed "roadmap" using the Spike-Counting technique and bifurcation analysis that provide an exhaustive information [2] 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. Once selected the basic bursting dynamics of isolated neurons, we analyze patterns evolution in the complete CPG.



By using Phase Resetting Curve (PRC) techniques, and later suitable symmetry reductions, the basic 6-neuron model can be reduced to a 3-oscillator model [1, 4, 7]. Therefore, a detailed bifurcation analysis of a 3-neuron model [6] is relevant. Also, the use of the roadmaps in the 3–cell CPG network reveals [3, 5] the existence of heteroclinic cycles between saddle fixed points (FP) and invariant cycles (IC). Such a cycle underlies a robust jiggling behavior in bursting synchronization [3].

The main problem is that the reduction techniques [1, 7] impose symmetries that make no possible to detect asymmetric patterns of movement. We introduce numerical techniques based on the combined use of several 3-cell analysis related to each side of the insect (that impose less symmetries) or the analysis of the complete system by performing automatic detection techniques combined with quasi-Monte-Carlo sweeping methodologies. These methods permit us to obtain a complete scheme [2] of the patterns evolution on the movement gaits of the insect once some of the parameters is changed (also associated to the active time of the involved neurons).

References

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

[2] R. Barrio, Á. Lozano, M. Rodríguez, S. Serrano. Insect movement gaits: neuron model, CPG and pattern bifurcations, preprint, 2019.

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

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

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

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

[7] A. Yeldesbay, T.I. Toth, S. Daun. The role of phase shifts of sensory inputs in walking revealed by means of phase reduction, *Journal of Computational Neuroscience*, 44(1), 313-339, 2018.

Sparse network connectivity revealed from physiology: What pairwise intracellular recordings can tell us about motor circuits

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During generation of rhythmic movements, most spinal neurons receive oscillatory synaptic drive. The neuronal architecture underlying this drive is unknown, and the corresponding network size and sparseness have not yet been addressed. If the input originates from a small central pattern generator (CPG) with dense divergent connectivity, it will induce correlated input to all receiving neurons, while sparse convergent wiring will induce a weak correlation, if any. Here, we use pairwise recordings of spinal neurons to measure synaptic correlations and thus infer the wiring architecture qualitatively. A strong correlation on a slow timescale implies functional relatedness and a common source, which will also cause correlation on fast timescale due shared synaptic connections. However, we consistently found marginal coupling between slow and fast correlations regardless of neuronal identity. The inhibitory connectivity was $< 1\%$, and the excitatory connectivity was even lower. This suggests either a sparse convergent connectivity, or a CPG network with pervasive recurrent inhibition that actively decorrelates common input.

Predictive coding and behavioural flexibility during probabilistic decision-making: multi-neuronal, multi-area, electrophysiological investigations of the macaque prefrontal cortex.

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Individual neurons are capable of encoding expectations about events, for example the probability of receiving a reward following an action; furthermore, they encode prediction errors when these expectations are not met, for example when a reward is not received after an action that was previously rewarded. In a dynamic or volatile environment, these prediction errors are useful to compute a new, updated prediction, about the likelihood of that event and this is a type of computation crucial for learning and flexible, adaptable behaviour. Single-cell neurophysiological recordings in monkeys have demonstrated that several prefrontal areas are involved in coding predictions and prediction error information. However, the study of single-cells and single-areas in isolation does not allow for elucidating how interactions between populations of neurons across different brain regions support complex predictive mechanisms that support learning and flexible behavior.

Here, we introduce the first study that seeks to address these questions by applying multi-electrode techniques to different frontal regions in the macaque monkey. We present exploratory results from two 64-electrode micro-arrays implanted in the anterior cingulate gyrus (ACC) and dorsolateral prefrontal cortex (dlPFC), which allowed us to record both single- and multi-unit as well as oscillatory activity, simultaneously from both areas, while the monkey is engaged in a novel two-step navigation task within a virtual dynamic maze involving probabilistic decision-making and flexible updating of behavioural plans.

We identified units that respond to task-relevant information - such as, for example, reward and reward expectation (in both ACC and dlPFC) and state transitions (in dlPFC) - and task-related changes in oscillatory activity in the beta and gamma bands. We also present evidence for changes in cross-region synchrony in the theta band that could be supporting network-level communication of task relevant information. We discuss these findings in the context of predictive coding models, as well as with regards to future applications of the task to investigate these mechanisms using advanced analysis tools to address network-level dynamics.

Fractional-order versions of neuronal models

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We present a stability and bifurcation analysis of three fractional-order versions of well-known neuronal models, based on previously obtained theoretical findings [1, 2]. For the continous cases, we consider the Caputo derivative, as it is more applicable to real world problems, while for the discrete-time counterpart, we use the Caputo h-difference [5]. The considered models are the Morris-Lecar neuronal model, the FitzHugh-Nagumo neuronal model and the discrete Rulkov neuronal model.

The classical Morris-Lecar neuronal model [4] describes the oscillatory voltage patterns of Barnacle muscle fibers. Mathematically, the fractional-order Morris-Lecar model is described by the following system of differential equations with two fractional orders $q_1, q_2 \in (0, 1)$:

$$\begin{cases} C_m(q) \cdot {}^cD^{q_1} V(t) = & g_{Ca} M_\infty(V)(V_{Ca} - V) + g_K N(V_K - V) + g_L(V_L - V) + I \\ {}^cD^{q_2} N(t) = & \overline{\lambda_N}^{q_2} \cdot \lambda(V)(N_\infty(V) - N) \end{cases} \tag{1}$$

where V is the membrane potential, N is the gating variable for K^+, C_m is the membrane capacitance, I represents the externally applied current, V_{Ca}, V_K and V_L denote the equilibrium potentials for Ca^{2+}, K^+ the leak current and g_{Ca}, g_K and g_L are positive constants representing the maximum conductances of the corresponding ionic currents, $\overline{\lambda_N}$ is the maximum rate constant for the K^+ channel opening, $C_m(q) = \frac{\tau^q}{R_m}$ is the membrane capacitance, R_m is the membrane resistance, τ is the time constant.

The FitzHugh-Nagumo neuronal model is a simplification of the well-known Hodgkin-Huxley model [3], which describes a biological neuron's spiking behavior. In this paper, we consider an extension of the classical FitzHugh-Nagumo model, by replacing the integer-order derivatives by fractional-order Caputo derivatives of orders $q_1, q_2 \in (0, 1)$:

$$\begin{cases} {}^cD^{q_1} v(t) = v - \dfrac{v^3}{3} - w + I \\ {}^cD^{q_2} w(t) = r(v + c - dw) \end{cases} \tag{2}$$

where v represents the membrane potential, w is a recovery variable and, I is an external excitation current.

As a discrete-time neuronal model, we analyze the following discrete-time fractional-order Rulkov-type model [6], describing the spiking behaviour of a biological neuron:

$$\begin{cases} {}^c\Delta^{q_1} x(n) = \dfrac{\alpha}{1 + x(n)^2} - x(n) + y(n) \\ {}^c\Delta^{q_2} y(n) = -\mu(x(n) - \sigma) \end{cases} \tag{3}$$

where x represents the membrane potential, y is a gating variable, with $0 < \mu \ll 1$, σ acts as an external current applied to the neuron , $\alpha > 0$ is a nonlinearity parameter and $q_1, q_2 \in (0, 1)$ are the fractional orders.

The occurrence of both continous and discrete Hopf bifurcations is also discussed. Numerical simulations are provided with the aim of exemplifying the theoretical results, revealing rich spiking behavior, in comparison with the classical integer-order neuronal models.

References

[1] O. Brandibur, E. Kaslik. Stability properties of a two-dimensional system involving one Caputo derivative and applications to the investigation of a fractional-order Morris–Lecar neuronal model, *Nonlinear Dynamics* 90 (4) pp. 2371–2386, 2017.

[2] O. Brandibur, E. Kaslik. Stability of two-component incommensurate fractional-order systems and applications to the investigation of a FitzHugh-Nagumo neuronal model, *Mathematical Methods in the Applied Sciences* 41 (17) pp. 7182-7194, 2018.

[3] A. Hodgkin, A. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve, *Journal of Physiology* 117 pp. 500–544, 1952.

[4] C. Morris, H. Lecar. Voltage oscillations in the barnacle giant muscle fiber, *Biophysical Journal* 35(1) pp. 193, 1981.

[5] D. Mozyrska, M. Wyrwas. Stability by linear approximation and the relation between the stability of difference and differential fractional systems, *Mathematical Methods in the Applied Sciences* 40(11) pp. 4080-4091, 2017.

[6] N. F. Rulkov. Regularization of Synchronized Chaotic Bursts, *Phys. Rev. Lett.* 86(1) pp. 183–186, 2001.

Fixed point attractors, chaos and sequences in networks with unsupervised Hebbian plasticity rules

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We recently found that differences between the statistics of neuronal responses to novel and familiar images in monkey inferior temporal cortex (ITC) are consistent with an unsupervised Hebbian plasticity rule operating on recurrent synaptic connectivity within ITC. This rule is characterized by a dependence on post-synaptic firing rate that is strongly non-linear, and biased towards depression, leading to a decrease in mean visual responses with familiarity. We studied the dynamics of initially random networks with such unsupervised rules. When the statistics of external stimuli to the network, and parameters of the learning rule are constrained to match the statistics of visual responses to novel and familiar stimuli, the network operates as a Hopfield-like attractor network, with fixed point attractors that are correlated with the external stimuli. When the coupling strength increases, fixed point attractors become unstable. 'Memory states' become chaotic, but in spite of the chaotic dynamics, the memory of the shown stimulus is maintained over time in sufficiently large networks. Finally, I will present a temporally asymmetric version of the rule, which is able to learn and retrieve sequences of network activity.

Mathematical Modelling of Low Grade Glioma Diffusion

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Gliomas are the most common type of primary brain tumors. Low-grade gliomas (LGGs) are aggressive and infiltrative with generally slow progression over time, however after a certain threshold LGGs become more malignant and turn into high-grade gliomas [1], [2]. It is therefore important to study the potential growth and diffusion of LGGs.
Over the years various mathematical models of cancer growth have been developed [3], [4] illustrating the progress made in understanding the dynamics of tumors cells invasions. Here we develop a stochastic approach to simulate low-grade glioma growth and malignant cells invasion of the surrounding normal tissue.

References

[1] Magdalena U. Bogdanska1, Marek Bodna, Monika J. Piotrowska, Michael Murek, Philippe Schucht, Juurgen Beck, Alicia Martinez Gonzalez, Victor M. Perez Garcia. A mathematical model describes the malignant transformation of low grade gliomas: Prognostic implications, *Plos*, August 1, 2017.

[2] Kristin R. Swansona, Carly Bridgea , J.D. Murray, Ellsworth C. Alvord Jr. Virtual and real brain tumors: using mathematical modeling to quantify glioma growth and invasion, *Journal of the Neurological Sciences*, 216 (2003) 1-10.

[3] Hana L.P. Harpold, BS, Ellsworth C. Alvord, Jr., MD, and Kristin R. Swanson. The Evolution of Mathematical Modeling of Glioma Proliferation and Invasion, *American Association of Neuropathologist*, 2007.

[4] Rick Durrett. Cancer Modeling: A Personal Perspective, March 2013.

Stochastic Approach To The Modeling of Sweet Taste Signaling

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Human taste system is responsible for sensing and responding to five qualities: bitter, salty, sour, sweet and umami. The first process of tasting starts at the level of the taste receptors cells (TRCs). Those cells are assembled on the tongue, in the taste buds. Researchers have identified four subtypes of the TRCs. The Type I is the glial-like cells, those cells detect salty taste. Type II, the G-protein coupled receptors (GPCRs), detect the sweet, umami, and bitter tastes. Type III, or the presynaptic cells, they sense the sour stimuli. And, the last type is the progenitor taste cells. In this work, we focus on the sweet taste receptors, specifically sweet taste signaling pathways. We describe how the information is conveyed from the sweet taste receptors to higher neural centers, using a stochastic model approach.

References

[1] Allen A.Lee, Chung Owyang Sugars, Sweet Taste Receptors, and Brain Responses, *Nutrients* 9 (7) pp. 653, 2017.

[2] Dale Purves , George J. Augustine, David Fitzpatrick , William C. Hall, et al. *Neuroscience,* Dale Purves , 2011.

A neural circuit model for learning a beat

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When listening to music, we typically lock onto and move to a beat. Behavioral studies on such sensorimotor synchronization abound [1], yet the neural mechanisms remain poorly understood. Time processing has been widely studied in the context of decision making, language, memory and perception [2]. Beat perception presents a special case of timing processing, relying on fast perception and learning of repetitive time intervals from 100 to 2000 ms. Some models of beat perception hypothesize that the brain contains an array of self-sustaining entrainable oscillators, which resonate when forced with periodic stimuli, i.e. musical rhythms [3]. In contrast, our approach, in the simplest case, assumes a single beat generator neuron (BG) which can adapt its frequency and phase to match that of an external rhythm. This represents a neuronal realization of Mates' dual-process algorithm, for learning the period and phase [4]. In our formulation, the BG is a conductance-based neuron, with ionic currents such as I_{NaP}, I_{CaT} and I_h. The model includes the novel use of naturally occurring gamma frequency oscillations to estimate time intervals. Based on these estimates, a biophysical parameter of the BG is iteratively adjusted to alter the BG's period and firing times. Analysis of the model demonstrates that accurate rhythmic time keeping can be achieved over a range of frequencies relevant to music, in a manner that is robust to changes in parameters and to the presence of noise. Additonally, the model makes generalizable predictions about the existence of asymmetries in the synchronization process, as well as specific predictions about resynchronization times after changes in stimulus tempo or phase. We then extend this BG-based, learning framework to develop network models for complex rhythms of interleaved combinations of loud and soft tones.

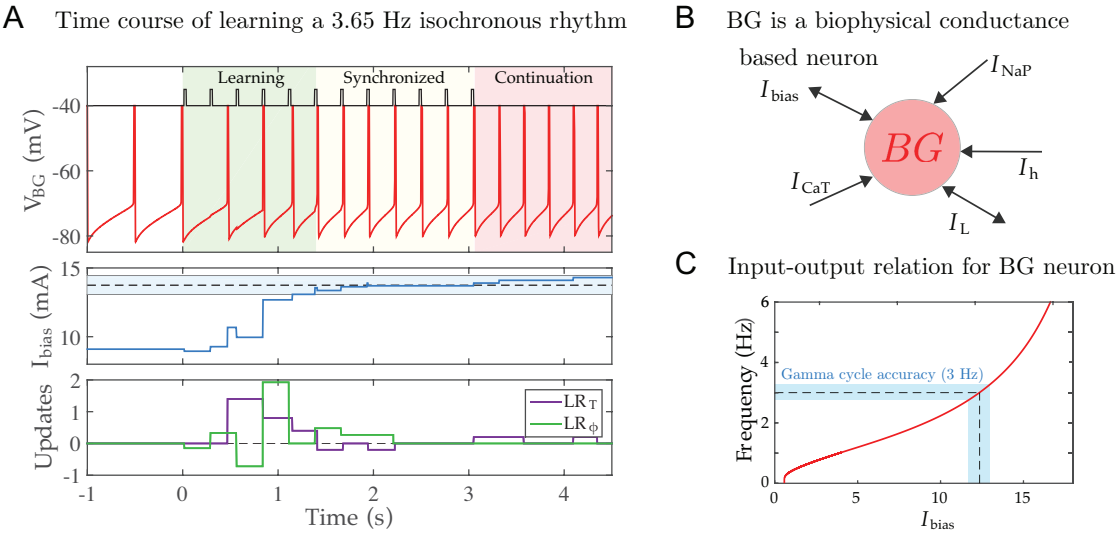

Figure 1: Model behavior and description

References

[1] Repp BH. Sensorimotor synchronisation; a review of the tapping literature. Psychonomic Bulletin & Review. 2005;12(6):969-992.

[2] Merchant H, Harrington DL, Meck WH. Neural basis of the perception and estimation of time. Annual Review of Neuroscience. 2013;36(1):313-336.

[3] Large EW, Almonte FV, Velasco MJ. A canonical model for gradient frequency neural networks. Physica D. 2010;239(12):905-911.

[4] Mates J. A model of synchronization of motor acts to a stimulus response. I. Timing and error corrections. Biological Cybernetics. 1994;70(5):463-473.

Slow coordinated fluctuations in neural activity in a balanced cortical network

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Asynchronous activity is a hallmark of cortical networks, and is characterized by a low degree of pairwise correlation across cells [1]. Theoretical models have successfully captured this form of activity by balancing excitatory and inhibitory synaptic inputs [2-4]. These models, however, do not capture the slow fluctuations in firing rate observed on a timescale of seconds in both spontaneous and evoked cortical activity [5]. In cortical areas including V1, population fluctuations are coordinated across neurons. These fluctuations are observed across brain states, cortical regions, and layers, and are present even in recordings with near zero pairwise correlations. Further, these global coordinated fluctuations are suggested to play a central role in neural coding of visual input by modulating the tuning curve of individual neurons embedded in local networks [6].

Here, we describe a theoretical framework that captures slow coordinated fluctuations in population activity by relying on two key mechanisms, namely short-term synaptic plasticity and a lognormal distribution of excitatory synaptic weights. Simulations of large-scale networks of leaky integrate-and-fire neurons that incorporate these mechanisms were able to reproduce several aspects of slow global fluctuations in population activity observed in primary visual cortex, including (i) a lognormal distribution of firing rates, (ii) a mean spike-count Fano factor that is greater than one and increases across time windows of increasing duration, and (iii) an eigenspectrum of the spike-count covariance matrix that is largely dominated by a single eigenmode. A dynamical systems analysis shows that lognormal synaptic connectivity allows the network to explore an unstable regime where fluctuations in population activity are driven by a small proportion of the strongest synapses. Taken together, results show that two biologically-motivated alterations to the standard framework of balanced networks, namely short-term plasticity and a lognormal distribution of excitatory synapses, provide the basis for a computational framework that captures the key statistics of population activity observed in cortical circuits. Further, this framework suggests an intra-cortical origin of slow fluctuations consistent with experimental recordings of isolated cortical circuits.

References

[1] M.R. Cohen, A. Kohn. Measuring and interpreting neuronal correlations, *Nature Neuroscience* 14 (7) pp. 811-819, 2011.

[2] C. van Vreeswijk, H. Sompolinsky. Chaos in neuronal networks with balanced excitatory and inhibitory activity, *Science* 274 (5293) pp. 1724-1726, 1996.

[3] A. Renart, J. de la Rocha, P. Bartho, L. Hollender, N. Parga, A. Reyes, K.D. Harris. The asynchronous state in cortical circuits, *Science* 327 (5965) pp. 587-590, 2010.

[4] A. Litwin-Kumar, B. Doiron. Slow dynamics and high variability in balanced cortical networks with clustered connections, *Nature Neuroscience* 15 (11) pp. 1498-1505, 2012.

[5] A.S. Ecker, P. Berens, R.J. Cotton, M. Subramaniyan, G.H. Denfield, C.R. Cadwell, S.M. Smirnakis, M. Bethge, A.S. Tolias. State dependence of noise correlations in macaque primary visual cortex, *Neuron* 82 (1) pp. 235-248, 2014.

[6] I. Arandia-Romero, S. Tanabe, J., Drugowitsch, A., Kohn, R., Moreno-Bote. Multiplicative and additive modulation of neuronal tuning with population activity affects encoded information, *Neuron* 89 (6) pp. 1305-1316, 2016.

Bifurcation analysis of a photoreceptor interaction model for Retinitis Pigmentosa

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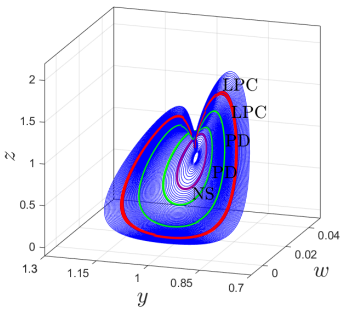
Retinitis Pigmentosa (RP) is an inherited disease affecting both the rod photoreceptors and cone photoreceptors in the retina. Particularly puzzling to researchers is that all manifestations of RP are caused by mutations in the rods, which cause them to die first, yet cone death always follows. The cones are necessary for daylight vision and acuity while the rods are responsible for night vision. Thus it is crucial to find a way to stop the demise of the cones. Unfortunately, patients typically come to the doctor and are diagnosed with RP once their daylight vision is beginning to be lost, which is often far into the disease progression. While numerous therapies exist that can slow the progression of RP, there is no cure for it.

We present a mathematical model of photoreceptor interactions, trophic and renewal processes, that aims to predict how a patient suffering from RP can go from a state in which all the photoreceptors are alive to one of complete blindness. The mathematical analysis focuses on the stability of the equilibrium solutions and limit cycles of the model and on tracking emergence of different regimes of stability in the empirical parameter space. The model predictions of various mathematical pathways to blindness is consistent with numerous different disease progressions experimentally observed in RP patients as well as the various animal models of the disease.

More specifically, a first analysis of the model examined stability of equilibrium solutions and saw the progression of the disease represented mathematically as a series of transcritical bifurcations leading to blindness as certain key parameters changed [2, 3]. Our more recent analysis focuses on identifying Hopf bifurcations, the emergence of stable limit cycles and the co-existence of multiple stable modes [4]. Our numerical results identified the existence of alternate stable solutions that are present for lower nutrient levels corresponding to the patient being closer to blindness. Stable limit cycles can be interpreted physiologically periodic variations in the levels of outer segment discs, due to their rhythmic shedding and renewal. Hence locating stable limit cycles, or other non-equilibrium stable attractors, could give insights into potential mechanisms to slow or stop the disease. Furthermore, existence of regimes of equilibrium/cycle bistability suggests that identifying RP in its early stages could avoid permanent blindness.



We discuss the need to focus on additional parameter ranges in which the life of the photoreceptors may be prolonged. Current experimental research is focusing on ways to increase the supply of glucose and nutrient uptake into the cell. Our work supports the importance of nutrients in preventing the disease from progressing, and may suggest other areas of parameter space that could be explored empirically. This line of research is also crucial in the developing field of designing retinal implants (in which photoreceptors are transplanted into an RP retina) since it can provide sets of initial conditions that would sustain one or more types of photoreceptors, even after blindness had occurred.

References

[1] A. Rădulescu, A. Pignatelli. Real and complex behavior for networks of coupled logistic maps, *Nonlinear Dynamics*, 87(2) 12951313, 2017.

[2] E.T. Camacho, M.A. Colón Vélez, D.J. Hernández, U. Rodríguez Bernier, J. van Laarhoven, S. Wirkus. A mathematical model for photoreceptor interactions. *Journal of Theoretical Biology*, 21: 638-646, 2010.

[3] E.T. Camacho, S. Wirkus. Tracing the progression of Retinitis Pigmentosa via photoreceptor interactions. *Journal of Theoretical Biology*, 317C:105-118, 2013.

[4] E.T. Camacho, A. Rădulescu, S. Wirkus. Bifurcation analysis of a photoreceptor interaction model for Retinitis Pigmentosa. *Communications in Nonlinear Science and Numerical Simulation*, 38: 267-276, 2016.

Application of the Mathematical Model for Autocrine Regulation with Diffusive Signalling Agent to GnRH Neurons Synchronization

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Gonadotropin-releasing hormone (GnRH) is synthesized and released from the GnRH neurons located in hypothalamus. The rhythmical pulses of GnRH are necessary for the correct reproductive function in mammals.

Based on experimental data, the autocrine regulation mechanism of the GnRH oscillations is widely accepted [1]. According to this mechanism, GnRH acts both as a regulator of the intracellular oscillations in a single GnRH neuron and as a signalling molecule that synchronizes the oscillation of the GnRH neurons spread out in hypothalamus. The mathematical model for such synchronization was based on the assumption of the well-stirred extracellular space with the averaged concentration of the signalling particles [2].

Recently, the mathematical model for the autocrine mechanism and synchronized release of GnRH has been introduced with the included diffusion and degradation processes for the signalling chemical in the extracellular space [3]. This model was developed with the Selkov cell kinetics for identical cells.

In our research, we study synchronization via diffusion using the model of a GnRH neuron developed by Khadra and Li [2] on the basis of experimental data and contemporary understanding of GnRH neuron regulation mechanisms. We show, both analytically and numerically, that the synchronized steady state is stable in the wide range of experimentally measured set of corresponding parameters. Moreover, even the nonhomogeneous population of GnRH neurons is able to synchronize their GnRH pulsation via diffusion.

The correlation with the experimental data proves the diffusive distribution of the signalling molecule concentration to be one more resource for the intercellular synchronization of the neuron oscillation.

References

[1] L. Krsmanovic et al. The hypothalamic GnRH pulse generator: multiple regulatory mechanisms, *Trends in Endocrinology and Metabolism* 20 (8) pp. 402-408, 2009.

[2] A. Khadra, Y.-X. Li. A model for the pulsatile secretion of gonadotripin-realising hormone from synchronized hypothalamic neurons, *Biophysical J.* 91 pp. 74-83, 2006.

[3] J. Gou et al. A theory of synchrony by coupling through a diffusive chemical signal, *Physica D* 339 pp. 1-17, 2017.

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The two compartment leaky integrate-and-fire neuronal model related to a one compartment integrate-and-fire model and the Gamma renewal process

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In [2] Lansky ad Rodriguez introduced and investigated a two-compartment leaky integrate and fire (LIF) neuronal model for the description of the neural activity. This model is composed of two interconnected parts: a dendrite and a trigger zone, with a white noise input in the dendritic compartment.

An alternate model describes the Inter spike Intervals (ISI) distribution as an Inverse Gaussian random variable. This distribution catches the heavy tail feature observed in some data. The pioneering work by Gerstein and Mandelbrot [1] motivated the use of Inverse Gaussian distribution introducing a one compartment Integrate and Fire model. The Inverse Gaussian is the First Passage Time distribution of Brownian Motion through a constant boundary. Hence, a natural model to obtain such distribution describes the membrane potential of the neuron as a one dimensional Wiener process. However, the same ISI distribution may arise also from different models.

A third model is of statistical nature and describes other types of data characterized by Gamma distribution. This last model does not pretend to relate membrane potential evolution and ISIs distribution. It simply considers a renewal process in which data follow the Gamma distribution [4].

Similarly to [3] here we relate these three models. The question investigated is the possibility of getting an Inverse Gaussian or a Gamma distributed output from a two compartment LIF model in the presence of coherent choices of the parameters. For this aim we introduce the inverse First Passage Time problem for multivariate Gauss-Markov processes and we investigate the boundary shape corresponding to Inverse Gaussian and Gamma FPT distributions for suitable choices of the parameters.

References

[1] G.L. Gerstein and B. Mandelbrot. Random walk models for the spike activity of a single neuron. *Biophys. J.* 4: 41–68, 1964.

[2] P. Lansky and R. Rodriguez. Two-compartment stochastic model of a neuron. *Physica D* 132: 267-286, 1999.

[3] P. Lansky, L. Sacerdote and C. Zucca. The Gamma renewal process as an output of the diffusion leaky integrate-and-fire neuronal model. *Biol. Cybern.*, 110 (2-3): 193–200,2016.

[4] N. Yannaros. On Cox processes and Gamma-renewal processes. *J. Appl. Probab.* 25: 423-427, 1988

[5] C. Zucca and L. Sacerdote. On the inverse first-passage-time problem for a Wiener process. *Ann. Appl. Prob.* 19 (4): 1319-1346, 2009.

Understanding Sensory Induced Hallucinations: From Neural Fields to Amplitude Equations

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Explorations of visual hallucinations, such as in [1], show that annular rings with a background flicker can induce visual hallucinations in humans that take the form of radial fan shapes and vice versa. The well-known retino-cortical map tells us that the corresponding patterns of neural activity in the primary visual cortex for rings and arms in the retina are orthogonal stripe patterns. The implication is that cortical forcing by spatially periodic input can excite orthogonal modes of neural activity.

To understand this phenomena, we adapt the work of [2] that shows how spatial forcing of the planar Swift-Hohenberg PDE model along one spatial axis can lead to the excitation of a pattern in the perpendicular direction. We consider a nonlocal neural field equation with a spatial forcing term,

$$\frac{\partial u(\mathbf{r},t)}{\partial t} = -u(\mathbf{r},t) + \int_{\mathbb{R}} w(|\mathbf{r}-\mathbf{r}'|) f(u(\mathbf{r}',t))\, \mathrm{d}\mathbf{r}' + \gamma u(\mathbf{r},t)\cos(k_f x), \quad \mathbf{r}=(x,y), \tag{1}$$

where $u(\mathbf{r},t)$ is the activity across the tissue, $w(|\mathbf{r}|)$ is the anatomical connectivity and $f(u)$ is the firing rate function. Beyond a Turing instability, solutions can be developed using a multiple-scale analysis [2]:

$$u(x,y,\chi,\Upsilon,\tau) \simeq \epsilon \left[A(\chi,\Upsilon,\tau)\mathrm{e}^{i(k_x x + k_y y)} + B(\chi,\Upsilon,\tau)\mathrm{e}^{i(k_x x - k_y y)} \right] + c.c., \tag{2}$$

where $\chi = \epsilon x$, $\Upsilon = \epsilon y$ and $\tau = \epsilon^2 t$.

The relevant amplitude equations for understanding pattern formation are found to be,

$$\beta_c \frac{\partial A}{\partial t} = \epsilon^2 \delta A - \Phi |A|^2 A - 2\Omega |B|^2 A + \frac{\gamma}{2}\beta_c B^*, \tag{3}$$

with a similar equation for the evolution of B. Here β_c is the bifurcation condition $\beta_c = 1/\widehat{w}(k_0)$, β_2 and β_3 are determined by the expansion of the firing rate, $\widehat{w}$ is the Fourier Transform of w, δ is the distance from the bifurcation point and ϵ is a small parameter. Also, the detuning parameter is $\nu = k_0 - k_f/2$, with k_0 the wavenumber of a Turing pattern that would be excited in the absence of forcing, k_f the forcing wavenumber and $\Phi = -3\beta_3 - 2\beta_2^2\left[\widehat{w}(2k_0)/(1-\beta_c\widehat{w}(2k_0)) + \Omega\right]$, $\Omega = 2\beta_2^2\widehat{w}(0)/(1-\beta_c\widehat{w}(0))$.

In turn we use these to uncover the parameter regimes which favour the excitation of patterns orthogonal to sensory drive, and thus shed light on the original psycho-physical observations in [1].

References

[1] V. A. Billock, B. H. Tsou. Neural interactions between flicker-induced self-organized visual hallucinations and physical stimuli, *Proceedings of the National Academy of Sciences* 104(20) 84908495, 2007.

[2] R. Manor, A. Hagberg, E. Meron. Wavenumber locking and pattern formation in spatially forced systems, *New Journal of Physics,* 11(6):63016, 2009.

Steady-states analysis of a mean-field model of interacting neurons

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We study a model of interacting neurons introduced by [De Masi et al., 2015]. We prove the existence and uniqueness of solutions of the associated mean-field equation and analyze its steady states. Depending on the value of the parameters, the long time behavior of this mean-field equation may be very rich. There can be one, two or three non-trivial invariant measures. Invariant measures may be unstable, leading in some cases to spontaneous oscillations.

We develop specific mathematical tools to better understand the long time behavior of this equation. Our findings include: 1. a robust proof that, for a small enough interaction parameter, the solution converges to the unique (in this case) invariant measure. 2. given any invariant measure, we propose a criteria to check its **local stability**. 3. the emergence of **spontaneous oscillations** in a fully excitatory network.

It is possible to extend these methods to study a network of neurons with excitatory and inhibitory connections.

We consider IF (integrate and fire) models: each neuron is characterized by its membrane potential and emits spikes. The system consists of N neurons all connected to the others. Between spikes, the dynamics of a neuron is deterministic; the potential of a neuron i solves a simple 1D-ODE:

$$dX_t^i = b(X_t^i)dt.$$

The spikes of the neurons are stochastic and occur at a rate which depends on their potentials: a neuron of potential x at time t has a probability $f(x)dt$ to spike between t and $t+dt$. The spiking rate f is a positive function and a parameter of the model.

When a neuron spikes, its potential is instantaneously reset to a resting potential X_{rest} and the $N-1$ other neurons see their potential to be increased by a kick of size J/N, where $J \geq 0$. J/N is the synaptic weight between the neurons.

It has been proven that this finite system converges as the number of neurons $N \to \infty$ to the solution of a non-linear McKean-Vlasov SDE (see [De Masi et al., 2015] and [Fournier and Löcherbach, 2016]):

$$dX_t = [b(X_t) + J\,\mathbb{E}\,f(X_t)]dt. \tag{1}$$

Here X_t spikes randomly as a Poisson process of intensity $f(X_t)$. After the spike, X_t is reset to X_{rest}. Existence and uniqueness of a strong solution of (1) is established using a fixpoint argument. We are then interested in its long time behavior. Given f and b, we prove in [Cormier et al., 2018] that if the interaction parameter J is small enough ($0 \leq J \leq \bar{J}(f,b)$ for some constant $\bar{J}(f,b) > 0$), then (1) has an unique invariant measure which is globally stable. For stronger J the situation may be more delicate.

Consider for instance $X_{\text{rest}} = 0$, $b(x) = \mu - x$ and $f(x) = x^2$, where $\mu > 0$ is a parameter. If μ is small enough, then depending on the value of J, (1) has exactly 1, 2 or 3 invariant measures. In the later case, numerical simulations show that two of the three invariant measures are stable, the other is unstable (bi-stability).

Consider now $b(x) = 2 - 2x$, $f(x) = x^{10}$ and $J = 1$. Then there is an unique invariant measure, but it is not a stable one. In fact spontaneous oscillations appears in this situation (see Figure 1).

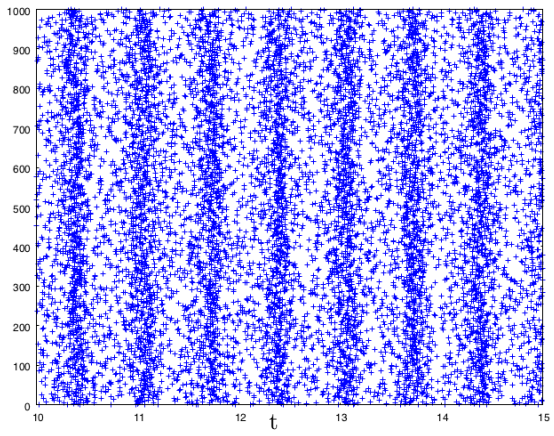

Figure 1: A raster plot in the case of spontaneous oscillations. Each cross corresponds to a spike of a neuron at a given time. Simulated with $N = 1000$.

Overall those examples motivate the following question: given b, f and an invariant measure of (1), at which condition this one is locally stable? To answer, we derive a criteria under which stability can be proven. This criteria is optimal in a certain sens and easy to check numerically.

References

[Cormier et al., 2018] Cormier, Q., Tanré, E., and Veltz, R. (2018). Long time behavior of a mean-field model of interacting neurons. *arXiv e-prints*, page arXiv:1810.08562.

[De Masi et al., 2015] De Masi, A., Galves, A., Löcherbach, E., and Presutti, E. (2015). Hydrodynamic Limit for Interacting Neurons. *Journal of Statistical Physics*, 158(4):866–902.

[Fournier and Löcherbach, 2016] Fournier, N. and Löcherbach, E. (2016). On a toy model of interacting neurons. *Annales de l'Institut Henri Poincaré, Probabilités et Statistiques*, 52(4):1844–1876.

Pattern formation in biological neural networks with rebound currents

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Waves and patterns in the brain are well known to subserve natural computation. In the case of spatial navigation the geometric firing fields of grid cells is a classic example. Grid cells fire at the nodes of a hexagonal lattice tiling the environment. As an animal approaches the centre of a grid cell firing field, their spiking output increases in frequency. Interestingly the spacing of the hexagonal lattice can range from centimetres to metres and is thought to underly the brain's internal positioning system. The mechanism for controlling this global spatial scale is linked to a local property of neurons within an inhibitory coupled population, namely rebound firing. This arises through the activation of hyperpolarisation-activated channels. For the case of grid cells in the medial enthorinal cortex this generates a so-called I_h current. Many other cells types also utilise rebound currents for firing, and in particular thalamo-cortical relay cells do so via slow T-type calcium channels (the I_T current). This can give rise to saltatory lurching waves in thalamic slices. Both of these examples show that rebound currents can contribute significantly to important spatio-temporal brain dynamics. Here we investigate such phenomenon from a mathematical perspective.

We begin by considering a rate based neural field model that incorporates a slow I_T current [1]. For a Heaviside firing rate a solitary lurching wave can be explicitly constructed. In comparison to solitary waves seen in excitable media it is found that the slower of the two branches of waves is stable. We then move on to treat a spike based (integrate-and-fire) neural field model that incorporates a piecewise linear I_h current [2]. Using techniques from nonsmooth dynamical systems we show how to construct periodic travelling waves (in one spatial dimension), and in particular the dispersion curve that determines how wave speed varies as a function of period. This exhibits a wide range of long wavelength solutions, reinforcing the idea that rebound spiking is a candidate mechanism for generating grid cell firing patterns. Importantly we develop a wave stability analysis to show how the maximum allowed period is controlled by the dynamical properties of the I_h current, thus providing a mechanism for the local control of pattern wavelengths.

References

[1] S Coombes 2003 Dynamics of synaptically coupled integrate-and-fire-or-burst neurons, Physical Review E, Vol 67, 041910

[2] M Bonilla-Quintana, K C A Wedgwood, R D O'Dea and S Coombes 2017 An analysis of waves underlying grid cell firing in the medial enthorinal cortex, Journal of Mathematical Neuroscience, 7:9

Dynamically relevant motifs in inhibition-dominated networks

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Many networks in the nervous system possess an abundance of inhibition, which serves to shape and stabilize neural dynamics. The neurons in such networks exhibit intricate patterns of connectivity whose structure controls the allowed patterns of neural activity. In this work, we examine inhibitory threshold-linear networks whose dynamics are constrained by an underlying directed graph. We develop a set of parameter-independent graph rules that enable us to predict features of the dynamics, such as emergent sequences and dynamic attractors, from properties of the graph. These rules provide a direct link between the structure and function of these networks, and may provide new insights into how connectivity shapes dynamics in real neural circuits.

Mixed-mode oscillations and chaotic dynamics in a model of rivalry

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We aim to understand the neural dynamics and mechanisms underlying perceptual bistability. This phenomenon occurs in binocular rivalry, when the two eyes are presented with incompatible stimuli and perception alternates between these two stimuli. Binocular rivalry has been investigated in two types of experiments: 1) Traditional experiments where the stimulus is fixed, 2) Eye-swap experiments in which stimulus periodically swaps between eyes many times in a second [1]. In spite of the rapid swapping between eyes perception can be stable for many seconds with specific stimulus parameter configurations. Wilson introduced a two-stage, hierarchical model to explain both types of experiment [2]. The first stage represents monocular neurons in primary visual cortex, and the second stage represents binocular neurons in higher cortical areas. Wilson's model and other competition models have been only studied with bifurcation analysis for fixed inputs and different dynamical behaviour that can occur with periodically forcing inputs have not been investigated. To fully explain this eye-swap experiments, we need to understand the bifurcations that distinguish different states: perception following the stimulus swaps and perception being stable for many seconds. To this end we report 1) a more complete description of the complex dynamics in the unforced Wilson model (Fig 1), 2) a bifurcation analysis with periodic forcing (in text).

Previously, bifurcation analysis of the Wilson model with fixed inputs has revealed three main types of dynamical behaviour: Winner-take-all (WTA), Relaxation oscillations (RIV), Simultaneous activity (SIM) (Fig 1A). Here, a more complete analysis has revealed mixed mode oscillations (MMO) emerging from high amplitude RIV oscillations (Fig 1B & E) and a cascade of period-doubling (PD) bifurcations emerging from low amplitude WTA (LAWTA) oscillations (Fig 1C & E). The bifurcation structure here appears similar to the canard induced MMO identified in a spiking neuron model [3], and they occur through a series of discrete branches. The discontinues transitions from one branch segment to the next one are similar to spike adding mechanism from [4]. The number of low amplitude oscillations and period both increase as we move down in the bifurcation parameter (Fig 1D).

We have also built a framework for studying competition models with periodic inputs using numerical continuation. Bifurcation analysis of periodic orbits shows that periodic forcing with high frequency (e.g. 18 Hz, known as flicker) modulates the three main types of behaviour that occur with fixed inputs with forcing frequency. However, dynamical behaviour will be different with low frequency periodic forcing (around 1.5 Hz, so called switch), and in addition to modulated-WTA and modulated-SIM, a cycle skipping behaviour occurs through a PD bifurcation from modulated-SIM behaviour. Another interesting behaviour in the forced case is the existence of chaotic behaviour through a cascade of PD bifurcations from modulated-WTA behaviour. An interesting avenue of investigation will be to understand how the low-amplitude PD cascade in the unforced case (Fig 1A) interacts with the forcing.

Whilst MMOs have been reported in a simpler rivalry model [5], the appearance of a PD cascade has revealed richer dynamics in the Wilson model. This provides the context to fully understand the periodically forced case.

References

[1] Nikos K Logothetis, David A Leopold, and David L Sheinberg. What is rivalling during binocular rivalry? *Nature*, 380(6575):621, 1996.

[2] Hugh R Wilson. Computational evidence for a rivalry hierarchy in vision. *Proceedings of the National Academy of Sciences*, 100(24):14499–14503, 2003.

[3] Bard Ermentrout and Martin Wechselberger. Canards, clusters, and synchronization in a weakly coupled interneuron model. *SIAM Journal on Applied Dynamical Systems*, 8(1):253–278, 2009.

[4] Jakub Nowacki, Hinke M Osinga, and Krasimira Tsaneva-Atanasova. Dynamical systems analysis of spike-adding mechanisms in transient bursts. *The Journal of Mathematical Neuroscience*, 2(1):7, 2012.

[5] Rodica Curtu. Singular hopf bifurcations and mixed-mode oscillations in a two-cell inhibitory neural network. *Physica D: Nonlinear Phenomena*, 239(9):504–514, 2010.

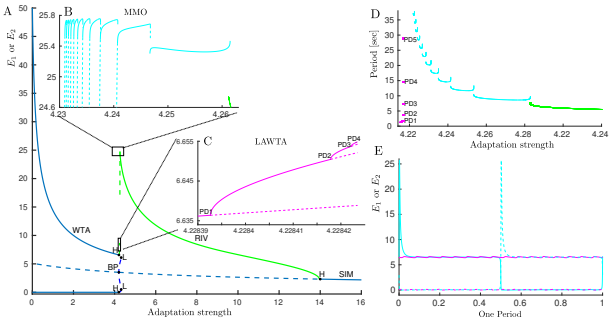

Figure 1: **A** & **B** & **C:** Bifurcation Diagram of Wilson model [2] with fixed inputs varying the adaptation strength. Five regions of dynamical behaviour are presented: 1) WTA fixed points, 2) LAWTA oscillations (magenta), 3) MMO (cyan), 4) Relaxation oscillations (RIV), 5) SIM fixed points. **D:** Periods of oscillations for three types of oscillatory dynamics. The period of oscillations increase sharply as we move toward a critical parameter value 4.22843. **E:** One period of MMO (cyan) and LAWTA oscillatory activity (magenta) for two neural populations (solid and dashed lines correspondingly). Here MMO solution has 16 low amplitude oscillations and LAWTA has 8 different low peaks.

Firing properties of a resonate-and-fire neural model with periodic forcing and noise

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The knowledge of the basic processes driving the response of a single neuron to stimulations plays a key role for the understanding of the information coding in neural populations [1, 2]. To this aim, the study of the dynamical behavior of neuron models, subject to periodic inputs, is a key ingredient to advance our knowledge on these phenomena. However, a strong limitation to make significant progresses comes from the intrinsic nonlinearity and complexity of the involved processes and corresponding mathematical models. Therefore, to counteract these difficulties a strategic and efficient approach is that of employing simplified, but still realistic, neuron models such as the class of integrate-and-fire models [3, 4, 5, 6, 7]. In particular, we studied the dynamics of a resonate-and-fire neural model in the presence of periodic driving and noise. The model was introduced in [8], by linearization of the well-known FitzHugh-Nagumo neural model, and it is a two dimensional nonsmooth dynamical systems with a threshold crossing firing mechanisms. Moreover, the parameters were chosen is such way that the stationary state of the FitzHugh-Nagumo was stable. We investigated the properties of the corresponding firing map by using the theoretical tools employed to study circle maps dynamics [9, 10]. We studied the effects of the harmonic forcing on the firing discharges generated by this model and, in particular, on its phase-locking patterns, either in the presence or absence of noise.

References

[1] W. Singer. Neuronal oscillations: unavoidable and useful?, *European Journal of Neuroscience* doi:10.1111/ejn.13796, 2018.

[2] E. Kheradpezhouh, M. Adibi, E. Arabzadeh. Response dynamics of rat barrel cortex neurons to repeated sensory stimulation, *Scientific Reports* 7 Article number: 11445, 2017.

[3] J.P. Keener, F.C. Hoppensteadt, J. Rinzel. Integrate-and-fire models of merve membrane mesponse to oscillatory input, *SIAM J. Appl. Math.* 41 pp. 503-517,1981.

[4] J. Laudanski, S. Coombes, A. R. Palmer, C. J. Sumner. Mode-Locked Spike Trains in Responses of Ventral Cochlear Nucleus Chopper and Onset Neurons to Periodic Stimuli, *Journal of Neurophysiology* 103 pp. 1226-1237, 2010.

[5] J.R. Engelbrecht, K. Loncich, R. Mirollo, M.E. Hasselmo, M. Yoshida. Rhythm-induced spike-timing patterns characterized by 1D firing maps, *J. Comp. Neurosci.* 34 pp. 59-71, 2013.

[6] W. Marzantowicz, J. Signerska. On the interspike-intervals of periodically-driven integrate-and-fire models, *J. Math. Anal. Appl.* 423 pp. 456-479, 2015.

[7] R. Brette. Dynamics of one-dimensional spiking neuron models., *J. Math. Biol.* 48 pp. 38-56, 2004.

[8] A. Di Garbo, M. Barbi, S. Chillemi. Dynamical behavior of the linearized version of the FitzHugh-Nagumo neural model, *Int. J. Bifurcation Chaos* 11) pp. 2549-2558, 2001.

[9] A. Lasota, M.C. Mackey. *Chaos, Fractals, and Noise* Springer, 1994.

[10] S. Wiggins *Introduction to Applied Nonlinear Dynamical Systems and Chaos* Springer, 2003

On diffusion neuronal models with multiplicative noise

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Nonlinear dynamical systems are often affected by different sources of noise and the usual belief is that the presence of noise can hinder or deteriorate the signal transmission in the system. However it has been observed, both in theoretical models and experiments, that random fluctuations can sometimes improve information processing. Mathematical models in neuroscience are one of the most prominent examples of phenomena for which the noise is of primary importance or even a part of the signal itself rather than a source of inefficiency and unpredictability (see for instance [4]).

Our aim is to contribute to the discussion on the role of noise, studying the effects of a multiplicative noise on the performance of a single neuron models using the analytical approach.

While there is an ongoing effort to incorporate detailed biological properties into realistic models, on the other hand, a compromise is usually made and the richness of details is sacrificed for computational or even analytical accessibility [5]. The leaky integrate-and-fire neuronal models with multiplicative noise go in this direction. These models incorporate the presence of postsynaptic reversal potentials and the state-dependency of the changes in the membrane depolarization preserving a relatively easy mathematical formulation.

We consider models where the evolution of the neuronal membrane depolarization between two consecutive spikes is described by a Feller process, an Inhomogeneous Geometric Brownian Motion or a Jacobi process [1]-[3]. We analyze the spiking activity of the neuron under study through the firing rate and the variability of the output and we describe the occurrence of a phenomenon of coherence resonance. In particular we present counterintuitive effects due to the presence of the multiplicative noise and its dependence on the input parameters.

References

[1] G.D'Onofrio, P.Lansky and E.Pirozzi, On two diffusion neuronal models with multiplicative noise: The mean first-passage time properties, *Chaos* 28(4) 043103, 2018.

[2] G. D'Onofrio, M. Tamborrino and P. Lansky, The Jacobi diffusion process as a neuronal model, *Chaos* 28(10) 103119, 2018.

[3] G. D'Onofrio, P. Lansky and M. Tamborrino, Inhibition enhances the coherence in the Jacobi neuronal model, *submitted*.

[4] M. D. McDonnell, L. M. Ward, The benefits of noise in neural systems: bridging theory and experiment, *Nature Reviews Neuroscience* 12 (10) 415–426, 2011.

[5] H. Tuckwell, *Introduction to Theoretical Neurobiology: Volume 2,* Nonlinear and Stochastic Theories (Cambridge University Press), 2005.

Percolation on dynamical random graphs provides a model for defining synaptic connections

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We study the development of connectivity in networks that are growing. The aim is to develop a mathematical model for a mechanism establishing synaptic connections in a network of *potential* connections which reflect solely the geometry of the network, more precisely the proximity between neuronal dendrites and axons [2].

We consider a collection of independent 2-dimensional branching random walks as a model for the morphological growth of dendritic and axonal arbors [1]. The initial states of these walks correspond to the spatial locations of neuronal somas. The parameters in this model are in a good agreement with other models of how neuronal growth builds networks of connections between the neurons [4].

We analyse first the probabilities of potential connections derived from the stochastic geometry of the original graph. This allows us to estimate the spatial distribution of the arborization of the dendritic trees. Then we define different algorithms of diluting the initial graph, and study the resulting subgraph. We show that even a random independent dilution of potential connections, which preserves the property that the probabilities of connections are proportional to the dendritic mass distribution, may lead to a subgraph whose properties such as the degree sequence and the largest connected component differ significantly from the characteristics of the original graph.

We consider also an inhomogeneous dilution of the connections in a population of neurons of different types. Such a dilution is considered to be biologically justified [3], and leads to a subgraph whose probabilities are less sensitive to the dendritic mass distribution in space.

Our approach utilises essentially the spatial graph of the potential connections. We show that using different pruning rules can lead to a variety of biologically relevant structures.

References

[1] Ajazi, F., Napolitano, G.M., Turova, T., Zaurbek I. Structure of randomly grown 2-d network, *Biosystems* 136, 105-112, 2015.

[2] Peters, A., and Feldman, M.L. The projection of the lateral geniculate nucleus to area 17 of the rat cerebral cortex. I. General description *J. of Neurocytology*, 5/1, 63-84, 1976.

[3] Rees, C.L., Moradi, K., and Ascoli, G.A. Weighing the Evidence in Peters' Rule: Does Neuronal Morphology Predict Connectivity? *Trends Neurosci.*, 40(2):63-71, 2017.

[4] van Pelt, J., and Uylings, H.B.M. Branching rates and growth functions in the outgrowth of dendritic branching patterns. *Network: Comput. Neural Syst.*, 13, 261-281, 2002.

Asymptotic behaviour of a network of neurons with random linear interactions

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We study the asymptotic behaviour for asymmetric neuronal dynamics in a network of linear Hopfield neurons [4, 5, 6]. The randomness in the network is modelled by random couplings which are centered *i.i.d.* random variables with finite moments of all orders. We consider a network of N neurons in interaction. Each neuron $i \in \{1, \cdots, N\}$ is characterized by its membrane potential $(V_t^{i,(N)})_t$ where $t \in \mathbb{R}_+$ represents the time. The membrane potential of neuron i is described by the stochastic differential equation

$$\begin{cases} \mathrm{d}V_t^{i,(N)} = -\lambda V_t^{i,(N)}\mathrm{d}t + \dfrac{1}{\sqrt{N}}\displaystyle\sum_{j=1}^{N} J_{i,j}^{(N)} V_t^{j,(N)}\mathrm{d}t + \gamma \mathrm{d}B_t^i \\ \mathcal{L}(V_0^{(N)}) = \nu_0^{\otimes N}, \end{cases}$$

The matrix $J^{(N)}$ is a square matrix of size N and contains the synaptic weights. The parameters λ and γ are real constants and $(B_t^i)_{t\geq 0}$ models the internal noise of the neuron i. The $(B_t^i)_t$, $i \in \{1, \cdots, N\}$ are N independent standard Brownian motions. We prove that if the initial condition of the network is a set of *i.i.d.* random variables with finite moments of all orders and independent of the synaptic weights, the thermodynamic limit of the system is described as the sum of the initial condition with a centered Gaussian process whose covariance function can be described in terms of a modified Bessel function. We also prove propagation of chaos results. We provide a rigorous proof of the results anounced in Sompolinsky et al. [7].

The originality of this neuronal system is in the scaling factor $1/\sqrt{N}$ used in the interaction term. Indeed, the very large majority of the studies for such systems used the scaling factor $1/N$, the mean field limit can be seen as a kind of Law of Large Numbers. Here, as the interactions are described by centered random variable, this setting corresponds to a balanced network where the synaptic inputs received by a neuron is in average equal to 0 and taking a $1/N$ scaling will give us a trivial mean-field limit. At this scale, the interactions will disappears in the macroscopic description. That is the reason why we place ourself in a context of Central Limit Theorem by taking a scaling in $1/\sqrt{N}$.

This problem is similar to the one considered by Ben Arous and Guionnet [2, 1, 3] in a context of spin glasses. The difference is that they applied large deviation techniques to study the thermodynamic limit of a network of spins interacting linearly. This approach contrains them to consider only *i.i.d.* centered Gaussian weights. Our method is essentially based on the Central Limit Theorem and the method of moments, this allows us to consider only *i.i.d.* centered synaptic weights without hypothesis on their precise distribution. We obtain propagation of chaos and convergence in law to a Gaussian process which is described almost surely with respect to the synaptic wieghts. This convergence is stronger than the one obtain by BenArous and Guionnet. This contribution is available on HAL.

References

[1] G. Ben-Arous and A. Guionnet. Large deviations for langevin spin glass dynamics. *Probability Theory and Related Fields*, 102(4):455–509, 1995.

[2] A. Guionnet. *Dynamique de Langevin d'un verre de spins*. PhD thesis, Université de Paris Sud, 1995.

[3] A. Guionnet. Averaged and quenched propagation of chaos for spin glass dynamics. *Probability Theory and Related Fields*, 109(2):183–215, 1997.

[4] J. J. Hopfield. Neural networks and physical systems with emergent collective computational abilities. *Proc. National Academy of Sciences, USA*, 79:2554–2558, 1982.

[5] J.J. Hopfield. Neurons with graded response have collective computational properties like those of two-state neurons. *Proceedings of the National Academy of Sciences, USA*, 81(10):3088–3092, 1984.

[6] J.J. Hopfield and D.W. Tank. Computing with neural circuits- a model. *Science*, 233(4764):625–633, 1986.

[7] H. Sompolinsky, A. Crisanti, and H.J Sommers. Chaos in Random Neural Networks. *Physical Review Letters*, 61(3):259–262, 1988.

The impact of mRNA localization on dendritic protein distribution and its dynamics

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Each location of the dendritic tree needs a sufficient amount of proteins to maintain synaptic plasticity. How neurons can meet this demand is currently poorly understood. Proteins are synthesized from their corresponding mRNAs in the soma or the dendrites while mRNA is produced exclusively in the soma. We developed a computational framework to understand how transport and turnover processes shape the distribution of mRNA and their corresponding proteins. In our model, which is represented by a system of linear one-dimensional drift-diffusion equations, protein expression is coupled to the availability of mRNA in the soma and the dendrites. First, we derived the spatial dendritic mRNA profile. Then we investigated how the somatic and the dendritic mRNA sources shaped the local amount of proteins and derived the dendritic protein profile. We further obtained time-dependent solutions and analyzed how long does it take for the newly synthesized mRNA and proteins to reach their steady-state levels.

To test our model, we have analyzed the high-resolution fluorescence data for CaMKIIα mRNA and protein in a cultured hippocampal neuron. CaMKIIα is an enzyme involved in a critical calcium signaling pathway that regulates synaptic transmission. From this data, we were able to determine diffusion and velocity coefficients that describe the molecular motion and found that these were in line with previous experimental reports. Finally, we compared the predictions of our model with a series of last experimental observations. For example, recent experiments (Akbalik et al., 2017) indicate that it can take up to 3-6 hours for newly transcribed mRNAs to reach a dendritic distance of 150 μm. This finding is consistent with the results we obtain using the time-dependent analytical solution of our model. Further, our model shows that the protein CamKIIα requires approximately 30 days to reach its equilibrium distribution. This result is in line with the timescales found in (Kaech and Banker, 2007) where neuronal dendritic arbors reach a plateau in their growth after 3-4 weeks.

Our work provides a novel biologically plausible and mathematically rigorous computational framework to understand coupled mRNA and protein dynamics. Although in this work we focused on CaMKIIα our model can be applied to other mRNA and proteins of interest.

References

G. Akbalik, K. Langebeck-Jensen, G. Tushev, S. Sambandan, J. Rinne, I. Epstein, I. Cajigas, I. Vlatkovic, and E. M. Schuman. Visualization of newly synthesized neuronal RNA in vitro and in vivo using click-chemistry. *RNA Biology*, 14(1):20–28, 2017.

S. Kaech and G. Banker. Culturing hippocampal neurons. *Nature Protocols*, 1:2406, Jan. 2007.

TMS-Induced Synchronisation in Human Brain Networks

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Transcranial Magnetic Stimulation (TMS) is a non-invasive method of provoking significant changes in mental states. While TMS has proven itself as a treatment for depression, schizophrenia and chronic pain, the neurological mechanisms behind the alleviation of these symptoms is poorly understood. TMS perturbs neurons by inducing a current along axons, facilitating excitatory activity and entraining neurons to synchrony. It is thought that this can fix disrupted functional connectivity that causes major depression, by activating the neural 'switch' that allows the brain to shift between two major brain subnetworks: the default mode and central executive networks [1].

Using a neural-mass model [2], we study the influence of TMS on networks of connected brain regions comprising millions of neurons. The model is particularly suited to studying TMS since simulated dynamics accommodate underlying neural population synchrony, yet within a course-grained framework appropriate for the modelling of macroscopic neural systems. Furthermore, connectivity is defined using human DTI data so that networks are neurologically relevant. In this way, the model comprises dynamics on a neuronal level as well as the much greater scale of whole-brain connectivity.

We reduce the model using the theory of weak coupling, so that the only state variable is the phase θ of each node, on some stable limit cycle of the system.

$$\dot{\theta}_i = \Omega + \epsilon \sum_j w_{ij} H(\theta_j - \theta_i), \text{ for node } i, \text{ with connected nodes } j \text{ and natural frequency } \Omega. \tag{1}$$

H is the phase-interaction function which determines the inter-population interactions, dependent on their phase differences. Treating $\sum_j w_{ij} H(\theta_j - \theta_i)$ as elements of a dynamic connectivity matrix, we can use existing theories to examine its eigenmodes to predict what functional connectivity patterns the model supports [3]. By adding delays in inter-mass interactions, we excite different eigenmodes to fit the model to a default mode network.

Changing the parameters of TMS delivery (frequency, amplitude, target region etc.), we explore how different methods of stimulation affect resultant functional networks and speculate which of these may relate to TMS 'fixing' an irregular connectivity. In particular, we use the metric of phase coherence to investigate how TMS can evoke new patterns of synchrony in the network model that relate to the switching between resting (default mode) and stimulated (central executive) network states, a proxy for the functional behaviour that would be expected in the brain of a healthy person. Graph theoretic methods of node centrality and clustering are employed to give a qualitative analysis of how the functional network has changed due to TMS.

References

[1] S. J. Iwabuchi, D. Peng, Y. Fang, K. Jiang, E. B. Liddle, P. F. Liddle and L. Palaniyappan. (2014). *Alterations in effective connectivity anchored on the insula in major depressive disorder*, European Neuropsychopharmacology 24 (11), 1784–1792.

[2] Coombes, S. and Byrne, Á., 2019. Next generation neural mass models. In Nonlinear Dynamics in Computational Neuroscience (pp. 1-16). Springer, Cham.

[3] Tewarie, P., Abeysuriya, R., Byrne, Á., O'Neill, G.C., Sotiropoulos, S.N., Brookes, M.J. and Coombes, S., 2019. How do spatially distinct frequency specific MEG networks emerge from one underlying structural connectome? The role of the structural eigenmodes. NeuroImage, 186, pp.211-220.

Spectral decomposition of refractory density equation for neural population dynamics

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In many areas of the brain neurons are organized in large groups with similar properties. For example in the columnar organization of the cortex all neurons of the same type and layer can be considered as a single population. It is therefore sensible to describe populations of neurons interacting by their population activity $A(t)$ rather than modeling the spike trains of every single neuron. Many attempts have been made to derive the temporal evolution of the population activity $A(t)$ from the properties of its individual neurons.

For neurons modeled by a time dependent renewal process, a common approach to obtain the population activity in response to an external stimulus is based on the temporal evolution of the refractory density [1], [2]. The refractory density equation is a partial differential equation and hence the dynamics is infinitely dimensional. Here, we aim at an efficient low-dimensional approximation for the dynamics of the population activity in form of ordinary differential equations.

Keeping only the two slowest modes, in an eigenfunction expansion of the refractory density equation, we derived a three-dimensional firing rate model. Rate-models are used for better analytical tractability, and involves a compromise between accuracy and simplicity. To explain some phenomenological properties, heuristic models were developed [3], whereas in our model the population activity $A(t)$ is derived from the properties of its individual neuron. In contrast to one dimensional firing-rate models, our model is able to reproduce firing-rate dynamics due to partial spike synchronization in a network.

The validity of the derived approximation is shown for a large homogeneous population of Poisson neurons with absolute refractoriness. However, the theoretical framework can be applied to any population of neurons modeled by a time dependent renewal process.

References

[1] W. Gerstner. Population dynamics of spiking neurons: Fast transients, asynchronous states, and locking. *Neural Comput.*, 12:43, 2000.

[2] T. Schwalger, M. Deger, and W. Gerstner. Towards a theory of cortical columns: From spiking neurons to interacting neural populations of finite size. *PLoS Comput. Biol.*, 13(4), 2017.

[3] H. R. Wilson and J. D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. *Biophys. J.*, 12(1):1, 1972.

The cluster duration distribution of Hawkes processes

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Hawkes processes are widely applied models of self-exciting and mutually exciting temporal point processes. They also have a long history in theoretical and mathematical neuroscience as stochastic models for the spiking activity in neural networks. We recently showed that growing networks of stochastically spiking neurons can self-organize into a nearly critical state [1]. In this state the network generates bursts of activity, also called neuronal avalanches, with power-law size and duration distributions. Avalanches in our model correspond to clusters of a self-exciting Hawkes point process [2] and we analytically derived their size and duration distributions. While it is relatively straightforward to obtain the cluster size distribution, e.g., [1, 2], the duration distribution generally requires solving a nonlinear integral equation [2, 3]. For Markovian Hawkes processes [4] we derived an ordinary differential equation whose solution directly determines the cluster duration distribution function [1]. This novel representation allowed us to establish the power-law tail of the duration distribution in the critical state.

Following a brief review of the results in [1] we here generalize our representation to a large class of self-exciting Hawkes processes. In a general self-exciting Hawkes process past points additively increase the instantaneous occurrence rate of future points in a time-varying manner described by a non-negative kernel function. For Markovian Hawkes processes this kernel is a decaying exponential function [4]. Here, we consider Hawkes processes with a matrix-exponential kernel, i.e., a kernel function given by the shape of the density of a matrix-exponential distribution [5]. Starting from the integral equation in [2, 3] we derive an analogue ordinary differential equation (system) whose solution determines the cluster duration distribution for the considered class of self-exciting Hawkes processes. Using this representation we investigate the effect of different kernel shapes on the duration distribution and assess the universality of its power-law tail in the critical regime. Furthermore, for experimental observations of neuronal avalanches, the duration distribution allows one to evaluate possible overlaps of clusters.

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[1] Kalle Kossio, F. Y., Goedeke, S., van den Akker, B., Ibarz, B., & Memmesheimer, R.-M. (2018). *Growing Critical: Self-Organized Criticality in a Developing Neural System.* Phys. Rev. Lett., 121(5), 058301.

[2] Hawkes, A. G., & Oakes, D. (1974). *A cluster process representation of a self-exciting process.* J. Appl. Probab., 11(3), 493–503.

[3] Møller, J., & Rasmussen, J. G. (2005). *Perfect simulation of Hawkes processes.* Adv. Appl. Probab., 37(3), 629–646.

[4] Oakes, D. (1975). *The Markovian self-exciting process.* J. Appl. Probab., 12(1), 69–77.

[5] Bladt, M., & Nielsen, B. F. (2017). *Matrix-Exponential Distributions in Applied Probability.* Springer US.

Stochastic neural field with smoothed noise

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We are interested in pattern formation by stochastic neural field equations, a class of space-time stochastic differential-integral equations using the Mexican Hat kernel. We explore, quantitatively, how the parameters that control the shape of the coupling kernel, coupling strength, and aspects of spatially-smoothed space-time noise, influence the pattern in the resulting evolving random field. We find that spatially-smoothed noise alone causes pattern formation even without direct spatial coupling. Our analysis of the interaction between coupling and noise smoothing allows us to determine parameter combinations that are optimal for the formation of spatial pattern.

The mathematics of self-organized neurobots

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Locomotion control is a primary task of the brain. Abstracting from the complexity of cortical dynamics it is hence important to classify basic neural controllers in terms of the mathematics of their respective working principles. We distinguish between top-down control, such as performed by central pattern generators (CPG), and embodied locomotion. For the latter a complex bifurcation diagram from fixpoint attractors to locomoting limit cycles can be observed within the sensorimotor loop as a function of the feedback strength.

Embodied controllers are well suited for a dynamical system analysis, as they dispose often of only a limited number of degrees of freedom. Typical are one or two neurons mapping the sensorial state of the actuator (propiosensation) to the motor command. The resulting feedback loop, the sensorimotor loop, is then closed by the physical forces the environment exerts on the body of the animal, or, respectively of the robot.

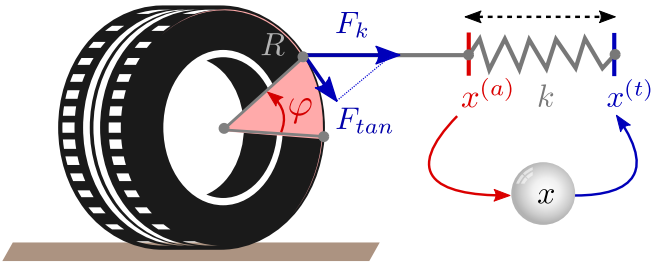

Fig. 1. Illustration of a one-neuron controller simulating the transmission of classical steam engines. The actual position $x^{(a)} = \cos(\varphi)$ of the wheel, as measured, drives the neural activity $y(x) = 1/(1 + \exp(-x))$, determining in turn the target position $x^{(t)} = y$.

For a simple class of embodied controllers the difference between the actual position $x^{(a)}$ and a target position $x^{(t)}$ of the actuator generates a driving force $F_k = k(x^{(t)} - x^{(a)})$, where k is a spring constant. This principle can be applied both for legged and for wheeled robots. For the latter, which is illustrated in Fig. 1, the force results in a torque $RF_{tan} = RF_k \sin(\varphi)$ acting on the wheel.

The embodied controller shown in Fig. 1 can be used to generate highly complex behavior for both simulated (click for movie) and for real-world (click for movie) robots, with regular limit-cycle and chaotic motion being equally possible. The resulting behavior is emerging, with the robot interacting non-trivially with the the environment.

From a dynamical system perspective a key question regards the route to locomotion. For small spring constants k, which determines the magnitude of the driving force, the dynamics is determined by a finite number of stable fixpoints, when projected to the degrees of freedom $(\varphi, \dot{\varphi})$ of the wheel. Locomotion cannot arise via a local bifurcation, that is via a Hopf bifurcation, which corresponds to small-amplitude (forth-and-back) oscillations around the non-moving fixpoints. We find that limit-cycle locomotion are generated via a global bifurcation, which occurs when the forth-and-back limit cycles expand until they touch in a series of heteroclinic bifurcations. We conclude that neural-controlled robots are an important and highly interesting emerging field within the mathematical neurosciences.

[1] B. Sandor, M. Nowak, T. Koglin, L. Martin, C. Gros, Kick control: using the attracting states arising within the sensorimotor loop of self-organized robots as motor primitives. Frontiers in Neurorobotics **12**, 40 (2018).

[2] L. Martin, B. Sandor, C. Gros, Closed-loop robots driven by short-term synaptic plasticity: Emergent explorative vs. limit-cycle locomotion. Frontiers in Neurorobotics **10**, 12 (2016).

[3] B. Sandor, T. Jahn, L. Martin, C. Gros, The sensorimotor loop as a dynamical system: How regular motion primitives may emerge from self-organized limit cycles. Frontiers in Robotics and AI **2**, 31 (2015).

A computational strategy to estimate synaptic conductances in spiking regimes

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Estimations of the time course of synaptic conductances impinging on a single cell are relevant to understand the functional connectivity of the brain. Although no general methods are available, many strategies have been developed to estimate excitatory/inhibitory synaptic conductances in low activity (subthreshold) regimes from membrane potential recordings. However, the estimation in spiking or more complex high activity regimes is still challenging. The main drawback is the predominance of ionic currents, which eventually mask the synaptic ones. Nevertheless, as we already showed in a caricature model, see [1], if one is able to extract substantial information about the contribution of ionic currents and track it during the spiking regime, then synaptic conductances can be identified as variations riding on the main ionic activity. For this purpose, the most natural observable from data in the spiking regime is the oscillation frequency. The knowledge of frequency-input relationships informs about the mean activity of the neuron which, of course, is not only due to the input stimulus but mainly to the activation of ionic currents that this input triggers. Fortunately, $f-I$ curves are prototypically monotone so that we have a bijection between frequency and input. Note also that the procedure naturally extends to experimental data, where $f-I$ curves are typically obtained, the only difference being the availability of data, which of course is scarce in experiments. However, synaptic conductances entail input currents that depend on the neuron's voltage itself ($I = g_{syn}(t)\,(v(t) - V_{syn})$) and then the estimation becomes highly sensitive to the fluctuations in g_{syn}. Therefore, a better frequency-input relationship would be knowing in advance the $f - g_{syn}$ curve rather than the $f-I$ curve, since it implicitly includes the voltage dependency of the synaptic current and thus mitigates the effects of the fluctuations. In a computational model, we can obtain the $f - g_{syn}$ curve numerically (in some cases, even analytically or quasi-analytically, see [1]). For experimental studies, retrieving the $f - g_{syn}$ curve requires using dynamic clamp techniques on the isolated cell for fixed g_{syn} values within a physiologically plausible interval.

In this contribution, we will first show, using a representative computational model (pyramidal cell), that the use of the $f - g_{syn}$ curve gives excellent predictions (MSE$\approx 10^{-7}$) of natural g_{syn} fluctuations in a regular spiking regime. We then deal with possible drawbacks that we could encounter in more realistic situations, namely, how to deal with the absence of an underlying mathematical model and how our strategy adapts to neuron's responses that alternate between spiking and subthreshold regimes. Concerning the absence of an underlying model, we show the level of adaptation of our method both when voltage traces are enough to fit the data to a generic neuron model (for instance, the EIF model) and when we have scarce experimental data. In the first case (fitting to an EIF model), we show as well that the quasi-analytical information that can be obtained from its mathematical expression (that is, the quasi-analytical expression of the period function) can help improving the estimations under alternations of spiking and subthreshold regimes. We also explore the required accuracy of the $f - g_{syn}$ curve and the effect of measurement noise on the estimations. We conclude that levels of noise below 1 mV do not compromise the estimations in a substantial way.

In summary, we go beyond the first proof-of-concept given in [1], and prove the suitability of frequency versus input relationships as a basis to estimate synaptic conductances in spiking regimes. In particular, we show how bifurcation theory can be used to obtain quasi-analytic estimation procedures. The method can be potentially extended with maximum likelihood or equivalent strategies to be useful to discern excitation and inhibition. As for many other estimation methods, it optimally works for stationary inputs, and does not capture high frequency fluctuations of the synaptic input, but still provides good estimations in mean in these cases.

References

[1] A. Guillamon, R. Prohens, A.E. Teruel and C. Vich. Estimation of synaptic conductances in the spiking regime for the McKean neuron model, *SIAM Journal on Applied Dynamical Systems* 16, pp. 1397–1424, 2017.

High-dimensional geometry of population responses in visual cortex

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A neuronal population encodes information most efficiently when its stimulus responses are high-dimensional and uncorrelated, and most robustly when they are correlated and lower-dimensional. We analyzed the dimensionality of the encoding of natural images by large visual cortical populations recorded from awake mice. Evoked population activity was high dimensional, with correlations obeying an unexpected power-law: the n^{th} principal component variance scaled as $1/n$. This scaling was not inherited from the $1/f$ spectrum of natural images, because it persisted after stimulus whitening. We proved mathematically that if the variance spectrum decayed any slower, the population code could not be smooth, allowing small changes in input to dominate population activity. The theory also predicts larger power-law exponents for lower-dimensional stimulus ensembles, which we validated experimentally. These results suggest that coding smoothness may represent a fundamental constraint governing correlations in neural population codes.

A Mathematical Analysis of Memory Lifetime in a simple Network Model of Memory

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Understanding how our brain can store so much information has long been a major problem in neuroscience. The memory process involves a huge number of chemical reactions, cascades, ion flows, protein states and even more mechanisms, which makes it really complex. Such a complexity stresses the need for simplified models: this has been done in network models of memory [1]. Such models are dedicated to the learning of external signals. More specifically, the analysis of the maximum number of stimuli that can be stored is investigated. Depending on the models, different approaches are proposed in order to answer whether a stimulus is learnt: more specific methods, based for example on attractor dynamics [2, 3], and more general methods, relying on a global quantity representing the memory trace of a stimulus [4–6]. The analysis of this global quantity is based on the dynamics of synaptic weights without giving information on how a stimulus can be retrieved. Here, we propose to add a retrieval process considering a mathematical analysis of the model of [4]. The advantage of this model is that it gives a plasticity rule depending on neural network responses to stimuli and it is simple enough to be tractable.

The following experimental protocol is modelled: an informative signal s_0 is sent to a recurrent network of N binary neurons. It puts the network in the state $\xi_0 \in \{0,1\}^N$. Neurons in state 1 (respectively 0) are selective (respectively non selective) to the signal with probability f, called the coding level. Then, the network is subjected to a sequence $(s_1, ..., s_p)$ of random stimuli (noise) putting neurons in states $(\xi_1, ..., \xi_p)$. Every signal affects the binary synaptic weight matrix $(J_1, ..., J_p)$ through a plasticity rule, $J_k \in \{J_-, J_+\}^{N^2}$. After the presentation of p_1 signals, the first stimulus is presented again and the ability of the network to recognize it is questioned. Hence, we study how much noise can be presented before forgetting the initial signal? The measure of forgiveness is based on the study of neuronal dendritic currents' distributions when receiving again the initial signal, after the presentation of p_1 stimuli. For the neuron i, this current is defined by:

$$h^i_{p_1} = \sum_{j \neq i}^{N} J^{ij}_{p_1} \xi^j_0.$$

Conditioning on the neuronal response to the first signal ξ^i_0, the dendritic current distributions knowing $\xi^i_0 = 0$ and the one knowing $\xi^i_0 = 1$ are initially well separated. As more and more stimuli are presented, both distributions converge to the same invariant measure, the signal is then totally forgotten. The speed of convergence is then crucial to evaluate forgiveness. Thus, we extend the analysis of Amit and Fusi first by computing the entire spectrum of the transition matrix of the process $\left(h^i_p\right)_{p \geq 0}$ and discover it has a nice expression. Then, we propose a statistical test on whether a neuron i could rely to retrieve the initial signal ξ^i_0. This test refers to a threshold decision based on the observation of its dendritic current h^i_p. From this test, we can define a probability error of estimation, denoted p_e that highly depends on the coding level, f. In the large N asymptotic, we analyse conditions on f under which we can evaluate p_e. Moreover, we find how f has to depend on N in order to minimise p_e. Then, we estimate the maximum number of random stimuli (noise) we can present before the probability of mistake reaches a given threshold. Finally, we use simulations to illustrate our results and to deal with cases not covered by our mathematical analysis.

References

[1] N. Brunel. *Course 10 - Network Models of Memory*, Methods and Models in Neurophysics 80 pp. 407-476 , 2005.

[2] J. J. Hopfield. *Neural networks and physical systems with emergent collective computational abilities*, PNAS 79 (8) pp. 2554-2558, 1982.

[3] D. J. Amit and G. Mongillo. *Spike-Driven Synaptic Dynamics Generating Working Memory States*, Neural Computation 15 (3) pp. 565-596, 2003.

[4] D. Amit, S. Fusi. *Learning in neural networks with material synapses*, Neural Computation 6 (5) pp. 957-982, 1994.

[5] C. Leibold and R. Kempter. *Sparseness Constrains the Prolongation of Memory Lifetime via Synaptic Metaplasticity*, Cerebral Cortex 18 (1) pp. 67-77, 2008.

[6] J. M. Luck and A. Mehta. *Slow synaptic dynamics in a network: From exponential to power-law forgetting*, Physical Review E 90 (3), 2014.

Mathematical tools for phase control and their role in neural communication

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Oscillations are ubiquitous in the brain. Although the functional role of oscillations is still unknown, some studies have conjectured that the information transmission between two oscillating neuronal groups is more effective when they are properly phase-locked [1]. Thus, studying phase dynamics is relevant for understanding neuronal communication.

The phase response curve (PRC) is a powerful and classical tool to study the effect of a perturbation on the phase of an oscillator, assuming that all the dynamics can be explained by the phase variable. However, factors like the rate of convergence to the oscillator, strong forcing or high stimulation frequency may invalidate the above assumption and raise the question of how is the phase variation away from an attractor.

In this talk, I will present powerful computational techniques to perform the effective computation of the phase advancement when we stimulate an oscillator which has not reached yet the asymptotic state (a limit cycle). I will show some examples of the computations we have carried out for some well-known biological models and its possible implications for neural communication.

References

[1] P. Fries. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence, *Trends in cognitive sciences* 9 (10) pp. 474-480, 2005.

Quantitative Analysis of Stochastic Axon Systems

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The brain contains many "point-to-point" projections that originate in known anatomical locations, form distinct fascicles or tracts, and terminate in well-defined destination sites. These projections are the focus of current connectomics projects and can be thought to represent the "deterministic brain." This brain coexists with a "stochastic brain" that is comparable in magnitude. The axons of the "stochastic brain" may initially travel in fascicles, but they eventually disperse in meandering trajectories, space-filling entire brain regions. Their cell bodies are typically located in the brainstem, as a component of the ascending reticular activating system (ARAS). ARAS axons (fibers) release serotonin, dopamine, norepinephrine, acetylcholine, and other neurotransmitters. They regulate perception, cognition, and affective states, and they also play major roles in human mental disorders (e.g., Major Depressive Disorder and Autism Spectrum Disorder).

Our interdisciplinary program [1, 2] seeks to understand at a rigorous level how the behavior of individual ARAS fibers determines their equilibrium densities in brain regions. These densities are commonly used in fundamental and applied neuroscience and can be thought to represent a macroscopic measure that has a strong spatial dependence (conceptually similar to temperature in thermodynamics). This measure provides essential information about the environment neuronal ensembles operate in, since ARAS fibers are present in virtually all brain regions and achieve extremely high densities in many of them.

A major focus of our research is the identification of the stochastic process that drives individual ARAS trajectories. Fundamentally, it bridges the stochastic paths of single fibers and the essentially deterministic fiber densities in the adult brain. Building upon state-of-the-art microscopic analyses and theoretical models, the project investigates whether the observed fiber densities are the result of self-organization, with no active guidance by other cells. Specifically, we hypothesize that the knowledge of the geometry of the brain, including the spatial distribution of physical "obstacles" in the brain parenchyma, provides key information that can be used to predict regional fiber densities.

In this presentation, we focus on serotonergic fibers. We demonstrate that a step-wise random walk, based on the von Mises-Fisher (directional) probability distribution, can provide a realistic and mathematically concise description of their trajectories in fixed tissue. Based on the trajectories of serotonergic fibers in 3D-confocal microscopy images, we present estimates of the concentration parameter (κ) in several brain regions. These estimates are then used to produce computational simulations that are consistent with experimental results. We also propose that other stochastic models, such as the superdiffusion regime of the fractional Brownian motion (fBm), may lead to a biologically accurate and analytically rich description of ARAS fibers, including their temporal dynamics. Since many properties of the fBm remain poorly understood, this interaction between neuroscience and stochastic analysis can stimulate both fields.

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References

[1] S. Janusonis, N. Detering. A stochastic approach to serotonergic fibers in mental disorders, *Biochimie*, 2018 (in press).

[2] S. Janusonis, K.C. Mays, M.T. Hingorani. Serotonergic fibers as 3D-walks, *ACS Chem. Neurosci.*, 2019 (in press).

Chimera States in Two-Population Network of Theta-Neurons

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A network of Theta-Neurons[1] is a dynamical system modeling the (electrical) signal traffic between neurons in the brain. Synchronization between neurons is a phenomenon considered to be important for the understanding of cognitive processes or pathologies.

The system under analysis can be reduced to a low-dimensional ordinary differential equation with the Ott-Antonsen ansatz[2, 3], a technique to capture the macroscopic (dynamical) behaviour of a large population of oscillators. The system under investigation is composed of two such populations such that neurons are coupled within a population and between populations via a mean-field.

In this project, we look for bifurcations and chimera states[4], depending on the intra- and inter-population coupling strengths and the inherent excitabilities of the neurons.

References

[1] G. B. Ermentrout, N. Kopell. Parabolic Bursting in an Excitable System Coupled with a Slow Oscillation, *SIAM Journal on Applied Mathematics*, Vol. 46, No. 2, 1986.

[2] E. Ott, T.M. Antonsen. Low dimensional behavior of large systems of globally coupled oscillators, *Chaos,* 18(3):037113, 2008.

[3] E. Ott, T.M. Antonsen. Long time evolution of phase oscillator systems, *Chaos,* 19(2):023117, 2009.

[4] D. M. Abrams, R. Mirollo, S. H. Strogatz, D. A. Wiley. Solvable Model for Chimera States of Coupled Oscillators, *Physical Review Letters,* PRL 101, 084103, 2008

A biophysical model for the tripartite synapse under metabolic stress

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The relevance of astrocytes in synaptic transmission at tripartite synapses is increasingly recognized as a major modulating factor. However, there are significant gaps in our understanding of the early changes in neuronal and astrocyte function during reduced energy availability. In this work we introduce a detailed single-cell biophysical model of the glutamatergic tripartite synapse under metabolic stress involving the dynamics of five relevant ions in a finite volume. We calibrate the model based on recent experimental findings on early events of physiological failure. The model explains about previously unclear mechanisms of early synaptic failure and cellular swelling during low energy conditions, as a function of ion clearance pathways by the astrocyte and extracellular space (ECS). We show that the latter relates to a higher vulnerability to metabolic stress. Using sensitivity and bifurcation analysis, we quantify key parameters of cellular physiological function with respect to metabolic stress. We also discuss key mechanisms associated with recovery from a pathological state upon restoring physiological conditions, thereby providing directions for future experiments.

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Optimal evidence accumulation on social networks

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Decision-making experiments in neuroscience primarily focus on individual organisms making decisions in isolation [1]. Studies seldom explore the neural computations of organisms making decisions as part of a group [2]. In such situations, subjects integrate their own individual stream of evidence along with information that comes from their network of social interactions. Normative models can provide a useful context for theorizing the neural computations underlying the integration of these two distinct evidence streams. Here, we formulate a normative model for agents making two choice decisions as part of a social network [3]. Primarily, we focus on two rational (Bayesian) agents making private measurements and observing decisions of their neighbors until they accumulate sufficient evidence to make an irreversible choice. Interestingly, both the presence and *absence* of a decision from a neighboring agent can communicate social information.

In our model, agent j computes a log likelihood ratio y_t^j (LLRs) between the either option of a binary choice task, based on observations of the world and their neighbors. In isolation, $y_t^j = y_{t-1}^j + \log \frac{P(\xi_t^j|H^+)}{P(x_t^j s|H^-)}$ where ξ_t are independent observations of agent j, and $P(\xi_t^j|H^\pm)$ are conditional probabilities of observing ξ_t^j given hypothesis $H^\pm$ is true. Agent j makes a decision $d_t^j = \pm 1$ when their LLR y_t^j crosses the threshold $\theta_\pm$ for hypothesis $H^\pm$. Coupling agents assumes agents can see their neighbors' decision states, which may be undecided ($d_t = 0$) or in favor of either hypothesis ($d_t = \pm 1$). In the example in Fig. 1a, agent 2 unidirectionally observes and incorporates agent 1's decision state into their own LLR (but agent 1 does not observe agent 2). When agent 1 has symmetric thresholds ($\theta_\pm = \pm\theta$), no information is conferred to agent 2 until agent 1 makes a decision (Fig. 1b), at which time there is a jump in agent 2's LLR of amplitude θ. On the other hand, when agent 1 has asymmetric thresholds ($\theta_- \neq -\theta_+$), social information is accumulated even prior to agent 1's decision according to:

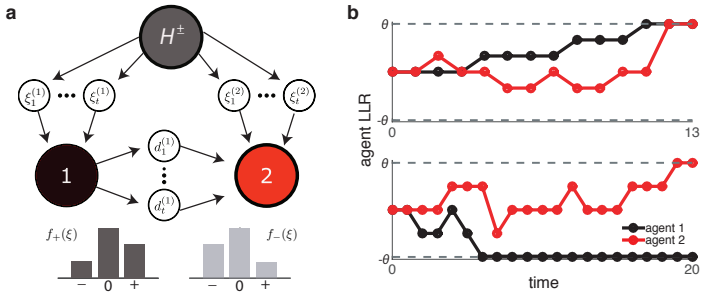

Figure 1: Two unidirectionally coupled agents deciding between the states $H^\pm$ based on private and social evidence. (a) Schematic of the information flow in the network. Agent 1 accumulates their own observations, $\xi_{1:t}^1$, resulting in a sequence of decision states, $d_{1:t}^1$, that is observed by agent 2. In addition, agent 2 gathers its own observations, $\xi_{1:t}^2$, to make a decision. (b) Sample trajectories for the beliefs (LLRs) of the agents. Decisions are made when an agent's belief crosses a threshold, $\theta_\pm = \pm\theta$ in this case. A decision of agent 1 leads to a jump in the belief of agent 2.

$$y_t^2 = \text{Priv}_{1:t}^2 + \text{Soc}_{1:t-1}^2 = \sum_{l=1}^{t} \log \frac{P(\xi_l^2|H^+)}{P(\xi_l^2|H^-)} + \log \frac{P(d_{1:t-1}^1|H^+)}{P(d_{1:t-1}^1|H^-)}.$$

The individual observations ξ_t^j agents 1 and 2 receive are independent, so we can split the private (Priv) and social (Soc) information agent 2 receives additively. Also, note (for technical reasons) there is a one timestep delay between when agent 1's decision state is detected by agent 2, so at time t agent 2 sees d_{t-1}^1. Social information can be computed from the survival probabilities of the distributions associated with agent 1's belief, assuming either hypothesis $H^\pm$.

We have extended these results to the case of recurrently coupled agents, in which case each agent must discount the information their neighbor has received from them to compute the net social information of their neighbor's decision state. Calculations are more involved, but still doable, as the size of the network grows: Agents must marginalize over all possible decision states of their neighbor's neighbors. Our work provides a firm mathematical footing for computing optimal evidence accumulation policies of organisms making decisions as part of a social network.

References: [1] JI Gold & MN Shadlen. Annu. Rev. Neurosci. 30 (2007) pp. 535-574; [2] S Tremblay, KM Sharika, & ML Platt. Trends Cog. Sci. 21 (2017) pp. 265-276; [3] B Karamched, S Stolarczyk, ZP Kilpatrick, & K Josić. SIAM Rev. (2019) in revision.

WILSON-COWAN NEURONAL INTERACTION MODELS WITH DISTRIBUTED DELAYS

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We generalize the original Wilson-Cowan model of excitatory and inhibitory interactions in localized neuronal populations that has been derived in 1972 [1], by considering distributed time delays. Based on the integral terms appearing in the original model as arguments of the threshold functions, model presented in [1], we obtain and analyze the following model with distributed delays:

$$\begin{cases} \dot{u}(t) = -u(t) + f\left[\theta_u + \int_{-\infty}^{t} h(t-s)\left(au(s) + bv(s)\right) ds\right] \\ \dot{v}(t) = -v(t) + f\left[\theta_v + \int_{-\infty}^{t} h(t-s)\left(cu(s) + dv(s)\right) ds\right] \end{cases} \tag{1}$$

In the above model, $u(t)$ and $v(t)$ represent the synaptic activities of the two neuronal populations, the coefficients a, b, c, d represent connection weights and θ_u, θ_v are background drives. The function f is called the activation function and it is considered to be increasing and of class C^1 on the real line, whereas $h : [0, \infty) \to [0, \infty)$ represents the delay kernel and is a probability density function representing the probability that a particular time delay occurs. So it is assumed to be bounded, piecewise continuous and it satisfies:

$$\int_0^\infty h(s)ds = 1, \quad \text{with the average time delay} \quad \tau = \int_0^\infty sh(s)ds < \infty.$$

Although mathematical models with particular classes of delay kernels shed a light on how distributed delays affect the dynamics differently from discrete delays, in the modeling of real world phenomena, one usually does not have access to the exact distribution, so approaches using general kernels is more appropriate [2, 3, 5, 6].

We present a stability and bifurcation analysis of the generalized model with respect to two characteristic parameters of the system and we plot the stability region in the characteristic parameter plane using several types of delay kernels, highlighting the importance of a careful choice of delay kernels in the mathematical model. To substantiate the theoretical results obtained so far, we also present some numerical simulations in which we consider a Dirac kernel and a strong Gamma kernel[2, 3, 5, 6]. We also compare our generalized model with the original one proposed and analyzed by Wilson and Cowan, thus highlighting the differences between the two models.

References

[1] Hugh R. Wilson and Jack D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons, *Biophysical Journal*, 12 (1) pp.1-24, 1972.

[2] Samuel Bernard, Jacques Bélair, and Michael C. Mackey. Sufficient conditions for stability of linear differential equations with distributed delay, *Discrete and Continuous Dynamical Systems Series B*, 1 (2) pp.233256, 2001

[3] S.A. Campbell and R. Jessop. Approximating the stability region for a differential equation with a distributed delay, *Mathematical Modelling of Natural Phenomena*, 4 (02) pp. 127, 2009.

[4] Stephen Coombes and Carlo Laing. Delays in activity-based neural networks, *Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences* 367 (1891) pp. 1117-1129, 2009.

[5] Yuan Yuan and Jacques Blair. Stability and Hopf bifurcation analysis for functional differential equation with distributed delay, *SIAM Journal on Applied Dynamical Systems* 10 (2) 551-581, 2011.

[6] Odo Diekmann, Mats Gyllenberg. Equations with infinite delay: blending the abstractand the concrete, *Journal of Differential Equations* 252 (2) pp. 819-851, 2012.

A method for estimating synaptic connections from parallel spike trains

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Advanced techniques of multiunit spike recording started to provide us with a huge number of spike trains. From the measured spike signal, we might infer the underlying neuronal circuitry, that is, the synaptic connections between neurons. Here we develop a method for estimating synaptic connections from spike trains recorded from multiple neurons based on the generalized linear model (GLM). The estimation performance of the model is evaluated by applying it to a synthetic data from a network of Hodgkin-Huxley type model neurons. Furthermore, our method is applied to rat hippocampal data.

Stochastic simulation of synaptic facilitation in Drosophila neuromuscular junction

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Synaptic transmission, where calcium-dependent release of neurotransmitter from synaptic vesicles is detected by the postsynaptic cell, is involved in all brain functions. An important aspect of this kind of transmission is the ability of the synapse to undergo use-dependent physiological changes. Short-term facilitation, where repeated stimulations over a short period of time yield an increase in the synaptic output, is an important example of such changes and can be observed in Drosophila Neuromuscular Junction as well as in many other synapses. However, the molecular mechanism underlying short-term facilitation is poorly understood and cannot be explained by the well-established models for neurotransmitter release alone.

Through analysis of new experimental data on the spatial distribution of synaptic vesicles, space-time simulation of calcium dynamics in the presynapse, and stochastic simulation of calcium binding and exocytosis, we identify necessary features of the molecular mechanisms underlying short-term facilitation. A prominent hypothesis suggests that two independent calcium sensors with different kinetics regulate the fusion rate and thereby produce the increase in the synaptic output. We show that this model alone cannot explain the observed facilitation. Furthermore, we propose another model in which calcium dependent mechanisms act on the release site in the cell membrane of the neuron instead of on the vesicle fusion process itself. This model is sufficient to reproduce the observed facilitation in the Drosophila Neuromuscular Junction.

This work is ongoing and not yet published. The paper referred to presents some of the experimental background for our work.

References

[1] Bohme MA., Grasskamp AT., Walter AM, et. al Active zone scaffolds differentially accumulate Unc13 isoforms to tune Ca(2+) channel-vesicle coupling, *Nature Neuroscience* 19 pp. 1311-1320, 2016.

Coordinate invariance as a constraint on the mutual information decomposition

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The value of Shannon's mutual information is commonly used to describe the total amount of information that the neural code transfers between the ensemble of stimuli and the ensemble of neural responses. In addition, it is often desirable to know which stimulus features or which response features are most informative. The literature offers several different decompositions of the mutual information into its stimulus or response-specific components, such as the specific surprise or the uncertainty reduction, but the number of mutually distinct measures is in fact infinite. We attempt to resolve this ambiguity by requiring the specific information measures to be invariant under invertible coordinate transformations of the stimulus and the response ensembles. We show that the Kullback-Leibler divergence is the only suitable measure of the specific information. We also discuss the impact of the reference frame change on the ultimate decoding accuracy. We speculate that the unwanted transformation covariance may be removed by considering the psychophysical scale based on the ideal observer paradigm.

References

[1] L. Kostal, P. Lansky. Coding accuracy is not fully determined by the neuronal model, *Neural Comput.* 27: 1051-1057, 2015.

[2] L. Kostal. Stimulus reference frame and neural coding precision, *J. Math. Psychol.* 71: 22-27, 2016.

[3] L. Kostal, G. D'Onofrio. Coordinate invariance as a fundamental constraint on the form of stimulus-specific information measures, *Biol. Cybern.* 112: 13-23, 2018.

Learning to control muscles with a brain-computer interface: a hierarchical and adaptive algorithm to optimally explore neural maps

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Each year, over 15 million people worldwide suffer major debilitating motor system injuries such as spinal cord trauma [1] or stroke [7]. A promising approach to help restore movement applies targeted, artificial stimulation of motor-related neural pathways, e.g. in motor cortex [4], spinal cord [3], or peripheral nerves [6] using brain-computer interfaces (BCI). New implantable devices which are microfabricated with many (>32) electrodes hold potential for targeted and specific stimulation, yet existing control algorithms do not fully take advantage of this, generally relying on incomplete and manual mapping. Two **important challenges towards designing algorithms to unveil and control neurostimulation-to-motor mappings** are: **(1)** the exploration of motor maps linking intensity and spatiotemporal patterns of electrical stimulation to muscle activation needs to be fast and efficient (exhaustive search is to be avoided for clinical reasons) **(2)** online learning needs to be flexible enough to track ongoing changes in these maps.

We propose a BCI stimulation search algorithm to address these issues in parallel with ongoing experiments in rat and non-human primate models. We achieve this via a **novel iterative process using Bayesian Optimization on increasingly complex signal spaces, leveraging acquired knowledge of muscle responses in low-dimensional spaces to build priors for *stim-to-EMG* maps in high-dimensional spaces**, where only correction terms are learned. The advantages of recursively learning correction terms, rather than a complete map, are threefold: **(1)** Convergence to optimal stimulation requires fewer exploratory stimuli than direct optimization on the space of all signals. **(2)** The algorithm can be used online and adapts quickly to changes in neural dynamics. **(3)** Our method precisely learns the nonlinearities introduced by network dynamics, and can track the evolution of population codes throughout recovery, thus allowing a mapping of circuit-level computations.

Further details: Motor circuits produce complex dynamics that contribute to the generation of nuanced, coordinated muscle activation, enabling animals to interact with the world. However, neural coding and plasticity mechanisms present in these circuits are not well understood, and are under intense study. As stimulating BCIs give the possibility to activate several neural sites with distinct temporal and intensity scales, what is the optimal stimulation strategy to achieve a targeted motor output? As networks' functional scopes change (either as a result of stimulation or normal plasticity mechanisms) how can we ensure that stimulation strategies adapt ? While isolated stimulation can selectively activate muscles with graded recruitment [2], designing stimulation patterns to evoke naturalistic synergies is still a major hurdle towards use for restoring movement to paralyzed limbs. We address these issues by developing a signal-to-motor-ouput mapping technique, while demanding as few exploratory stimuli as possible. The resulting algorithm can be used in a variety of stimulation modes, and is applied to distinct experimental procedures such as stimulation of the primary motor cortex (M1) through an intracortical multielectrode array (Fig 1 A), or microstimulation of peripheral nerves that can selectively activate muscles with graded recruitment [2].

We consider electrical stimulation signals that are composed of discrete pulses (e.g. single electrical pulses or short pulse trains) that can be delivered to one of N channels. A stimulation containing k pulses is a tuple $s_k = (n_1, \dots n_k, a_1, \dots, a_k, \Delta t_1, \dots, \Delta t_{k-1})$ where $n_i = 1 \dots N$ indicates the channel of the i^{th} event, a_i its amplitude, and Δt_i is the inter-pulse interval between pulses i and $i+1$. Each s_k generates a noisy pattern of EMG activity $g(s_k)$. Our goal is to optimize an objective function $C(g(s_k))$. Here C is flexible; it can be extracting the maximum output of a single EMG, or measuring a distance between evoked pattern $g(s_k)$ and a target pattern g_{target}.

We illustrate our procedure using a synthetic objective C to be minimized, shown in Fig. 1, evaluated over the 2D space of dual-pulse stimulations (with fixed a and Δt). This signal is parameterized by $s_2 = (n_1, n_2)$: the identities of the electrodes delivering the two pulses. Evoked EMG patterns are denoted $g(n_1, n_2)$. We write $g(n_1)$ for the EMG pattern evoked by the stimulation of electrode n_1 only. Suppose we want to find the minimum of an objective function $C(g(n_1, n_2))$. Our first step is to fit a Gaussian Processes (GP) [5] over the space of single-pulses, minimizing $C(g(n_1))$ (dotted red line in Fig. 1 A) and providing an estimate $\hat{g}(n_1)$. The main assumption of our approach is that evoked patterns from concatenated stimulation signals combine in a simple way so that $g(n_1, n_2) \simeq f(\hat{g}(n_1), \hat{g}(n_2))$ for a chosen function f (we often assume linearity). Using this approximation, we build a prior for our objective function in 2D, here chosen to be

$\tilde{C}(g(n_1, n_2)) = C(f(\hat{g}(n_1), \hat{g}(n_2)))$ (Fig. 1 B). For illustration, we set $f(\hat{g}(n_1), \hat{g}(n_2)) = \hat{g}(n_1) + \hat{g}(n_2)$. Crucially, our toy $C(g(n_1))$ in shown in Fig. 1 A, and we let $C(g(n_1, n_2)) = C(g(n_1) + g(n_2) + \epsilon(n_1, n_2))$ where $\epsilon(n_1, n_2)$ is a Gaussian bump meant to shift the 2D minimum away from the minimum of $C(g(n_1))$ (see Fig. 1 B). We then use a GP in the (n_1, n_2) parameter space to learn the difference between this prior and the true response: $\Delta g = \tilde{f}(\hat{g}(n_1), \hat{g}(n_2)) - g(n_1, n_2)$, while minimizing $C(f(\hat{g}(n_1), \hat{g}(n_2)) + \Delta g)$. For comparison, we train a GP to minimize C over the (n_1, n_2) parameter space directly, using a flat prior.

Fig. 1 C,D shows the number of exploration stimuli used by the two GPs to find the minimum. Importantly, the total number of iterations necessary for our method (including those to build $\hat{g}(n_1)$) is smaller than that of the 2D GP, and this discrepancy only shrinks as more dimensions are considered (not shown). **Thus our method suggests that combining EMG maps of low-D stimulations into priors for maps of high-D stimulations, provides a fast and efficient way to optimize an objective target.**

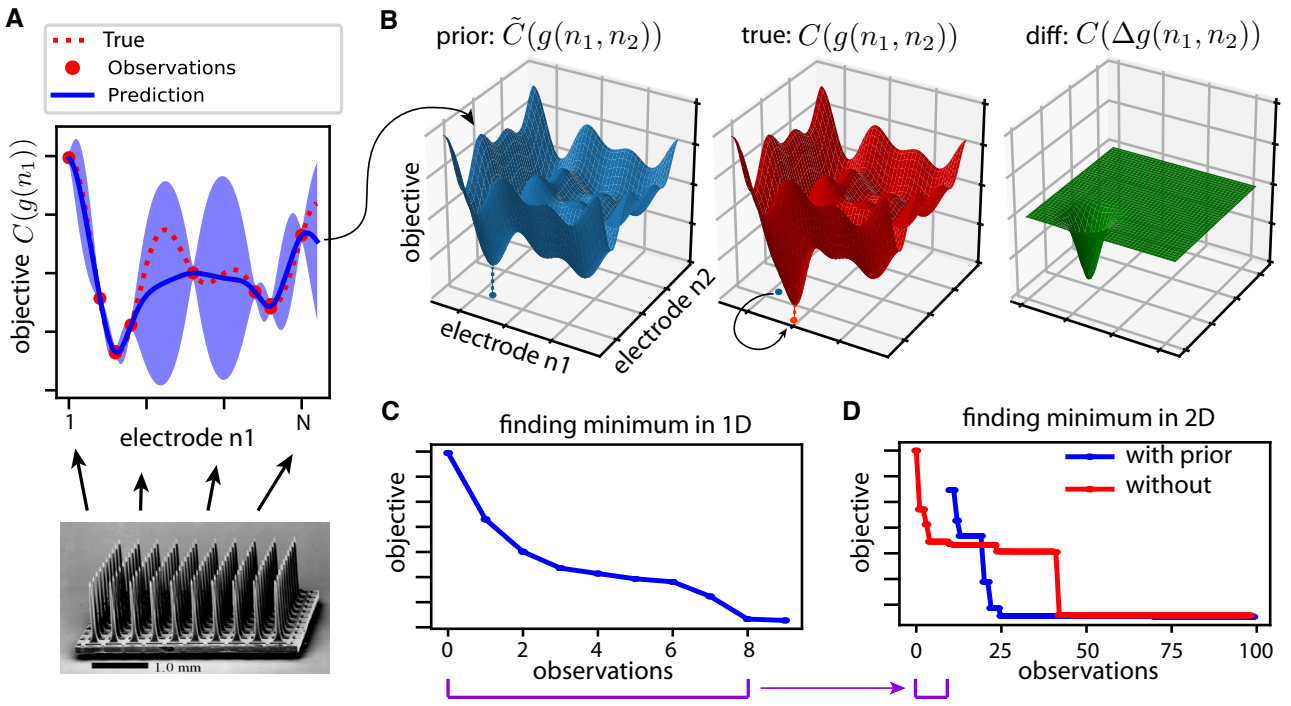

Figure 1: **A:** Example GP approximation (blue) fitted to a true objective (dotted red) over the space of single pulse signals (1D). **B:** (from left to right) Prior objective, true objective and difference between the two, over the space of dual pulse stimulations (2D). Notice the shifted minimum. **C:** Predicted minimum of objective v.s. number of observations in 1D (see also panel A). **D:** Predicted minimum of objective v.s. number of observations in 2D, with and without use of prior from 1D. Number of observations for case using prior includes those used to find 1D.

References

[1] Spinal cord injury. http://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury. Accessed: 2018-11-15.

[2] Tim Boretius et al. A transverse intrafascicular multichannel electrode (time) to interface with the peripheral nerve. *Biosensors and Bioelectronics*, 26(1):62–69, 2010.

[3] Marco Capogrosso et al. A brain-spine interface alleviating gait deficits after spinal cord injury in primates. *Nature*, 539(7628):284–288, 11 2016.

[4] Simon A Overduin, Andrea d'Avella, Jose M Carmena, and Emilio Bizzi. Microstimulation activates a handful of muscle synergies. *Neuron*, 76(6):1071–1077, 12 2012.

[5] Carl Edward Rasmussen and Christopher K. I. Williams. *Gaussian Processes for Machine Learning (Adaptive Computation and Machine Learning)*. The MIT Press, 2005.

[6] S. Raspopovic et al. Experimental validation of a hybrid computational model for selective stimulation using transverse intrafascicular multichannel electrodes. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 20(3):395–404, 2012.

[7] Amanda G Thrift et al. Global stroke statistics. *International Journal of Stroke*, 12(1):13–32, 2018/11/15 2016.

Threshold-Linear Networks and Mutations of Oriented Matroids

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Many networks in the brain exhibit internally generated patterns of activity that arise from intrinsic properties of the network rather than by an external input. Such dynamics are believed to underlie many brain functions, ranging from central pattern generators for locomotion to emergent sequences in cortex and hippocampus. To isolate the role of connectivity in shaping emergent dynamics we study competitive threshold-linear networks. TLNs are firing rate models with simple, perceptron-like neurons on which we impose uniform external input, ensuring that the emergent dynamics are controlled solely by the structure of the connectivity. Specifically, the dynamics is given by $\frac{d\mathbf{x}}{dt} = -\mathbf{x} + [W\mathbf{x} + \theta]_+$, where $\mathbf{x}(t) \in \mathbb{R}^n$ is a vector of firing rates, W is an $n \times n$ matrix of connection strengths, and $[y]_+ = \max\{0, y\}$ is the nonlinear transfer function.

In [1, 2], intrinsic properties of the network connectivity, W, were extracted in the form of a directed graph. The graph is defined by the rule $i \to j$ in G if and only if $W_{ji} > -\theta$. It was shown there that this graph constrains both the transient activity and the fixed point supports of the network. The support of a fixed point is defined to be the subset of coactive neurons in the fixed point.

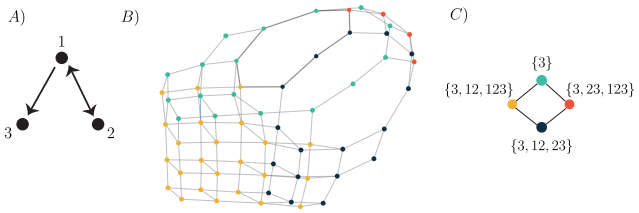

Figure 1: (A) A directed graph capturing combinatorial properties of a matrix W. (B) The mutation graph of the graph in (A). (C) The resulting bifurcations of fixed points that are possible on this architecture.

In this work, we show that the directed graph G can be extended to an oriented matroid which, in some sense, captures the full combinatorial data of W. This oriented matroid can be understood geometrically as a collections of signs of determinants encoding the combinatorial geometry of a hyperplane arrangement associated to W. The notion of mutation of a hyperplane arrangement provides a powerful language for understanding local perturbations of the network and the bifurcations of fixed points that arise. By viewing G as the fixed network architecture and computing the corresponding mutation graph we obtain combinatorial constraints on the bifurcations that can arise over this fixed architecture (see Figure 1.)

To understand how variations in the parameters of the network realize these bifurcations we consider slices of the parameter space corresponding to the rows of the matrix W. For a network of three neurons this gives an arrangement of lines whose cell structure determines the local changes to the network corresponding to pre-synaptic plasticity of neuron i (see Figure 2.) Using these diagrams we can classify every bifurcation of fixed points in a threshold-linear network of three neurons and in addition, provide a sequence of variations in the synaptic weights that realizes these bifurcations.

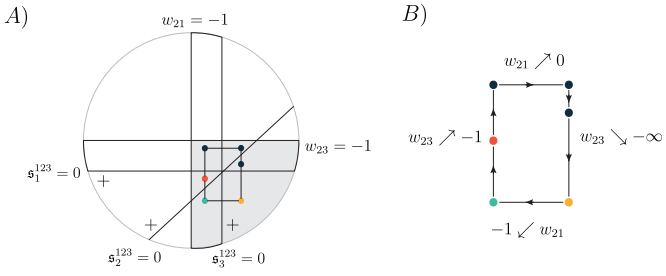

Figure 2: (A) Parameter slice for neuron two (B) By cyclically varying the parameters w_{21} and w_{23} we obtain every bifurcation of fixed points that is possible on the architecture defined by Figure 1A.

References

[1] K.Morrison, A. Degeratu, V.Itskov, C. Curto Diversity of emergent dynamics in competitive threshold-linear networks: a preliminary report, Available at https://arxiv.org/abs/1605.04463. 2016

[2] C. Curto, J. Geneson, K. Morrison *Fixed points of competitive threshold-linear networks* Neural Computation, 2018.

Modeling the initiation of cortical spreading depression triggered by the hyperactivity of GABAergic neurons

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Familial hemiplegic migraine type 3 (FHM3) is a rare but severe form of migraine with aura, i.e. preceded by sensory disturbances. Cortical spreading depression (CSD) is a wave, slowly propagating in the cortex, of intense neuronal firing followed by a sustained depolarization which silences electrical activity for several minutes. It is commonly accepted as an underlying mechanism of migraine with aura [1]. Experiments suggest that this wave indirectly stimulates the trigeminal nociceptors innervating the meninges, activating pain pathways and provoking the headache [2]. FHM3 is know to be caused by mutations of the gene coding for $Na_V1.1$ [3], a sodium voltage-gated channel mainly expressed in GABAergic neurons and crucial for their excitability. However, the pathological mechanism through which these mutations can lead to CSD remains unclear. Several studies, e.g. [4], suggest that they cause a gain of function of the channel, i.e. increase its activity, leading to hyperexcitability of GABAergic neurons. Could the hyperactivity of GABAergic neurons, which classically have an inhibitory role, trigger the initiation of a CSD?

To investigate this counterintuitive hypothesis, Desroches et al. developed a Hodgkin-Huxley based model of a pair of coupled neurons: a GABAergic neuron and a pyramidal cell [5]. Since CSD is characterized by the disruption of ionic gradients, they take into account modifications of the reversal potentials for the pyramidal cell due to its transmembrane currents, to diffusion or buffering of extracellular potassium and to potassium currents of the GABAergic neuron. The latter couples both cells, in addition to synaptic coupling. For simplicity, they assume that the other ion currents of the GABAergic neuron have no effect on the extracellular concentrations and that its reversal potentials are constant. They show that, in this model, moderate firing of the GABAergic neuron inhibits the pyramidal cell, whereas intense firing induces a depolarizing block in the pyramidal cell, which can be interpreted as the initiation of a CSD. Furthermore, after exploring different trails (efficacy of the KCC2 cotransporter, GABA and glutamate levels), they conclude that the key factor for the transition to CSD is, here, the accumulation of extracellular potassium. Intense firing of the GABAergic neuron, and of the pyramidal cell in a positive feedback loop, generates a potassium build-up. It increases the potassium reversal potential of the pyramidal cell, which has a depolarizing effect and promotes CSD induction. This computational result is consistent with current experimental findings [6].

Following on from this work, we extended the model to consider the effects of ion currents on the dynamics of the reversal potentials of both neurons, for consistency. To model $Na_V1.1$ mutations, we also implemented a persistent sodium current for the GABAergic neuron, in addition to the usual fast inactivating one. We found that this facilitates CSD ignition, which can be put in perspective with similar experimental results in preparation. Finally, we used bifurcation analysis, to study transitions between different regimes or the sensitivity of the system to parameters whose biological values are uncertain, e.g. the maximal conductance of the sodium leak current. In the future, this model could be used to inspire building blocks of a spatial model to study the propagation of CSD, or to further investigate the role, raised for example in [7], of astrocytes in maintaining ion homeostasis in the context of CSD.

References

[1] M. Lauritzen. Pathophysiology of the migraine aura: The spreading depression theory, *Brain* 117 (1), pp. 199-210, 1994.

[2] M. D. Ferrari, R. R. Klever, G. M. Terwindt, C. Ayata et al. Migraine pathophysiology: lessons from mouse models and human genetics, *The Lancet Neurology* 14 (1), pp. 65-80, 2015.

[3] M. Dichgans, T. Freilinger, G. Eckstein, E. Babini et al. Mutation in the neuronal voltage-gated sodium channel *SCN1A* in familial hemiplegic migraine, *The Lancet* 366 (9483), pp. 371-377, 2005.

[4] S. Cestèle, E. Schiavon, R. Rusconi, S. Franceschetti et al. Nonfunctional $Na_V1.1$ familial hemiplegic migraine mutant transformed into gain of function by partial rescue of folding defects, *PNAS*, pp. 17546-17551, 2013.

[5] M. Desroches, O. Faugeras, M. Krupa, M. Mantegazza. Modeling cortical spreading depression induced by the hyperactivity of interneurons, *https://hal.inria.fr/hal-01520200*, v1, working paper or preprint, 2017.

[6] O. Chever, S. Zerimech, M. Ayrault, F. Duprat et al. Hyperexcitability of GABAergic neurons triggers cortical spreading depression: New mechanism of migraine?, *Society for Neurosciences Meeting* Poster 288.14/D35, 2017.

[7] G. Huguet, A. Joglekar, L. Messi, B. Matamba et al. Neuroprotective role of gap junctions in a neuron astrocyte network model, *Biophysical journal* 111 (2), pp. 452-462, 2016.

Numerical Investigation of a Neural Field Model Including Dendritic Processing

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We consider a neural field model which treats the voltage on a dendrite as the primary variable of interest in a simple one-dimensional model of neural tissue. At each point along a *somatic* coordinate $x \in \mathbb{R}$ we envisage a fibre with voltage dynamics at a point $\xi \in \mathbb{R}$ described by the cable equation with a non-local input current arising as an integral over the outputs from all somatic regions (where $\xi = 0$). Denoting the voltage by $V(x, \xi, t)$ we have an integro-differential equation for the continuous function $V : \mathbb{R}^2 \times [0, T] \to \mathbb{R}$ of the form

$$\frac{\partial}{\partial t} V(x, \xi, t) = \left(-\frac{1}{\tau} + D \frac{\partial^2}{\partial \xi^2} \right) V(x, \xi, t) + \int_{\mathbb{R}^2} \mathrm{d}y \, \mathrm{d}\xi' K(x, y, \xi, \xi') S(V(y, \xi', t)), \qquad t \in [0, T], \tag{1}$$

for some typically sigmoidal firing rate function S. Here D is the diffusion coefficient and τ the membrane time-constant of the cable. This model is completed with the choice of the generalised connectivity function K. Assuming that the synaptic contact occurs in an ϵ-neighbourhood of a point ξ_0 on the cable we have the decomposition

$$K(x, y, \xi, \xi') = \delta_\epsilon(\xi - \xi_0) \delta_\epsilon(\xi') W(|x - y|), \tag{2}$$

where W describes the strength of interaction across the somatic space and is chosen here to be translationally invariant and δ_ϵ is a Gaussian function with standard deviation $\epsilon \ll 1$.

The aim of the present work is to introduce a computational method for approximating the solution of (1), with initial condition $V(x, \xi, 0) = V_0(x, \xi)$, and to apply it to the numerical simulation of the model for the choice of (2). For the time discretisation we adopt the implicit Euler method; the space discretisation is based on a finite-difference scheme to approximate the diffusion term and uses the trapezoidal rule to approximate the integral. Other discretisations, including generic differentiation matrices for the diffusion term, Gauss quadrature for the integrals, and Runge-Kutta schemes for time stepping are also possible. By way of validation we compare the outputs a numerical realisation to theoretical predictions for the onset of a Turing pattern when W has a Mexican hat shape, and to the speed and shape of a travelling front when W is exponentially decaying and the firing rate is a Heaviside function. We find that they are in excellent agreement.

References

[1] Neural Fields, 2014, Ed. S Coombes, P beim Graben, R Potthast and J J Wright, Springer Verlag

High-dimensional geometry of population responses in visual cortex

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I present a simple microscopic stochastic model describing short term plasticity within a large homogeneous network of spiking interacting neurons. I will show how in this framework short time memory can be described as the tendency of the system to keep track of an initial stimulus by staying within a certain untypical region of the space of configurations during a short but macroscopic amount of time. The main technical tool is a rigorous justification of the passage to a large population limit system.

Wandering bumps in a stochastic neural field: a variational approach

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Neural field theory concerns the analysis of nonlinear integro-differential equations arising from a coarse-grained continuum model of spatially-structured neural tissue. The associated integral kernels represent the spatial distribution of neuronal synaptic connections. Neural fields are an important example of spatially extended excitable systems with nonlocal interactions, and exhibit a wide range of self-organizing spatiotemporal patterns analogous to those found in nonlinear partial differential equation (PDE) models of diffusively coupled excitable systems. One topic of current interest is how these patterns are affected by the addition of spatially extended noise terms. Much of the recent focus has been on traveling fronts and bumps (stationary pulses) in one-dimensional neural fields. The analysis of stochastic fronts was originally developed using formal perturbation methods [1], and was subsequently extended to the case of wandering bumps in single-layer and multi-layer neural fields [4]. Stannat *et al* also extended the analysis [5] using a gradient-descent definition of the phase. In this talk we continue the analysis of wandering bumps that was started in [4].

The bump solution is marginally stable with respect to uniform spatial translations. This means that one has to treat longitudinal and transverse fluctuations of the bump or wave separately in the presence of noise. This is implemented by decomposing the stochastic neural field into a deterministic bump profile, whose spatial location has a slowly diffusing component, and a small error term. (There is always a non-zero probability of large deviations, but we prove that this is negligible up to some exponentially long stopping time.) However, this decomposition is non-unique unless an additional mathematical constraint is imposed. Within the context of formal perturbation methods, the latter takes the form of a solvability condition that ensures that the error term can be identified with fast transverse fluctuations, which converge to zero exponentially in the absence of noise.

One advantage of formal perturbation theory is that it provides a relatively straightforward method for deriving an explicit SDE for the diffusive-like wandering of the deterministic component in the weak noise regime. However, it is not rigorous and does not provide bounds on the size of transverse fluctuations. Therefore, in this paper, we show how the explicit results of formal perturbation theory can be derived more rigorously using variational methods. This requires generalizing the analysis of [3] by taking perturbations to belong to the Hilbert space $L^2(U,\rho)$ for an appropriately chosen weight ρ, rather than $L^2(\mathcal{U})$, where $\mathcal{U}$ is the spatial domain of the neural field. That is,

$$\langle u,v\rangle_\rho = \int_{\mathcal{U}} u(x)v(x)\rho(x)dx < \infty, \quad u,v \in L^2(\mathcal{U},\rho).$$

The reason that we must do this is that in the weighted space the deterministic dynamics is linearly stable with respect to the bump of excited activity. Since the spatial domain of the ring model is S^1 is compact, the spectrum of the linear operator obtained by linearizing about a bump solution is discrete. We can then adapt the methods of [3] to prove that the variational definition of the phase is accurate over exponentially long periods of time. This in turn facilitates a long-time analysis of the wandering of the bump. We determine the leading order asymptotic behavior of the occupation measure: which indicates the typical probability of the bump being in a particular location over long time intervals. We investigate how the occupation measure is affected by a weak external stimulus and different types of underlying stochasticity.

References

[1] P C Bressloff and M. A. Webber. Front propagation in stochastic neural fields. SIAM J. Appl. Dyn. Syst., 11: (2012) 708–740.

[2] P. C. Bressloff and J. Maclaurin. A variational method for analyzing stochastic limit cycle oscillators. SIAM J. Appl. Dyn. 17 (2018) pp. 2205-2233.

[3] J. Inglis and J. MacLaurin, A general framework for stochastic traveling waves and patterns, with application to neural field equations, SIAM J. Appl. Dyn. Syst., 15 (2016) 195-234.

[4] Z P Kilpatrick, and G. B. Ermentrout. Wandering bumps in stochastic neural fields. SIAM J. Appl. Dyn. Syst., 12 (2013) 61–94.

[5] M Kruger and W Stannat. Front propagation in stochastic neural fields: a rigorous mathematical framework. SIAM J. Appl. Dyn. Syst., 13 (2014) 1293–1310.

Accuracy of Mass-Action vs Stochastic Modeling of Calcium-Dependent Vesicle Release

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A distinguishing feature of synaptic and endocrine secretory vesicle release is the high degree of variability in all steps of the process, from the opening of Ca^{2+} channels to the final membrane fusion. Stochastic Ca^{2+} channel gating is a major source of this stochasticity [1-9]. The associated fluctuations can be quite large since only a small number of Ca^{2+} ions enter the cell through a single channel during an action potential, and further increased by the stochasticity in the Ca^{2+} binding to Ca^{2+} buffers and sensors [8-9]. This leads to a widely-held assumption that solving mass-action reaction-diffusion equations for buffered Ca^{2+} diffusion does not provide sufficient accuracy for modeling Ca^{2+}-dependent cell processes. However, several comparative studies showed a surprising close agreement between deterministic and trial-averaged stochastic simulations of Ca^{2+} diffusion, buffering and binding, as long as Ca^{2+} channel gating is not strongly Ca^{2+} dependent [1-9]. We present further analysis and comparison of stochastic and mass-action simulations, focusing on Ca^{2+} dynamics downstream of Ca^{2+} channel gating and considering full spatial reaction-diffusion in 3D. Smoldyn is used for stochastic simulations [10], while CalC is used for deterministic simulation [11]. We show that the discrepancy between deterministic and stochastic approaches can be surprisingly small even when only as few as 40 ions enter per single channel-vesicle complex, despite the majority of ions quickly binding to Ca^{2+} buffers. The reason for the close agreement is that in the absence of Ca^{2+}-induced Ca^{2+}-release, the non-linearities in the exocytosis process involve only bi-molecular reactions. Therefore, the discrepancy between the two approaches is determined by the correlations between reactant molecule number fluctuations rather than the fluctuation amplitudes of individual reactants. Further, contrary to naïve intuition, mass-action reaction-diffusion description yields the full vesicle release latency probability density function [9], since it agrees with the differential equation for the first passage time distribution under the simplifying assumption of negligible correlations. This explains the close match between stochastic and mass-action simulations of Ca^{2+}-dependent exocytosis, despite the high variability in Ca^{2+} diffusion, buffering and binding. The small size of molecule number correlations is in turn determined by the relationship between the rate of diffusion relative the rate of Ca^{2+} buffering and binding. This work is supported by NSF grant DMS-1517085.

[1] Hake J, Lines GT: Stochastic binding of Ca2+ ions in the dyadic cleft; continuous versus random walk description of diffusion. Biophys J 2008, 94:4184-4201.

[2] Modchang C, Nadkarni S, Bartol TM, Triampo W, Sejnowski TJ, Levine H, Rappel WJ: A comparison of deterministic and stochastic simulations of neuronal vesicle release models. Phys Biol 2010, 7:026008.

[3] Tanskanen AJ, Greenstein JL, Chen A, Sun SX, Winslow RL: Protein geometry and placement in the cardiac dyad influence macroscopic properties of calcium-induced calcium release. Biophys J 2007, 92:3379–3396.

[4] Flegg MB, Chapman SJ, Erban R. The two-regime method for optimizing stochastic reaction-diffusion simulations. J R Soc Interface 2012, 9:859–868.

[5] Flegg MB, Rudiger S, Erban R: Diffusive spatio-temporal noise in a first-passage time model for intracellular calcium release. J Chem Phys 2013, 138:154103.

[6] Wieder N, Fink RHA, von Wegner F: Exact stochastic simulation of a calcium microdomain reveals the impact of Ca2+ fluctuations on IP3R gating. Biophys J 2015, 108:557–567.

[7] Weinberg SH, Smith GD: Discrete-state stochastic models of calcium-regulated calcium influx and subspace dynamics are not well-approximated by ODEs that neglect concentration fluctuations. Comput Math Methods Med 2012:897371.

[8] Weinberg SH, Smith GD: The influence of Ca2+ buffers on free [Ca2+] fluctuations and the effective volume of Ca2+ microdomains. Biophys J 2014, 106:2693–2709.

[9] Weinberg SH: Microdomain [Ca^{2+}] Fluctuations Alter Temporal Dynamics in Models of Ca2+-Dependent Signaling Cascades and Synaptic Vesicle Release. Neural Comput 2016, 28:493–524.

[10] Andrews SS, Bray D: Stochastic simulation of chemical reactions with spatial resolution and single molecule detail. Phys Biol 2004, 1:137-151.

[11] Matveev V, Sherman A, Zucker RS: New and corrected simulations of synaptic facilitation. Biphys J: Biophys J 83:1368-1373.

Data-driven estimation of drift-diffusion-jump neural processes

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Reconstructing Langevin-type stochastic differential equations from experimental time series is possible by estimating the drift and diffusion functions of the associated Fokker-Planck equation via the Kramers-Moyal expansion. In certain neural systems, however, large and abrupt events - such as dendritic spikes or large EPSPs in single neuron recordings - can also be seen concurrently with drift-diffusion dynamics. It becomes a huge challenge to disentangle all these contributions to neural activity and pinpoint their respective origins. These abrupt events further violate the assumptions of the Langevin approach. We provide a novel method that reconstructs a jump-drift-diffusion stochastic differential equation based solely on process realizations. We first threshold the increments of the process to "approximately" detect jumps in the time series. This is followed by an iterative scheme that compensates for the presence of diffusive fluctuations that are falsely detected as jumps. Our approach is based on probabilistic calculations associated with these fluctuations, and on the use of the Fokker-Planck and the differential Chapman-Kolmogorov equations. Our method is validated numerically by showing that the drift function, diffusive noise intensity, jump rate, and jump amplitude distribution of the true process are accurately estimated. We then successfully apply this method to recordings of membrane noise in pyramidal neurons that display large, jump-like depolarization events at random times, the biophysics of which is unknown. Our approach reveals how these cells increase both the random voltage jump rate and the diffusive noise intensity as the potential approaches the spike threshold, while the drift function and distribution of jump amplitudes remain relatively unchanged. In particular, this gives novel insight into synergistic effects of signal and noise in this sensory system, namely into the boosting of signal detection by voltage-dependent diffusive and jump noise (voltage-dependent stochastic resonance). As our method is fully data-driven, it provides a valuable means to investigate the functional role of jump-like events without relying on more detailed, albeit unconstrained biophysical models. The method is also applicable to population level recordings as well as behavioural data.

Using dynamic neural fields to examine loci of plasticity in supervised and unsupervised auditory category learning

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Summary Humans encounter many different stimuli from the environment; the ability to categorize similar stimuli is important for survival. In particular, language acquisition requires auditory categorization. For example, speech sounds are grouped into categories that combine features which are generalized between speakers. A fundamental question asks what mechanisms form the foundation for auditory category learning. We propose a dynamic neural network framework that combines plausible biological mechanisms and the theory of dynamic neural fields to model this process. The model simulates a task in which a listener is presented with a sequence of pairs of tones with each pair corresponding to one of four categories defined by their frequencies. The subject first passively listens to tones for approximately 20 minutes. Then the subject engages in a supervised task and is instructed to associate each tone-pair with a physical object representing one of the four auditory categories. Corrective feedback is given to the subject in the supervised task. The mathematical model is used to manipulate mechanisms through which hypotheses can be made about the category learning process. We present preliminary results from model simulations of the experiment and compare them with implementations of the experiment on human subjects.

Network Description and Results We consider a dynamic neural field consisting of multiple layers, allowing for multiple locations of plasticity involved in the learning process that can be manipulated and tested. The incoming sounds are projected onto a one-dimensional tonotopically organized feature space associated with subcortical auditory fields. Neural units along this space are tuned to specific frequencies and interact through local excitatory and inhibitory synapses. Auditory inputs in this field drive activation in regions of primary and secondary auditory cortex. These regions are then mapped into the category layer composed of 4 neural units representing the 4 categories defined in the task. These nodes are hypothesized to represent regions in auditory-related temporal cortical regions such as superior temporal gyrus (STG) [2] and the inferior frontal gyrus in humans or in layer 2/3 of auditory cortex and prefrontal cortex in rats [1]. In the theoretical network, the categories are represented by four nodes connected through mutual inhibition competing in a winner-take-all setting. The model is designed so that above threshold activation peaks in the category layer are interpreted as experimentally detectable responses. Parameters within the model are tuned so that responses in the category layer closely match behavioral results obtained from implementations of the experiment on human subjects. In simulations we varied stimuli distributions, category prototypes, and category boundaries to match implementations of the task with human subjects. The model predicts category learning at rates consistent with those found experimentally.

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References

[1] Nikolas A Francis, Daniel E Winkowski, Alireza Sheikhattar, Kevin Armengol, Behtash Babadi, and Patrick O Kanold. Small networks encode decision-making in primary auditory cortex. *Neuron*, 97(4):885–897, 2018.

[2] Nima Mesgarani, Connie Cheung, Keith Johnson, and Edward F Chang. Phonetic feature encoding in human superior temporal gyrus. *Science*, 343(6174):1006–1010, 2014.

Effects of excitatory/inhibitory neuron ratio on neural activities and network structures

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Inhibitory neurons play a crucial role in controlling excessive firings and synchronization in neural networks. From physiological experiments, it is widely acknowledged that there are approximately 80% of excitatory neurons and 20% of inhibitory neurons in the cerebral cortex[1]. However, it has not been clarified yet why this ratio is appropriate for the brain functions and how the neural activities will be affected by this ratio. Then, we investigated the effects of neural activities and network structures if the ratio of the numbers of the inhibitory neurons and excitatory neurons using a mathematical model of the STDP learning rule only for excitatory neurons[2].

We first investigated the average firing rates by changing the inhibitory neuron ratio r_{IN} after a sufficient time for learning convergence (Fig. 1(a)). Then, we found that all firing rates take the highest value when $r_{\mathrm{IN}} \simeq 0.2$ and they decrease when $r_{\mathrm{IN}} \geq 0.2$. This is because that the increase of the number of inhibitory neurons suppressed the firing of the whole neural network. Next, we investigated the effects of the change in the ratio of inhibitory neurons on the STDP learning. We calculated the average variability of synaptic strength for synapses from inhibitory neurons to excitatory neurons and those from excitatory neurons to excitatory neurons (Fig. 1(b)). If the average variation value is greater than 0, the effect of LTP is stronger than that of LTD, and if less than 0 it means the opposite. In Fig. 1(b), for the synapses from excitatory neurons to inhibitory neurons, the effect of LTP is stronger than that of LTD regardless of the ratio of inhibitory neurons. However, in case of the synapses from excitatory neurons to excitatory neurons, the effect of LTD is superior to that of LTP when r_{IN} takes between 0 and 0.3. When r_{IN} is larger than 0.3, or more, the effect of LTP exceeds the effect of LTD. These results indicate that the STDP learning rule suppresses synapses from excitatory neurons to excitatory neurons. This suppression arises from the fact that LTD has stronger effects than LTP in the STDP learning window[3]. However, this suppression decreases when the number of inhibitory neurons increases.

Furthermore, we analyzed the neural network structures from the viewpoints of complex networks. We calculated weighted directed cluster coefficients with the synaptic strength of the neural network after the STDP learning converged[4] (Fig.1(c)). Three nodes with edges between nodes are considered. The triangle with the cycle structure is evaluated by C_{cyc}. If one node has a structure that mediates between the remaining two nodes, it is C_{mid}. The input structure is evalutated by C_{in}, and the output structure is evaluated by C_{out}. Most of the cluster coefficients did not depend on the ratio. However, only the cluster coefficients C_{cyc} changed, and the minimum value was obtained at $r_{\mathrm{IN}} \simeq 0.2$. This result suggests that the structure formation of the feedforward network by the STDP learning rule may correspond to the activation of neural activities.

In conclusion, we observed firing suppression by inhibitory neurons and the suppression of synaptic strength between excitatory synapses changed by the STDP learning rule. These suppressions depend on the ratio of inhibitory neurons. It is considered that the firing activities of the whole neural network were activated when both suppressions were unlikely to occur. It was also indicated that the feedforward structure emerges but depends on the ratio of inhibitory neurons. These results suggest that such a network structure is relevant to the activation of neural activities. This research is partially supported by the JSPS Grant-in-Aid for Scientific Research (No. 18K18125, 16K16138, 15KT0112 and 17K00348).

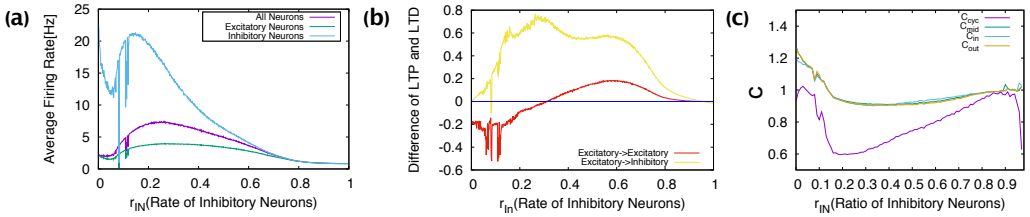

Figure 1: (a) Average firing rates after learning convergence, (b) The average variability of synaptic strength change by LTP and LTD, and (c) the weighted directed cluster coefficients[4] of the neural network after learning convergence, when changing inhibitory neurons ratio.

References

[1] DeFelipe J. and Farinas I., "The pyramidal neuron of the cerebral cortex: morphological and chemical characteristics of the synaptic inputs," *Progress in neurobiology*. Vol. 6, No. 39, pp. 563-607, 1992.
[2] Izhikevich E. M., "Polychronization: computation with spikes." *Neural Computation* Vol. 2, No. 18, pp. 245–282, 2006.
[3] Bi G. Q. and Poo M. M., "Synaptic modifications in cultured hippocampal neurons; dependence on spike timing, synaptic strength, and postsynaptic cell type," *The Journal of Neuroscience*, Vol. 18, No. 8, pp. 10464–10472, 1998.
[4] Fagiolo G., "Clustering in complex directed networks," *Physical Review E*, No. 76, Vol.2, 026107, 2007.

Emergent sequences from recurrent network motifs

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Sequences of neural activity arise in many brain areas, including cortex, hippocampus, and central pattern generator circuits that underlie rhythmic behaviors like locomotion. Moreover, fast sequences during ripple events in hippocampus are believed to be critical for memory processing and cortico-hippocampal communication. While the network architectures supporting sequence generation vary considerably, a common feature is an abundance of inhibition. Roughly speaking, inhibition creates competition among neurons, resulting in a tendency for neurons to take turns reaching peak activity levels and thus to fire in sequence. In particular, inhibition-dominated networks exhibit emergent sequences even in the absence of an obvious chain-like architecture, such as a synfire chain.

In this presentation, we focus on the mechanisms for sequence generation in recurrently-connected networks with inhibition-dominated dynamics but arbitrary architectures. Specifically, we focus on emergent sequences in threshold-linear networks (TLNs), and a tightly-controlled sub-family called combinatorial threshold-linear networks (CTLNs). Such networks naturally give rise to an abundance of sequences, but the relationship of the sequences to the architecture is far from clear. We show that for CTLNs, sequences can be understood in terms of a decomposition into "core" and "peripheral" components, with the core being a network motif that supports a sequential attractor, and the periphery consisting of additional neurons that are recruited by the attractor, and are thus inserted into the core sequence. We develop a number of parameter-independent graph rules to identify and characterize these core motifs. These rules provide a direct link between the structure and function of these networks, and may provide new insights into how connectivity shapes dynamics in real neural circuits.

Shaping chaotic dynamics and signal transmission by single neuron properties in random neural networks

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Cortical neurons exhibit rich dynamics, shaped by the presence of history-dependent biophysical mechanisms such as adaptation over different timescales. In the brain, neurons are embedded in highly recurrent networks, that can be described using random network models. It is known that large random networks with strong connectivity exhibit chaotic dynamics even if single neurons have simple dynamics [SCS88]. This chaotic phase can be quantitatively analyzed using dynamical mean-field theory (DMFT) [SCS88], even in the presence of additional biological constrains [KS15, MO18]. However, these results hold for one-dimensional rate neurons, that cannot capture the richness of cellular mechanisms present in real neurons. How these additional biophysical mechanisms at the level of single-neuron dynamics affect the activity patterns of a recurrent random network is an open question.

We analyze how the dynamical properties of single neurons and recurrent connections interact to shape the effective dynamics in large randomly connected neural networks. We extend DMFT to the case of strongly connected networks of multi-dimensional rate units. Using our theoretical framework, we show that the power spectrum of the network activity in the chaotic phase emerges from a nonlinear sharpening of the frequency response function of single units [MGS18].

As a biologically relevant application of our theoretical framework, we consider two-dimensional rate units with adaptation. We find that a network of such units exhibits a state of "resonant chaos", that corresponds in the mean-field theory to robust, narrow band stochastic oscillations. The coherence of stochastic oscillations is maximal at the onset of chaos and their correlation time increases with the adaptation timescale of single units [MGS18]. Surprisingly, the resonance frequency can be predicted from the properties of isolated units, even in the presence of heterogeneity in the adaptation parameters. Finally, we show that when the network is in this resonant chaotic state, the transmission of weak, low-frequency signals is strongly enhanced by adaptation, whereas signal transmission is not influenced by adaptation in the non-chaotic regime.

Our results can be readily applied to other mechanisms at the level of single nodes, such as synaptic filtering, refractoriness or spike synchronization, and even to infinite-dimensional models, such as rate neurons with power-law adaptation. These results advance our understanding of the interaction between the dynamics of single units and recurrent connectivity, which is a fundamental step toward the description of biologically realistic network models in the brain, or, more generally, networks of other physical or man-made complex dynamical units.

References

[KS15] J. Kadmon and H. Sompolinsky. Transition to chaos in random neuronal networks. *Phys. Rev. X*, 5:041030, 2015.

[MGS18] Samuel P. Muscinelli, Wulfram Gerstner, and Tilo Schwalger. Single neuron properties shape chaotic dynamics in random neural networks. *ArXiv e-prints*, page arXiv:1812.06925, 2018.

[MO18] F. Mastrogiuseppe and S. Ostojic. Linking connectivity, dynamics, and computations in low-rank recurrent neural networks. *Neuron*, 99(3):609 – 623.e29, 2018.

[SCS88] H. Sompolinsky, A. Crisanti, and H. J. Sommers. Chaos in random neural networks. *Physical Review Letters*, 61(3):259–262, 1988.

Stochastic spike-diffuse-spike model of propagation in randomly demyelinated nerves

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We present a novel theoretical and computational framework for assessing the effects of demyelination on axonal transmission. The stochastic spike-diffuse-spike (SSDS) model describes the stochastic saltatory conduction along axons with random demyelination. It models transmission through nodal and internodal compartments with two types of operations: a stochastic integrate-and-fire operation models nodal excitability, and a linear filtering operation based on a Green's function approach models internodal propagation. The effects of demyelinated segments on the probability of transmission, transmission delay and spike time jitter are investigated in this framework. In addition, we model sodium channel remodeling as a homeostatic control of nodal excitability. We find that the effects of mild demyelination on transmission probability and delay can be largely counterbalanced by an increase of the density of sodium channels at the nodes surrounding the demyelination. The spike timing jitter, however, reflects the level of demyelination regardless of whether sodium channel densities are fixed or are allowed to change in compensation. This jitter can accumulate over long axons and leads to a broadening of the compound action potential, linking microscopic defects to a mesoscopic observable. The method can also be used to link images of demyelinated tissue obtained e.g. through nonlinear microscopy to scores of nerve functionality, providing a new tool to investigate the elusive relation between pathology and function in diseases such as MS.

Clusters in nonsmooth oscillator networks

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For coupled oscillator networks with Laplacian coupling, the master stability function (MSF) has proven a particularly powerful tool for assessing the stability of the synchronous state. Using tools from group theory, this approach has recently been extended to treat more general cluster states. However, the MSF and its generalizations require the determination of a set of Floquet multipliers from variational equations obtained by linearization around a periodic orbit. Since closed form solutions for periodic orbits are invariably hard to come by, the framework is often explored using numerical techniques. Here, we show that further insight into network dynamics can be obtained by focusing on piecewise linear (PWL) oscillator models. Not only do these allow for the explicit construction of periodic orbits, their variational analysis can also be explicitly performed. The price for adopting such nonsmooth systems is that many of the notions from smooth dynamical systems, and in particular linear stability, need to be modified to take into account possible jumps in the components of Jacobians. This is naturally accommodated with the use of saltation matrices. By augmenting the variational approach for studying smooth dynamical systems with such matrices we show that, for a wide variety of networks that have been used as models of biological systems, cluster states can be explicitly investigated. By way of illustration, we analyze an integrate-and-fire network model with event-driven synaptic coupling as well as a diffusively coupled network built from planar PWL nodes, including a reduction of the popular Morris-Lecar neuron model. We use these examples to emphasize that the stability of network cluster states can depend as much on the choice of single node dynamics as it does on the form of network structural connectivity. Importantly, the procedure that we present here, for understanding cluster synchronization in networks, is valid for a wide variety of systems in biology, physics, and engineering that can be described by PWL oscillators.

References

[1] R. Nicks, L. Chambon and S. Coombes. Clusters in nonsmooth oscillator networks, *Phys Rev E.* 97: 032213, 2018.

Is the hippocampus timing truly a population-based endeavor?

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For over four decades we have known and used the fact that the hippocampus has specialized "place cells" that seem to ramp-up their firing when the subject is in a specific spatial location [1]. While spatial and temporal dimensions are related, it has been about a decade since we learned that hippocampus also has "time cells" that seem to ramp-up their firing when the subject is at a specific temporal marker in a behavioral test [2]. Single-cell recordings from hippocampus showed that the firing rate of the time cells correlates with the to-be-timed duration [3]. They found that an entire population of hippocampus time cells span the to-be-timed duration and time cells selectively and repeatably peak at specific moments during the to-be-timed duration [3]. Among other properties, the spread of the firing interval, i.e. the width of the Gaussian-like activity, for each time cell is proportional to the time of the peak activity. Although such a linear relationship between the the estimation error and the to-be-timed duration has been know for decades in behavioral neuroscience as the scalar property of timing [4, 5], these new since-cell recordings [3, 2] suggest a possible cellular-level origin of scalar timing.

This study focuses on the mathematical modeling interval timing starting with a population of hippocampal time cells and a dynamic learning rule [6, 7]. We hypothesized that during the reinforcement trials the subject learns the "boundaries" of the temporal duration. The envisioned mechanism is similar to "place cells" learning the spatial boundaries of the environment during the exploratory phase of the trials [1]. Once the temporal boundaries of the behavioral experiment are learned a population of time cells is recruited and coverers the entire to-be-timed duration. At this stage, the population of time cells simply produces a uniform average time field since all time cells contribute equally to the average. We hypothesized that dopamine could modulate the activity of time cells during reinforcement trials by enhancing/depressed their activity. A possible neurobiological structure involved in strengthen/weaken the weights associated to individual time cells could be attributed to striatum, which is known to serve as a coincidence detector. Therefore, the striatum could selectively enhance the activity of time cells that peak close to the to-be-timed duration and depress others, producing a Gaussian-like average time field. Our numerical simulations of the model re in agreement with the behavioral experiments.

References

[1] O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology* 51, 78 – 109.

[2] Pastalkova, E., Itskov, V., Amarasingham, A., and Buzsaki, G. (2008). Internally generated cell assembly sequences in the rat hippocampus. *Science* 321, 1322–1327.

[3] MacDonald, C. J., Lepage, K. Q., Eden, U. T., and Eichenbaum, H. (2011). Hippocampal time cells bridge the gap in memory for discontiguous events. *Neuron* 71, 737–749.

[4] W. H. Meck, R. M. Church, and D. S. Olton. Hippocampus, time, and memory. *Behavioral Neuroscience*, 98(1):3–22, 1984.

[5] Gibbon, J. and Allan, L. (1984). Time perception - introduction. *Annals of the New York Academy of Sciences* 423

[6] Sorinel A. Oprisan, Tristan Aft, Mona Buhusi, and Catalin V. Buhusi. Scalar timing in memory: A temporal map in the hippocampus. *Journal of Theoretical Biology*, 438:133 – 142, 2018.

[7] Sorinel A. Oprisan, Mona Buhusi, and Catalin V. Buhusi. A Population-Based Model of the Temporal Memory in the Hippocampus. *Front Neurosci*, 12:521, 2018.

Is empirical mode decomposition better than delay embedding for analyzing optogenetic data?

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Optogenetically evoked local field potentials (LFPs) were recorded from the medial prefrontal cortex (mPFC) of male PV-Cre mice (B6; 129P2 - Pval$^{btm1(Cre)Arbr/J}$ Jackson Laboratory (Bar Harbor, ME, USA) infected with the viral vector (AAV2/5. EF1a. DIO. hChR2(H134R) - EYFP. WPRE. hGH, Penn Vector Core, University of Pennsylvania) [1]. We recorded multiple basal conditions followed by a systemic injection with D1 receptors antagonist SCH23390 and/or D2 antagonist sulpiride. Optical stimulation was provided by a blue laser (473 nm) stimulus delivered to mPFC through a fiber optic every 2 seconds and each trial was repeated 100 times [2, 3]. As in the previous study, we used a surrogate data method to check that nonlinearity is present in the experimental LFPs and only used the last 1.5 seconds of steady activity to measure the LFPs phase resetting induced by the brief 10 ms light stimulus. The extracellular signals were sampled at 10 kHz and stored for offline analysis.

In this study, we compared the results obtained by using the traditional nonlinear dynamics approach, i.e. delay embedding of one-dimensional data (time series) of the membrane potential [2, 3], to the empirical mode decomposition (EMD) or Hilbert-Huang transform [4]. While delay embedding is a reliable method for identifying nonlinear structures of stationary times series, biophysically relevant time series are often (a) too short (b) non-stationary, and (c) the data represent nonlinear processes. The EMD extracts intrinsic mode functions (IMFs) from the original time series based on smooth envelopes defined by local maxima and minima of the sequence. The first iMF is the difference between the original time series and the mean of these envelopes. The same algorithm is applied then to the first IMF to find the second IMF, and so on. We compared the phase resetting determined using the delay embedding dendrogam against the Hilbert transform of IMFs and found a good agreement between the two methods. At the same time, we identified limitations of the delay embedding due to a too short time series that could be addressed using EMD method.

References

[1] JE Dilgen, T Tompa, S Saggu, T Naselaris, and A Lavin. Optogenetically evoked gamma oscillations are disturbed by cocaine administration. *Frontiers in Cellular Neuroscience*, 7:213, 2013.

[2] Sorinel A. Oprisan, Patrick E. Lynn, Tamas Tompa, and Antonieta Lavin. Low-dimensional attractor for neural activity from local field potentials in optogenetic mice. *Frontiers in Computational Neuroscience*, 9:125, 2015.

[3] Sorinel A. Oprisan, J. Imperatore, J. Helms, Tamas Tompa, and Antonieta Lavin. Cocaine-induced changes in low-dimensional attractors of local field potentials in optogenetic mice. *Frontiers in Computational Neuroscience*, 12:1, 2018.

[4] Huang N. E., Shen Z., Long S. R., Wu M. C., Shih H. H., Zheng Q., Yen N. C., Tung C. C., Liu H. H. The Empirical Mode Decomposition and the Hilbert Spectrum for Nonlinear and Nonstationary Time Series Analysis. *Proceedings of the Royal Society of London A*, 454: 903?995, 1998.

Synfire Chain-Like Activity Underlies Swimming and Turning of the Scyphozoan Jellyfish *Aurelia aurita*

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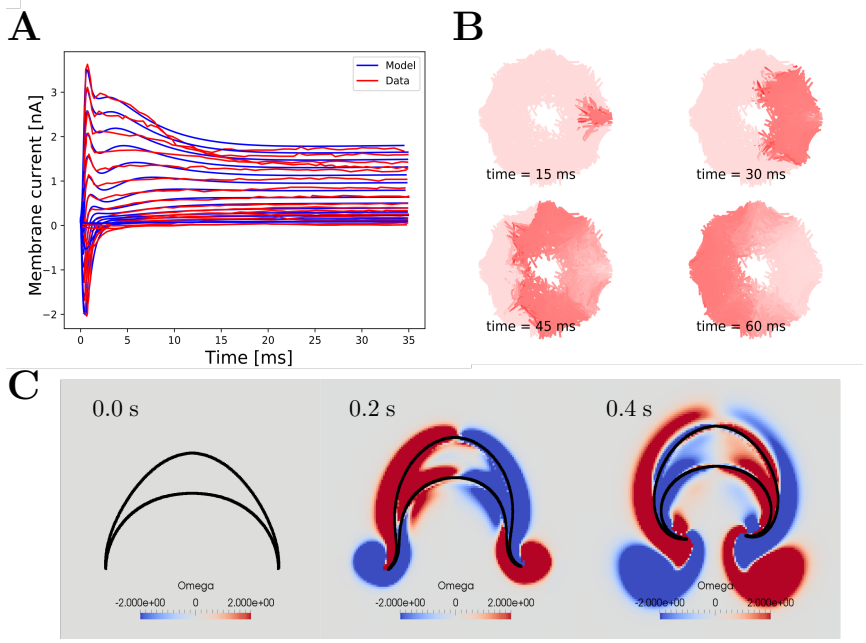
Understanding how biophysical properties of single neurons give rise to emergent network behavior is an important goal in theoretical neuroscience. Such a link between single neuron dynamics and functional biological networks is often hard to establish, yet crucial to understand how nervous systems enable organisms to survive in their natural environment and ultimately shape behavior and cognition. Here, we present a biophysically realistic bottom-up computational model of the nervous system of a scyphozoan jellyfish. We use voltage-clamp data [1] to fit Hodgkin-Huxley type neurons. Based on key structural features we further build a model of the two nerve nets in charge of motor control. From simulations of the resulting nerve nets we can extract the muscle activity during swimming with high spatial and temporal resolution. We then use the immersed boundary method to simulate the fluid interactions of the jellyfish swimming motion in 2D. We find that the distribution of neurons in the scyphozoan nerve net is optimized to conduct excitation waves across the jellyfish bell and prove that upon stimulation, the excitation travels in a synfire chain-like manner through the nerve net such that every neuron fires exactly once. After coupling a muscle model to the spiking activity, experimentally observed features of the swimming motion emerge simply from the structure of the nerve net. In addition to the first nerve net-based simulation of the jellyfish turning mechanism, we find a potential alternative turning mechanism that increases the level of control on the swimming motion of the animal. Our model suggests that the jellyfish is able to fine-tune its swimming motion by precisely timed activation of its two nerve nets. Since the nervous system of jellyfish is thought to represent an evolutionary ancestral state, this model can not only be used to further investigate the nervous system of one of the simplest neuron-bearing animals but also to advance our understanding of the evolutionary origins of nervous systems.



A: Biophysical neuron model fitted to the voltage-clamp data. The model (blue) follows the data (red) described in [1] where clamping ranged from -20 mV to +90 mV with a step size of 7.5 mV.
B: Time series of an MNN pulse with 2000 neurons. The activity of each neuron at different times after the stimulation of a single pacemaker neuron. Color level indicates the voltage of the neuron.
C: A swimming stroke after an MNN pulse with 2000 neurons. The MNN is activated at the left bell margin. Color indicates vorticity, where red indicates a clockwise eddy and blue an anticlockwise eddy.

References

[1] P.A.V. Anderson. Ionic currents of the Scyphozoan *In: Evolution of the First Nervous Systems, Springer;* pp. 267-280, 1989

Homoclinic organization in fold/hom bursters: the Hindmarsh-Rose model

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Mathematical neuroscience has a significant role nowadays. To understand how an incredibly sophisticated system such as the brain works, a natural first step is to achieve a better understanding of the dynamics of neurons, its basic units. One of the relevant phenomena that can be found in many neurons is *bursting*, that is, the alternation between periods of spiking and periods of quiescence, which is usually modeled using fast-slow systems. When a neuron goes from producing n spikes per burst to producing $n+1$, we talk about the process of spike-adding. We are interested in studying this spike-adding process and its relationship with the bifurcation diagram of the system. Since [1], it is known that if the process is continuous, to gain one spike, a periodic orbit needs to pass through two fold bifurcations. Between them, the orbit grows via a canard mechanism. In [2, 3] it has been shown that in the Hindmarsh-Rose model (a typical model of fold/homoclinic bursting) the fold bifurcations have their origin in degenerated homoclinic connections (of codimension two). The intricate homoclinic bifurcation diagram has been studied in [4] in a three-parametric context. In [5] we are trying to determine the exact relationship between the bifurcation surfaces of periodic orbits (responsible of the spike-adding process) with the homoclinic codimension-two curves, since there are different scenarios that could be possible.

References

[1] Terman, D. Chaotic spikes arising from a model of bursting in excitable membranes, *SIAM J. Appl. Math.*, 51 (5), pp. 1418–1450, 1991.

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

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

[4] R. Barrio, S. Ibáñez, L. Pérez. Homoclinic organazation in fold/hom bursters: the Hindmarsh-Rose model. *Preprint*, 2019.

[5] R. Barrio, S. Ibáñez, L. Pérez, S. Serrano. Homoclinic structure in spike-adding process in fold/hom bursters. *Preprint*, 2019.

The Numerical Solution of Neural Field Models Posed on Realistic Cortical Domains

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In this work we show how neural field equations (NFEs) [1] can be solved numerically on arbitrary geometries. We explore the numerical schemes required for the solution of NFEs of the form

$$\frac{\partial}{\partial t}u\left(\boldsymbol{x},t\right)=-u\left(\boldsymbol{x},t\right)+\int_{\Omega}W\left(\boldsymbol{x},\boldsymbol{x}'\right)f\left(u\left(\boldsymbol{x}',t\right)\right)dm\left(\boldsymbol{x}'\right), \tag{1}$$

where Ω is a 2-manifold in $\mathbb{R}^3$, modelling a realistic cortex, including gyri and sulci. Here u represents cortical activity, W is an arbitrary connectivity kernel, and f is a typically sigmoidal firing rate function. The integral is a surface integral over Ω. We discretise the domain to obtain a system of ordinary differential equations using the Nyström method. This method works by applying a quadrature rule to the integral and choosing the quadrature nodes to coincide with the spatial collocation nodes of (1). The Human Connectome Project (HCP) [5] has a large collection of data available which we have incorporated into the NFE. This includes real strucural connectivity estimates collected from a number of subjects, as well as the cortical domain meshes.

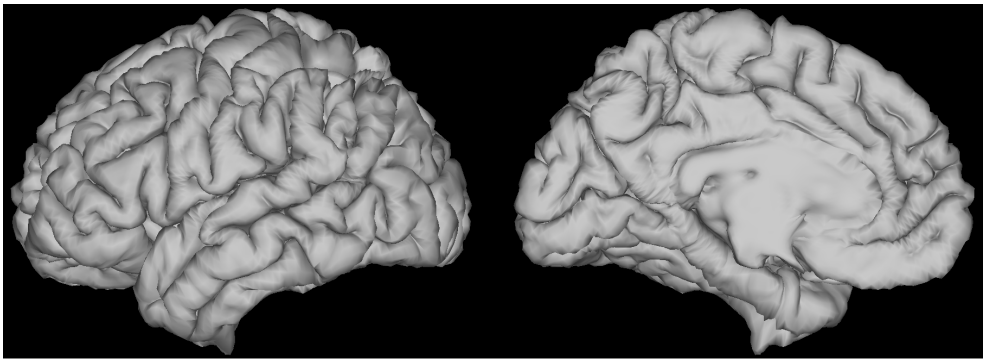

Figure 1: Example cortical surface mesh for the left hemisphere of the brain.

Due to the highly heterogeneous nature of the problem posed with the HCP data, analytic solutions are unavailable. We shall, however, present some convergence results for the numerics for domains in $\mathbb{R}^1$ and $\mathbb{R}^2$ [3]. We will also present preliminary results for the incorporation of delays into the equations and the numerical techniques required to solve delay NFEs. We have developed a delay differential equation (DDE) solver that combines an adaptive Runge-Kutta 3(2) timestepper with a 3rd order Hermite interpolant [2, 4].

[1] S. Coombes, P. beim Graben, R. Potthast, and J. Wright. *Neural fields: theory and applications*. Springer, 2014.

[2] E. Hairer, S. P. Norsett, and G. Wanner. Solving ordinary differential equations I, computational mathematics, vol. 8, 1987.

[3] P. M. Lima and E. Buckwar. Numerical solution of the neural field equation in the two-dimensional case. *SIAM Journal on Scientific Computing*, 37(6):B962–B979, 2015.

[4] E. Süli and D. F. Mayers. *An Introduction to Numerical Analysis*. Cambridge University Press, 2003.

[5] D. C. Van Essen, K. Ugurbil, E. Auerbach, D. Barch, T. E. J. Behrens, R. Bucholz, A. Chang, L. Chen, M. Corbetta, S. W. Curtiss, et al. The Human Connectome Project: a data acquisition perspective. *Neuroimage*, 62(4):2222–2231, 2012.

Neuronal firing rate models with electrical and chemical synapses

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Firing rate models are powerful tools for the analysis of the collective dynamics of networks of spiking neurons. Within such a network, the principle communication channels between neurons comprise chemical and electrical synapses the latter are also referred to as gap junctions. Despite a recent increase in interest, the effect of gap junctions on a networks dynamics remains poorly understood. Starting from a heterogeneous network of quadratic integrate-and-fire neurons that include both types of synapses, we derive a concise firing rate model. This model is exactly solvable and allows, in particular, to analytically prove the relevance of gap junctions to synchronization and collective oscillations. In addition, we can disentangle the complementary roles of chemical and electrical coupling in shaping the collective dynamics of networks of spiking neurons.

Dissecting Molecular Contributions to Interspike Interval Variability in Conductance-Based Neural Models via Stochastic Shielding

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Current fluctuations arising from randomly gated ion channels provide an important source of dynamical variability, at the level of single neurons. Exact Markov Chain (MC) simulations are the gold standard for numerical simulations of stochastic conductance based models (SCBMs), but can be prohibitively costly for multi-state channel models or large channel populations[1]. Several authors have proposed Langevin stochastic differential equation (SDE) models to approximate MC models for SCBMs, e.g. for stochastic Hodgkin-Huxley (HH) kinetics[2–11]. Meanwhile, Schmandt and Galán[12] introduced the stochastic shielding (SS) approximation as an efficient and accurate method for approximating SCBMs. The SS method exploits the observability structure of the ion channel process to selectively neglect noise generated by "hidden" ion channel state transitions that do not change the channel conductance. Thus, rather than aggregating ion channel states, SS effects dimension reduction by selectively eliminating those independent noise sources that have the least impact on current fluctuations[13;14].

In this contribution, we report two main results. First, we establish pathwise equivalency among a family of Langevin SCBMs that includes most previously proposed models[2–4;6–11], including the alternative formulation given in Fox's recent critique of the earlier Fox-Lu model[5]. Within this class of Langevin models, we identify a 14-dimensional version of the HH-model with a particularly simple SDE structure, for which stochastic shielding can be easily applied. As our second main contribution, we show analytically that the variance of the interspike interval (ISI) for the stochastic 14-D HH model can be decomposed into a sum of contributions from individual channels and molecular channel state transitions, in the limit of small noise (large system size limit). We establish this decomposition through a perturbation analysis, and support it through numerical simulations. Previous analysis of stochastic shielding was restricted to the voltage-clamp scenario[13;14], in which the ion channel process is Markovian. Under current clamp conditions, the channel state fluctuations, current fluctuations, and voltage fluctuations are mutually interdependent. Therefore, the contribution of each directed edge to the variance of the ISI cannot be directly inferred from its contribution under voltage clamp. Our new analysis quantifies the relative contributions of individual ion channel state transitions to ISI variability, and shows that the edges making the largest contribution to current fluctuations under voltage clamp do not necessarily make the greatest contribution to ISI variance under current clamp, and vice-versa.

References

[1] Anderson, D. F, Ermentrout, B. and Thomas, P. J. (2015). *J. Comput. Neurosci*, 38(1):67–82.

[2] Dangerfield, C. E., Kay, D., and Burrage, K. (2012). *Phys. Rev. E*, 85(5):051907.

[3] Fox and Lu (1994). *Phys. Rev. E*, 49(4):3421–3431.

[4] Fox, R. F. (1997). *Biophys. J*, 72(5):2068–2074.

[5] Fox, R. F. (2018). *arXiv preprint arXiv:1807.07632*.

[6] Goldwyn, J. H. and Shea-Brown, E. (2011). *PLoS Comput. Biol*, 7(11):e1002247.

[7] Güler, M. (2013). *Neural Computation*, 25(1):46–74.

[8] Huang, Y., Rüdiger, S., and Shuai, J. (2013). *Phys. Rev. E*, 87(1):012716.

[9] Linaro, D., Storace, M., and Giugliano, M. (2011). *PLoS Comput. Biol*, 7(3):e1001102.

[10] Orio, P. and Soudry, D. (2012). *PLoS One*, 7(5):e36670.

[11] Pezo, D., Soudry, D., and Orio, P. (2014). *Front. Comput. Neurosci*, 8:139.

[12] Schmandt, N. T. and Galán, R. F. (2012). *Phys. Rev. Lett*, 109(11):118101.

[13] Schmidt, D. R., and Thomas P. J. (2014) *J. Math. Neurosci*, 4(1):6

[14] Schmidt, D. R., Galán, R. F., and Thomas, P. J. (2018). *PLoS Comput. Biol*, 14(6):e1006206.

Age Dependent Hawkes Process

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In the last decade, Hawkes processes have received a lot of attention as good models for functional connectivity in neural spiking networks. In this paper we consider a variant of this process; the Age Dependent Hawkes process, which incorporates individual post-jump behaviour into the framework of the usual Hawkes model. This allows to model recovery properties such as refractory periods, where the effects of the network are momentarily being suppressed or altered. We show how classical stability results for Hawkes processes can be improved by introducing age into the system. In particular, we neither need to a priori bound the intensities nor to impose any conditions on the Lipschitz constants. When the interactions between neurons are of mean field type, we study large network limits and establish the propagation of chaos property of the system.

References

[1] Mads Bonde Raad, Susanne Ditlevsen and Eva Löcherbach. Age dependent Hawkes process, arXiv:1806.06370, 2018.

Predicting dynamics from hardwiring in canonical low-dimensional coupled networks

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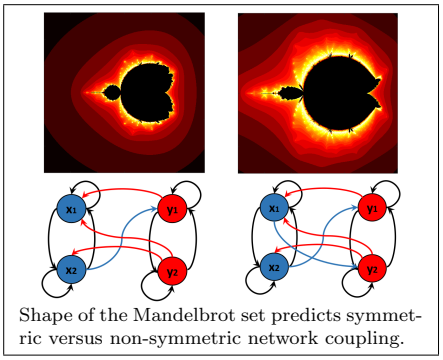
A point of great interest in computational neuroscience has been to explain how the hardwired *structure* of a network (such as the brain) affects its temporal *function*. The question has crucial applications and has earned its own subfield of study (currently known as "dynomics"). However, the task of translating connectivity patterns to ensemble temporal behavior presents the difficulty of simultaneously addressing the complexity of the graph and the richness of the coupled dynamics. This may be computationally intractable, even for relatively small network sizes and for reduced models of node-wise neural dynamics.To shed light on this relationship, a recent strategy has been to investigate it in basic theoretical models, where one may more easily identify and pair specific structural patterns to their effects on dynamics. For example, in threshold linear networks (TLN), complex ensemble behavior emerges from simple, almost linear node-wise dynamics. This makes it feasible to identify relationships between specific configurations and corresponding dynamic patterns [1]. While this represents remarkable progress, it would be important to establish whether this type of predictive analysis can be applied to other classes of models.

We use quadratic maps as a canonical way to model a neural response function in each of the network nodes. In this case, one can conveniently use the system's asymptotic (Julia and Mandelbrot) sets to calculate, visualize and interpret the long-term behavior of the system (in both phase and parameter spaces, with the network structure acting as a bifurcation parameter [2, 3]). The advantage is that of using clear topological markers (e.g., connectedness of a set) as the signature for the global dynamics of the system, amenable for prediction and classification. For example, we were able to identify an optimal parameter locus for which configurations which have identical Julia sets for one node-wise function (determined by the parameter c) do so for all c. This suggests means to produce robust classifications of ensemble behavior based entirely on the network architecture, independently on the node-wise dynamics (described by c). In this scenario, it is sufficient for the network to know in advance which hardwired structure is most effective to use in order to obtain a desired effect or avoid another, and then it can plastically modify its structure on a continuous basis, adapting online to new behavioral requirements.



Shape of the Mandelbrot set predicts symmetric versus non-symmetric network coupling.

We compare our results with those in other simplified models, proposing that some aspects may be universal to nonlinear networks, and hence could be further applied to physiological models with more complex dynamics. By the intrinsic properties of the quadratic node-wise dynamics, as well as by the nature of the methods and measures used in conjunction with these dynamics, our approach is fundamentally different from those being currently used to address other network types. One of our main directions of interest is to investigate how our results compare with predictions and classifications in other small networks with basic node dynamics. To fix our ideas, we will look at classification of attractor sets in threshold linear networks (studied by Curto et. al [1]) and at synchronization and clustering in inhibitory Hodgkin-Huxley neuronal networks (studied by Rinzel [4]). In each case, we will use the appropriate measures of synchronization and stability to assess and classify long-term dynamics; then we will check if there is any overlap (universality) in these classifications.

References

[1] C. Curto, K. Morrison. Pattern completion in symmetric Threshold-Linear Networks, *Neural Computation* 28 (12) pp. 2825–2852, 2016.

[2] A. Rădulescu, A. Pignatelli. Real and complex behavior for networks of coupled logistic maps, *Nonlinear Dynamics*, 87(2) 12951313, 2017.

[3] A. Rădulescu, S. Evans. Asymptotic sets in networks of coupled quadratic nodes, *Journal of Complex Networks*, 2018.

[4] D. Golomb, J. Rinzel. Clustering in globally coupled inhibitory neurons, *Physica D: Nonlinear Phenomena* 72 (3) pp. 259–282, 1994.

Geometry-based estimates of glutamate transporter density in astrocytes

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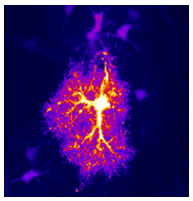
Glutamate is the main excitatory neurotransmitter released in the brain. Its removal from the extracellular space is important to terminate synaptic transmission between neurons, and prevent build-up of neurotoxicity. The removal process is intermediated by non-neuronal cells called astrocytes. These take in the excess extracellular glutamate via tiny cross-membrane transporters densely expressed in the wall of the cell membrane. To understand their impact on neurotransmission efficiency, one needs to estimate the density of transporters for an average astrocyte [1, 2].

Existing computations are based on simplifying assumptions of spherical cellular shape. However, the actual, 3-dimensional fractal geometry of a typical astrocyte may drastically reduce this number, due to the rigidity implied by the condition that transporters cannot collide with each other. We use a geometric modeling argument, based on the known crystal structure of the transporter, to study how the structural complexity of astrocytic processes influences the surface density of transporters. Making only basic simplifying assumptions of regularity and symmetry for the cell geometry, we consider a cell model built around a spherical soma, surrounded by a three-dimensional branching tree. The geometry of the branching processes follows certain spatial restrictions, and the length and diameter of the branches depend on their position in the tree (e.g., generational distance from the soma). The transporters can be well approximated to have prismatic shape, with an equilateral triangular base. Using a combination of trigonometry and a variety of traditional and new integration algorithms, we compute the number and fraction of the cellular membrane occupied by transporters, under the geometric constraint that the intra-cellular ends of the transporters cannot meet.



We compare our results to existing empirically-based estimates based on assumptions of simpler geometry, and we discuss the significance of the improvement that geometrically-informed estimated may bring to the field. We use Monte Carlo reaction-diffusion simulations to determine whether our theoretical estimates challenge our knowledge of how glutamate transporters shape efficiency of synaptic transmission.

References

[1] J.S. Diamond. Deriving the glutamate clearance time course from transporter currents in CA1 hippocampal astrocytes: transmitter uptake gets faster during development. *The Journal of Neuroscience*, 25(11) 2906-2916, 2005.

[2] A. Scimemi et al. Neuronal transporters regulate glutamate clearance, NMDA receptor activation, and synaptic plasticity in the hippocampus. *The Journal of Neuroscience*, 29(46) 14581-14595, 2009.

Periodic forcing of auditory bistability: modelling and experiments

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The auditory streaming paradigm (van Noorden 1975), in which alternating high- A and low-frequency tones B appear in a repeating ABA- pattern, has been shown to be perceptually bistable [1] for extended presentations (order of minutes). For a fixed, repeating stimulus, perception spontaneously changes at random times between an integrated interpretation with a galloping rhythm and segregated streams, switching every 2–8 s. However, streaming in a natural auditory environment requires segregation of auditory objects with features that evolve over time. With the relatively idealized ABA- triplet paradigm, we begin to explore switching in a non-static environment, by considering slowly and periodically varying stimulus features.

Our recent study introduced the first neuromechanistic competition model of auditory bistability [2], capturing the dynamics of alternations in a system of stochastic differential equations. Our model departs from idealizations, common for perceptual rivalry models, with percept-based inputs. It uses dynamic inputs that directly link to sensory features as represented by the neuronal responses of pre-competition stages: inputs based on electrophysiologically-recorded primary auditory cortex (A1) responses to interleaved A and B tones (Micheyl et al 2005). The work was recently extended to account for build-up (early bias towards integration) and the effects of stimulus interruptions and perturbations [3].

Exploration of periodically modulated stimuli in the model lead to the following predictions: 1) switches into segregated (integrated) occur on the DF upswing (downswing), with most switches occurring before the maximal (minimum) DF values 2) stronger entrainment occurs when the DF modulation rate matches the percept durations from the unmodulated case. Fig 1A shows the DF modulation profile and Fig 1B shows the predicted timing of switches into segregated (red) occurring before the peak in DF and into integrated before the trough. Our experimental data confirm these predictions and show that perceptual switches are entrained to the periodically modulated stimulus.

We have demonstrated perceptual entrainment for slowly varying stimuli, which carries practical implications for future auditory bistability experiments with human listeners and animal models. Our results add weight to support auditory bistability as a noise-driven bistable system. In contrast with similar experiments and modelling of binocular rivalry [4, 5], we see less prominent resonance peaks, which can be explained by larger subject-to-subject variability for auditory bistability. Knowledge of the likely perceptual state as dependent on instantaneous phase could allow for performance of human participants in other tasks to be measured with a time-locked a priori expectation of their perceptual state. This knowledge could prove useful for animal models where invasive recording is possible, but objective measures of perception are limited [6].

References

[1] D Pressnitzer and JM Hupé. Temporal dynamics of auditory and visual bistability reveal common principles of perceptual organization. *Curr Biol*, 16(13):1351–1357, 2006.

[2] J Rankin, E Sussman, and J Rinzel. Neuromechanistic model of auditory bistability. *PLOS Comput Biol*, 11(11):e1004555, 2015.

[3] J Rankin, PJ Osborn Popp, and J Rinzel. Stimulus Pauses and Perturbations Differentially Delay or Promote the Segregation of Auditory Objects: Psychoacoustics and Modeling. *Front Neurosci*, 11, 2017.

[4] M Riani and E Simonotto. Stochastic resonance in the perceptual interpretation of ambiguous figures: A neural network model. *Phys Rev Lett*, 72(19):3120, 1994.

[5] Yee-Joon Kim, Marcia Grabowecky, and Satoru Suzuki. Stochastic resonance in binocular rivalry. *Vision Res*, 46(3):392–406, 2006.

[6] Kate L Christison-Lagay and Yale E Cohen. Behavioral correlates of auditory streaming in rhesus macaques. *Hear Res*, 309:17–25, 2014.

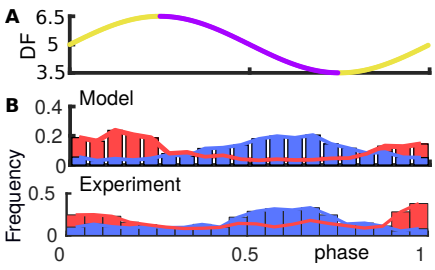

Figure 1: **A**: Shows one cycle of frequency difference (DF) modulation between 3.5 and 6.5 semitones with the phase normalised to the interval [0,1] (stimuli were periodically modulated about the equidominance condition DF=5. Increasing phase is yellow, decreasing purple. Period of modulation was 10 s, which is roughly double the intrinsic perceptual duration of 5 s with fixed DF=5). **B**: Phase-histogram of times of switches from integrated to segregated (red) and from segregated to integrated (blue) from model and experiment with $N = 7$ participants.

A stochastic model of postsynaptic plasticity based on dendritic spine Ca^{2+} downstream proteins

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Dendritic spines are protrusions in neuron arbor and the main hub in neuron-to-neuron excitatory communication, a small structure regulating our brain activity lasting from few milliseconds to a lifetime. The current standpoint on synaptic plasticity, called calcium hypothesis (CH), targets the calcium dynamics as the main factor determining the plasticity observed in dendritic spines. The hypothesis claims the high influx of post-synaptic calcium leads to long-term potentiation (LTP), whereas moderate levels lead to long-term depression (LTD). Against that, calcium imaging and paired stimulation protocols - spike-time-dependent plasticity (STDP) - applied to hippocampal synapses reveal that plasticity outcomes can significantly differ even under a similar level of calcium (1). This experiment suggesting a CH flaw inspired us to seek for additional means by which the plasticity mechanisms embedded in the dendritic spines are able to decode the calcium signal. Here, we design a biophysical model of dendritic spine able to reproduce the calcium observed experimentally and to predict synaptic plasticity by merging data obtained by fluorescence studies in electrophysiology and calcium downstream proteins (CDP).

Previous models attempted to capture the dynamics of calcium to understand the plasticity in the neuronal response to stimuli. Jdrzejewski-Szmek et al. (2) proposed a plasticity model using calcium location, but for a limited number of STDP protocols applied to dopaminergic striatum neurons. They approach the calcium mechanisms zoo and its diffusion in the whole neuron, however, do not explore complex firing patterns containing more than a single BAp and EPSP. Graupner and Brunel (3) proposed a model able to reproduce the post-synaptic calcium in complex firing patterns. Their plasticity prediction uses the outcome calcium to emulate a simplified version of CDP, however adding to the calcium a single external noise neglecting the multiple sources experienced by the dendritic spines. Our model simulates the stochasticity of each calcium source in order to investigate how the spines deal with the noise build-up, also how they generate the plasticity in the STDP experiment recently used to suggest CH flaws (1).

Integration of excitatory post-synaptic potential (EPSP) and back-propagated action potential (BAp) modifies the synaptic strength and response to a new stimulus due to changes in the dendritic spines. To model it we describe its interaction with the fundamental blocks of STDP. Glutamate neurotransmitter released by synaptic vesicles generate the EPSP, our model incorporates effects of AMPA and NMDA structure to reproduce the voltage and calcium rise in the spine. Sent by the soma the BAp is sensed mainly by the voltage-sensitive calcium channels (VGCC) with its few units adding noise. Additionally, our model incorporates short-term plasticity (STP) mechanisms to model the adaption caused by vesicle depletion, back-propagation decay, and channel/receptor desensitization. Different time scales adaptations ultimately will produce a specific calcium signal interacting with the CDP reactions. Our CDP model uses dynamics from CaN and CaMKII which lately had its behavior associated respectively with LTD and LTP (4). Mapping the activity of such proteins allow us to observe that similar calcium profiles can generate different outcomes of protein activity. This effect was used to predict plasticity changes and was anticipated by Fuji et al. that CaN and CaMKII are non-linear filters of the firing patterns in the neuronal level (4).

References

[1] C. M. Tigaret, V. Olivo, J. H.L.P. Sadowski, M. C. Ashby, and J.R. Mellor. Coordinated activation of distinct Ca^{2+} sources and metabotropic glutamate receptors encodes Hebbian synaptic plasticity, *Nature communications*, 2016.

[2] J. JdrzejewskaSzmek, S. Damodaran,D. B. Dorman and K. T. Blackwell. Calcium dynamics predict direction of synaptic plasticity in striatal spiny projection neurons, *European Journal of Neuroscience, 45(8), 1044-1056*, 2017.

[3] M. Graupner and N. Brunel. Calcium-based plasticity model explains sensitivity of synaptic changes to spike pattern, rate, and dendritic location. *Proceedings of the National Academy of Sciences*, 2012.

[4] H. Fujii, M. Inoue, H. Okuno, Y. Sano, S. Takemoto-Kimura, K. Kitamura, M. Kano and H. Bito, Nonlinear decoding and asymmetric representation of neuronal input information by CaMKII and calcineurin. *Cell reports* 2013.

Spike-timing-dependent plasticity effect on the patterns of neural synchrony

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Synchronization of neural activity has been associated with several neural functions. Abnormalities of neural synchrony may underlie different neurological and neuropsychiatric diseases. Neural synchrony in the brain at rest is usually very variable and intermittent. Experimental studies of neural synchrony in different neural systems report a feature, which appears to be universal: the intervals of desynchronized activity are predominantly very short (although they may be more or less numerous, which affects average synchrony) [1,2,3]. This kind of short desynchronization dynamics was conjectured to potentially facilitate efficient creation and break-up of functional synchronized neural assemblies.

Cellular, synaptic, and network mechanisms of the short desynchronizations dynamics are not yet understood. In this study we use computational neuroscience methods to investigate the effects of spike-timing-dependent plasticity (STDP) on the temporal patterns of synchronization. We employed a small network of conductance-based model neurons mutually connected via excitatory STDP synapses. The dynamics of this model network was subjected to the time-series analysis methods used in prior experimental studies.

We found that STDP is able to alter synchronized dynamics in the network in several ways depending on the time-scale of action of plasticity. However, in general, the action of STDP tends to promote dynamics with short desynchronizations (i.e. dynamics similar to those observed in prior experiments). Complex interplay of the cellular and synaptic dynamics may lead to the activity-dependent adjustment of synaptic strength in such a way as to facilitate short desynchronizations in the activity of weakly coupled intermittently synchronized neurons.

References

[1] S. Ahn, L.L. Rubchinsky. Short desynchronization episodes prevail in the synchronous dynamics of human brain rhythms, *Chaos* 23 p. 013138, 2013.

[2] S. Ahn, L.L. Rubchinsky, C.C. Lapish. Dynamical reorganization of synchronous activity patterns in prefrontal cortex - hippocampus networks during behavioral sensitization, *Cerebral Cortex* 24 pp. 2553-2561, 2014.

[3] S. Ratnadurai-Giridharan, S.E. Zauber, R.M. Worth, T. Witt, S. Ahn, L.L. Rubchinsky. Temporal patterning of neural synchrony in the basal ganglia in Parkinsons disease, *Clinical Neurophysiology* 127 pp. 1743-1745, 2016.

Copulas and shuffles as statistical tools to recognize hidden dependences between neurons stimulated by periodic signals

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Recorded spike trains may exhibit patterns determined both by the direct interactions between the neurons and by their simultaneous stimulation from external inputs. Recovering the structure of the network from the study of simultaneously recorded spike trains is a challenging topic. For this reason, it is not surprising that, despite the existence of several methods helping to detect the existence of links between neurons [1], the problem is still open.

Motivated by the study of simultaneous recordings of two neurons of the electric fish, we reconsider the copula-method discussed in [2] to include the presence of periodic stimula. What is known about the electric fish is that its neurons are regularly stimulated by a periodic signal, and it has been recently hypothesized the existence of an inhibitory action between neurons [5]. Here we propose to merge copulas with a careful use of shuffling, to recognise the two causes of dependences: one determined by the common periodic input and the other by the direct connection between the neurons.

After recalling the definition of copula, its relation with joint distributions through Sklar's theorem [3] and introducing empirical copulas, we propose an improvement of the copula-method proposed in [2]. In particular, we study the copulas between the interspike intervals (ISIs) of the two neurons and between the ISIs of a neuron and the forward times of the other neuron, as in [2], and between the ISIs of a neuron and the backward times of the other neuron, following [4]. This first study allows to guess the existence of possible dependences between neurons and their direction. However, the presence of an underlying periodic stimulus does not allow to discriminate the nature of connections. To tackle this, we propose to study also the copulas of the shuffled samples. Depending on the type of shuffling, we expect to destroy different types of dependences. Hence, the comparison between copulas with or without shuffling suggests the cause of the observed dependences.

First, we validate the proposed method on simulated data obtained from a toy model including both a common periodic stimulus and inhibition of one neuron to the other.Then we apply the method to experimental data from the electric fish.

References

[1] R.E. Kass, S.I. Amari, K. Arai, E. N. Brown, C. O. Diekman, M. Diesmann, B. Doiron, U.T. Eden, A.L. Fairhall, G.M. Fiddyment Computational183-214, 2018.

[2] L. Sacerdote, M. Tamborrino and C. Zucca Detecting dependencies between spike trains of pairs of neurons through copulas, *Brain research* 1434 pp. 243-256, 2012.

[3] R.B. Nelsen. *An Introduction to Copulas* , Springer-Verlag, 2006.

[4] P. Verzelli, L. Sacerdote. A study of dependency features of spike trains through copulas, *Submitted*

[5] A. Author, B. Author. A.C. Pereira, A. Rodrguez-Cattneo, A.A. Caputi The slow pathway in the electrosensory lobe of Gymnotus omarorum: Field potentials and unitary activity, *Journal of Physiology-Paris* 108 (2-3) pp. 71-83, 2014.

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We thank Prof. Caputi who provided us the experimental data from the electric fish, recorded in his lab. An extensive study with the physiologist group will follow.

Estimation of Connections between Neurons only from Inter-Spike-Interval

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In the field of neural science, one of the important issues is to estimate neural network structures, or identify connections between neurons. However, it is not so easy to estimate connections, particularly directions of connections, between neurons only from observed spike data. As a causal estimation method using observed time series data, a method called convergent cross mapping (CCM) has already been proposed [1], which can correctly estimate causal relations, or directions of connections, even when connection strength between elements is relatively weak [1].

In this paper, we proposed a method to estimate connections between neurons only from observed spike time series using the CCM. First, we obtained firing timing from the membrane potential time series data of the Izhikevich neuron model with gap junction [2,3]. Then, we converted the firing timing time series data into inter spike interval (ISI). Finally, we applied the CCM to ISI to estimate connection between neurons. The Izhikevich neuron model with gap junction is expressed as follows : $\dot{v}_i = 0.04v_i^2 + 5v_i + 140 - u_i + I_i + \sum_{i\neq j, j=1}^{N} w_{ij}(v_j - v_i)$ and $\dot{u}_i = a_i(b_i v_i - u_i)$ when $v_i \geq 30$, $v_i \leftarrow c_i, u_i \leftarrow u_i + d_i$.

We conducted two numerical experiments, one is the case that neurons are connected in both directions ($w_{ij} \neq 0$), and the other is in the case of neurons are not connected ($w_{ij} = 0$). Then, we set parameters of two Izhikevich neuron models ($N = 2$) as follows : (i) $w_{ij} \neq 0$, $a_1 = a_2 = 0.03, b_1 = b_2 = 0.3, c_1 = c_2 = -55, d_1 = d_2 = 2, I_1 = I_2 = 10$ and $w_{12} = w_{21} = 0.05$, and (ii) $w_{ij} = 0$, $a_1 = 0.02, a_2 = 0.0201, b_1 = 0.498, b_2 = 0.4981, c_1 = -47.6, c_2 = -47.61, d_1 = d_2 = 2, I_1 = I_2 = 10$ and $w_{12} = w_{21} = 0$. We reconstructed the state space from observed ISI time series, with the embedding dimension of two and the time delay of unity when we applied the CCM to the ISI.

Figures 1 and 2 show the results of the numerical experiments. Figure 1 shows the results of the case that neurons are connected, and Fig.2 shows the results of the case that neurons are not connected. Figures 1 (a) and 2 (a) show the spike time series, and Figs. 1 (b) and 2 (b) show the result of applying the CCM for the ISI. In Figs. 1 (b) and 2 (b) ρ_{ij} represents the estimation accuracy of connecting from the i th neuron to the j th neuron.

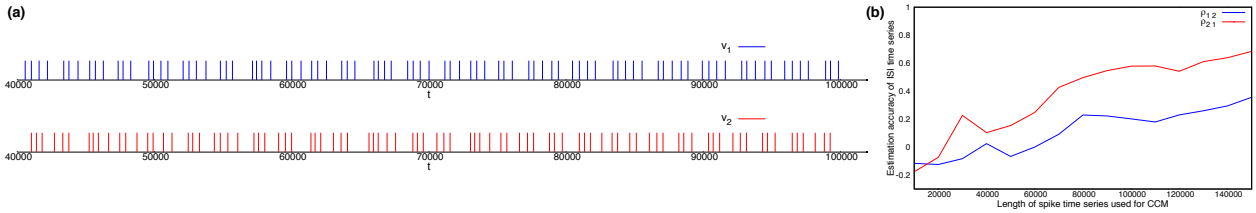

Figure 1: Results in case that two neurons are connected

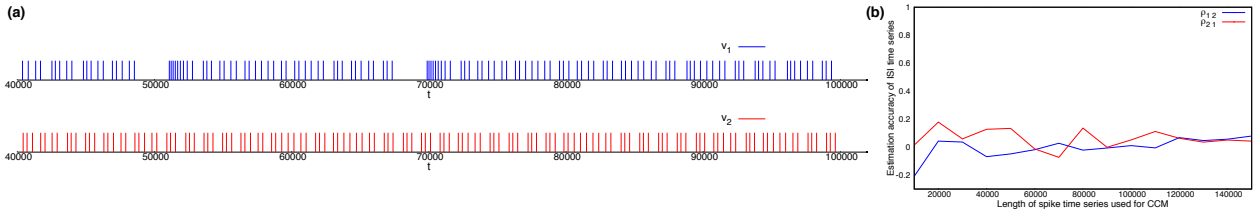

Figure 2: Results in case that two neurons are not connected

From Fig.1 (b), the estimation accuracy rises when the length of the time series used for estimation increases when two neurons are connected. In contrast to Fig.1 (b), the estimation accuracy does not increase even if the length of the time series used for estimation increases in Fig.2 (b), because there is no connection. From the results of numerical experiments, we can estimate the coupling with directions between two neurons by using the ISI. One of the important issues is to apply this method to large scale networks. We will present these results at the conference. This research is partially supported by the JSPS Grant-in-Aid for Scientific Research (No. 15KT0112, 17K00348 and 18K18125).

References

[1] G. Sugihara, et al., *Science*, Vol. 338, No. 6106, pp. 496–500, 2012.
[2] E.M. Izhikevich, *IEEE Trans. on Neural Networks*, vol. 14, No. 6, pp. 1569–1572, 2003.
[3] K. Naiki, et al., *Proc. of NOLTA2016*, pp. 257-260, 2016.

Non-Poisson firing statistics of spiking neurons with delayed feedback

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We consider 2 classes of spiking neuronal models with delayed feedback known in real biological neural networks, namely, the excitatory neuron with delayed feedback and inhibitory neuron with fast *Cl*-type inhibitory feedback. Both self-excitation [1] and self-inhibition [2] are common features in real biological neural networks. The classes of neuronal models (without feedback) are defined by a set of conditions typical for basic threshold-type models, such as the leaky integrate-and-fire or the binding neuron model and also for some artificial neurons. A neuron is fed with a Poisson process. Each output impulse is applied to the neuron itself after a finite delay Δ.

We derive a general relation which allows calculating exactly the probability density function (pdf) $p(t)$ of output interspike intervals of a neuron with feedback (excitatory or fast inhibitory) based on known pdf $p^0(t)$ for the same neuron without feedback, intensity of the input stream and the properties of the feedback line (the Δ value).

The course of $p(t)$ has a δ-function peculiarity in case of excitatory feedback or a jump for interspike intervals of duration Δ in case of fast inhibitory feedback. This fact contributes to the discussion about the possibility to model neuronal activity with Poisson process, supporting the no answer.

References

[1] V. Aroniadou-Anderjaska, M. Ennis, M.T. Shipley. Dendrodendritic recurrent excitation in mitral cells of the rat olfactory bulb, *Journal of Neurophysiology* 82 (1) pp. 489-494, 1999.

[2] G. Tams, E.H. Buhl, P. Somogyi. Massive autaptic self-innervation of GABAergic neurons in cat visual cortex, *Journal of Neuroscience* 17 (16) pp. 6352-6364, 1997.

Towards a reduced model of ripple oscillations in recurrent inhibitory networks

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Ripple oscillations, as observed in the hippocampal local field potential (LFP), have long been implicated in important cognitive functions such as memory consolidation or planning [1,2]. The mechanisms underlying ripple generation however are still under debate. One hypothesis is that inhibitory interneurons act as the primary pacemaker. Modeling studies have shown that a recurrent network of interneurons (INT-INT type) can indeed produce oscillations in the ripple band (140-220 Hz), when driven with sufficient feedforward excitatory input [3,4]. Furthermore, INT-INT networks were shown to reproduce the experimentally observed intra-ripple frequency accommodation (IFA) – an asymmetry in the instantaneous network frequency during a transient ripple event [4,5].
Here we develop a minimal model that reflects the core features of INT-INT networks required for the emergence of both ripple oscillations and IFA.
We hypothesize that there is a direct link between IFA and a network's steady-state profile, i.e. its response to excitatory feedforward input of constant intensity. The steady-state profile of the network described in [4] shows three distinct dynamical regimes: (i) an asynchronous irregular regime at low excitatory input levels with single units firing sparsely and irregularly and no significant oscillation in the network; (ii) a sparsely synchronized regime at intermediate input levels beyond the bifurcation point, with a ripple-range network oscillation much faster than the mean unit firing rate and largely independent of the input level; (iii) a fully synchronized regime where network and unit frequencies coincide and rise quasi-linearly with the input level. It has been proposed that IFA is a direct consequence of such a steady-state profile, in particular the nonlinearity in the network's frequency response [4].
In an effort to determine the critical network features for such a steady-state profile, we performed model reductions. We find that sparseness in the recurrent inhibitory connections is not critical. On the other hand, we could show a systematic dependence of the steady-state profile on the strength of correlations in the feedforward inputs. The desired nonlinearity in the network frequency response is only preserved for weakly correlated or independent excitatory inputs. These feedforward inputs however do not require synaptic filtering, so we could make a diffusion approximation without altering the steady-state profile. On the contrary, synaptic filtering in the inhibitory connections is necessary to maintain network frequencies in the ripple band. All in all, the model from [4] can be reduced to a population of LIF neurons with global inhibitory synaptic coupling receiving only weakly correlated, stochastic excitatory input. We propose this as the minimal INT-INT-type model for ripple oscillations that can also reproduce IFA.
This model reduction not only enhances our understanding of the crucial network components for ripple generation and IFA, but might also be the basis for deriving the network frequency in an analytical fashion. So far, the network frequency at the onset of oscillations has been shown to depend mainly on the short synaptic time constants [3], yet only for certain INT-INT network architectures that do not include the one presented here.
IFA could be a useful additional criterion to narrow down the selection of possible ripple generating mechanisms. Understanding the range of INT-INT-type network architectures that reproduce IFA is therefore crucial to assess the plausibility of interneuron networks as the main pacemaker of ripple oscillations.

References

[1] M. Wilson, B. McNaughton. Reactivation of hippocampal ensemble memories during sleep, *Science* 265(5172), pp: 676-679, 1994.

[2] G. Buzsáki. Two-stage model of memory trace formation: a role for "noisy" brain states, *Neuroscience* 31(3), pp: 551-570, 1989.

[3] N. Brunel, X.-J. Wang. What determines the frequency of fast network oscillations with irregular neural discharges? I. Synaptic dynamics and excitation-inhibition balance, *Journal of neurophysiology* 90(1), pp: 415-30, 2003.

[4] J. Donoso, D. Schmitz, N. Maier, R. Kempter. Hippocampal ripple oscillations and inhibition-first network models: Frequency dynamics and response to GABA modulators, *Journal of Neuroscience* 38(12), pp: 3124-3146, 2018.

[5] A.A. Ponomarenko, T.M. Korotkova, O.A. Sergeeva, H.L. Haas. Multiple GABAA receptor subtypes regulate hippocampal ripple oscillations, *European Journal of Neuroscience* 20 (8), pp: 2141-2148, 2004.

Mesoscopic population equations for spiking neural networks with synaptic short-term plasticity

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Deriving coarse-grained models of neural population activity at mesoscopic scales from an underlying microscopic model of a spiking neural network is an essential step for building multi-scale models of the brain. A ubiquitous feature of microscopic neural dynamics with significant functional implications is short-term plasticity (STP) of synaptic connections. Although accurate models of STP for a single synapse exist [1], a systematic mean-field theory for mesoscopic neural populations with STP is presently lacking.

Here [2], we extend a recent theory for mesoscopic population dynamics with static synapses [3] to the case of dynamic synapses exhibiting STP. Under the assumption that spike arrivals at synapses have Poisson statistics, we derive stochastic mean-field dynamics for a single effective connection between two populations consisting of a finite number of neurons that interact via dynamic synapses. More specifically, we derive two different sets of equations : a set of *first order* mean field equations obtained by a first order moment-closure approximation and a set of *second order* mean field equations obtained by a second order moment-closure approximation.

Comparison with extensive Monte Carlo simulations of the microscopic model show that in a feedforward network the mesoscopic model accurately reproduces the exact realisation of the total synaptic input into a postsynaptic neuron. It is further shown that the *second order* mean field exhibits the same first- and second-order statistics over the full parameter space, whereas the *first order* mean field largely underestimate finite-size noise when the firing rate is high.

We then test the mesoscopic model for STP on a homogeneous, fully connected population of neurons. First, we consider Poisson-neurons and show that the mesoscopic model accurately predicts finite-size induced population spikes (like the ones observed in neural cultures) and finite-size induced Up and Down state switches, except for certain parameter regimes where the *first order* mean field approximation error leads to inaccurate predictions that are corrected with the *second order* mean field. Finally, we test the mesoscopic model in the case of Generalized Intagrate-and-Fire neurons and show that it correctly predicts finite-size induced population spikes.

This extended mesoscopic population theory of spiking neural networks with STP may be useful for a systematic reduction of detailed biophysical models of cortical microcircuits to efficient and mathematically tractable mean-field models.

References

[1] M. Tsodyks, K. Pawelzik, H. Markram Neural networks with dynamic synapses. *Neural computation* 10(4) 821-835, 1998.

[2] V. Schmutz, W. Gerstner, T. Schwalger Mesoscopic population equations for spiking neural networks with synaptic short-term plasticity. *arXiv preprint* arXiv:1812.09414, 2018.

[3] T. Schwalger, M. Deger, W. Gerstner Towards a theory of cortical columns: From spiking neurons to interacting neural populations of finite size. *PLoS Computational Biology* 14(3) e1005507, 2017.

Exact avalanche distributions for inhomogeneous networks of non-leaky integrate and fire neurons

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Abstract: Cortical networks have been shown to self-organize to a critical dynamics, a state between order and chaos characterized by scale-free distributions of neural avalanche sizes. Previous analytical studies investigated neural avalanches in networks of discrete neurons characterized by transition probabilities from inactive to firing states [2, 3]. However, this simplified avalanche dynamics makes unrealistic assumptions such as independence of membrane potentials and novel analytical methods that go beyond mean field analysis are needed to rigorously model avalanche dynamics in finite, inhomogeneous networks with nontrivial topologies. In this contribution, we derive avalanche distributions for a finite network of randomly driven excitatory non-leaky integrate-and-fire-neurons [4] on arbitrary networks topologies. In extension of previous studies we found that this system is equivalent to a semi-group action of translations on the N-torus and obtain it's ergodic measure, from which avalanche probabilities are calculated as state space volumes. We find that membrane potentials are only independent on directed acyclic graphs, which prohibits units to transition independently from inactive to firing in recurrent networks. Remarkably, our approach allows a closed form solution for avalanches that establishes a close link to graph theory via the matrix tree theorem and graph cuts. As example applications we demonstrate qualitative changes of avalanche distributions for small changes in connection strength for two coupled subnetworks with strong intra- and weak inter network couplings (emergence of synchronized states) and for a change of boundary conditions transforming a neural chain to a ring (system size events).

Supporting information: Our model extends the EHE-model [4], which is used in mathematical studies of self organized criticality [5, 6], to arbitrary non-negative coupling matrices. We use the notation $[N] = \{1, \dots, N\}, W_{I,J} = (\sum_{j\in J} W_{i,j})_{i\in I}$ and assume $W \geq 0, W_{[N],[N]} < 1$ (componentwise). The potential of a randomly chosen unit is increased at each step on a slow timescale. If this unit crosses the threshold, an avalanche evolves deterministically on a fast timescale in which spiking units send excitation to connected units and that stops when all potentials are below the threshold. This dynamics leads to a uniform equilibrium distribution supported on a subset of $[0, 1)^N$ that depends on the coupling matrix W. We vastly simplify treatment of the model by introducing a topology based on a linear transformation that is homeomorphic to the N-torus, in which the system acts as a translation upon receiving external input. This transformation allows to prove ergodicity for arbitrary W (closing an open conjecture [5]) and it's determinant provides a simple expression for the inhabited phase space volume $|\operatorname{Id}_N - W|$. Using this tools we establish a link to graph theory in the closed form expressions for probabilities that unit i_s starts an avalanche in which exaclty the units in $I \subseteq [N]$ fire.

$$P(I, i_s) = |\operatorname{diag}(W_{I\setminus\{i_s\},I}) - W_{|I}||\operatorname{diag}(1 - W_{[N]\setminus I,I}) - W_{|[N]\setminus I}|/|\operatorname{Id}_{N-1} - W_{|[N]\setminus\{i_s\}}|$$

The first determinant is a cofactor of the $W_{|I}$ Laplacian and favors sets allowing a high number of spanning trees (matrix tree theorem), while the second determinant penalizes connections in the cut set of the $(I, [N] \setminus I)$ graph cut. In summary, we rigorously connect avalanche distributions resulting from spiking neurons to network topology and provide new tools to study the role of avalanches in neural computations.

References

[1] J. Beggs, D. Plenz. Neuronal avalanches are diverse and precise activity patterns that are stable for many hours in cortical slice cultures. *Journal of neuroscience* 24.22 pp. 5216-5229, 2004.

[2] D. Larremore, W. Shew, J. Restrepo. Predicting criticality and dynamic range in complex networks: effects of topology, *Physical review letters* 106.5 058101, 2011.

[3] D. Larremore, M. Carpenter, E. Ott, J. Restrepo. Statistical properties of avalanches in networks, *Physical Review E* 85.6, 066131, 2012.

[4] C. Eurich, M. Herrmann, U. Ernst. Finite-size effects of avalanche dynamics, *Physical review E* 66.6 066137, 2002.

[5] M. Denker, A. Levina. Avalanche dynamics, *Stochastics and Dynamics*, 16(02) 1660005, 2016.

[6] M. Denker, A. Rodrigues. Ergodicity of avalanche transformations, *Dynamical Systems* 29.4 pp. 517-536, 2014.

Hazard rate approach to spiking neural networks with background noise

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Population rate models such as Wilson-Cowan equations are widely used for modeling neural computations and dynamics in cortical circuits. They are highly amenable to mathematical and statistical analysis but, being heuristic models, they lack a clear link to biophysical parameters. On the other hand, cortical circuits can be simulated by means of large-scale spiking neural network models. A popular choice for such microscopic models are networks of integrate-and-fire (IF) neurons driven by external Poisson noise representing background activity from outside the network. Microscopic models can be constrained by experimentally measured biophysical parameters, but do not permit a direct theoretical understanding of emergent dynamics. To understand cortical computations from the underlying complex network dynamics of thousands of spiking neurons, it is thus necessary to bridge the gap between microscopic network models and mesoscopic or macroscopic population rate models. However, linking these different levels remains a largely unsolved theoretical problem because of several biological constraints such as spike-history dependencies of individual neurons, finite system size and heterogeneity of parameters.

Here, I propose a systematic mathematical reduction from microscopic models to population rate models based on a hazard rate approach. In our recent work [SDG17], we have developed refractory density equations for the dynamics of homogeneous, finite-size ("mesoscopic") populations of generalized integrate-and-fire (GIF) models. The mesoscopic refractory density equations are stochastic integro-partial-differential equations, which accurately reproduce activities of finite-size populations of neurons exhibiting refractoriness and adaptation. The central object in these equations is a hazard rate function. The rich functional form of the hazard rate is explicitly known for populations of GIF neurons with "escape noise" via a quasi-renewal and mean-field approximation. For the common model of IF neurons driven by external background noise, however, the hazard rate is not known. In fact, the knowledge of the hazard rate is equivalent to knowing the first-passage-time density of the membrane potential with respect to an arbitrarily time-varying threshold, which is an unsolved problem. Using a reduction of the Wiener-Rice series for level-crossing processes and a novel correlation theory for upward-crossing times, I present an approximate solution to this problem. The resulting hazard rate yields a novel mapping from diffusive noise to escape noise. Using this mapping allows us to extend the mesoscopic refractory density equations to IF networks driven by external background noise. Comparison with microscopic simulations as well as an alternative hazard-rate theory [CG08] reveals an excellent agreement (Fig. 1). Finally, I show how the refractory density dynamics can be reduced to efficient low-dimensional dynamics of Wilson-Cowan type, based on an eigenfunction expansion.

In conclusion, our theory suggests a mathematical framework to systematically reduce spiking neural network models with external background noise to biologically more realistic, yet tractable, population rate models.

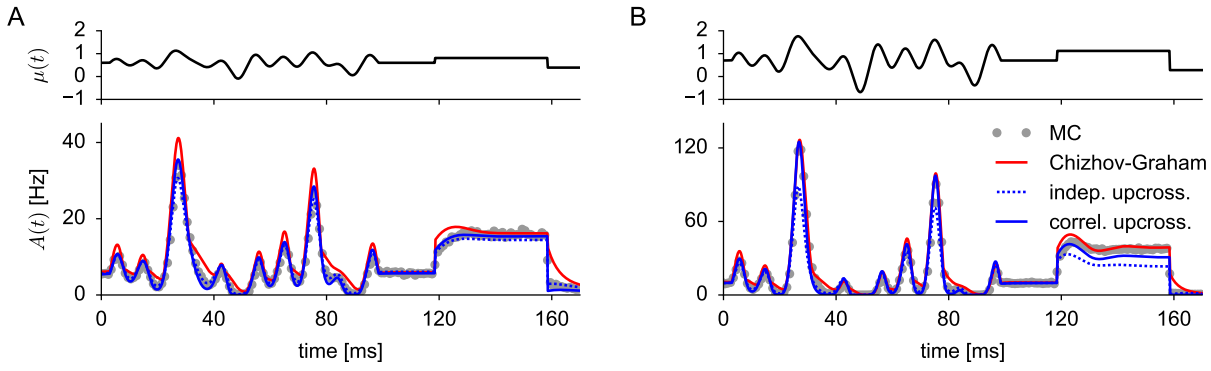

Figure 1: Population rate $A(t)$ of LIF neurons with colored noise in response to subthreshold (A) and suprathreshold (B) time-dependent stimuli $\mu(t)$. Circles: simulations, solid blue line: level-crossing theory, red line: theory by [CG08].

References

[CG08] A. V. Chizhov and L. J. Graham. Efficient evaluation of neuron populations receiving colored-noise current based on a refractory density method. *Phys. Rev. E*, 77(1):011910, 2008.

[SDG17] T. Schwalger, M. Deger, and W. Gerstner. Towards a theory of cortical columns: From spiking neurons to interacting neural populations of finite size. *PLoS Comput. Biol.*, 13(4):e1005507, 2017.

Anticipation in the retina and the primary visual cortex : towards an integrated retino-cortical model for motion processing

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The retina is able to perform complex tasks and general feature extraction, allowing the visual cortex to process visual stimuli with more efficiency. With regards to motion processing, an interesting and useful task performed by the retina is anticipation and trajectory extrapolation. Anticipation in the retina lies in the fact that the peak of retinal ganglion cells response is shifted, occurring before the object reaches the center of the receptive field, and can be explained by gain control mechanisms occurring at the level of bipolar and ganglion cells [1] . Trajectory extrapolation on the other hand is related to a rise in the activity before the object enters the receptive field of the cell and is carried out through electrical synapses (gap junctions) connecting ganglion cells [2]. This extrapolation has also been observed at the level of the primary visual cortex, where lateral propagation drives the activity ahead of the input, denoting predictive computations [3]. Motion encoding in the retina also involves amacrine cells, which connect bipolar cells to either bipolar or ganglion cells, but their role has not been investigated yet in motion anticipation.

The first contribution of our work lies in the development of a generalized 2D model of the retina with three layers of ganglion cells : Fast OFF cells with gain control accounting for anticipation, direction selective cells connected via gap junctions, and Y-cells connected through amacrine cells, accounting for motion extrapolation.This model affords a mathematical analysis via dynamical systems theory and allows to outline the role of lateral connectivity (gap junctions and amacrine cells) in motion perception, anticipation and trajectory extrapolation. The second contribution is the use of the output of our retina model as an input to a mean field model of the primary visual cortex to reproduce motion anticipation as observed in VSDI recordings of V1 [4]. We present results of the integrated retino-cortical model for motion processing, and study how anticipation and extrapolation depend on stimuli parameters such as speed, shape and trajectory. Through the integrated retina-cortical model we emphasize the mechanisms defining motion anticipation, due to the cooperation of gain control and lateral connectivity at the level of the retina and lateral connectivity in the cortex. Moreover, we show how cortical nonlinearities due to a different gain between excitatory and inhibitory neurons shape the cortical response thus affecting object recognition.

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References

[1] E. Y. Chen, O. Marre, C. Fisher, G. Schwartz, J. Levy, R. Azeredo da Silveira, & M. J. Berry, Alert Response to Motion Onset in the Retina, *The Journal of Neuroscience* 2013.

[2] S. Trenholm, D. J. Schwab, V. Balasubramanian & G. B. Awatramani Lag normalization in an electrically coupled neural network., *Nature Neuroscience* 2013.

[3] G. Benvenuti, S. Chemla, A. Boonman, G. Masson, F. Chavane Anticipation of an approaching bar by neuronal populations in awake monkey, *The Journal of Vision* 2015.

[4] M. di Volo, A. Romagnoni, C. Capone & A. Destexhe Biologically realistic mean-field models of conductance-based networks of spiking neurons with adaptation, *bioRxiv* 2018.

Shot Noise, diffusion limits and suitable approximations

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Suppose that events (e.g., jumps representing the excitatory inputs impinging on a neuron) occur in accordance to a Poisson process $N(t)$ with constant rate $\lambda > 0$. Associated with the ith event is a positive random variable J_i, which quantifies the event (e.g., its amplitude). Denote by τ_i the time of the ith event. Consider the stochastic process X(t) given by [4]

$$X(t) = \sum_{i=1}^{N(t)} J_i e^{-\alpha(t-\tau_i)}, \qquad X(0) = x_0 \tag{1}$$

where $\alpha > 0$ is a constant determining the exponential decay rate. When the J_i are independent and identically distributed random variables, independent of the Poisson process $N(t)$, the process $\{X(t), t \geq 0\}$ is called *shot noise process*.

We study the shot noise process (1) from two different perspectives. First, we consider different distributions for the jump amplitudes J_i and calculate the corresponding first three moments and stationary distribution of the shot noise process $X(t)$. The obtained results are compared with the corresponding statistics of some well known process, e.g., the Ornstein-Uhlenbeck and the Feller processes, to investigate under which conditions these diffusion processes can satisfactorily approximate the shot noise $X(t)$.

Second, we consider a sequence of shot noise processes, $\{X_n(t)\}_{\{n\geq 1\}}$, with $\mathbb{E}[J_{i;n}] \to 0, \mathbb{E}[J_{i;n}^2] \to 0, \lambda_n \to \infty$, i.e. jump amplitudes going to 0 and jump frequencies going to ∞ as $n \to \infty$. Under which conditions does the sequence of shot noise processes converge to a diffusion process $Y(t)$? Is there any shot noise process fulfilling these conditions? If not, what type of limiting process $Y(t)$ do we obtain? How is the distribution of $J_{i;n}$ changing the properties of $Y(t)$?

We will discuss our results [5] in the framework of neuronal models, and in particular Leaky Integrate-and-Fire models, where shot noises are used to model synaptic input currents [1, 2, 3] and diffusion approximations are commonly considered to replace the shot noise input with a Gaussian white noise.

References

[1] F. Droste and B. Lindner. Exact analytical results for integrate-and-fire neurons driven by excitatory shot noise, *J Comput Neurosci*, 43:81–91, 2017. ISSN 1573-6873

[2] K. Rajdl and P. Lansky. Shot-noise Fano factor, *Phys. Rev. E*, 92, 052135, 2015.

[3] M. J. E. Richardson and W. Gerstner. Statistics of subthreshold neuronal voltage fluctuations due to conductance-based synaptic shot noise, *Chaos*, 16, 026106, 2006.

[4] S. M. Ross. *Stochastic processes*, Wiley, 1983. ISBN 0471099422

[5] M. Tamborrino, P. Lansky. On the shot noise process, its characterization and diffusion limit, submitted, 2019.

Annihilation phenomenon in a PWL version of the FitzHugh-Nagumo system

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Many biological systems have the capability to operate in a stable manner in two different regimes, by switching from one to the other as a response to an external input. These bistable systems are usually described by differential equations exhibiting two different attractors. The basin of attraction of both attractors are bounded by an unstable object. This unstable object can be, thus, considered as a threshold between the two stable regimes.

Planar saddle-node bifurcation of limit cycles, also called fold of limit cycles, is a qualitative change in the behaviour of a system. In this change, the phase portrait passes from exhibiting two hyperbolic limit cycles, surrounding an equilibrium point, to the disappearance of such cycles through their collision in a non-hyperbolic semistable limit cycle. Saddle-node of limit cycles, in particular the configuration where the equilibrium point in the interior of both limit cycles and the outer limit cycle are stable, is an instance for bistability. In this case, the thresold is the unstable inner limit cycle.

This configuration helps to explain some phenomena associated to bistability, as for instance annihilation and single-pulse triggering [2]. In such phenomenon, an oscillatory behavior is ceased by injecting a sub-threshold pulse, and then, the activity is restarted by injecting a supra-threshold pulse. Annihilation has been described in several biological oscillators, such as the activity of the sinoatrial node [3], the eclosion rhythm of fruit flies, the circadian rhythm of bioluminescence in marine algae and biochemical oscillators, see [5].

Connected with the annihilation phenomenon is the problem of fine-tuning the injected pulse, in order to minimize the required energy to carry the system from the oscillatory behaviour to the resting behaviour, and vice versa.

Piecewise linear (PWL) systems have showed their ability for mimicking behaviours exhibited by the general nonlinear systems, but in a context which is more friendly for computations. These properties have been used for developing strategies of parameter estimation. In particular, in [4] authors present a strategy for the estimation of the synaptic conductance in the neural McKean model.

In this contribution we present a first proof of concept for solving the fine-tuning problem in a PWL version of the FitzHugh-Nagumo model. The strategy is based on the knowledge of the value of the injected pulse, at which the system exhibits a saddle-node limit cycle [1], and in the assumption that the given oscillatory voltage trace corresponds to a limit cycle which is close to the saddle-node limit cycle.

References

[1] V. Carmona; S. Fernndez-Garca; A. E. Teruel. Saddle-node of limit cycles in planar piecewise linear systems and applications. *Submited to DCDS-A*, 2019.

[2] M. Guevara. Bifurcations Involving Fixed Points and Limit Cycles in Biological Systems, *In: "Nonlinear Dynamics in Physiology and Medicine",* edited by Beuter A, Glass L, Mackey MC, Titcombe MS. Springer-Verlag, New York, pp. 41-85 (2003).

[3] M. Guevara and H. Jongsma. Three ways of abolishing automaticity in sinoatrial node: ionic modeling and nonlinear dynamics, *Am. J. Physiol.* (262) pp. H1268–H1286, 1992.

[4] A. Guillamon; R. Prohens; A. E. Teruel; C. Vich. Estimation of synaptic conductances in the spiking regime for the McKean neuron model, *SIADS,* 16(3), pp 1397-1424, 2017

[5] A. T. Winfree. The Geometry of Biological Time, *Interdisciplinary Applied Mathematics,* Springer-Verlag New York, (12), 2001.

Runaway excitation-like behavior in networks of PPGLM-type spiking neurons

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In recent years, nonlinear Hawkes processes implemented as point process generalized linear models (PPGLMs) have been proven to be a useful tool for analyzing microelectrode array recordings of neuronal ensemble spiking activity. They are related to classical models of neuronal dynamics (GIF, spike response model) and, unlike ODE-based neuron models, PPGLMs can be fitted directly to the spike-times data, using standard optimization tools.

Roughly speaking, a (multivariate) nonlinear Hawkes process is vector of point processes on the real line, whose (stochastic) intensity at every moment in time depends on the past event history of all the coordinate processes involved; and this dependence has a particular form — spike trains are convolved with fixed filters, summed and passed through a nonlinearity. Nonlinearity is necessary to allow the model to reproduce self and cross inhibition.

One of the obstacles in using data-driven PPGLMs is that sometimes they can display non-physiologically high firing rates, when simulated. To make nonlinear Hawkes PPGLMs useful for long-term prediction of neuronal activity and simulation studies, it is important to understand which model features cause the firing rates to become excessively large ("runaway excitation" phenomena). This questions were studied to some extent for univariate PPGLMs but not in multivariate (network) case.

There are several existing approaches based on statistical physics-inspired methods developed for the analysis of similar systems, but their performance in the context of data-driven PPGLMs has not been assessed yet. We compared the accuracy of several theoretical approaches for predicting the occurrence of excessively high firing rates in multivariate Hawkes processes. The approaches are based on the following theoretical approaches: mean field approximation, 1-loop fluctuation expansion based on stochastic path integral formulations, quasi-renewal approximation and the regular spiking limit test. These approaches are quite different conceptually, having been introduced in different settings and having limitations in different aspects.

Based on simulation studies, we identify model features that make some approaches work better than others. Furthermore, we demonstrate how these theoretical approaches work when applied to multivariate PPGLMs fitted to the spikes trains generated by a synthetic cortical model and also to those from nonhuman primate cortex data. Finally, we also illustrate an algorithm for efficient simulation of arbitrary nonlinear Hawkes process networks.

References

[1] P. Brémaud and L. Massoulié, Stability of nonlinear Hawkes processes *The Annals of Probability*, 1996, pp 1563–1588

[2] F. Gerhard, M. Deger, W. Truccolo, On the stability and dynamics of stochastic spiking neuron models: Nonlinear Hawkes process and point process GLMs, *PLoS computational biology* 2 (13), 2017.

[3] G. Ocker, K. Josić, E. Shea-Brown, M. Buice, Linking structure and activity in nonlinear spiking networks, *PLoS computational biology*, 6 (13), 2017.

[4] Yu Chen, Qi Xin, V. Ventura, R. Kass, Stability of point process spiking neuron models, *Journal of computational neuroscience*, 2018

The neurophysiology of visual attention - quantitative approaches to the shaping of sensation into perception

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Area V5/MT in primate visual cortex is arguably the best understood area in primate extrastriate visual cortex in terms of its representation of the incoming (bottom-up) sensory information. MT is considered to be of critical importance for our ability to perceive the visual motion patterns in our environment.

This level of understanding of the neural representation of sensory information in one cortical area is an excellent basis for a quantitative analysis of the top-down influences exerted by various types of attention onto sensory information processing.

The talk will give an overview of the multitude of attentional effects that have been discovered using single-cell recordings in awake rhesus monkeys, ranging from attentional modulations of target and distractor stimuli encoding, to multiplicative and non-multiplicative modulations of tuning curves and receptive field profiles, modulations of firing patterns, peri-saccadic effects, as well as effects on the representation of change events in the environment.

From these investigations a clear pattern emerges that turns MT into a model area for the interaction of sensory (bottom-up) signals with cognitive (top-down) modulatory influences that characterizes visual perception. These findings also document how this interaction enables visual cortex to actively generate a neural representation of the environment that combines the high-performance sensory periphery with selective modulatory influences for producing an integrated saliency map of the environment.

Spectral Density-Based and Structure-Preserving Approximate Bayesian Computation for Partially Observed SDEs With an Invariant Measure: *A Demonstration on the Jansen and Rit Neural Mass Model and the FitzHugh-Nagumo Model*

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Stochastic differential equations (SDEs) have become an established and powerful tool for modelling the oscillatory activity of both single cells and large populations of neurons. Let us consider a n-dimensional SDE whose solution process is only partially observed through a one-dimensional and parameter-dependent output process admitting an invariant distribution. We aim to infer the parameters from discrete time measurements of the invariant output process. Due to the increased model complexity, needed to understand and reproduce the real neural data, the underlying likelihood is often unknown or intractable. Among several likelihood-free inference methods, we focus on the Approximate Bayesian Computation (ABC) approach [1].

When applying ABC to stochastic processes, two difficulties arise. First, different realizations from the output process with the same choice of parameters may show a large variability, due to the stochasticity of the model. Second, exact simulation schemes are rarely available for general SDEs and, thus, a numerical method for the synthetic data generation within the ABC framework has to be derived. We tackle these issues as follows. To reduce the randomness coming from the underlying model, we propose to make use of the structural properties of the SDE, namely the existence of a unique invariant distribution. We map the synthetic data into their estimated invariant density and invariant spectral density, almost eliminating the variability in the data and, thus, making hidden information about the parameters accessible. Since our ABC algorithm is based on the structural property, it can only lead to successful inference when the invariant measure is preserved in the synthetic data simulation. To achieve this, we propose to use a structure-preserving numerical scheme that, differently from the commonly used Euler-Maruyama method, preserves the properties of the underlying SDE.

Here, we illustrate our proposed Spectral Density-Based and Structure-Preserving ABC Algorithm on the stochastic Jansen and Rit Neural Mass Model (JR-NMM) [2] and the stochastic FitzHugh-Nagumo model (FHN) [3]. Both models are ergodic, which results in the output process admitting an invariant measure. The use of numerical splitting schemes guarantees the preservation of the invariant distribution in the synthetic data generation step. With our new approach, we succeed in the simultaneous estimation of the three most crucial parameters of the JR-NMM and of all four parameters inherent in the FHN model. Finally, we apply our method to fit the JR-NMM to real EEG alpha-rhythmic recordings.

References

[1] M.A. Beaumont, W. Zhang, D.J. Balding
"Approximate Bayesian computation in population genetics".
In: Genetics, 162(4), pp.2025-2035 (2002)

[2] M. Ableidinger, E. Buckwar, H. Hinterleitner.
"A Stochastic Version of the Jansen and Rit Neural Mass Model: Analysis and Numerics."
In: The Journal of Mathematical Neuroscience 7(8) (2017)

[3] J. R. Leon, A. Samson.
"Hypoelliptic stochastic FitzHugh-Nagumo neuronal model: mixing, up-crossing and estimation of the spike rate."
In: Annals of Applied Probability 28(4), pp.2243-2274 (2018)

[4] E. Buckwar, M. Tamborrino, I. Tubikanec. "Periodogram-Based and Structure-Preserving Approximate Bayesian Computation for Partially Observed Diffusion Processes Admitting an Invariant Measure. A Demonstration on Hamiltonian SDEs." *in preparation.*

[5] E. Buckwar, A. Samson, M. Tamborrino, I. Tubikanec. "Periodogram-Based and Structure-Preserving Approximate Bayesian Computation Applied to the Hypoelliptic Stochastic FitzHugh-Nagumo Neuronal Model." *in preparation.*

Strategies used by humans and monkeys in transparent coordination games

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The question of how living agents coordinate their actions is highly relevant for the social neuroscience. To tackle it simultaneous and sequential games have been studied in humans and recently were also employed in monkeys [1, 2]. Yet, assumptions of classic game theory are often not fulfilled in social behaviours since humans and animals rarely act strictly simultaneously or sequentially. Instead, they observe their partners and adjust actions accordingly. To account for such action visibility we developed a game-theoretic setting of "transparent games" [3, 4], providing a realistic model of interactions under time constraints, where each player has a certain probability to observe the partner's choice before deciding on its own action. This probability is determined by the action times of the players. We consider a transparent version of a Bach-or-Stravinsky (BoS) game, where players choose between 2 options, each associated with higher payoff for one of the players. Players can either insist on their own preference or accommodate the preference of the partner. Jointly selecting the same option adds an equal bonus to the payoff of each player, so the maximal joint payoff is obtained when one player insists, and the other accommodates. Yet this results in an unequal (i.e. unfair) reward distribution. Our analysis shows that action visibility influences optimal behaviour already for the one-shot BoS, and Nash equilibria (NE) depend on the probabilities of players to see partner's choice. If these probabilities are low for both players, there are 2 pure-strategy NE and 1 mixed-strategy NE as in the simultaneous BoS. High probabilities of seeing the partner's choice result in a single pure-strategy NE: insist if you do not see partner's choice or if you see the partner accommodating; otherwise accommodate. Evolutionary simulations employed to study the iterated transparent BoS reveal 3 major strategies: *challenging* (players insist until one gives in and switches to accommodation), *turn-taking* (alternation between insisting and accommodating) and *leader-following* (the slower player follows the faster's choice). Higher probabilities to see a partner's choice are associated with more effective coordination. To check whether these predictions hold true for living agents, we studied performance of humans and rhesus macaques in a transparent iterated BoS. For this we used a novel setup in which 2 agents sit vis-à-vis separated by a transparent display with 2 touchscreens, allowing them to observe each other while reaching targets in the shared workspace. Most human and macaque pairs established coordination. Humans mainly used *turn-taking* to equalize payoffs, but some pairs employed cooperative forms of *leader-following* and *challenging*. Monkeys relied on selecting the same side or on *challenging*. To verify that monkeys were able to dynamically take a partner's choice into account, two monkeys underwent training with a human confederate, who alternated between insisting and accommodating in blocks. After the training monkeys coordinated their choices with the confederate, actively observing the human. When these monkeys then played together, they adhered to *leader-following*. Unlike in humans, the leader mainly insisted and the second monkey accommodated. In two sessions where monkeys showed similar average reaction times a *competitive turn-taking* pattern emerged: each monkey led and followed in blocks. In those sessions, the probability to see the other's action (derived from the difference in reaction times in each trial) correlated strongly with the actual choice behaviour. Our results corroborate findings in [5], showing that action visibility enhances human performance in coordination games and results in more fair reward distribution. Moreover, we provide a game-theoretical explanation for this effect and show that it also takes place to some degree in rhesus macaques.

References

[1] K. Haroush, Z.M. Williams. Neuronal prediction of opponent's behavior during cooperative social interchange in primates, *Cell* 160 (6), pp. 123345, 2015.

[2] R. Báez-Mendoza, W. Schultz. Performance error-related activity in Monkey striatum during social Interactions, *Scientific Reports* 6, 37199, 2016.

[3] A.M. Unakafov, T. Schultze, I. Kagan, S. Moeller, S. Eule, F. Wolf F. Emergence and suppression of cooperation by action visibility in transparent games, *bioRxiv* 314500, 2018.

[4] A.M. Unakafov, T. Schultze, I. Kagan, S. Moeller, A. Gail, S. Treue, S. Eule, F. Wolf F. Evolutionary successful strategies in a transparent iterated Prisoner's Dilemma, *bioRxiv* 524348, 2019.

[5] R.X.D. Hawkins, R.L Goldstone. The formation of social conventions in real-time environments, *PloS ONE* 11 (3), e0151670, 2016.

Dynamics of a mean field limit of interacting 2D nonlinear stochastic spiking neurons

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Bridging the gap between microscopic and macroscopic description of biological neural networks is one of the current challenges in neuroscience. But how can we explain the macroscopic measurements from the microscopic description and more precisely, how the intrinsic firing properties of the isolated neurons influence or are influenced by the collective dynamics? The family (1) of two-dimensional (2D) nonlinear spiking neuron model [GKNP14] is efficient in reproducing the majority of observed membrane potential behaviour (like bursting) while having a flow much simpler than that of the celebrated Hodgkin-Huxley model.

$$\frac{d}{dt}v(t) = F(v(t)) - w(t) + I := V(v(t), w(t)), \quad \tau_w \frac{d}{dt}w(t) = b\, v(t) - w(t) := W(v(t), w(t)). \tag{1}$$

Taking inspiration in [DMGLP15, FL16], we use a stochastic firing mechanism of jump type with rate function $\lambda(v)$ only depending on the membrane potential. The jump implementing the reset is $(v, w) \to (\bar{v}, w + \bar{w})$. We then consider a large number N of excitatory neurons, each being connected to approximately N other ones, chosen at random. The firing of one neuron induces a jump of size $\frac{J}{N}$ of the membrane potential of the postsynaptic neurons. The goal of the present work is to analyse the (heuristic) mean field limit in link with the question stated above. General studies of this problem are scarce (but see [NLC15])

The contributions of this work are two fold: theoretical and numerical. The main theoretical advances are the proof of existence of invariant distribution which is notoriously difficult for jump processes. The is done by showing that an isolated neuron with arbitrary current is ergodic taking advantage of the fact that the embedded Markov chain $(\bar{v}, w_n)_n$ is one dimensional in our case. We then prove a local Doeblin condition for the Markov chain before showing that the continuous process has a unique invariant measure. The last step is non trivial as the mean firing time under the invariant measure of $(w_n)_n$ has to be finite. All the above analysis relies on the fact that we have a relatively good understanding of the 2d flow. We then analyse the PDE limit (2) which is a nonlocal transport equation by showing its well-posedness and analyse its equilibrium and their (linear) stability based on the analysis of the isolated neuron. This allows to predict collective oscillations.

$$\partial_t \mu(t) + \partial_v\big(\mu(t)\, V_{\mu(t)}(v, w)\big) + \partial_w\big(\mu(t)\, W(v, w)\big) = -\lambda(v)\, \mu(t) + \delta_{\bar{v}}(v) \int_{\mathbb{R}^2} \lambda(v')\, \tau_{\bar{w}}(\mu)(t, dv', dw') \tag{2}$$

where $V_\mu(v, w) := V(v, w) + J \int \lambda(v')\mu(dv', dw')$ and $\tau_{\bar{w}}(\mu)(t, v, w) := \mu(t, v, w - \bar{w})$.

On the numerical side, we develop an adaptive implicit positive and conservative scheme which has second order accuracy in time in order to simulate the dynamics of the mean field limit. Without this scheme, the simulation of the mean field is extremely unstable due to the reset mechanism. The scheme is based on a Finite Volume Method for which we prove the above properties, namely positivity and invertibility of the discretised divergence which we could not find in the literature for general 2d flows. Finally, based on theoretical analysis of the invariant measure, we provide an iterative procedure (with fast convergence rate) to numerically compute the equilibrium of the PDE. This procedure also provides a way to compute the spectrum of linearised equation. We are thus able to perform numerical bifurcation analysis of the PDE and predict multi-stability and collective oscillations.

By combining theoretical and numerical analysis of the mean field, we are able to predict how the intrinsic firing properties of the isolated neurons impact or are impacted by the collective dynamics at the level of the mean field. We then compare these predictions to the dynamics of the finite network which is simulated on GPU.

References

[DMGLP15] A. De Masi, A. Galves, E. Löcherbach, and E. Presutti. Hydrodynamic Limit for Interacting Neurons. *Journal of Statistical Physics*, 158(4):866–902, February 2015.

[FL16] Nicolas Fournier and Eva Löcherbach. On a toy model of interacting neurons. *Annales de l'Institut Henri Poincaré, Probabilités et Statistiques*, 52(4):1844–1876, November 2016.

[GKNP14] Wulfram Gerstner, Werner M. Kistler, Richard Naud, and Liam Paninski. *Neuronal dynamics: from single neurons to networks and models of cognition*. Cambridge University Press, Cambridge, United Kingdom, 2014.

[NLC15] Wilten Nicola, Cheng Ly, and Sue Ann Campbell. One-Dimensional Population Density Approaches to Recurrently Coupled Networks of Neurons with Noise. *SIAM Journal on Applied Mathematics*, 75(5):2333–2360, January 2015.

Characterising the temporal dynamics of stimulus processing through unconstrained decoding

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In this talk, I will introduce a technique designed to track trial-specific neural dynamics of stimulus processing and decision making with high temporal precision. Based on the use of decoding analysis, this method addresses a major limitation of the traditional decoding approach which is that it relies on consistent timing of these processes over trials. Using a temporally-unconstrained approach, the temporal differences in neural processing between presentations of the stimulus (or decisions to make) are explicitly accounted for.

By applying this novel method to a perceptual template-matching task, we tracked representational brain states associated with the cascade of neural processing, from early sensory areas to higher order areas, that are involved in integration and decision making. This way, we found that the timing of the cognitive processes involved in perceptual judgments can vary considerably over trials, even though the sequence of processing states was consistent for all subjects and trials. Furthermore, we found that the specific timing of states on each trial was related to the quality of performance over trials.

Altogether, in this talk I will highlight the serious pitfalls and misleading interpretations that result from assuming stimulus processing to be synchronous across trials, and I will also discuss how this type of analysis could open avenues to investigate learning, memory consolidation and plasticity.

Shape *versus* timing: linear responses of a limit cycle with hard boundaries under instantaneous and static perturbation

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The existing methods of infinitesimal phase response curve (iPRC) and variational analysis are well established for smooth systems and recently have been extended to nonsmooth dynamics with transversal crossing boundaries [1, 2, 4, 3]. But many rhythmic motions make and break contact with hard boundaries, leading to limit cycles with sliding components (LCSC). In this work, we extend both variational and iPRC methods to the LCSC in nonsmooth systems, for both instantaneous and parametric perturbations. The classical variational analysis neglects timing information and restricts to instantaneous perturbation. By defining an *infinitesimal shape response curve* (iSRC), we incorporate timing sensitivity of an oscillator to describe the shape response of this oscillator to parametric perturbations. In order to extract timing information, we further develop a *local timing response curve* that measures the timing sensitivity of a limit cycle within any given region. We demonstrate in a specific example that taking into account local timing sensitivity improves the accuracy of the iSRC over global timing analysis given by the iPRC. In addition, we investigate the isochrons of a simple LCSC system, and find nonsmooth kinks in the asymptotic phase function, propagating away from the hard boundary along a grazing trajectory emanating from an osculating point, in reverse time. Potential applications of our method include analysis of motor control systems in which the organism makes and breaks contact with a physical substrate (including walking, swallowing, and wiping motions), neural network models with a hard boundary at zero firing rate, and mechanical systems such as the stick-slip oscillator.

References

[1] Remco I Leine and Henk Nijmeijer. *Dynamics and bifurcations of non-smooth mechanical systems*, volume 18. Springer Science & Business Media, 2013.

[2] Youngmin Park. *Infinitesimal phase response curves for piecewise smooth dynamical systems*. PhD thesis, Case Western Reserve University, 2013.

[3] Youngmin Park, Kendrick M Shaw, Hillel J Chiel, and Peter J Thomas. The infinitesimal phase response curves of oscillators in piecewise smooth dynamical systems. *European Journal of Applied Mathematics*, pages 1–36, 2018.

[4] Sho Shirasaka, Wataru Kurebayashi, and Hiroya Nakao. Phase reduction theory for hybrid nonlinear oscillators. *Physical Review E*, 95(1):012212, 2017.

Neural field model of matching law behavior

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Neural field models describing the average activity of continuous networks of interacting neurons generally take the form of first-order integro-differential equations [1]. The rigorous analysis of pattern formation in these networks have become a powerful tool in theoretical neuroscience, to model higher-level cognitive functions such as memory and decision mechanisms [2]. In classical neural fields of Amari type, decision making is implemented by a winner-takes-all competition between sufficiently active neuronal populations [1]. The accumulation of input from sensors and connected populations leads to a continuous increase of population activity until a read-out threshold is reached. Strong later inhibition within the field ensures that only one population may become suprathreshold at any time. The decision process with competing alternatives may be driven not only by the accumulation of currently available sensory evidence, but also by the history of previous decisions or rewards. The accumulated evidence from choices made over a period of time is modeled as an input that preshapes neural populations. Consistent with the notion of priors in the Baysian sense [3], this preshaping input may bias the decision process. Behavioral evidence indicates that preference is given to choices associated with the highest reward probability but also choices with lower probability may win the competition from time to time. Stated mathematically, the behavior can be described by the so-called matching law asserting that the fraction of choices made to any option will exactly match the fraction of total rewards earned from that option [4, 5].

Here we report simulation results of a model consisting of coupled neural fields that addresses the neural representation of subjective choice valuation leading to the matching behavior. Central to our approach is the robust integration of rewards of competing alternatives over a given number of trials. This is achieved by a novel 2-population neural integrator model [6] representing the relative value of each choice by a stable bump solution with a height proportional to the reward frequency.

The integration of reward history in the decision process is tested in two possible scenarios: (1) a stationary environment with fixed reward rate over a long series of trials ("global matching law") , and (2) a dynamic environment with varying reward rate and an accumulation over a limit number of trials ("local matching law").

References

[1] S. Amari. Dynamics of pattern formation in lateral-inhibition type neural fields, *Biological Cybernetics,* 27 (2) pp. 77-87, 1977.

[2] W. Erlhagen and E. Bicho. The dynamic neural field approach to cognitive robotics, *Journal of neural engineering,* 3 (3) pp. R36, 2006.

[3] R. H. Cuijpers and W. Erlhagen. Implementing Bayes' rule with neural fields, *International Conference on Artificial Neural Networks,* pp. 228-237, 2008.

[4] L. P. Sugrue, G. S. Corrado, and W. T. Newsome. Matching behavior and the representation of value in the parietal cortex, *Science,* 304 (5678) pp. 1782–1787, 2004.

[5] B. Lau and P. W. Glimcher. Dynamic response-by-response models of matching behavior in rhesus monkeys, *Journal of the experimental analysis of behavior,* 84 (3) pp. 555-579, 2005.

[6] W. Wojtak, S. Coombes, E. Bicho and W. Erlhagen. Combining spatial and parametric working memory in a dynamic neural field model, *International Conference on Artificial Neural Networks,* pp. 411-418, 2016.

Communication Between Time Cells Leads to the Linear Increase of Noise

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Many organisms can time arbitrary time intervals flexibly with high accuracy but substantial variability between trials. One of the core psychophysical properties of interval timing function is the proportionality of the standard deviation of timed responses to their mean (time scale invariance). Recent experimental evidence show the existence of time cells that fire sequentially with progressing time. The time interval between consecutively firing time cell ensembles is shown to increase with the progressing time. When time is calculated by adding distributions of time intervals between time cell ensembles firing one after another, the noise is compressed by the square root function because of the way the standard deviation is calculated. So, how should the communication between successive time cell ensembles be so that noise increases linearly with progressing time? We came up with a simplified model of time cells that proposes a mechanism for the synaptic communication of time cells that fire one after another [1]. When the model is simulated with noisy conductances multiple times, the standard deviation of spike times of the time cells increases with mean spike-times. In addition, the model is shown to remain robust with respect to the changes in the key model parameters.

References

M. Zeki, F. Balci. Communication Between Time Cells Leads to the Linear Increase of Noise, *Frontiers in Computational Neuroscience* in press.

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