Brain Dynamics and Statistics: Simulation versus Data

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1 Motivation

The human brain is arguably the most complex biological structure. Making sense of its inner workings poses an enormous challenge. Different components of its activity evolve over periods ranging from one thousandth of a second to years, and over distances of one millionth of a meter to the size of the skull. Experiments perturb and probe activity over these scales of time and space, yielding reams of data. Our cohort of scientists is leading the effort to organize these data into a coherent picture using state-of-the-art mathematical modelling techniques. This picture encompasses deterministic and random components. This is a consequence of the fact that part of the brain's activity seems to evolve in a predictable structured manner, while other parts are unpredictable, even when responding to the same stimulus or initiating the same action.

The goal of this workshop was to develop methods to characterize these components, how they interact with each other, and how this interaction changes when stimuli impinge on the brain or the brain acts upon its environment. The techniques and advances that were discussed are at the forefront of two fields that seldom come together, namely dynamics and statistics, which respectively address the predictable and unpredictable aspects of the brain's behaviour. The rising and established experts brought together by this workshop aim to gain a deeper understanding of the brain's operational principles in the presence of variability, an understanding grounded in quantifiable ”statistical” certainty. The group is also driven by potential novel directions in mathematics that the intersection of concepts from dynamics and statistics will offer.

2 Overview of the topic

The primary goal of the workshop was to inspire collaboration among researchers in theoretical and experimental neuroscience, by discussing statistical methods, stochastic modeling tools, and experimental possibilities.

The data come from intra- and extracellular recordings of single neurons, revealing both spiking and subthreshold patterns, local field potential data, spatio-temporal measurements which show us spatial patterns with the extra dimension of time, EEG and fMRI data. Specific questions are: What are the important modes of information transmission in the brain? Does it occur via spiking patterns, or time averages of patterns? Are various rhythms also important? Surprisingly little is known. We know about some simple aspects of the operation of primary visual cortex, such as how single cells code for edges or movement at different angles; but the representation of the many features that make up a stimulus across different spatio-temporal scales of activity is an unsolved puzzle.

In order to make progress we needed to bring together people who gather neural data and understand lab work, people who have an extensive but usually specialized current knowledge about the brain, people who work in the mathematics of dynamical systems, particularly stochastic dynamical systems, and people who have facility in the statistics of stochastic processes. The common requirement is that these people are devoted to understanding the dynamics of the brain.

Despite a considerable recent body of literature on statistical inference and stochastic modeling in neuroscience, there remain substantial unsolved problems and challenges, some of which we addressed during the workshop. Examples are: understanding the role of stochasticity in the brain, developing efficient Monte Carlo methods for inference, understanding the relationship between system behavior (i.e. bifurcations and their stochastic counterparts) and statistical properties of estimates based on data from these systems, and reconstructing the structure of network models from partially observed data.

The workshop discussed the way data are processed and understood in the biological sciences, from a dynamical stochastic approach. Neuroscience is experiencing an imbalance between prowess in data collection and deficiency in data interpretation. The improved models for data processing are expected to be of significant theoretical interest from biophysical, mathematical and statistical viewpoints. Our work contributes to all parts of neuroscience, from single cell analysis to the understanding of neuronal network dynamics, and potentially beyond.

3 Main subjects of the workshop

- The role of stochastic dynamics in the Brain
  - Single neuron models
  - Mean field models
  - Network models
  - Hypoelliptic models and the statistical challenges
- Information transmission, encoding and decoding
- Applications of neural modeling to brain physiology
  - Control of Oscillatory Brain Dynamics
  - EEG data during anaesthesia in humans
  - Artifical neural network, biological instantiation of processing
  - The weakly electrical fish
  - Red-eared turtle

4 Presentation Highlights

We next give an overview of the presentations within the overall headings above, together with abstracts.

The role of stochastic dynamics in the Brain

Peter Thomas: Noise in the Brain: Statistical and Dynamical Perspectives There is growing interest in applying statistical estimation methods to dynamical systems arising in neuroscience. The discipline of statistics provides an intellectual framework for quantifying and managing uncertainty. For statistical methods to apply, one must consider a system with some variability. Depending on where one locates the source of variability, different methods suggest themselves. The talk will discuss some challenges and opportunities in linking statistical and mathematical perspectives in theoretical neuroscience, including the problem of quantifying "phase resetting" in stochastic oscillators, the problem of identifying the most significant sources of noise in a finite state Markov model, the problem of inferring control mechanisms in brain-body motor control systems, and the problem of parameter identification in noisy conductance-based models.

Adeline Samson: Hypoelliptic stochastic FitzHugh-Nagumo neuronal model: mixing, up-crossing and estimation of the spike rate Joint work with J.R. Leon (Universidad Central de Venezuela). In this presentation, we will introduce the hypoelliptic stochastic neuronal model, as diffusion approximation of intracellular or extra-cellular models. Then we will specifically focus on the FitzHugh-Nagumo model, and detail some of its properties: stationary distribution, definition of spikes, estimation of spiking rate.

Eva Löcherbach: Memory and hypoellipticity in neuronal models I will discuss the effect of memory in two classical models of neuroscience, first the stochastic Hodgkin-Huxley model, considered in a series of papers by R. Höpfner, M. Thieullen and myself, and second, a model of interacting Hawkes processes in high dimension which has been studied recently by S. Ditlevsen and myself. I will explain why memory leads to hypoellipticity and then discuss the probabilistic and statistical consequences of this fact.

Antoni Guillamon: At the crossroad between invariant manifolds and the role of noise I will drift along several topics in which we are currently involved. They all contain some treatment of recent tools from dynamical systems, mainly related to invariant manifolds, intertwined with the role of stochasticity. We aim at sharing our research interests to boost discussion and eventual collaborations. The first example will be on bistable perception where we are exploring up to which extent noise is necessary to explain data obtained from psycophysical experiments, as opposed to the information provided assuming quasi-periodic forcing. Second, we will focus on phase response curves (PRC) for oscillating neurons, a well-known tool to study the effectiveness of information transmission between cells; we have extended the notion of PRC to that of phase response field/function (PRF), also valid away from pure periodic behaviour. Stochastic PRCs have been already studied but PRFs constitute a more natural setting when neurons are subject to noisy inputs; we have neither explored the impact of noise on PRFs nor the extension of the concept to stochastic processes yet and, moreover, we also seek for experimental tests of our theoretical findings. Therefore, we think it can be interesting to address these open questions in this audience. If time allows, we will comment on some other issues (estimation of conductances and short-term synaptic depression) that combine concepts of dynamical systems with the presence of noise.

Zachary Kilpatrick: Maintaining spatial working memory across time in stochastic bump attractor models We discuss various network mechanisms capable of making spatial working memory more robust to noise perturbation and error. The canonical example we begin with arises from classic oculomotor delayed response tasks whereby a subject must maintain the memory of a location around a circle over the period of a few seconds. Asymptotic methods are used to reduce the dynamics of a bump attractor to a stochastic differential equation whose dynamics are governed by a potential that reflects spatial heterogeneity in the network connectivity. Heterogeneity can serve to reduce the degradation of memory overtime, ultimately increasing the transfer of information forward in time. We also show that connectivity between multiple layers of a working memory can further serve to stabilize memory, especially if they possess propagation delays. We conclude by discussing recent work, where we are modeling the phenomenon whereby a previous trials response attracts the current trials response, sometimes called repetition bias.

Lawrence Ward: Pattern formation via stochastic neural field equations The formation of pattern in biological systems may be modeled by a set of reaction-diffusion equations. A form of diffusion-type coupling term biologically significant in neuroscience is a difference of Gaussian functions used as a space-convolution kernel. Here we study the simplest reaction-diffusion system with this type of coupling. Instead of the deterministic form of the model, we are interested in a *stochastic* neural field equation, a space-time stochastic differential-integral equation. We explore, quantitatively, how the parameters of our model that measure the shape of the coupling kernel, coupling strength, and aspects of the spatially-smoothed space-time noise, control the pattern in the resulting evolving random field. We find that a spatial pattern that is damped in time in a deterministic system may be sustained and amplified by stochasticity, most strikingly at an optimal space-time noise level.

Laura Sacerdote: Integrate and Fire like models with stable distribution for the Interspike Intervals In 1964, Gernstein and Mandelbrot [1] proposed the Integrate and Fire model to account for the observed stable behavior of the Interspike Interval distribution. Their study of histograms of ISIs revealed the stable property and they suggested modeling the membrane potential through a Wiener process in order to get the inverse Gaussian as first passage time distribution, i.e. a stable distribution. Holden (1975) [2] observed that stable distributions determine a simple transmission pathway. Later many variants of the original model appeared with the aim to improve its realism but meanwhile researches forgot the initial clue for the model. The Leaky Integrate and Fire model that has not stable FPT distribution gives an example. The same holds for many other variants of this model. More recently Persi et al. (2004) [3] studying synchronization patterns, proposed a time non homogeneous integrate and fire model accounting for heavy tail distributions. The existence of heavy tails, typical of stable distributions is well recognized in the literature (see for example Tsubo et al [4] , Gal and Morom [5] and references cited therin) Signals from different neurons are summed up during the elaboration. Different ISIs distributions would determine an incredible variety of firing distributions as the information progresses in the network. However, it seems unrealistic to admit ISIs that cannot reproduce the same distribution when summed. This suggest the development of Integrate and Fire models using stable distributions. Furthermore, the stable ISIs paradigm gives rise to a more robust transmission algorithm since a possible lack of detection of some spike from the surrounding neurons does not change the nature of the final distribution. Here we rethink to the problem, taking advantage of the mathematical progresses on Lévy processes [6]. Hence, we propose to start the model formulation from the main property, i.e. the stable nature of the ISIs distribution. We follow the Integrate and Fire paradigm but we model the membrane potential through a randomized random walk whose jumps are separated by intertimes with stable distribution (or in the domain of attraction of such distribution). Observing that the supremum of the modeled membrane potential results to be the inverse of a stable subordinator allows to determine the Laplace transform of the ISIs distribution. This is a preliminary contribution since we limit ourselves to some aspects of the modelling proposal ignoring any attempt to fit data. We are conscious that these are preliminary results and some further mathematical study will be necessary to obtain models fitting data. In particular we expect an important role of tempered stable distributions [7]. [1] Gerstein G.L., Mandelbrot B. (1964) Random walk models for the activity of a single neuron. Biophys. J. 4: 41-68. [2] Holden, A.V. (1975) A Note on Convolution and Stable Distributions in the Nervous System. Biol. Cybern. 20: 171-173. [3] Persi E., Horn D., Volman V., Segev R. and Ben-Jacob E. (2004) Modeling of Synchronized Bursting Events: the importance of Inhomogeneity. Neural Computation 16: 2577-2595. [4] Tsubo Y., Isomura Y. and Fukai T. (2012) Power-Law Inter-Spike Interval Distributions infer a Conditional Maximization of Entropy in Cortical Neurons PLOS Computational Biology 8, 4: e1002461. [5] Gal A., and Marom S. (2013) Entrainment of the Intrinsic Dynamics of Single Isola Neurons by Natural-Like Input The Journal of Neurosciences 33(18), 7912-7918. [6] Kyprianou, A. (2014) Fluctuations of Lvy Processes with Applications. Springer Verlag, Berlin/Heidelberg. [7] Rosinski, J. (2007) Tempering stable processes. Stochastic Processes and their Applications. 117, 6: 677-707

Jonathan Touboul: Noise in large-scale neuronal networks, brain rhythms and neural avalanches It is now folklore that intracellular membrane potential recordings of neurons are highly noisy, owing to a variety of random microscopic processes contributing to maintenance. At macroscopic scales, reliable, fast and accurate responses to stimuli emerge, and are experimentally described through various quantities. I will focus in particular on mathematical models of large neuronal networks can account for the type of experimental data observed in synchronized oscillations (sources of brain rhythms) or neural avalanches. These two quantities are relevant in that rhythms reportedly support important functions such as memory and attention, while distributions of avalanches were reported to reveal that the brain operates at criticality where it maximizes its information processing capacities. I will show that a simple theory of large-scale dynamics allows understanding under a common framework both phenomena. In particular, I will show the relatively paradoxical phenomenon that noise can contribute to synchronization of large neural assemblies, and that the experimentally reported heavy-tailed distributions of avalanche durations and sizes may be in fact related to Boltzmanns molecular chaos that naturally emerges in limits of large interacting networks with noise. These works were developed with Alain Destexhe and Bard Ermentrout.

Janet Best: Variability and regularity in neurotransmitter systems In this talk I will discuss a couple of recent themes in my work: (1) Population models of deterministic neural systems enable one to capture the biological variability in individuals. These models can explain how the same circuits can operate differently in different individuals or can change in time in individuals because of dynamic changes in gene expression. They can be used to discover the characteristics of subpopulations in which drugs are efficacious or deleterious and are therefore useful for clinical trials; (2) In volume transmission neurons don't engage in one on one transmission but project changes in biochemistry over long distances in the brain. Thus, the nuclei containing the cell bodies (like the dorsal raphe nucleus for serotonin) are basically acting as endocrine organs. Recent work with Sean Lawley shows why volume transmission works, that is why concentrations of neuromodulator in the extracellular space are very even despite the fact that terminals and varicosities are distributed unevenly and firing may be random.

Shigeru Shinomoto: Emergence of cascades in the linear and nonlinear Hawkes processes The self-exciting systems as represented by neural networks are known to exhibit catastrophic chain reaction if the internal interaction exceeds an epidemic threshold. Recently, we have shown that the same systems may exhibit nonstationary fluctuations already in the subthreshold regime [1,2]; cascades of events or spikes may emerge in the Hawkes process even in the absence of external forcing. In a practical situation, however, systems are subject to time-varying environment in addition to internal interaction between elements. Here we attempt to estimate the degree in which the nonstationary fluctuations occurring in the system are induced by external forcing or internal interaction. [1] T. Onaga and S. Shinomoto, Bursting transition in a linear self-exciting point process. Physical Review E (2014) 89:042817. [2] T. Onaga and S. Shinomoto, Emergence of event cascades in inhomogeneous networks. Scientific Reports (2016) 6:33321.

Romain Veltz: Quasi-Synchronisation in a stochastic spiking neural network I will discuss a recent mean field (from E. Löcherbach and collaborators, R. Robert and J.Touboul) of a stochastic spiking neural network from a dynamical systems perspective. More precisely, I will present some recent results concerning the quasi-synchronisation of the neurons as function of the different parameters of the network (gap junction conductances, synaptic strength...).

Information transmission, encoding and decoding

Massimiliano Tamborrino: Novel manifestation of the noise-aided signal enhancement We discuss various type of noise-aided signal enhancements. Since not all stimulus levels can be decoded with the same accuracy, it is of paramount interest to determine which stimulus intensities can be discriminated most precisely. It is well known that the presence of noise corrupts signal transmission in linear systems. Nevertheless, noise may have a positive effect on signal processing in nonlinear systems, as confirmed by the stochastic resonance phenomenon. Stochastic resonance is typically observed in systems with a threshold in presence of a weak signal. However, the subthreshold regime is not a necessary condition when considering more than one neuron, since, for example, a suprathreshold signal may be also enhanced by noise in a network of threshold devices. Other phenomena where noise enhances the signal are for example coherence resonance and firing-rate resonance. We present a study of the decoding accuracy of the stimulus level based on either the first-spike latency coding or the rate coding (from the exact spike counting distribution) in a neuronal model as simple as the perfect integrate-and-fire model. We report counter-intuitive results, representing a novel manifestation of the noise-aided signal enhancement which differs fundamentally from the usual kinds reported on.

Benjamin Lindner: Spontaneous activity and information transmission in neural populations In my talk I will first review features of the spontaneous activity of nerve cells in neural populations and in recurrent networks, ranging from effects of cellular properties (e.g. noise and leak currents) and slow external noise (up/down transitions in a driving population) to the slow fluctuations that can build up due to the recurrent connectivity. I will then discuss how these features affect information transmission and stimulus detection, for instance, enable or suppress information filtering, benefit overall population coding, or lead to the detection of a short single cell stimulation in a large recurrent network.

Richard Naud: Burst ensemble multiplexing: connecting dendritic spikes with cortical inhibition Two distinct types of inputs impinge on different spatial compartments of pyramidal neurons of the neocortex. A popular view holds that the input impinging on the distal dendrites modulates the gain of the somatic input encoding. This gain modulation is thought to participate in top-down processes such as attention, sensory predictions and reward expectation. Here we use computational and theoretical analyses to determine how the two input streams are represented simultaneously in a neural ensemble. We find that dendritic calcium spikes in the distal dendrites allows multiplexing of the distal and somatic input streams by modifying the proportion of burst and singlet events. Two ensemble-average quantities encode the distal and somatic streams independently: the event rate and the burst probability, respectively. Simulations based on a two-compartment model reveal that this novel neural code can more than double the rate of information transfer over a large frequency bandwidth. To corroborate these findings, we determined analytically the parameters regulating mutual information in a point process model of bursting. Secondly, we find that an inhibitory microcircuitry combining short-term facilitation and short-term depression can decode the distal and somatic streams independently. These results suggest a novel functional role of both active dendrites and the stereotypical patterns with which inhibitory cell types interconnect in the neocortex. Burst ensemble multiplexing, we suggest, is a general code used by the neural system to flexibly combine two distinct streams of information.

Applications of neural modeling to brain physiology

Jeremie Lefebvre: State-Dependent Control of Oscillatory Brain Dynamics Numerous studies have shown that periodic electrical stimulation can be used not only to interfere with the activity of isolated neurons, but also to engage population-scale synchrony and collective rhythms. These findings have raised the fascinating prospect of manipulating emergent brain oscillations in a controlled manner, engaging neural circuits at a functional level to boost information processing, manipulate cognition and treat neurobiological disorders (so called oscillopathies). Capitalizing on this, it has been shown that brain stimulation can be tuned to alter perception and task performance. Rhythmic brain stimulation forms the basis of a control paradigm in which one can manipulate the intrinsic oscillatory properties of cortical networks via a plurality of input-driven mechanisms such as resonance, entrainment and non-linear acceleration. But the brain is not a passive receiver: outcomes of brain stimulation, either intracranial or non-invasive, are highly sensitive to ongoing brain dynamics, interfering and combining with internal fluctuations in non-trivial ways. Exogenous control on brain dynamics has indeed been shown to be gated by neural excitability, where effects of brain stimulation are both state-dependent and highly sensitive to stimulation parameters. To understand this phenomenon, we here used computational approach to study the role of ongoing state on the entrainment of cortical neurons. We examined whether state-dependent changes in thalamo-cortical dynamics could implement a gain control mechanism regulating cortical susceptibility to stimulation. We found that the resulting increase in irregular fluctuations during task states enables a greater susceptibility of cortical neurons to entrainment, and that this phenomenon can be explained by a passage through a bifurcation combined to stochastic resonance. We also investigated the relationship between the stimulation parameters, such as amplitude and frequency, on entrainment regimes for different levels of sensory input. Taken together, our results provide new insights about the state-dependent interaction between rhythmic stimulation and cortical activity, accelerating the development of new paradigms to interrogate neural circuits and restore cognitive functions based on the selective manipulation of brain rhythms.

Rune W Berg: Neuronal population activity involved in motor patterns of the spinal cord: spiking regimes and skewed involvement Motor patterns such as chewing, breathing, walking and scratching are primarily produced by neuronal circuits within the brainstem or spinal cord. These activities are produced by concerted neuronal activity, but little is known about the degree of participation of the individual neurons. Here, we use multi-channel recording (256 channels) in turtles performing scratch motor pattern to investigate the distribution of spike rates across neurons. We found that the shape of the distribution is skewed and can be described as log-normal-like, i.e. normally shaped on logarithmic frequency-axis. Such distributions have been observed in other parts of the nervous system and been suggested to implicate a fluctuation driven regime (Roxin et al J. Neurosci. 2011). This is due to an expansive nonlinearity of the neuronal input-output function when the membrane potential is lurking in sub-threshold region. We further test this hypothesis by quantifying the irregularity of spiking across time and across the population as well as via intra-cellular recordings. We find that the population moves between supra- and sub-threshold regimes, but the largest fraction of neurons spent most time in the sub-threshold, i.e. fluctuation driven regime. Read more about this work here: Peter C Petersen, Rune W Berg ”Lognormal firing rate distribution reveals prominent fluctuationdriven regime in spinal motor networks” eLife 2016;5:e18805

Axel Hutt: Model and prediction of anaesthetic-induced EEG The monitoring of patients under general anaesthesia is an essential part during surgery. To interpret correctly measured brain activity, such as electroencephalogram (EEG), it is essential to first understand the possible origin of EEG and hence classify the physiological state of the patient correctly. Moreover, it would be advantageous to even predict the development of the brain activity to anticipate severe changes of the physiological state. The talk presents a novel model explaining major EEG features under light anaesthesia, such as the spectral smile effect, by a denoising of brain dynamics. In a second part, the talk shows how to predict EEG under anaesthesia by applying a data assimilation technique.

Mark McDonnell: What can we learn from deep-learning? Models and validation of neurobiological learning inspired by modern deep artificial neural networks In the field of machine learning, deep-learning has become spectacularly successful very rapidly, and now frequently achieves better-than-human performance on difficult pattern recognition tasks. It seems that the decades-old theoretical potential of artificial neural networks (ANNs) is finally being realized. For computer vision problems, convolutional ANNs are used, and are often characterized as biologically inspired. This is due to the hierarchy of layers of nonlinear processing units and pooling stages, and learnt spatial filters resembling simple and complex cells. However, this resemblance is superficial. An open challenge for computational neuroscience is to identify whether the spectacular success of deep-learning can offer insights for realistic models of neurobiological learning that are constrained by known anatomy and physiology. I will discuss this challenge and argue that we need to validate proposed neurobiological learning rules using challenging real data sets like those used in deep-learning, and ensure their learning capability is comparable to that of deep ANNs. To illustrate this approach, in this talk I will show mathematically how a standard cost-function used for supervised training of ANNs can be decomposed into an unsupervised decorrelation stage and a supervised Hebbian-like stage. With this insight, I argue that this form of learning is feasible as a neurobiological learning mechanism in recurrently-connected layer 2/3 and layer 4 cortical neurons. I will further show that the model can learn to very effectively classify patterns (e.g. images of handwritten digits from the MNIST benchmark); error rates are comparable to state of the art deep-learning algorithms, i.e. less than 1.

Jonathan D. Victor: How high-order image statistics shape cortical visual processing Several decades of work have suggested that Barlow’s principle of efficient coding is a powerful framework for understanding retinal design principles. Whether a similar notion extends to cortical visual processing is less clear, as there is no ”bottleneck” comparable to the optic nerve, and much redundancy has already been removed. Here, we present convergent psychophysical and physiological evidence that regularities of high-order image statistics are indeed exploited by central visual processing, and at a surprising level of detail. The starting point is a study of natural image statistics (Tkacic et al., 2010), in which we showed that high-order correlations in certain specific spatial configurations are informative, while high-order correlations in other spatial configurations are not: they can be accurately guessed from lower-order ones. We then construct artificial images (visual textures) composed either of informative or uninformative correlations. We find that informative high-order correlations are visually salient, while the uninformative correlations are nearly imperceptible. Physiological studies in macaque visual cortex identify the locus of the underlying computations. First, neuronal responses in macaque V1 and V2 mirror the psychophysical findings, in that many neurons respond differentially to the informative statistics, while few respond to the uninformative ones. Moreover, the differential responses largely arise in the supragranular layers, indicating that the computations are the result of intracortical processing. We then consider low- and high-order local image statistics together, and apply a dimension-reduction (binarization) to cast them into a 10-dimensional space. We determine the perceptual isodiscrimination surfaces within this space. These are well-approximated by ellipsoids, and the principal axes of the ellipsoids correspond to the distribution of the local statistics in natural images. Interestingly, this correspondence differs in specific ways from the predictions of a model that implements efficient coding in an unrestricted manner. These deviations provide insights into the strategies that underlie the representation of image statistics.

Volker Hofmann: Population coding in electric sensing: origin and function of noise correlations In many cases, great knowledge regarding single neuron activity during the encoding of sensory signals or the generation of behavioral outputs has been achieved. On another scale, however, we still lack detailed information of the mechanisms of concerted neuronal activity, i.e. population coding. This is crucial to understand the neuronal code and remains a central problem in neuroscience. Extrapolating the knowledge of single unit activity to the scale of a neuronal population is often complicated by the fact that the activities of neurons are typically correlated rather than being independent. Such correlations, which can arise in terms of the average responses to different stimuli as well as in terms of trial to trial variability, were shown to substantially impact the efficacy of population codes. To investigate the sources and function of correlations we use the weakly electric fish Apteronotus leptorhynchus as a model system, due to the wealth of physiological and anatomical knowledge that is available with regard to electrosensory processing. These fish sense electric fields with an array of electroreceptors that project to three parallel segments of the medullary electrosensory lateral line lobe (ELL). Previous studies established, that the size and the organization of receptive fields differs substantially between pyramidal neurons in the different segments, which should consequently result in very different amounts of correlations in each segment. In contrast to this, our experimental recordings revealed very similar levels of correlation magnitudes. To explain this surprising result, we investigated the differential receptive field interactions using a modeling approach. Considering the antagonistic center-surround organisation of receptive fields, we were able to show that very different receptive field organization can give rise to very similar amounts of correlations. After establishing the presence of noise correlations in the ELL, we assessed their potential impact and function for the encoding of electrosensory stimuli. Our preliminary results suggest that ELL noise correlations encode stimuli independent of classical measures of neuronal activity (i.e. firing rate). The stimulus dependent changes in correlation levels are potentially modulated via the recurrent ELL connectivity which will be a focus of our future investigations to unravel the mechanisms mediating this independent additional channel of information transmission in the brain.

5 Posters

Each poster presenter had 5 minutes to introduce their poster to the full workshop. During our 45 minutes breaks, the posters were discussed in smaller groups. Having the posters up for the full meeting gave ample time to discuss and study the posters.

- Catalina Vich: Different strategies to estimate synaptic conductances
- Timothy Whalen: Pallidostriatal Projections Promote Beta Oscillations in a Biophysical Model of the Parkinsonian Basal Ganglia

- Jacob Østergaard: Capturing spike variability in noisy Izhikevich neurons using point process GLMs
- Peter Rowat: Stochastic network thinking applied to firing patterns of stellate neurons
- Wilhelm Braun: Spike-triggered neuronal adaptation as an iterated first-passage time problem
- Mareile Grosse Ruse: Modeling with Stochastic Differential Equations and Mixed Effects
- Kang Li: Mathematical neural models for visual attention
- Pietro Quaglio: SPADE: Spike Pattern Detection and Evaluation in Massively Parallel Spike Trains
- Alexandre René: Dimensionality reduction of stochastic differential equations with distributed delays

6 Impact Reports from Participants

Participants were asked to write a few lines telling about what they learned. Below are individual reports, also giving hints at outstanding problems in the field, and new directions for future research.

Laura Sacerdote, Torino: The workshop was a great occasion to meet very interesting people in a wonderful environment. We had contributions from theoricians and experimentalists with a challenging alternance that allowed each one to learn from the others. I already knew some of the scientists attending to the workshop but the discussions after each talk, as well as the long coffee breaks, gave me the opportunity to know new people and to propose new scientific links for my research. The presence of a very mixed group during my talk, gave me hints for interesting improvements of my work. The size of the workshop was perfect, in a small group it becomes easy to start to talk with the others, learning from posters and talks but also from many private discussions.

Benjamin Lindner, Berlin: The schedule was much better than that of many other workshops I have attended: long talks with sufficient time for questions during and after the talks, long breaks for even more informal discussions. The relaxed schedule, the number and kind of participants, the way the sessions were chaired - all of this was encouraging for a creative atmosphere during this workshop that I enjoyed a lot.

I met old friends and colleagues (Susanne Ditlevsen, Axel Hutt, Jeremie Lefebvre, Andre Longtin, Mark McDonnell, Richard Naud, Laura Sacerdote, and Peter Thomas) and talked with them about old times and new research projects. I was happy to make new acquaintances (Wilhelm Braun, Cindy Greenwood, Volker Hofmann, Zachary Kilpatrick, Eva Löcherbach, Massimiliano Tamborrino, Jonathan Touboul, Romain Veltz, Jonathan Victor, Lawrence Ward), to learn about exciting new research directions, and to get a bit of feedback on my own research efforts too.

I was especially inspired by the mixture of presentations on fundamental math problems related to stochastic processes in neuroscience (stochastic dynamics of excitable systems) and talks that were devoted to more data-driven and biology-centered topics - I think this was an excellent mixture that met many of my research interests. I know from many conversations that I was not the only one who felt like that.

Thank you again for organizing this marvelous workshop.

Mariele Groβe Ruse, Copenhagen, Denmark: What I appreciated a lot was the atmosphere among our group and that I all the time felt very welcome and included. No matter the ”academic status”, all participants were open, happy to talk/discuss, happy to provide inputs/feedbacks/ideas and also to chat about topics beyond research. I got very good inputs regarding applicability of my model to different kinds of input, which is useful for my PhD project. I talked to people with various background, which I always perceive as very interesting. Definitely, I learned a lot, although there was as much I did not understand, due to me having not really a background in neuroscience.

Mark McDonnell, Australia: I enjoyed discussions with a lot of slightly more junior researchers who were familiar with my work on stochastic resonance from the time of my PhD and just after. This was an enjoyable experience to see the new directions these researchers are following in that field, and have the opportunity to discuss with them. I also enjoyed many discussions with people about their experiences with machine learning and how it might benefit their future research.

A potential collaboration is in progress with Jonathan Touboul, whom I met at the workshop for the first time.

And of course the workshop was an opportunity to continue work on existing collaborations with Cindy Greenwood and Lawrence Ward.

Zachary Kilpatrick, Boulder Colorado: Thanks so much for organizing this workshop! It was wonderful. My current work and future plans were impacted in several different ways from my experience at the BIRS workshop. One of the first conversations I had at the conference was over dinner with Andre Longtin, and he shared his experience in balancing research, teaching, and service with me, providing some useful ideas for how to use my time wisely in my career. Peter Thomas provided some excellent feedback after my talk on different information theoretic measures and error quantification I could use to better think about the way the brain might optimize working memory systems. Furthermore, he was gracious enough to give me extensive details on his recent work on asymptotic phase for stochastic systems, taking me through some special cases. I learned a lot! Other conversations with Jonathan Touboul, Benjamin Lindner, and Axel Hutt gave me excellent ideas for future projects. Wilhelm Braun took the time to ask me some of my own advice about how to proceed at his stage (as an early postdoc) in view of getting an academic job in the future. Furthermore, I had an excellent conversation with Susanne Ditlevsen about planning current and future meetings for the International Conference on Mathematical Neuroscience.

Peter Thomas, Case Western University: Benjamin Lindner and I, who had been working together previously, were able to complete and finally submit a paper to the Journal of Statistical Physics while we were at Banff together, and began work on our next paper. I also learned a great deal from the workshop talks. Adeline Samson and Eva Löcherbach's talks on Hypoelliptic stochastic systems gave me ideas for how to show that a certain kind of nerve cell "resets" (in a stochastic sense) each time it fires, which is something my biological collaborator has conjectured repeatedly but which we did not know how to formulate. Antoni Guillamon's talk give me new ideas about how to represent the phase and amplitude of stochastic oscillators, a long standing interest of mine. Rune Berg's talk gave me new ideas for a project with a different collaborator involving mathematical modeling of motor control systems. I benefitted from side conversations with many participants, including the three organizers (Greenwood, Ditlevsen, and Longtin). I particularly appreciated the chance to discuss data assimilation techniques with an expert in this area, Axel Hutt. And snowshoeing up the back side of Mount Sulphur in subzero temperatures with Zach and Wilhelm was a real treat.

Jonathan Victor, Cornell: First, Romain Veltz: following my presentation, we had a substantive discussion about new approaches to understanding cortical dynamics, which may provide a way to account for some of the puzzling features of the data I had discussed. (The basic idea here is that patches of visual cortex don't represent just an orientation (as is traditionally thought), but rather, three parameters – an orientation, a dispersion, and a scale – effectively a 2x2 symmetric matrix. The implications are that cortical dynamics don't live on a torus, but rather, on a stack of Poincare disks.) Second, Volker Hofmann: with whom I had a series of discussions on active sensation, and the parallels and contrasts between the electric sense in weakly electric fish, and vision.

But most importantly, I really want to thank you for inviting me to this very stimulating event.

Timothy Whalen, Carnegie Mellon University: As a younger PhD student, it was a great learning experience to meet with experts in neural data analysis from across the experimental-mathematical spectrum. Several of the talks and discussions in the poster hall inspired ideas on how to address difficult, quantitative questions in my data and better relate these to my simulations. The Banff Center proved to be a fantastic venue for this purpose, streamlining everything so that we attendees could focus on the content of the workshop. The fellow researchers I've connected with and the new ideas I've learned from the workshop will not soon be forgotten!

Lawrence Ward, UBC, Vancouver: I was very happy to meet and converse with Axel Hutt and Jonathan Touboul, having previously known of their work in this field. I of course learned many new things about brain dynamics from the talks, but also from my conversations with their authors. Again, the work of Hutt, Touboul, Lindner, Kilpatrick, Veltz and Thomas was very revealing, and in some cases new to me (esp. Hutt on effects of anesthesia, Kilpatrick on memory and bumps). All of this will stimulate my future work on stochastic neuron models as well as on brain dynamics.

Axel Hutt, INRIA, France: The workshop gathered most of the top-level researchers working in the research field. This allowed to learn directly the primary current hot topics in the field and who works on what. The rather informal meeting made it possible to chat with researchers at a beer on general and specific science what was elucidating in several cases. I would say the workshop was quite valuable scientifically and definitely worth making the long trip from Europe.

Kang Li, Copenhagen: It was a great experience for me, in terms of both academic studies and mountain viewing. I brought a poster and there were some who came by and discussed with me. Among them were Eva, Adeline, Laura, and some others but I can't remember their names. I presented my work and future ideas and received interesting and useful feedbacks. The posters and talks from participants are brilliant and inspiring, from parameter estimations of point & diffusion processes, to the synchronization and coherence of spike trains, and to the emerging application of deep neural networks, etc. I was trained as a statistician and have been focusing on model inference, but there are obviously many different areas beyond mine which I really learned a lot from.

Eva Löcherbach, Paris: Personally, I found it very interesting to meet Peter Thomas; in particular his question how to distinguish between variability that is intrinsically generated versus the one that is extrinsically generated is a problem that I would like to study in models such as Hawkes processes in high dimension, subject to mean-field interactions within a spatially structured system of neurons which are arranged in populations. I also would like to study phase response curves in such models - and this is certainly inspired by some of the talks presented at the conference. The talk of Adeline Samson was also very interesting for me, in particular her question how to decide whether there is presence or not of channel noise for example (can we write a real statistical test for this?). Other talks that inspired me a lot were those of Zachary Kilpatrick, of Shigeru Shinomoto and certainly also Benjamin Lindner. Finally, let me say that the posters that were presented were very interesting and that I really appreciated the way those posters were shortly presented during the conference.

Adeline Samson, Grenoble: This conference was very productive for me, starting a new project with Massimiliano Tamborrino around some good beers in the cafe!

Toni Guillamon, Barcelona: The facilities provided by BIRS and the Banff Center are excellent; staying there is so easy and confortable that you can keep your mind occupied with the scientific problems and, at the same time, you forget you are working. The information provided along the whole process is very clear and all is prepared to arrive at Banff and work efficiently. The lodging quality is excellent, as well as the food in the restaurant, and the leisure activities. Among them, I will remember our walk on the Tunnel Mountain, the excursion to the Sulphure mountain, and the chats during the meals and around a glass of wine (sorry for the alcoholic reference) at the "bistrot".

I find also worth to mention the job made by the organizers of the workshop, mainly in selecting the lectures and the attendants. They were able to put together a group of excellent persons, with common interests but non-coincident backgrounds, and with a sincere desire to understand each other's work. More personally speaking, I come from dynamical systems theory and I've been working mainly on deterministic treatment of brain dynamics with an increasing interest in statistics and stochastic processes. In this workshop, it has been very rewarding to see how my research could link to the interests of other participants, most of them experts on aspects that I do not know but I do need! At the end, I came back home with a long list of stimulating suggestions as well as a group of colleagues which whom I can eventually interact in the future. I wish I could say the same of every meeting I'm attending!

In virtue of my sincere words in the above paragraph, thanks again for organizing it.

Volker Hofmann, McGill University: 1. I met researchers that work in my immediate field (weakly electric fish) and approach common question with employing different methods (i.e. by theoretical means). I am happy to have met Andre Longin and Benjamin Lindner at this work shop that allowed me to discuss a few things regarding recent and coming publications in the field. In addition to that I have had conversations with a number of researchers that share interests in certain more general research questions and use different animal models and/or methods. Also seeing how these people combine methodological expertise which I share, with further methods and techniques was of particular interest and will most probably help me to develop my own profile further down the road. Particularly my conversations with Rune Berg and Jonathan Victor were interesting in this respect.

2. To me, who is doing his very first steps in computational modeling this workshop was a jump start into the field and gave me a good overview of the aspects that are ”cutting edge problems” in neuronal modeling and ”mathematical neuroscience”. While I will probably not be working on any of these problems soon, I think this broad overview is helpful for me to see where the field of computational modeling is at the moment and where it is going in the near future. I actually learned about some problems that I didn’t know were problems.

3. The very positive and accommodating atmosphere at this workshop has positively reinforced my own work. I have become some good feedback after the presentation of my talk and this feedback has led to ideas that I am testing at the moment in the revision of one of my submitted publications.

Massimiliano Tamborrino, Linz: I have been honoured of being invited as a speaker to the workshop ”Brain Dynamics and Statistics: Simulation versus Data”. Without any doubt I can state that it has been the most inspiring and successful workshop I have ever attended. First of all, it gave me the opportunity of presenting myself and my research to a group of eminent professors and researchers, half of them I never met before. The organizers made an excellent job selecting the workshop participants and I believe that was one of the reason of the success of the workshop. All participants share an interest towards neuroscience, coming from different background though, e.g. statistics, mathematics, physics, experimental neuroscience, etc. More importantly, each participant was willing to listen, share and discuss ideas and open problems, making the workshop the perfect spot for starting new collaborations and being inspired by new topics. I wish there could be more of these workshops.

7 Outcome of the Meeting

This workshop brought together researchers from several different disciplines to work on the problem of understanding stochastic brain dynamics and statistics. This involved statisticians, probabilists, physicists, mathematicians and experimentalists. The experimental neuroscientists attending the workshop have been selected, in part, because of their interest in neuronal modeling and understanding stochastic effects in the brain. Their input was essential in our discussion.

The workshop has enabled us to cristalize and update the current directions and main goals in this area. We have forged links among people working in various directions, all being important for the advancement of the field. We have obtained a more focussed view of the current state of the field, and become aware of directions and activities of the various groups, the latest results in diverse areas, and where to find expertise within subtopics.

Our field has had a slow development. It is a rather complicated topic, having many modeling and physiological aspects, as well as statistical challenges. Treatments of this subject have generally been focussed on one or another of these aspects. In this meeting we have had a group of people with different emphasis of research. Several people join biological research with modeling, and have presented creative methods to address the statistical challenges of this particular field.

The workshop integrated graduate students and postdocs. All of the participants presented their work during the meeting, either with a talk or a short presentation and subsequent discussion of their poster in smaller groups. It is important to note that these young people were excellent in their ability to communicate their ideas and research to the diverse audience attending the workshop.

Informal feedback from workshop participants has been very positive with many new ideas emerging and the participants have all learned a great deal. All participants heartily thank BIRS and its staff for providing truly exceptional facilities and organization to support the meeting.

Some Key References

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