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Neural Coding 2012

Book of Abstracts

Prague, Czech Republic,
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Contents

Using the structure of inhibitory networks to unravel mechanisms of spatiotemporal patterning

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We established a relationship between an important structural property of an inhibitory network, its colorings, and the dynamics it constrains. Using a model of the insect antennal lobe we show that our description allows the explicit identification of the groups of inhibitory interneurons that switch, during odor stimulation, between activity and quiescence. This description optimally matches the perspective of the downstream neurons looking for synchrony in ensembles of pre-synaptic cells.

On dependency properties of the ISIs generated by a two compartmental neuronal model

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One dimensional Leaky Integrate and Fire neuronal models describe Interspike Intervals as a renewal process and disregard the geometry of the neuron. Multicompartment models account for the geometrical features of the neuron but they are too complex for their mathematical tractability. Leaky Integrate and Fire two compartment models seem a good compromise between mathematical tractability and an improved realism. Indeed they allow to relax the renewal hypothesis, typical of one dimensional models, without introducing too strong mathematical difficulties. Our aim is to enlarge the analysis of the two compartment model studied by Lansky and Rodriguez, using some specific mathematical tools together with simulation techniques. This model is one of the simplest models allowing the dependence between interspike intervals (ISIs). This fact motivates its study, as a first prototype of a model neuron of non renewal type.

Keywords: Two compartment neural model, ISI dependency properties

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Modelling of Sensory Pathway of Swimming Initiation in Young Frog Tadpole Spinal Cord: a Developmental Approach

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The relationship between structure and function of neuronal circuits is a challenging problem in neuroscience which has two main aspects: 1) How does a dynamical pattern of spiking activity lead to functions like cognitive behaviour? 2) What methods can identify the neuronal connections which lead to appropriate activity of a circuit?

In our previous work [1] we have developed a biologically realistic anatomical model of the tadpole spinal cord which is based on the developmental approach. The idea of this method is to analyze available experimental data on neuron anatomy, function and synaptic connections and extract their "characteristic features" which are then used for modelling. Thus, the model is able to generate an extended set of "artificial data" with the same characteristic features as the more limited experimental evidence.

The anatomical model is expanded to include both the hide brain and the spinal cord. A new model is based on three chemical gradients and some other simple rules which generate realistic neuronal axonal projection patterns for each of the neurons in the network. For each neuron type we therefore distribute cell bodies along the neuronal axis and generate axon projections using the growth model. We map the axons onto a two-dimensional nervous system and allow connections to form with a certain probability where axons cross the fixed dendrites assigned to each neuron. This gives us what we call a "connectome", a pattern of connections between all the different types of neurons [2].

To model spiking activity on the neural network, we use a conductance-based Hodgkin-Huxley type model with parameters set according to available neurophysiological measurements for each neuron type ([3]). Connections in the neuronal network are according with the connectome.

Functioning of the model is based on two main principles: 1) pacemaker activity, mutual excitation and Post-Inhibitory Rebound (PIR) in excitatory descending Inter-Neurons (dIN); 2) inhibition of activity on opposite side by the commissural Inter-Neurons (cIN). Oscillator half centres on each side of the body include both excitatory dIN and inhibitory cIN neurons.

Swimming initiation is modeled by a brief simulation of three nearby sensory neurons (RB cells) at some point on one side of the body. Although stimulation is possible at any point of the body, an excitation of sensory neurons is delivered by the network (with connections according to the connectome) to the hind brain and the rostral part of the spinal cord to excite dIN neurons at the rostral position of the spinal cord. From the rostral part, activity of dIN neurons propagates along the body (metachronal wave). Due to the inhibitory activity of the commissural cIN neurons, left and right sides of the body demonstrate anti-phase oscillations.

A remarkable result of this modelling is that the spatio-temporal pattern of spiking activity corresponds to swimming. This activity pattern is stable in some region of the parameter space. Our model is probably the first demonstration of how a biologically realistic connectome (structure) leads to a proper spatio-temporal pattern of spiking activity (function).

Keywords: connectome, spiking activity, swimming pattern

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Determinism, Randomness and the Question of the “Free Will” – Examined from a Neural Coding Perspective

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The existence of a “free will” has repeatedly been questioned since ancient times. In recent years, attacks against the “free will” specifically came from neuroscience. EEG recordings [1] as well as more recent fMRI data [2], have demonstrated that action related brain activity (readiness potentials, BOLD signals) occurs up to several seconds before an individual becomes aware about his/her decision to perform the action. As neuronal mechanisms are obeying physical laws it has been proposed that all decisions are fully determined already before the individuals become aware of those, only having the “illusion” of a free will.

Whether these experimental data can really disprove the existence of a “free will” has controversially been discussed [3, 4], also with critical contributions of Libet himself [5]. Here, only the argument of determinism shall be considered, thereby specifically reminding on basic neurophysiology knowledge that, in principle, is already known since 60 years (`www.cnsorg.org/hodgkin-huxley60`) when Hodgkin and Huxley have published their groundbreaking work about the generation and conduction of action potentials, modeled by voltage dependent rate constants[6]. In between, it could be demonstrated in innumerous experiments that the rate constants, indeed, reflect transition probabilities between open and closed ion channel states [7]. This indicates that there exists a particular type of randomness, apparently driven by Brownian motion that is principally unavoidable as long as the temperature does not fall to absolute zero, i.e. under all life compatible conditions. This randomness (or “noise”) is different from common stochasticity which may result from a manifold of unknown influences that are not under control.

Ion channel openings and closings, of course, first of all depend on physiological parameters, e.g. membrane potential or neurotransmitters and neuromodulators. Nevertheless, certain randomness always remains. An example is shown in Fig.1 relating an ion current activation curve to the underlying transitions rates of ion channel open and closing probabilities demonstrating significant fluctuations around deterministically expected steady state values. This “channel noise” of course, is becoming smaller with further increasing number of ion channels. Nevertheless, the deterministic value would only be reached with an infinitely high number of ion channels or, alternatively, after an infinitely long time. Hence, in real life there is no chance to get rid of randomness in neural coding and brain functions.

Noteworthy, even small channel noise can be dramatically blown up especially when it originates from subthreshold currents with slow activation and inactivation kinetics [8]. While the shape of an action potential is essentially determined by fast Na^+- and K^+-currents, the timing of action potential initiation - and fluctuations – depends on subthreshold currents, often generated by comparably few ion channels. The thereby induced variations in the temporal pattern of action potential generation lead to a principally unavoidable component also of synaptic noise. As a consequence, ion channel fluctuations can be dramatically blown up when propagated through individual neurons’ action potential generation to synaptic effects in neuronal networks. At each level the direct or indirect impact of channel noise can further be enhanced by cooperative effects with the systems’ inherent nonlinearities. Hence, a significant part of the well-known randomness of brain functions at all levels may be the result of principally unavoidable channel noise.

Principle unpredictability has been discussed in different contexts, specifically emphasized in physics by Heisenberg’s uncertainty relation. In biology, the relations between “chance and necessity” seem to achieve a particular relevance not only for random mutations in evolution [9] but also for everyday life of neural coding. There are neurons in diverse brain nuclei (e.g. amygdala and

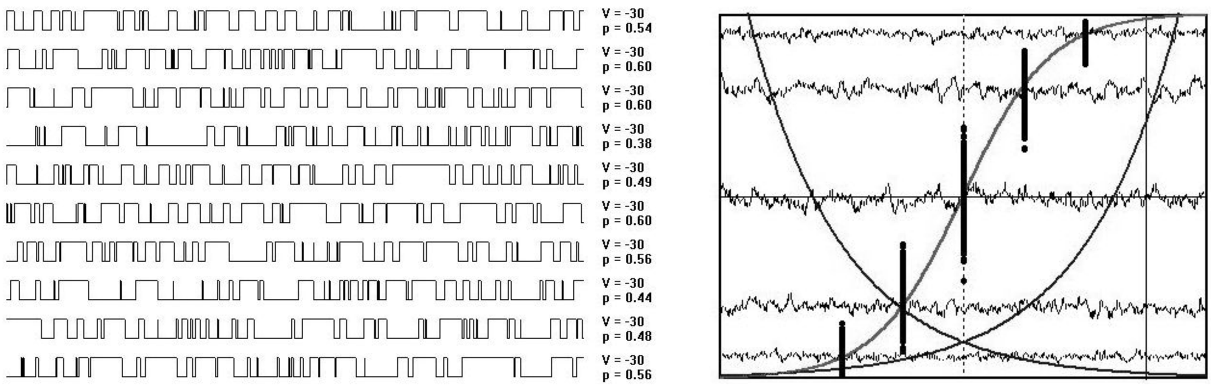

Figure 1: Left diagram: Sigmoid curve of voltage dependent ion current activation $a = 1/(1+\exp(-s(V-Vh))$ ($Vh = 30\,\mathrm{mV}, s = 0.14$) related to exponential voltage dependencies of ion channel transitions probabilities between open and closed states $p_{o,c} = x * \exp(y(V - Vh)$ (per ms). that are implemented symmetrically with unit value at Vh and $x = 0.1, y = (-)0.065$. Right diagram: Examples of random ion channel switching over 50ms at half activation voltage $Vh = 30$mV, p indicating the relative open state. With one thousand of such simulation runs (i.e. ion channels) the time course of compound current activation, plotted in the left diagram for different voltages, still shows significant fluctuations. Bars of black circles indicate the variation range of 50ms simulations runs as shown on the right.

entorhinal cortex) as well as sensory receptors (thermo- and electroreceptors [10]) that apparently take advantage of random fluctuations for their proper functioning.

In conclusion, randomness in neural coding and brain functions is principally unavoidable. This, of course, is not a proof of "free will" – but determinism, for sure, is also not a good argument against.

Keywords: ion channels, action potential, noise, chance, Hodgkin-Huxley

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Fast learning in single synapses and behavioral learning times

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Human can learn new facts and rules in a few seconds from a single presentation of a stimulus [1]. There is little experimental information on the speed of onset of synaptic changes in biology.

The first part of this paper estimates learning speed from synaptic depression and spine growth data, to determine how fast weight changes can actually take place. The resulting learning speed of a S-R association in a multilayer network of LIF neurons developed in [2] is then examined. This has implications on the number of synaptic relays that can practically be involved in fast learning and on the representation of sensory information.

Learning speed estimation from synaptic depression. Given that LTP requires the insertion of new AMPA receptors in the synapse, information on the speed of the process can be gained from observing the recovery from synaptic depression, although it is difficult to separate pre-synaptic vesicle replenishing effects, postsynaptic AMPAR recovery processes and diffusive contributions. Recovery is probably dominant for large synapses while diffusion and vesicle depletion dominate for small synapses [3]. When intracellular calcium concentration is increased through NMDA activation, the recovery from depression is slowed down, indicating that diffusion effects can be the limiting factor in the recovery time from depression. Thus, recovery time constants from depression represents a lower bound on the receptors influx time during learning. From data published in [3], the full synaptic conductivity is restored in approximately 100ms.

Estimation from the speed of growth of new spines. There is a good correlation between synapse area and number of AMPA receptors in a synapse [4]. Therefore, another source of information on the speed of learning is the observation of the speed of growth of spines. Several experiments have shown very fast growth of new spines in the presence of glutamate produced by uncaging. In [5], a spine can grow by 1um with an average spine head area of 0.4um2 in as little as 10 seconds. This is produced by 20 uncaging pulses produced at 2Hz. The same growth can be produced by 20 pulses at 0.5Hz, in a total time of 40 sec. The process requires NMDA activation. The independence of pulse frequency suggests that a certain amount of growth occurs for each pulse with a rate of at least 0.23um2/sec. In [4] synapses with a radius of 0.1um have no AMPAR, while those with 0.2um have a maximum number. The area difference is 0.19um2, which could be grown in just less than 1 second.

Implications for fast learning. The data presented above provide a maximum time of learning per synapse of 1 sec based on spine growth and a minimum of around 100ms corresponding to the recovery time from depression. With an input stimulus firing at around 100Hz, these boundaries allow for between 10 and 100 spikes to induce the desired synaptic weight. In a 6-layer multilayer system such as the one described in [2], we have set the learning rate so that 2, 20, 50 and 100 spikes are needed to set a weight, the learning times are found to be respectively 680 ms, 1066 ms, 1615 ms, and 2764 ms (fig. 1)

Fig 1A and 1B indicate that the learning time scales with the number of trained layers. Fig 1C shows that the total learning T time scales linearly with the number m of input spikes needed to learn one weight: $T = 700 + 21m$. For up to 20 spikes needed to train one synapse, the overall learning time is less than 1 second, a duration that is behaviorally realistic. However, if more spikes were needed, then one would need to reduce the number of layers to keep the learning time below 1 sec. Such a reduction would require an appropriate representation to have been pre-trained in deeper layers. It is surprising that a 50 fold decrease of the rate of synaptic weight change only causes a 2.4 fold increase of the learning time. Fig 1C reveals a basic learning-rate-independent

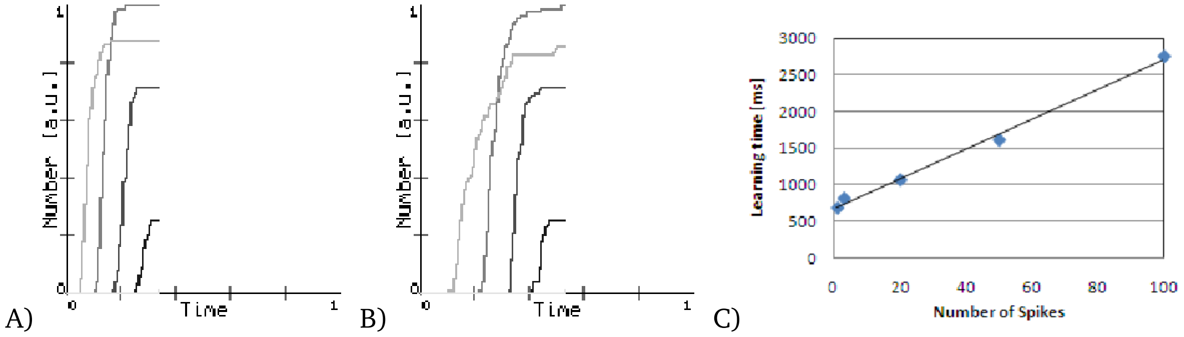

Figure 1: Fraction of active nodes in successive layers as learning progresses and learning time. The x-axis in A) and B) represents a duration of 2 seconds. A: Condition where the new weight is effective from the second input spike on each synapse. B: Condition where 20 spikes are needed to bring the weight to the same level. All active inputs fire Poisson spike trains at 100Hz. The weight of each synapse converges towards W_0/n where W_0 is the size of an initial pool of weight resource, e.g. extra-synaptic surface AMPAR, and n is the number of active inputs of the neuron . More details can be found in [2]. C: Learning time as a function of the number of spikes needed.

learning time, possibly linked to the stochastic arrival of the inputs, to which the weight build-up process adds a component that increases linearly with the number of spikes needed.

Keywords: Synaptic learning. Receptors mobility. AMPAR pool.

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A Simple Algorithm for Simulating Firing Times predicted by a LIF Model

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The problem of first passage time is widely known as one of the most difficult matters in the theory of stochastic processes, even if it plays a crucial role in various application contexts, i.e. in quantitative finance, in theoretical biology, in engineering, in chemistry, in epidemiology.

In the context of the firing of a single neuron the membrane potential is often described by means of a Gaussian diffusion process (IF, LIF, EIF models) whose excursion is limited above by an absorbing barrier, called firing threshold, at attainment of which there is the emission of the so-called action potential or spike. The shape of the stereotyped function describing the action potential depends on each family of neurons. Here, considerable importance is given to the determination of the distribution of the firing times, or alternatively, to the determination of its main statistical indexes.

In this specific application, the problem of the firing time of a neuron can be even more complicated than the underlying problem of the first passage time described above. In fact, even assuming that, subsequently the emission of an action potential, the membrane potential is initialized, after a fixed absolute refractory period, at a pre-assigned value, the time dependency of the deterministic stimulus may cause different conditions for next evolutions towards the threshold firing.

It may then be useful to have methods to simulate the interspike intervals (ISIs). This can be done, for example, by simulating trajectories of the membrane potential by means of numerical methods suitable for the stochastic differential equations of diffusive type (see [1] and [2]), or exploiting the underlying known Gaussian bridge distribution (see [3]). However, as the above cited authors point out, it is necessary to evaluate the probability that a spike arises within each interval of the temporal mesh before the time of the observed spike.

With this aim, in [2] the authors applied a Monte Carlo method, while in [3] via theoretical considerations an useful bound is obtained.

We now propose the application of the simulation method based on the hazard function ([4]) that for the first passage time problem represents the related instantaneous rate: the ratio between the probability density function and the survival function. For this purpose it would be known the first passage time probability density function that is, unfortunately, the unknown desired function. The method proposed by us is based on the use of the integral equation ([5], [6]), known in the literature as the singularity removed probability current equation ([7]). According the available computational facilities, one can use several methods to obtain suitable numerical approximations of the required probability density.

Taking account that the application of the method of the hazard function can also lead to the evaluation of the above density in times considerably larger than the integration step, the proposed method is particularly operative when the hazard function tends, as time increases, to a constant or a periodic function. We prove that it happens, asymptotically respect to the firing threshold, in the case of the LIF model with constant or periodic stimulus. The same result is obtained in the LIF model in which the time constant and the resting potential are substituted with appropriate time dependent functions.

Keywords: Hazard Rate Method, Gauss-Diffusion Processes, Instantaneous Firing Rate.

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Precise coding of interaural level differences in the auditory brainstem

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Interaural level difference (ILD) is one of basic binaural clues supporting the localization of a sound source. Due to acoustic shadow cast by the head, deviation of a sound source from the medial plane results in an increased sound level at the nearer ear and a decreased sound level at the averted ear. In mammalian auditory brainstem, the ILD is evaluated by neurons in the lateral superior olive (LSO), which receive excitatory projections from the ipsilateral side and inhibitory projections from the contralateral side. As the sound level is encoded predominantly by neuronal discharge rate, the principal function of LSO neurons is to estimate the difference between discharge rates of the two inputs. Both psychophysical and neurophysiological studies in mammals have shown that the ILD is assessed with a remarkable precision, the just noticeable differences (JND) ranging from 0.5 dB to 4 dB [2]. Such a precision imposes severe requirements on precision of both sound level coding and the ILD evaluation mechanism. Employing computer simulations and signal detection theory, the current work explores the theoretical JNDs of ILD depending on various parameters of the input spike trains and the evaluation mechanism.

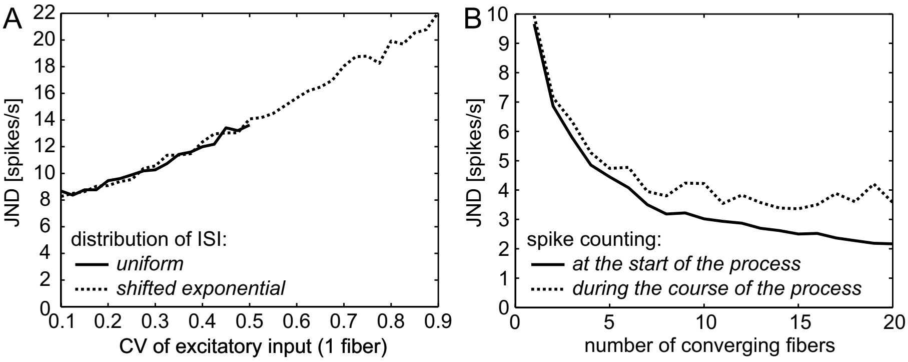
The afferent inputs to the LSO may be either primary-like, preserving precisely the discharge patterns in the auditory nerve, or choppers with regular rhythmic response [1]. These two types of firing were modeled by a dead-time Poisson process with shifted exponential distribution of inter-spike intervals (ISI), and a process with a uniform distribution of ISI, respectively. Only asynchronous firing with no phase-lock to the stimulus waveform was considered.

The temporal variability of neuronal discharge patterns may be expressed using the coefficient of variation (CV: standard deviation of ISI divided by mean ISI) or Fano factor (FF: spike count variance divided by mean spike count over some counting interval). A higher variability of firing leads to a lower precision of the rate code. Intuitively, if a repeated presentation of a given stimulus evokes each time a different spike count, then to distinguish between two different stimuli, the associated spike count change must be larger than the spike count variability.

The JND of ILD may be evaluated, e.g., by fixing the contralateral sound level and varying the ipsilateral sound level. However, as the relationship between the sound level and the corresponding discharge rates at the LSO input depends on many factors (such as auditory nerve rate-level function, RLF), the current work does not evaluate the ILD itself, but the just noticeable changes of firing rate of the excitatory LSO input. The corresponding ILDs may be estimated by considering that the slope of auditory nerve RLFs is on average 5 spikes/sec/dB [3]. In the simulations, the theoretical JNDs are evaluated using ideal subtraction of excitatory and inhibitory firing rates using a given counting window.

The results show that the JND increases nearly linearly with increasing CV of the excitatory or inhibitory input (see Fig. 1A), the distribution of ISI of the inputs does not play a role. The length of the counting window Δ strongly influences the JND. The longer the Δ, the smaller the JND, explicitly, $\mathrm{JND} = K/\sqrt{\Delta}$, where K is some positive constant. An analogous dependence may be found between the JND and overall input firing rate. Given a constant CV of the inputs, the JND grows with the square root of the input rates. This leads to a paradox that to keep the JND constant, higher input rates must be accompanied by longer counting windows.

The above results hold for excitatory and inhibitory inputs each comprising a single random renewal process with given ISI distribution and CV. As multiple excitatory and inhibitory fibers may converge at an LSO cell, such situation was considered by modeling each input as a sum of multiple independent random renewal processes with identical statistics. Importantly, despite that the converging fibers are independent, JND decreases for an increasing number of fibers. Although a sum of multiple non-Poisson processes has nearly an exponential distribution of ISI, the result



Parameter setting

A: *excitatory firing rate*: 100 sp/s
inhibitory firing rate: 50 sp/s
CV of inhibitory fiber: 0.5
counting window: 200 ms

B: *excitatory firing rate*
(each fiber): 100 sp/s
inhibitory firing rate
(each fiber): 50 sp/s
CV of excitatory fiber: 0.25
CV of inhibitory fiber: 0.5
counting window: 200 ms

Figure 1: JND depending of the excitatory CV and on number of converging fibers.

is not a renewal process and on longer time scales, it preserves the properties of the individual component processes [4]. The simulations show that in the case of a renewal process, Fano factor is proportional to the square of CV. However, if we sum up multiple processes each having CV=0.25, the resulting CV quickly approaches 1, yet the resulting FF corresponds to the CV of an individual component process (i.e., FF $\sim 0.25^2$), leading to markedly lower JNDs. Furthermore, the summary process is not renewal, hence the spike counts (and thus also the JNDs) obtained at the beginning of the process are different from those obtained during the course of the process (see Fig. 1B), which may have implications for ILD perception: JNDs of ILD may be lower when evaluated using short tone pips than when using continuous signals.

Concluded, the lowest theoretical JNDs of ILD are similar or better than the experimental values. However, the LSO cells hardly behave as an ideal detector; a certain worsening of JND is to be expected. Given that the lowest excitatory and inhibitory CVs are approx. 0.2 and 0.7, respectively [1, 3], then to attain the desired precision, the counting window should be at least 200 ms long, ca. 10 excitatory and 10 inhibitory fibers should converge at one cell, and the input firing rates should be kept low. Furthermore, spike timing must be conveyed accurately from the auditory afferents to the LSO.

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Keywords: Binaural interaction, Lateral superior olive, Subtraction of firing rates.

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Image coding at the electrosensory lobe of pulse gymnotiforms

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Electric fish explore their environment using an electric organ discharge. The electric field is modified by the presence of nearby objects allowing the fish to identify different object attributes related to their impedance, shape, position in the electric field, size and distance. This study is focused on the early processing of electro-sensory images in the electro-sensory lobe of *Gymnotus omarorum*.

The electro-sensory lobe, the first neural relay of electro-sensory images, contains two different sensory streams: the fast and the slow electro-sensory pathways. At the electro-sensory lobe the fast electro-sensory pathway shows a single spiking onset neuron type whose intrinsic properties and role in information processing was recently disclosed [1]. The slow path shows a complex circuitry with several cell types [2]. The main output cells of the slow path are two types of pyramidal cells differentiated anatomically by the presence or absence of a basilar dendrite. While basilar pyramids are excited by the stimulus increase at the center of the receptive field, non-basilar pyramids are inhibited [3]. The firing patterns of these cells in response to changes in electro-sensory stimuli as well as the roles of this dual output of the electro-sensory lobe are still unknown in pulse gymnotiforms.

The aim of this study was to investigate the post-EOD probability pattern discharge of pyramidal neurons in the chronically implanted, freely discharging and non-anesthetized fish. We found a general pattern of discharge. There is an early silent phase, starting about 4 ms and lasting up to 12 ms after the EOD. This silent period is followed by the active phase lasting the rest of the inter-EOD interval. Different firing modalities were distinguished in the phase histogram that usually was bimodal. Histogram modes were characteristically timed and modulated up or down by local signals allowing us to classify the recorded units according to their post-EOD firing pattern and their response to the presence of conductive or non- conductive objects and global changes in their environment (tube hiding).

Keywords: electrosensory system, unitary recording in freely moving fish, pyramidal neurons

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Interplay between Endogenous and Exogenous Rhythms in Recurrent Networks with Conductance-Based neurons

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A central issue in computational neuroscience is to determine the way cortical activity originates from the interplay between external stimuli and internal dynamics [1]. This is crucial to understand how the brain combines external and internal sources of information to produce its functions. In previous works, we begun the investigation of the effect upon cortical dynamics (as measured by Local Field Potentials – LFPs) of the interplay between endogenous and exogenous rhythms by studying the dynamics of recurrent excitatory and inhibitory integrate-and-fire networks, that were stimulated with various types of dynamic external inputs arising from the thalamus [2, 3, 4]. We modelled LFPs because we focused on network-scale (rather than single cell) rhythms. These rhythms are indeed more easily measured experimentally with LFPs, which include contributions from different neural phenomena (expressing a wide range of frequencies) that are not easily captured when recording extracellularly the spiking activity of small groups of neurons. In the previous studies we found that, in agreement with experimental results [4, 5], low and high LFP frequency bands expressed by our networks conveyed independent information about simulated external stimuli with complex, natural-like temporal dynamics [2, 3]. The power of low frequency (<10 Hz) LFP oscillations carried information about the corresponding low frequency components of the simulated external input because the latter entrained the first, whereas the information carried by the power of internally generated LFP oscillations in the gamma range (50-100 Hz) was about the intensity of the simulated external input.

A limitation of our previous work was that it did not take into account the dependence of the post synaptic current (PSC) on the membrane potential of the post synaptic neuron and that it neglected certain types of sources of endogenous oscillations, such as adaptation currents that are known to enable the network to display endogenous slow LFP fluctuations, potentially leading to Up and Down states [6]. These limitations did not enable us to study the interplay between external stimuli and certain classes of internal dynamics. Here, we present results obtained with a network having the same architecture of the one studied in [2, 3], but with conductance-based neurons (in which the PSC depends on the membrane potential of the post synaptic neuron) and pyramidal cells displaying activity-dependent adaptation current.

We found that our conductance-based model was able to replicate several aspects of cortical dynamics. In particular, it could replicate well the shape of field potentials, the dependence of LFP information about visual stimuli upon the LFP frequency [5], and the cross-frequency coupling between phase of slow oscillations and power of gamma oscillations. This suggests that the hypotheses about the network mechanism generating slow (<10 Hz) and fast (50-100 Hz) information components in LFPs, that arose from our previous models [2, 3], are robust enough to hold also in the presence of more realistic conductance based synaptic dynamics.

The presence of an adaptation current [7] did not disrupt the gamma oscillation regime induced in the network by sufficiently strong stimuli. Only when the ratio of the excitatory and inhibitory input to the excitatory population was above a given threshold, the interplay between recurrent excitation and adaptation current led to the presence of a dynamics resembling the Up and Down states.

Keywords: Integrate and fire networks, Conductance based model, Local field potential oscillations

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Independent components of wing kinematics in the fruit fly Drosophila

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Flies are known for their supreme flight maneuverability that is facilitated by their highly specialized flight apparatus. In the fruit fly Drosophila melanogaster, the wing motion is modulated by the activity of a group of around 18 miniscule steering muscles at the base of each wing. Our study is motivated by the hypothesis that a small number of muscle co-activation synergies gives rise to the changes in wingbeat responsible for flight maneuvers. Complementary to existing electrophysiological studies of selected muscles, our approach is to study the neuromotor control mechanism of the flight apparatus as a whole. We have developed a statistical method based on independent component analysis [1] to classify the wing motion patterns of the fruit fly during tethered flight. This method identifies components of the wing motion that are maximally statistically independent of each other; such components may be viewed as the basic neuromotor flight control modes.

Wing motion of tethered flying flies was recorded using a high speed computer vision system (TrackFast, SciTrackS.com) [2]. Angular positions of the two wings at 12 equispaced phases of the wingbeat cycle were considered as 24 separate time series and analyzed using independent component analysis (ICA). Out of the 24 least dependent components obtained from each test, only 6 to 8 were found to have a non-flat spectral density (Wiener entropy below 0.8), while the remaining components had the characteristics of broad-band noise. Thus, the wing beat variability during a segment of tethered flight is composed of only a few types of mutually independent characteristic variations.

Our present study focuses on variations that we found repeatedly in test flights of individual flies and between flies. These variations were reproduced even when only 2 phase points per wing (the dorsal and ventral reversal angles of each wing) were considered as 4 input signals for the ICA. Each test flight was analyzed in segments of 2500 wing strokes, and components represented by similar linear combinations of the four signals in distinct segments were clustered. Clusters from different test flights and from separate flies were then grouped based on the characteristic properties of the dominant variations in their elements (Fig. 1).

Three distinct groups of least dependent components were obtained. Components in the first group were dominated by sharp features at a time scale of 40 to 70 wing beat cycles and had almost no correlation (< 0.2) with wing beat period. During these events, the ventral reversal angle of one wing decreased, while that of the other wing increased (Fig. 1). Such a change corresponds to

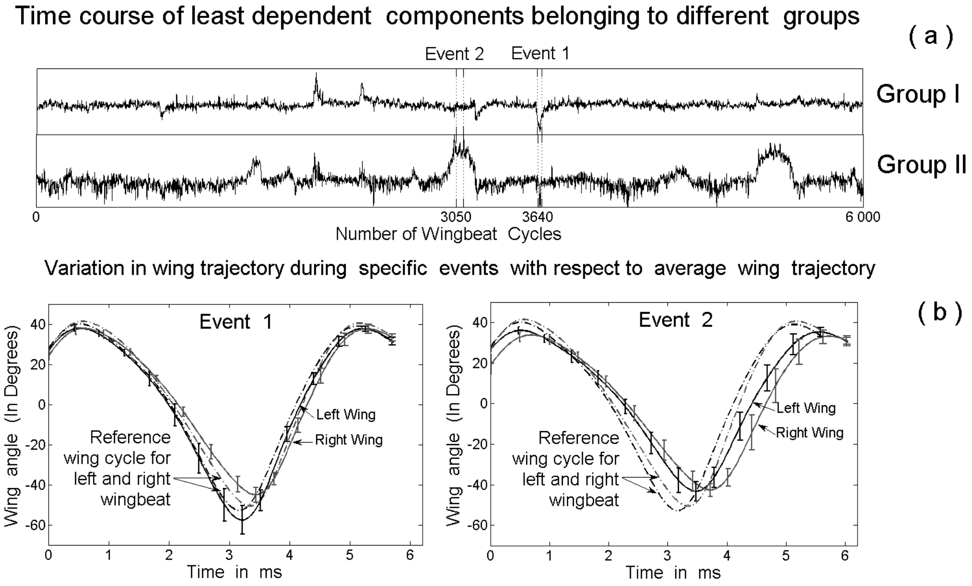

Figure 1: *Example of mutually independent wing variations. a) Time course of ICA components belonging to two distinct groups. Events 1 and 2 mark two intervals, in which variation corresponding to one of the components occurs exclusively. b) Mean wing trajectory during events 1 and 2. Dashed lines show wing trajectory averaged over 2000 cycles.*

the well-known fast turning maneuvers of flies during free flight, called body saccades [3]. Components in the second group have period-correlated (> 0.45) variations at a time scale of 200 to 500 wing beat cycles (Fig. 1). These events comprised bilaterally symmetrical alterations of wing beat amplitudes, corresponding to a lift maneuver during free flight. The third group of components was obtained from the difference of dorsal reversal angles and had no identifiable characteristic time course. The first two types of variations were occasionally found to occur simultaneously and ICA resolved them as distinct components. In conclusion, our findings suggest that the muscle synergies that generate lift and saccade maneuvers operate independently from each other.

Keywords: Flight control, muscle synergy, independent component analysis.

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FM responses of midbrain auditory neurons modeled with artificial neural network based on multiple trigger features

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Frequency modulation (FM) is an important building block of complex sounds including speech signals. Mechanisms on neural processing of complex sounds remain largely unclear. Attempts have been made to predict neural responses to complex sounds using various computer models, but often without much success especially targeted at the higher levels of the auditory pathways [1, 2]. The failure is generally attributed without to 'non-linear' properties of the central circuits [3]. We had previously reported that such unsatisfactory results are partly due to the lack of knowledge on the complexity of trigger features [4]. When the trigger features are better delineated and incorporated into the model, performance would usually improve [5]. Here, we attempt to model auditory neurons with multiple trigger features. Single spike activity was first recorded from midbrain auditory neurons of anesthetized rats in response to a battery of sounds (random FM tones of different carrier frequencies and different modulation profiles). We then applied spike-trigger averaging to extract the raw trigger features which were further segregated into individual components following a scheme of 'progressive thresholding' and 'spike de-jittering' algorithms we have developed earlier [6, 7]. We then carefully grouped the peaks in peri-stimulus time histogram of the spike response to FM sound in accordance with the trigger features and simultaneously taking into account of the performance of trained artificial neural network in predicting the response. The artificial neural network is a finite impulse response artificial neural network of simple architecture (1-1-1). Separate modeling of groups of peaks was subsequently performed. Results showed that such approach of separate modeling provide satisfactory prediction of FM response to modulation envelope unknown to the trained model. Our findings are in support that trigger features are likely more important than non-linearity in successful modeling at least for some FM-sensitive neurons in the auditory midbrain.

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Keywords: Frequency modulation, spectro-temporal receptive field, inferior colliculus, neural modeling.

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Coding of woody and fruity odorant mixtures: Interactions of odorants with olfactory receptors and receptor neurons match the perceptual dynamics

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The present study aimed to create a direct bridge between peripheral and central responses to odorant mixtures and their components. Three experiments were performed using mixtures of fruity (isoamyl acetate, ISO) and woody (whiskey lactone, WL) odorants known to contribute to some of the major notes in Burgundy red wine. These experiments consisted of *(i)* calcium imaging of human embryonic kidney cells (HEK293T) transfected with olfactory receptors (ORs); *(ii)* single-unit electrophysiological recordings from olfactory receptor neurons (ORNs) and analyses of electro-olfactogram (EOG) responses in the rat nose in vivo; and *(iii)* psychophysical measurements of the perceived intensity of the mixtures as rated by human subjects.

The calcium imaging and electrophysiological results revealed that ISO and WL can act simultaneously on single ORs or ORNs and confirm that receptor responses to mixtures are not the result of a simple sum of the effects of the individual mixture compounds. The addition of WL to ISO principally suppressed the ORN activation induced by ISO alone and was found to enhance this activation in a subset of cases. In the human studies, the addition of high concentrations of WL to ISO decreased the perceived intensity of the ISO. In contrast, the addition of low concentrations of WL enhanced the perceived intensity of the fruity note (ISO) in this mixture, as it enhanced EOG responses in ORNs.

Thus, both OR and ORN responses to ISO+WL mixtures faithfully reflected perceptual response changes, so that the odour mixture information is set up since the peripheral stage of the olfactory system.

Keywords: Odour coding, odour mixture, olfactory receptors, olfactory receptor neurons

Patterns of single-trial auditory evoked potentials on the human temporal cortex extracted with the adaptive filter

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Human auditory evoked potentials especially recorded intra-cranially especially over the superior temporal cortices are valuable in understanding neural coding of speech sounds. Such electrical recordings from the temporal cortex are usually obtained from consent neurosurgical patients undergoing investigatory procedures during short stays in the hospital [1]. Consequently, datasets obtained from these subjects are of limited sample size. To extract the auditory evoked responses from such small samples, the conventional ensemble averaging often fails to suppress the relatively large ongoing background EEG activity over the association auditory cortices where large inter-trial variations in response could occur, likely related to the fluctuation of attention during experiment [2]. Effective methods to extract evoked potentials especially on single-trial basis are therefore important. Here we applied the technique of adaptive filter [3] to extract the stimulus-evoked single-trial potentials at the superior temporal cortices recorded with chronically-placed surgical grid electrodes. We found that the method was able to successfully extract single-trial evoked potentials in the face of large inter-trial variations in both response amplitude and latency. Furthermore, we found an apparent gradient of inter-trial variability and response latency from dorsal to ventral, and from posterior to anterior aspects over the superior temporal cortices. This gradient appeared to be related if not extended from a similar gradient along the long axis of the nearby primary auditory field. Based on the extracted single-trial evoked response, subtle differences could be detected when two sounds sharing similar spectral property but different temporal property (e.g., fast-slow versus slow-fast FM tone) are presented in the same session. Greater differences are detected for sounds with greater spectral and temporal disparity (e.g., clicks versus AM tone). Similar findings were also observed with the gamma band responses to sounds at the same recording locations. Results are consistent with the notion that inputs to the various cortical fields could be segregated to some extent for effective processing of the complex sounds. Depending on the acoustic property of the stimulus sounds, the underlying neural processing could take place on similar or different areas of the superior temporal cortices.

Keywords: evoked potentials, adaptive filter, superior temporal cortex

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Diffusion approximation of neuronal models revisited

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Stein's neuronal model with reversal potentials (see [1]) has number of diffusion approximations, each depending on the form of random amplitude of excitatory, resp. inhibitory postsynaptic potentials (see [2, 3]). Probability distributions of the first passage time and of the steady state value of the membrane potential in the original model and its diffusion approximations are numerically compared in order to find which of the approximations is the most suitable one. Importance of the properties of the random amplitudes of postsynaptic potentials is discussed. It is shown on a simple example that quality of the approximation depends directly on them.

Keywords: Stein's model with reversal potentials, Diffusion approximation.

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Some remarks on a spike train model of interacting neurons

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Since spikes have very short duration, counting processes are commonly used as probability models of spike trains. Aiming to include the neuronal refractory period and to describe properties of spike trains, various authors follow an approach based on the assumption that the non-homogeneous Poisson process describing the number of neuronal firings has a conditional intensity function expressed as product of the *free firing rate function* and a suitable *recovery function*; see Berry and Meister (1998), Johnson and Swami (1983), Kass and Ventura (2001), Miller (1985), and, more recently, Chan and Loh (2007). Such model is based on a point process $N(t)$, $t \geq 0$, which denotes the number of spikes of a single neural unit in the time interval $[0, t]$, and on the following conditional intensity function:

$$\lambda(t \,|\, \tau_1, \tau_2, \ldots, \tau_{N(t)}) = \lim_{\delta \downarrow 0} \mathrm{E}[N(t+\delta) - N(t) \,|\, \tau_1 < \tau_2 < \ldots < \tau_{N(t)}] \ \text{ a.s.}$$

In order to include the effect of the refractory period, the above authors proposed the Markovian model in which the conditional intensity function has the following form:

$$\lambda(t \,|\, \tau_1, \tau_2, \ldots, \tau_{N(t)}) = \begin{cases} s(t), & \text{if } N(t) = 0, \\ s(t)\, r(t - \tau_{N(t)}), & \text{if } N(t) \geq 1, \end{cases}$$

where s and r are non-negative functions, s being known as the free firing rate function and r as the recovery function, and where τ_j is the j-th spike time.

We purpose to extend the above model to the case of a network of excitatory neuronal units, where the recovery function of the conditional intensity function of the i-th unit depends on the last spiking unit. A suitable choice of the recovery function allows to include the effect of the refractory period and the interactions among the neurons of the network.

In the special case of a network formed by two neurons characterized by constant free firing rate $s(t) = \lambda$, we evaluate the probability that a spike of a generic unit, occured at a generic instant, is followed by a spike of the same unit. The special form of the recovery function yields that the spiking activity of the network is described by a Poisson process with intensity λ. We finally investigate

(i) the distribution of the number of spikes that occur in $[0, t]$ and that are followed by spikes of the same unit,

(ii) the distribution of the index of the last neuron firing in $[0, t]$.

Keywords: Neuronal network, Free firing rate function, Recovery function.

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Firing mechanisms in the stochastic Morris-Lecar neuron model and its embedded leaky integrate-and-fire model

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Stochastic leaky integrate-and-fire models are popular tools to describe the stochastic fluctuations in the neuronal membrane potential dynamics due to their simplicity and statistical tractability. They have been widely applied to gain understanding of the underlying mechanisms for spike timing in neurons, and have served as building blocks for more elaborate models. Especially the Ornstein-Uhlenbeck process is popular, but also other models like the square-root model or models with a non-linear drift are sometimes applied. However, experimental data show varying time constants, state dependent noise, a graded firing threshold and time-inhomogeneous input, and higher dimensional, more biophysical models are called for.

The stochastic Morris-Lecar neuron is a two-dimensional diffusion which includes ion channel dynamics. We study the firing mechanism in the model as well as in experimental data from a spinal motoneuron, and relates it to a leaky integrate-and-fire model.

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Brain States revealed by Bispectral Analysis of Microsleep

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Neurology and neuropsychiatry are for long facing a great duty and challenge: Detect as early as possible pathological states, follow their evolution $with$ or $without$ treatment and assess the success of the latter. This means to identify and further detect specific global, regional or local brain states which further implies to develop techniques allowing to explore functional brain connectivity in the least invasive way. Scalp EEG is the least invasive electrophysiological tool whose resolution seems too low to discriminate any states but the most global like wakefulness, sleep stages etc.

This hold true when considering visual inspection and linear signal analysis. This might not be true with the use of third order cumulant analysis of the electrophysiological recordings used to measure the phase-coupled frequencies corresponding to non-linear coupling of spectral frequency components, somewhat analogous to frequencies of resonance [1, 2]. Frequency pairs corresponding to bispectra peaks different from zero were tested for bicoherence. The sum of the two frequencies in each pair defined the frequency of resonance [5]. Bispectral analysis, a non linear signal analysis method which detect interactions between pairs of signals with frequency and phase locking such as two different generators $G1$ and $G2$, generating frequencies $F1$ and $F2$, generate together a third one, called harmonic, which is the sum or difference of these two frequencies ($F3 = F1 + F2$ or $F3 = F1 - F2$) with a similar phase relationship ($\phi_3 = \phi_1 + \phi_2$ or $\phi_3 = \phi_1 - \phi_2$). These harmonic components indicate a kind of cross modulation of the $G1$ and $G2$ signals called quadratic phase coupling (QPC) and indicate some mutual interaction of the $G1$ and $G2$ generators (groups of neurons).

We used bispectral analysis to assess the follow-up of cognitive-behavioral therapy of patients affected by primary insomnia [3]. This analysis was able to characterize very well sleep stages and could also be used to discriminate normal and pathological brain states, such as epilepsy [4]. The aim of the current study is to extend further the investigation of bispectral analysis for assessing sleep disorders and to reveal more basic mechanisms related to sleep neurophysiology.

We examined the EEG of 7 patients having a confirmed obstructive sleep apnea syndrome with daytime sleepiness and therefore possible microsleeps (MS) while in relaxed resting position. Microsleeps were recorded during a maintenance wakefulness test (MWT) consisting of 4 sessions of 40 min. every two hours. Patients were told to rest relaxed, without sleeping, in the comfortable arm-chair of a quiet and dark room. MS scoring was done visually according to general literature, i.e. with the complete disappearance of alpha rhythm on frontal, central and occipital derivations, and the apparition of theta rhythm. lasting at least 3 s and no more than 14 s. Patients were further divided in 2 groups for comparison: Big Microsleepers (BM) with more than 40 MS (2 patients) and Small Microsleepers (SM) with less than 20 MS (5 patients).

We analysed and compared the 10s EEG segments (AA) preceding MS onsets with the full MS (MA) segment. We also compared the 3 first seconds of MS (M1) with the 3 segments of 3 s (A1, A2, A3) immediately preceding the MS onset. In order to be reliable, bispectra must be estimated over a number of epochs greater than the number of samples of a single epoch. As we used 1s epochs with a 200 Hz sampling rate one needs at least 200 epochs to detect significant QPCs. As the number of

MS is to low for reliability we assume that the QPC content do not change much over a 3 epoch long segment, thus multiplying the number of epochs by three. Even with this assumption the number of epochs remains too low. By further assuming that patients share common QPC features when similarly related to MS onsets, we pooled all MSs of each group of patients as if they where issued by a single patient. This concatenation of event related data segments from subjects of a given group allow to ensure a low variance while hopefully enhancing the common features of this group.

To compare the BM synthetic subject with the SM one (the control) we compared their MS segments with each of the pre-MS in the frontal (Fr), central (Cr) and occipital (Or) regions as these later do not "compute" the same kind of information. These comparisons were made by running a Kolmogorov-Smirnov test (with $p < 0.01$) between distributions of the harmonic frequencies of the detected QPCs, both for auto (aF3) and cross (xF3) bispectra.

For all regions and for both aF3 and xF3, the M1 *vs.* MA and the A1 *vs.* AA comparisons showed no differences for SM and systematic differences for BM, indicating dynamic changes of the AA and MA segments in the BM subjects. Both for aF3 and xF3, SM and BM subjects did not differ at all in Or for all segments and only for A1 in Fr and Cr indicating a weak, if any, involvement of occipital region and the first pre-MS segment in all regions. The Fr-Cr comparison showed a SM-BM difference only for A3 with aF3, whereas the Cr-Or one differed for A3 and E1 only for xF3. The Fr-Or SM-BM difference exists for A1 and AA both for aF3 and xF3 with the additition of A3 for xF3. Other analysis like the IRF (index of resonnant frequencies) [3] were made to evaluate the low-high frequency relationships and structures in bispectral QPC harmonics.

In conclusion, our results indicate that Big Microsleepers represent a specific population and open a way to higher topographical and time resolution bispectral studies to better understand microsleep and other brain states.

Keywords: quadratic phase coupling, microsleep, bispectrum.

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Coding in the presence of adaptation

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A population of adapting neurons encodes a time-dependent input in the instantaneous firing rate of the population (spike count in a small window averaged across the population), a quantity which we call 'population activity'. In this talk, I present a novel analytical expression of the population activity, show how coding and decoding is possible, and relate population activity to measured dynamics of individual neurons.

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A simple estimator for mutual information

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A possible approach to study how the brain encodes information to the activity of neural populations deals with concepts from information theory. In this framework the quantity of interest is the information about a given stimulus contained in the neural response. In particular mutual information between the stimulus and the response gives a measure of the gained information about the stimulus obtained by knowing the response. It is a quantity that measures the mutual dependency of two variables taking into account both linear and non linear correlations.

From a statistical point of view the direct estimation of mutual information is difficult. Firstly, the joint stimulus–response distribution requires a prohibitive amount of data and usually any real experiment only yields a finite number of trials, see [1, 2, 3]. A different approach is the so called “binless” strategy that allows an estimation of the information without relying on response discretization into a “binary” word using bins of finite temporal precision [4, 5, 6].

We propose here a new and simple estimator for the mutual information. We rely on the equation that links the entropy of the copula (dependence structure) and the mutual information of two random variables [7]. Hence the problem is reduced to the estimation of the entropy, once the sample is suitably transformed. The properties of the new estimator are illustrated through simulative examples and performances are compared to the best estimators in the literature.

Keywords: Information Theory, Mutual Information, Estimation.

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Neural Encoding of Saccadic Stimuli in the Retina

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Natural vision is structured into brief episodes of fixation, separated by rapid gaze shifts, called *saccades*. Nearly all animals with a sense of vision perform such saccades, either by movements of the eyes or of the head and body [1]. The saccadic nature of vision provides a strong spatio-temporal structure to visual stimuli that impinge on the retina: brief presentations of nearly stationary images are separated by rapid global motion signals. Under laboratory conditions, however, visual systems are often studied with stationary stimulation or simple light flashes.

In the retina, the global motion signal that occurs during a saccade has been shown to cause bursts of activity in some neurons [2] while suppressing activity in others [3]. Moreover, the beginning of a new fixation after a saccadic motion is often marked by bursts of activity that are particularly informative about the newly fixated image [4]. Yet, little is known about how neurons in the retina encode specific stimulus features in the presence of saccades.

To better understand the neural code of the retina under saccadic stimulus presentation, we performed extracellular recordings of spiking activity in isolated retinas of salamander and mouse. We used multi-electrode arrays to record spikes of retinal ganglion cells while stimulating the retina with images that were projected onto the photoreceptor layer and shifted in a saccade-like fashion. Specifically, we asked how the observed spiking responses depended on the image prior to the saccade, on the image after the saccade, and on the transition between the fixated images.

For both salamander and mouse, we found that many of the encountered cells defy the picture of simple stimulus filters that is commonly used to describe the function of retinal ganglion cells, based on investigations with simplistic or stationary visual stimuli. Instead, a large fraction of cells show highly nonlinear response properties. Furthermore, they encode the transition from the image prior to the saccade to the new image rather than the new image by itself. In the salamander retina, we found many cells that transfer information about the image transition in a precise spike-timing code, similar to previous observations for flashed images [5]. By systematically varying the saccade characteristics, we were able to disentangle the contributions of the new image, the previous image, and the motion trajectory to the generation of the response.

For mouse retina, we found a more diverse picture of response patterns and classified these into several distinct types. While some cells responded primarily to the spatial structure of the newly fixated image, other response types could be characterized as detectors of change or similarity in fixated images across the saccadic transition. These response types have an intrinsically nonlinear nature and cannot be captured by standard receptive field models. Rather, the findings suggest that

the saccadic image presentation triggers specific circuit elements that provide different cell types with characteristic response features of potentially high behavioral relevance.

Keywords: retina, saccade, neural code.

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Inter Neuron Nearest Spike Intervals based Method to Measure Synchrony under Low Firing Rates

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A common interest in electrophysiological studies is synchrony among neurons under several conditions, such as different kinds of stimuli. In this work we present a synchrony measure that can be easily adapted to different firing rates scenarios. Usually, synchrony measures are based on 1-1 matches along binned trains [3][4][2]. Our method is based on the time elapsed between spikes of the different trains, thus no binning is required. This method is flexible enough to work in low firing rate scenarios such as spontaneous activity. In some experimental settings, getting many recordings of one group of neurons is very difficult or impossible. The proposed method can be used to measure the synchrony with small amounts of trials. We discuss tests to determine (1) whether the synchrony observed is due only to chance and (2) whether there exist differences in synchrony between experimental conditions.

Consider two neuronal recordings described by the counting processes $\{N_i(t), t \in [0,\infty)\}$ for neurons $i = 1,2$ and let X_{ij}, $j = 1,\ldots,J_i$ be the time points where neurons fire. Define de Inter Neuronal Nearest Spike Intervals (INNSI) as the time that elapses between the spikes of one neuron and the closest spike of the other neuron. Let n_δ be the frequency of INNSI smaller or equal to δ, where δ can be chosen by the researcher according to the problem. Let $\bar{n}_\delta$ be the frequency of the INNSI that are larger than δ. We define the INNSI-based Synchrony Estimator (ISE) as:

$$ISE = \frac{n_\delta}{n_\delta + 2\bar{n}_\delta}$$

This is just the proportion of INNSI that are smaller than δ in the total amount of INNSI, giving double weight to the ones that are greater than δ.

The ISE can be assumed to be time dependent by applying the function on sliding windows. At time t, spiking activity in a window of length 2ν is used. Controlling ν, low firing rate is outweighed by the use of neighborhood activity in the estimation of n_δ at time t: $n_\delta(t,\nu)$.

We propose the use of binomial Generalized Additive Models (GAM) [5]. Since the ISE estimator can be regarded as the success probability for an event INNSI$< \delta$, the ISE measure can be estimated via the use of a Binomial process, $n_\delta \approx \text{Binomial}(n, \pi_\delta)$. An autoregressive term in the parametric part is suggested to account for dependence between responses at consecutive time points. Time should be considered as a covariate in the smooth terms together with any other covariates under study.

To make sure that the proposed synchrony measure is not driven by firing in proximity just by chance, we compare the method with the theoretical synchrony expected under independence of spike trains. Also, a bootstrap procedure is proposed to build confidence bands for the predictions of the GAM model. These confidence bands can be used to test different hypothesis [8].

The data used to exemplify the use of ISE was provided by the NEUROcom Group of the Universidade da Coruña. The spike trains were recorded simultaneously in the primary visual cortex of an anesthetized cat. Recordings were made under spontaneous activity and two types of electrical stimulations were carried out. These stimulations were made in two areas of the brain that module the wake-sleep cycle: the brainstem (bs) and the forebrain (bf) [7][1][6]. When stimulating these areas, a wake-like state is induced and then the sleep-like state is gradually recovered. We study synchrony of a pair of spike trains under the two stimulation conditions. Firing rates are very low through out the experiment and only three trials of each condition are available.

The best GAM was selected using the AIC criterion and was used to build confidence bands and test the following hypothesis:

- $H_0^1 : \pi_\delta^A(t) = \pi_\delta^0$ for every t after the condition onset. Here, π_δ^0 represents the baseline synchrony before the stimulus. A similar hypothesis can be formulated for condition B.
- $H_0^2 : \pi_\delta(t) = \pi_0$, where π_0 stands for random synchrony.
- $H_0^3 : \pi_\delta^A(t) = \pi_\delta^B(t)$. With this test we aim to detect differences in the synchrony profile induced by the experimental conditions.

Results show significant differences between baseline synchrony and under stimuli (H_0^1). Regarding H_0^2 we found that encountered synchrony is almost all the time higher to that theoretically expected under independence. Finally, differences between synchrony under the different conditions are found significant after stimulation while they are not so before stimulation.

Keywords: bootstrap, generalized additive models, spike train, synchrony.

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The Mechanism of Orientation Selectivity in Primary Visual Cortex without a Functional Map

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Most neurons in primary visual cortex (V1) have an orientation selective response. This is true for animals such as cats and primates, in which V1 has an orientation map [1], as well as for animals without such a map, e.g. rodents [2]. The mechanism for orientation selectivity (OS) remains a matter of debate. Whether selectivity is primarily due to feedforward connectivity or to recurrent interactions has not been settled. If the mechanism is primarily feedforward, the presence or absence of an orientation map hardly matters, but if recurrent interactions are important the spatial organization of preferred orientations could affect the mechanism. Theoretical studies of OS have, up to now, focused on models of V1 with orientation map. The proposed recurrent mechanisms rely on the fact that, with a map, neurons mostly receive recurrent connections from cells with similar preferred orientations [3].

The connectivity in V1 without map is hotly debated [5]. Unclear is whether connections depend on the difference in stimulus feature preferences. With such a preference, the distributions of orientations of cells projecting to a neuron would be similar to that in cortices with a map and the same mechanism could operate. In contrast, when connectivity is independent of difference in preferred orientation, this distribution is flat. How can orientation tuning arise in this case? Here we argue that OS arises naturally in V1 without feature dependent connectivity if it operates in the balanced regime. To this end, we consider a network consists of an excitatory and an inhibitory population of randomly connected neurons with, on average, K recurrent inputs from each population. The strengths of the recurrent connections are of order $1/\sqrt{K}$. Neurons also receive a feedforward input, with an untuned part of order $\sqrt{K}$ and a random orientation dependent part of order 1. Feedforward input, total excitatory and total inhibitory feedback are all much larger than the rheobase. Nevertheless neurons fire at a reasonable rate because the net feedback approximately cancels the feedforward input. Because of the connectivity, the total excitatory and inhibitory feedback are almost untuned. As a result, the untuned part of the feedforward input is approximately canceled by the feedback, but its much smaller tuned part is not. This results in an output of the cells with significant orientation tuning. The heterogeneity in tuning curves is large. Our study predicts that the average voltage of the neurons, relative to rest, shows clear orientation tuning, but the size of the voltage fluctuations are orientation independent.

Recent experiments have investigated the effect of manipulating the activity of subsets of GABAergic interneurons on the response of primary visual cortex (V1) of mice. Atallah et al [7] optogenetically suppressed or stimulated parvalbumin expressing (PV) interneurons. For physiologically reasonable changes of the PV activity, the amplitude of the Pyramidal (Pyr) cells response was modulated by a factor 0.7–1.2, upon visual stimulation. Yet, both the orientation tuning and the shape of the contrast response function were largely unaffected. It was also shown that manipulating the PV cell activity modifies the inhibitory synaptic input into the Pyr cells, but does not significantly change their excitatory input upon visual stimulation. What do the recent optogenetic experiments tell us about the V1 network? The fact that manipulating the PV input affects the Pyr activity, but hardly changes the excitatory input into these cells, implies that the recurrent excitation is weak. We show that this increases the selectivity of the Pyr cells. Because the E-E connections are weak, for the input into the Pyr neurons to be balanced, their recurrent inhibition just cancels the feedforward excitation. Thus, if the network consisting only of Pyr and PV neurons, it responds to changes in the external input into PV cells by changing the Pyr activity in such a way that E to I input must just cancels the extra feedforward input into the PV cells, leaving the PV firing rate unaffected. Hence, to account for the effect of optical stimulation on the PV activity the presence of a second inhibitory population is essential. With two inhibitory populations in the model we can account for the experiments. Activation/suppression of the PV activity leads to a multiplicative increase/decrease in the response of the Pyr neurons. Furthermore, as in the experiments, this change in the gain of the Pyr neurons leaves their tuning properties unaffected. Finally we argue that the second inhibitory population can be identified with the somatostatin expressing interneurons. Indeed, we show that this population is more sharply tuned than the PV cells.

Very recently, Chen et al. [6] measured calcium signals in spines on pyramidal neurons in layer 2/3 of the mouse auditory cortex. They found that inputs to neighboring spines are tuned to sound with very different preferred frequencies. Nevertheless, the responses of the neurons are sharply selective to frequency. The ideas developed in this work can readily be extended to explain strong selectivity in primary auditory cortex or indeed other sensory cortices.

Part of this work has been published in [8].

Keywords: Neuronal networks, balanced state, interneurons.

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Genesis, dynamics and role of nested theta to gamma oscillations in an attractor network model of cortical memory

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Oscillations constitute an ubiquitous aspect of neural dynamics. Their cognitive as well as behavioural correlates have been extensively studied at different levels of brain organisation. Numerous reports discuss the relevance of these rhythms in the context of working memory tasks (for review, see Klimesch, 1996; Benchenane et al., 2011), perceptual processes (e.g. Tallon-Baudry, 2009; Romei et al., 2010), attentional modulation (for review, see Benchenane et al., 2011) and early sensory processing (for review, see Koepsell et al., 2010). Despite extensive research effort, the understanding of the origins and mechanisms underlying these cognitive correlates of theta to gamma oscillations is limited.

In our attempt to study functional aspects of the cortical oscillatory activity, a computational modelling approach was adopted to examine a hypothesis that memories, either evoked by external stimuli or activated as a result of internal processing, are manifested as distributed cell assemblies oscillating at gamma-like frequencies with lifetimes within a theta scale. To this end we continued to investigate a meso-scale attractor network model (Lundqvist et al., 2006) allowing for the examination of oscillatory phenomena as an emergent feature of neuronal activity and, most importantly, as a correlate of the network's functional states in simulations of two memory paradigms: stimulus-triggered memory recall and multi-item working memory maintenance by periodic replay (cf. Fuentemilla et al., 2010). This biophysically detailed cortical model of cortical layer 2/3, operating in bistable mode, has previously been shown to faithfully reproduce single cell firing statistics (Lundqvist et al., 2010) and qualitative effects of modulation of the synchronous population activity in working memory as well as long-term memory tasks (Lundqvist et al., 2011). The focus here was on investigating spatially dependent coherence within distinct frequency components of the synthesised local field potentials as well as cross-frequency interactions, specifically nested oscillations. The nesting phenomenon has been mainly reported as coupling between the amplitude of gamma and the phase of theta rhythm in experimental work on sensory and memory systems (Chrobak and Buzsaki, 1998; Lakatos et al., 2005; Tort et al., 2008). In the model, the same nested hierarchy of gamma (25-35 Hz) and theta (2-5 Hz) rhythms was shown to arise during activation of memory patterns (coding attractor state) in the two simulated paradigms. Additionally, 10-Hz alpha rhythm emerged as part of this nested hierarchy when memory retrieval was triggered by a stimulus. The activity in the gamma band was associated with selective activation of local neural subpopulations and the 10-Hz rhythm appeared due to heterogeneity of excitability within these subpopulations. Theta was correlated with coordinated activation of more globally distributed assemblies consisting of several such local subpopulations. The network also exhibited idling activity manifested as an upper alpha/lower beta rhythm (15-25 Hz) in the absence of nested oscillations during a non-coding state, thus reflecting the readiness to process input.

In conclusion, the model was demonstrated to be consistent with the concept that gamma oscillations are a manifestation of local computations while theta oscillations reflect the activation of global, distributed assemblies. We hypothesise that the dynamics of coherent theta constitute an important aspect of the formation and replay of the encoded memory items. Finally, it should be mentioned that this computational study has been, to the best of our knowledge, the first attempt to explore the rich oscillatory dynamics with spatial aspects of coherence and synchronisation patterns, and cross-frequency effects emerging in a biophysically detailed model with strong commitment to functionality.

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A computational modelling approach to the problem of odour mixture segmentation

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Odorants in natural environments are dominated by multi-ligand mixtures and their blends, many of which are composed of a large and complex variety of chemical components. Some of the most challenging directions in the olfactory research to date have involved the problem of coding, processing and, ultimately, perception of odour mixtures in the olfactory systems. Despite intensive investigations pursued at a wide range of levels ranging from molecular, electrophysiological to psychophysical and psychological, there is still a plethora of open questions and debatable hypotheses. We adopt a different approach to studying the mammalian olfactory system and attempt to understand general principles of olfactory information processing by constructing a large-scale computational model. The key objective of this contribution was to propose a neural mechanism underlying cortical segmentation of odour mixtures and study its functional implications.

Since we treated the system holistically, besides the olfactory cortex (OC) our model encompassed the first and the second stages of mammalian early olfactory processing. Olfactory stimuli patterns, both single- and multi-ligand odour objects, were synthesised and their processing in the olfactory epithelium (OE) was simulated in the form of activations of olfactory receptor neurons (ORNs), modelled as graded units with sigmoidal response characteristics (Rospars et al., 2000). To ensure a satisfactory level of biological plausibility of the model, the distribution of ligand-olfactory receptor (OR) affinities was generated to account for key statistical features of widely reported olfactory response patterns to naturalistic odour stimuli (e.g., Hallem and Carlson, 2006; Yoshida and Mori, 2007). The process of mixing odour molecules modelled at the OR level complied with one of the most predominant hypoadditive syntopic interaction type (Rospars et al., 2008). The resulting static rate-based codes were then processed in the reduced model of the olfactory bulb (OB). OB computations were performed within the modular structure of glomerular columns and the transformation of the primary to the secondary odour representation followed a novel interval concentration coding scheme (Sandström et al., 2009). Self-organization of the feedforward connectivity from the OB to the OC based on statistical properties of synthetic olfactory stimuli with the support of synaptic plasticity provided the capacity for generating sparse and distributed cortical representations (Benjaminsson et al., 2010). The OC model, which handled odour recognition functionality lying at the heart of this study, was implemented in the framework of an associative attractor network with modular architecture and sparse recurrent connections trained with Hebbian plasticity. The proposed odour mixture segmentation mechanism was based on the neural adaptation phenomena at the level of cortical units.

The network was first trained to perform concentration invariant identification of single-ligand odours. A range of different training scenarios were implemented to mimic various psychophysical experimental conditions. In the evaluation stage the olfactory system model was exposed to mixtures of two up to five ligands and the segmentation performance was analysed analogously to classical behavioural studies (Laing and Francis, 1989; Livermore and Laing, 1998). In consequence, we managed to reproduce some qualitative psychophysical effects reported in the context of olfactory perceptual learning (Wilson and Stevenson, 2003), e.g. impeded segmentation capability at low concentrations (Duchamp-Viret et al., 1990), correlation between a so-called glomerular overlap and mixture perception (Frederick et al., 2009) or a profile of the performance drop with an increasing number of odour components (Laing and Francis, 1989) among others. In a broader perspective, the results obtained in this computational study pave the way for a discussion on mechanistic origins of a wide range of perceptual phenomena observed in mixture segmentation. Finally, it should be emphasised that the holistic modelling approach adopted here facilitated insights into the impact of early olfactory coding, stimulus representations and the system dimensionality on the odour recognition performance.

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Activity Patterns in Networks Stabilized by Background Oscillations

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There are many background oscillations in a brain, in particular those having frequencies in the theta and gamma bands. An interesting question is what these background oscillations might enable an array of neurons to do. To investigate this question, we consider the same question for an array of oscillators, each of which is based on a heuristic for the Hodgkin-Huxley system. The array is initialized in some configuration of states, which is referred to here as being an image. We show that the background oscillations may provide energy to stabilize the initial image, and it will persist until a new image is presented to the array or until the background oscillation is removed or its frequency content is changed. A computer simulation of this phenomenon is presented.

Channel Capacity of a Spiking Neuron

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In order to understand the information processing in the brain, the information channel capacity[5] is an important quantity. Since a fundamental information processing in the brain is the information transfer through a single neuron, some attempts have been made to compute the capacity of a single neuron[3, 6]. However, some of the results range much larger than measurements[1], or lacks mathematical proof. The computation of the capacity is not simple because it depends on various issues, such as the stochastic characteristics of the communication channel and optimisation over input distributions. We have considered two different models, the temporal coding, and the rate coding, and computed the capacity for each of them[2]. We have employed a spiking neuron model that the ISI follows a gamma-distributed random variable, where the shape parameter κ is fixed and the scale parameter θ varies over time. Theoretical studies prove that the distribution of inputs, which achieves the channel capacity, is a discrete distribution with finite mass points for temporal and rate coding under a reasonable assumption. The proof follows the steps firstly shown by Smith[4]. This allows us to compute numerically the capacity of a neuron. Numerical results are in a plausible range based on biological evidence to date.

Keywords: Information capacity, spiking neuron.

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Inverse Problem for Leaky Integrate-and-Fire Neuronal Models using Spike-Times Data: The sinusoidally-driven case

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We aim to estimate structural parameters (the coefficients) of a stochastic leaky-integrate and fire neuronal model given only data for the interspike intervals (ref. [4, 5, 3]). Building on the Fortet Integral Equation method introduced for this problem in [2] and the classical Fokker-Plank equation, we extend the methods to the case of a time-dependent drift, in particular a sinusoidal term with unknown amplitude, a situation common for sensory neurons [1].

Thus the voltage trajectory, X, is assumed to follow the following trajectory (in non-dimensional form):

$$dX_s = (\alpha - X_s + \gamma \sin((s + \phi)))\, \mathrm{d}s + \beta\, \mathrm{d}W_s. \tag{1}$$

until X hits a threshold at which time a spike is recorded and X is reset. Here, $\mathrm{d}W_s$ is an increment from standard Brownian motion.

The main difficulty in estimating the parameters for these dynamics from spike-data only is that the observed interspike-intervals of the inferred stochastic process do not form a renewal process due to the phase differences in the sinusoidal term at the beginning of each interval (at each spike). We propose to deal with this difficulty by binning the data into several bins each of which with approximately the same phase and then to treat each bin with the methods developed for renewal processes (the Fortet Equation and the Fokker-Plank equation). Both algorithms are iterative and so we also introduce a simple and constructive initialization procedure to provide them with initial guesses for the parameters directly and automatically from the data. The initializer works on approximating the distribution of spike dynamics as an advected Gaussian bell, whose mean and std. deviation can be estimated from the quantiles of the ISI distribution.

Results to Present

We attempt to estimate the parameters for four (4) distinct regimes, which we call: 'Super-Threshold', 'Critical', 'Sub-Threshold' and 'Super-Sinusoidal'. The regimes' respective parameters are in tab. 1. These regimes try to represent the following scenarios: in the 'Super-Threshold', the bias current, α is strong enough to trigger spikes on its own and the noise and sinusoidal currents only create jitter around the regular spiking; in the 'Critical' regime the two deterministic currents, α and $\gamma \sin()$ are barely strong enough to spike without noise; in the 'Sub-Threshold', the neuron spikes only due to the stochastic fluctuations; while the 'Super-Sinusoidal' is like 'Super-Threshold', but here it is the sinusoidal $\gamma \sin()$ term that dominates and that is the primary driver of the spikes.

The estimation results for 16 spike trains are shown in Fig. 1. We see that the estimation procedures are most accurate for the 'Super-Threshold' and the 'Critical' regimes. We also find the Fortet-equation method to be more accurate usually, but less robust, meaning it is more likely to be way off. In contrast, the Fokker-Plank-equation method is more robust. We also find that the proposed initializer is doing an effective job, starting the iterative methods close to the true parameter values.

Keywords: inverse first-passage times, stochastic neuron models, parameter estimation from stopping times, Fortet integral equation, Fokker-Plank equation.

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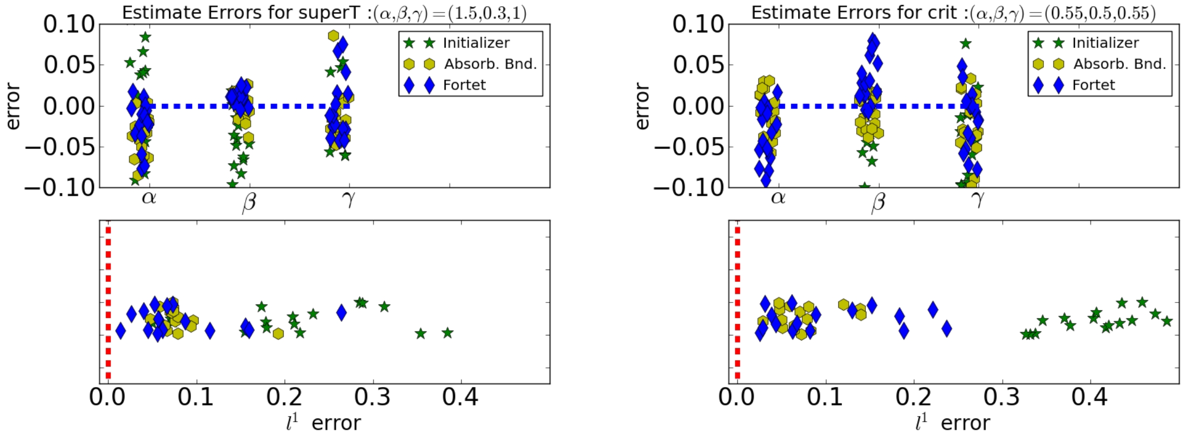
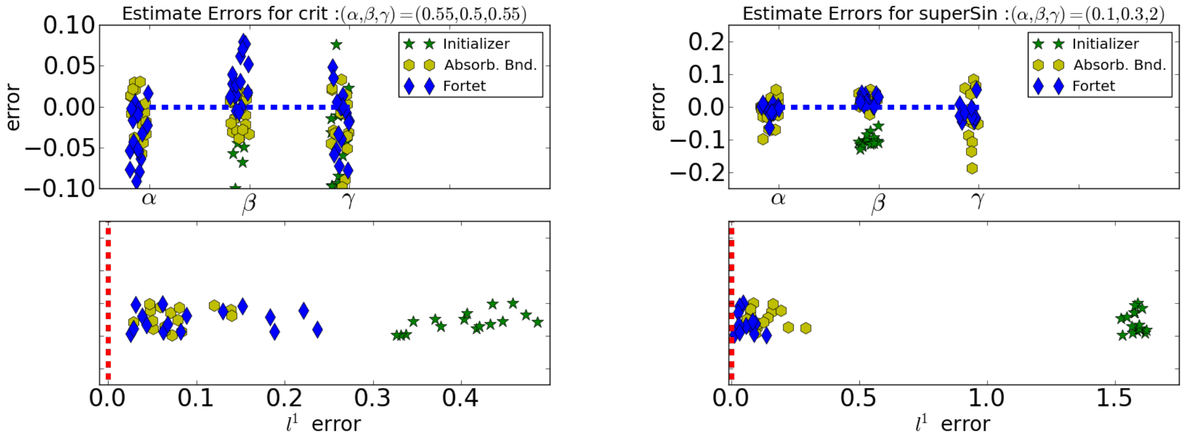
Regime Name	α	β	γ
Super Threshold	1.5	0.3	1.0
Critical	0.55	0.5	.55
Sub-Threshold	0.4	0.3	.4
Super Sinusoidal	0.1	0.3	2

Table 1: α, β, γ parameters for the different regimes.



(a) SUPER THRESHOLD

(b) CRITICAL



(c) SUB THRESHOLD

(d) SUPER SINUSOID

Figure 1: Absolute errors of the parameter estimation routines for the 4 different spike regimes. The upper panel shows the difference between the estimated and the real value for each parameter, e.g. $\tilde{\alpha} - \alpha$. The lower panel shows the sum of the absolute errors, i.e. $|\tilde{\alpha} - \alpha| + |\tilde{\beta} - \beta| + |\tilde{\gamma} - \gamma|$. NOTE: figures have different scales.

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Can discrete Response-Stimulus Correlation distinguish Integration from Coincidence Detection?

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Whether neurons operate as integrators or coincidence detectors may determine the role of the cortical neuron [1, 3] and might give an insight as to the nature of the neural code. For this, a simple measure is needed that can both be used for *in vitro/vivo* neuron recordings as well as investigated analytically. Unfortunately, the most likely candidate, the response-stimulus correlation (RSC) or reverse correlation has been shown numerically [2, 5] and can be shown analytically not to be able to distinguish between the two modes.

As an alternative, we introduce a discrete, response-stimulus correlation related measure, based on spike times. The discrete response-stimulus correlation (dRSC) consists of two values: (1) a phase locking value indicating whether the stimulus actually drives the neuron or serves as background noise, and (2) a coincidence value indicating whether the stimulus is used as source of temporal integration or as source of coincidences to detect. We tested both values of the measure on a leaky integrate-and-fire (LIF) neuron and confirmed their validity.

In order to be able to fully assess the validity of the measure under various conditions analytically, we also introduce a re-formulated LIF model, where the single excitatory stimulus is modelled by spike intervals instead of single points in time and the differential equations describing the neuron are discretised. The new model (which we call the interval neuron) consists of one single system tensor, which describes the neural behaviour. Using matrix algebra the dRSC can then be calculated for a given set of neural parameters. This interval neuron cannot only be derived and built from an LIF neuron, but from any mathematical neuron model, or even from *in vitro/vivo* recordings.

We will apply the dRSC measure to corner cases created with both neural models (LIF and interval neuron) in order to see whether in these cases the neurons operate as temporal integrators or coincidence detectors. This verdict will then be compared with the results of other measures (like the one proposed in [4]) for the same corner cases. The results will be presented and fully discussed at the conference.

Keywords:
integration, coincidence detection, discrete response-stimulus correlation

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Estimating Nonstationary Inputs from Firing Rate and Non-Poisson Irregularity in a Single Spike Train

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Neuroscience researchers have measured neuronal firing rates in correlation to animals' behavior, largely ignoring detailed patterns of spike times. We examine spike timing in the present study to collect additional information about the dynamics of unobserved neuronal populations, based on the assumption that neuronal spike timing can provide information about the population activities of excitatory and inhibitory neurons.

Each cortical neuron constantly receives spiking signals from thousands of other neurons. The random arrival of several synaptic inputs results in uncorrelated fluctuations that can be characterized by their mean and amplitude. Mathematical methods have been developed, assuming that presynaptic neuronal activities are constant over time [1]. Recently, to analyze situations in which input parameters vary in time, several methods have been proposed using a time-dependent stimulus traces [2] or averaging over repeated trials [3]. Inputs to individual neurons, however, are not entirely controlled by animal behavior or reproduced exactly under identical behavioral conditions. Instead, they might fluctuate from trial to trial. Therefore, it is necessary to develop a method capable of estimating time-varying inputs in a single trial.

For this purpose, we constructed a method for estimating nonstationary inputs from a single spike train using a two-step analytical method [4]. First, the instantaneous firing characteristics consisting of the spike rate and non-Poisson irregularity are estimated using a computationally feasible state-space method. Then, we transform the firing characteristics into input parameters by inverting the forward transformation from input to output signals, which can be done rapidly. By analyzing spike trains recorded in vivo, we found that neuronal input parameters are similar in the primary visual cortex V1 and middle temporal area, whereas parameters in the lateral geniculate nucleus of the thalamus were markedly different.

Keywords: Non-Poisson irregularity, State-space method, Leaky integrate-and-fire model.

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A model-based inference of synaptic connectivity from simulated multi-neuronal spike data

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Synaptic connectivity is one of the most essential factors for neural mechanisms. As multi-neuron recoding techniques are rapidly developed, to capture synaptic connectivity from a multi-neuronal spiking activity is gaining in importance for understanding of the neural mechanisms.

To address this issue, we employed several methods to infer synaptic connections on the simulated spike data of the realistic local cortical network model, which enables us to directly compare the inferred connections with synapses of the model. We examined performances of the employed methods of model-free (information-geometric measure and transfer entropy) and model-based (coupled escape rate model) methods changing the network topology of the computational model by the way used in the small-world-network paradigm.

Irrespective of the employed methods, the evaluation of similarity between the synaptic connectivity and the inferred connectivity by ROC (Receiver Operating Charateristic) and related analyses indicated that the network with a highly clustered, near regular or small-world, connectivity was more correctly inferred than a random network. Among the employed methods, the model-based method showed the best performance in terms of the higher similarity, less sensitivity to change in the threshold and less required data length. Considering the evidence that a cortical connectivity posses highly clustered features, our results suggested the possibility to infer the underlying synaptic connectivity of the local cortical network exhibiting a spontaneous activity.

Keywords: functional connections, network topology, large-scale simulation.

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A Bayesian approach for estimating time-varying input signals from membrane potential of a neuron

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Neurons transmit information by transforming synaptic inputs into action potentials. It is essential to investigate the dynamics of the synaptic inputs to understand the computational mechanism in the brain.

We consider an estimation problem of input parameters from a single voltage trace of a neuron obtained by intracellular recordings. Previous methods are based on the assumption that the input parameters are constant over time [1, 2]. However, it is natural to expect that neuronal activity in vivo is time-variable, reflecting the variable external conditions.

Here, we propose a Bayesian method to estimate the time-varying input parameters from a voltage trace of the Ornstein—Uhlenbeck neuronal model [3]. The proposed method is extended for more realistic models, i.e., Hodgkin—Huxley type models [4]. It is shown that both time-varying input signals and ion channel state can be deduced from a single voltage trace of a neuron. The proposed method is verified by applying it to simulated data and to in-vitro experimental data.

Keywords: Statistical inference, Single neuron models, Empirical Bayes method

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On reliable information transmission in simple neuronal systems

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The nature of information processing in single neurons and neuronal networks is one of the most intensively studied topics in the field of computational neuroscience. The fundamental mathematical framework for the theoretical approach to this problem is often provided by information theory [1]. The theory quantifies, under certain assumptions, the ultimate limit on reliable information transfer by means of information channel capacity. However, channel capacity is known to be essentially an asymptotic quantity, as the code length and the associated coding/decoding complexity tends to infinity. In this contribution we address both the ultimate limits (capacity) and the bounds on non-asymptotic performance for a given code length, taking into account the probability that the stimulus is decoded incorrectly by employing the maximum likelihood decoding scheme. Metabolic cost of neuronal activity is also taken into account.

Keywords: Neural coding, Reliable information transfer, Metabolic cost

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Input synchrony estimation in the Ornstein-Uhlenbeck model through the slope of depolarisation at threshold crossing

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We present a method of estimating the input parameters and through them, the input synchrony, of a stochastic leaky integrate-and-fire (LIF) neuron based on the Ornstein-Uhlenbeck (OU) process when it is driven by time-dependent input mean μ and variance σ. Driving the neuron using sinusoidal inputs, we simulate the effects of periodic synchrony on the intracellular voltage and the firing of the neuron. Our estimation methods allow us to measure the degree of synchrony driving the neuron in terms of the input sine wave parameters, using the slope of the membrane potential during threshold crossing.

In a recent publication [1] we demonstrated how the degree of synchrony at the input of a LIF neuron can be estimated, using the slope of the membrane potential in a small period prior to firing. The degree of pre-synaptic synchrony is related to the operational mode of the neuron, which can lie anywhere on a continuum between temporal integration and coincidence detection [2, 3]. The operational mode is in turn related to the way the neuron encodes information into spike trains, which is usually considered to be based either on a rate or on a temporal coding scheme. Our previous methods required defining a temporal window within which the pre-spike slope was averaged for each response spike. This was necessary due to the trajectory of the LIF's membrane potential being discontinuous. However, the stochastic variant of the LIF, the OU model, has a continuous membrane voltage and can be used for further investigation into more accurate input synchrony estimation methods. In addition, our formulation of the OU model's input also accounts for inhibitory inputs, which our previous model did not include.

Our work is based on expressions of the OU's membrane potential slope during firing to define estimators for the values of the input parameters [4]. Preliminary results show that the slope of the membrane potential provides greater accuracy in the estimation methods than estimators based on the inter-spike interval (ISI) distribution alone. The accuracy of our results will be presented using numerical simulations across a wide range of parameters.

Keywords: synchrony, parameter estimation, integrator, coincidence detector

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Coding efficiency and detectability of rate fluctuations with non-Poisson neuronal firing

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Characterizing the statistical features of spike time sequences in the brain is important for understanding how the brain represents information about stimuli or actions in the sequences of spikes. Although the spike trains recorded from *in vivo* cortical neurons are known to be highly irregular [7, 10], a recent non-stationary analysis has revealed that individual neurons signal with non-Poisson firing, the characteristics of which are strongly correlated with the function of the cortical area [8].

This raises the question of what the neural coding advantages of non-Poisson spiking are. It could be that the precise timing of spikes carries additional information about the stimuli or actions [2, 5]. It is also possible that the efficiency of transmitting fluctuating rates might be enhanced by non-Poisson firing [1, 6]. Here, we explore the latter possibility.

In the problem of estimating firing rates, there is a minimum degree of rate fluctuation below which a rate estimator cannot detect the temporal variation of the firing rate [4, 3, 9]. If, for instance, the degree of temporal variation of the rate is on the same order as that of the noise, a constant rate might be chosen as the most likely estimate for a given spike train. It is, therefore, interesting to see how the minimum degree of rate fluctuation depends on the non-Poissonian feature of spike trains.

In this study, we investigate the extent to which the non-Poissonian feature of spike trains affects the encoding efficiency of rate fluctuations. In addition, we address the question of how the detectability of rate fluctuations depends on the encoding efficiency. For this purpose, we introduce the Kullbuck-Leibler (KL) divergence to measure the encoding efficiency, and assume that spike sequences are generated by time-rescaled renewal processes. With the aid of analytical and numerical studies, we suggest that the lower bound of detectable rate fluctuations, below which the empirical Bayes decoder cannot detect the rate fluctuations, is uniquely determined by the KL divergence. By examining three specific models (the time-rescaled renewal process with the gamma, inverse Gaussian (IG) and lognormal interspike interval (ISI) distributions), it is shown that the KL divergence, as well as the lower bound, depends not only on the first- and second-order moments, but also significantly on the higher-order moments of the ISI distributions. We also find that among the three ISI distributions, the IG distribution achieves the highest efficiency of coding information on rate fluctuations.

Keywords: Non-Poisson firing, firing rate estimations, Kullbuck-Leibler divergence.

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Non-markovian spiking statistics of a neuron with delayed feedback in the presence of refraction

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Any neural network can be described as a set of neurons and inter-neuronal communication lines – axons. When a neuron fires a spike, this spike propagates through communication line and reaches its target neuron after some temporal delay. Future firing moments of neurons depend on present position of impulses in axons which, in the reverberating network, depends on previous firing moments of those same neurons. That is why delayed feedback interconnections may result in non-renewal statistics of neuronal firing, even if the network is stimulated with a renewal process.

In order to reveal the influence of delayed feedback presence on neuronal firing statistics, we consider the simplest possible construction with delayed feedback interconnection, namely, a single neuron with delayed feedback. The neuron receives input impulses from other neurons and sends its output impulses to its own input through the feedback line with a fixed time delay Δ. As input stimulation we take a Poisson stream — the simplest renewal process. As neuronal model be take the binding neuron [1], as it allows rigorous mathematical treatment.

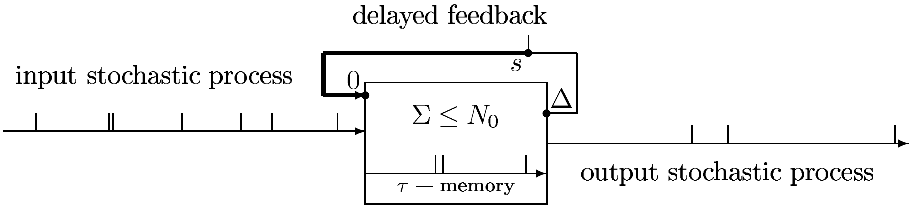

Figure 1: Binding neuron with feedback line under Poisson stimulation. Multiple input lines with Poisson streams are joined into a single one here.

In our previous paper [2], we considered the case, when refraction time r of a neuron equals to zero, $r = 0$, which allows receiving and generating impulses immediately after the previous spike. In the case of no refraction, the neuron is potentially able to generate an arbitrary large finite number of output impulses within a finite time window Δ, needed for impulse to pass the feedback line. Thus, the impulse from the feedback line at the moment of its arrival can provide information about a very distant previous firing moment. We prove rigorously in [2], that in the case of no refraction the sequence of output inter-spike intervals (ISIs) of a neuron with delayed feedback cannot be represented as a Markov chain of any finite order.

In this work, we check if this result can be violated by presence of non-zero refraction time, $r > 0$. In the presence of refractoriness, the number of output spikes (and, eventually, ISIs), which can be generated while the feedbacked impulse is traveling through the feedback line, is limited with $[\frac{\Delta}{r}]$, were $[x]$ gives an integer part of x. That means, that at the moment of its arrival, the impulse from the feedback line could provide information about the moment of one of $[\frac{\Delta}{r}]+1$ previous firings, but cannot bring any information about the earlier ones. That is why, one could expect the finite Markov order to be found for the output ISI stream in the presence of refraction. The goal of this work is to check if this is the case.

In order to reveal the influence of refractoriness, we take the limiting case

$$1 < \frac{\Delta}{r} < 2, \tag{1}$$

when no more than one output firing is possible while impulse passes the feedback line. In this case, the refractoriness, taking more than half of the delay time within the feedback line, could reduce correlations beetween ISIs for the most part.

We consider the m-order conditional probability density $P(t_{m+1} \mid t_m, ..., t_0)$, which gives the probability to obtain an output ISI having its duration within the range $[t_{m+1}; t_{m+1} + dt_{m+1}[$, provided previous ISIs had durations $t_m, \ldots, t_1$ and t_0, respectively. We derive exact analytical expression for $P(t_{m+1} \mid t_m, ..., t_0)$ for an arbitrary m. We prove exactly, that $P(t_{m+1} \mid t_m, ..., t_1, t_0)$ does not reduce to $P(t_{m+1} \mid t_m, ..., t_1)$ for any $m \in \mathbb{Z}^+$. It means, that even for the case (1) the output ISI stream cannot be represented as a Markov chain of any finite order.

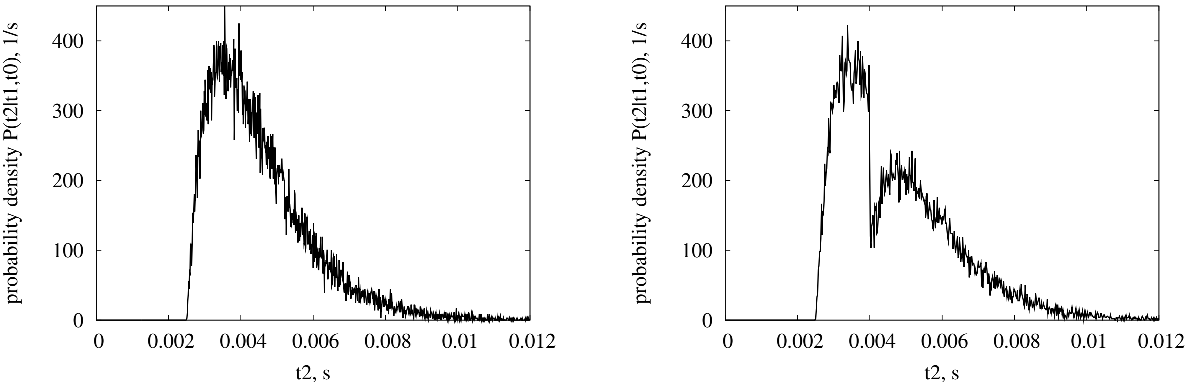

Figure 2: Conditional probability density $P(t_2 \mid t_1, t_0)$ vs. t_2, found numerically by means of Monte-Carlo method. On both pannels all the parameters are equal except the value of condition t_0. It is clearly seen, that the figures are different.

We conclude, that refractoriness does not affect qualitatively the non-Markovian character of neuronal firing statistics, which is due to the delayed feedback presence. We suggest, that this result should be taken into account, when analyzing experimental records of spiking statistics from any network with delayed feedback interconnections.

Keywords: Non-Markovian statistics, Delayed feedback, Refraction time.

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Estimating latency in the case of inhibitory response

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Stimulus response latency is the time period between the presentation of a stimulus and the occurrence of a change point in the neural firing rate evoked by the stimulation. While the response latency was explored and methods of its estimation were proposed mostly for the case if the response to stimulus is excitatory, which means that the neuron reacts to the stimulus by an increase in the firing rate, the opposite kind of reaction was so far of less attention. Here we focus only on the estimation of the response latency in the case of inhibitory response.

Our approach is based on the measurements of the time from the stimulus presentation to the occurence of the first spike after the stimulus (forward reccurrence time) in n independent trials. Two simple models of a spike train are used and probability distribution of the forward reccurence time under the assumption of known response latency is derived for each of them. The distribution is then employed in three different methods of detecting the response latency. Two of them, moment estimators and maximum-likelihood estimators, are applications of generally known estimation methods. The third method is based on a comparison of the theoretical cumulative distribution function of the forward reccurence time under the condition of no change in the firing rate with empirical cumulative distribution function obtained from the experiment. Finally, all three methods are applied on simulated data and the results are compared.

Keywords: response latency, inhibitory response, moment estimator, maximum-likelihood estimator, Kolmogorov-Smirnov test

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Information filtering by stochastic neurons

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Do stochastic neurons prefer to encode information about fast or about slow components of a time-dependent stimulus? In my talk, I will consider the frequency-dependent information transmission of model neurons of the integrate-and-fire type, both at the level of a single spiking neuron and at the population level. I will discuss under which conditions short-term synaptic plasticity or subthreshold oscillations may suppress or enhance the flow of information in certain frequency bands.

An electrophysiological study of cortico-thalamic networks in PV depleted mice

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The thalamus is considered as the sensory gateway to cerebral cortex and the reticular nucleus (NRT) 'might be considered the Guardian of that gateway' as mentioned by Francis Crick in 1984. Typically, the NRT receives excitatory inputs from the lateral geniculate nucleus (LGN) and from the visual cortex (VC), and sends back an inhibitory projection to the LGN. Parvalbumin (PV) is a Calcium buffer protein, which is highly expressed in NRT neurons [1]. Recently [2] we suggest the lack of PV affects the firing properties and the burst discharge dynamics of the main population of NRT neurons. For this study we performed *in vivo* extracellular recording with multiple electrodes across RTN, thalamus and cerebral cortex in anesthetized wildtype (WT) and PV-knockout (KO) mice. General anesthesia was induced by Equithesin at a dose corresponding to $130 mg/kg$ chloral hydrate and $30 mg/kg$ pentobarbital. Simultaneous extracellular single-unit activity was recorded during spontaneous activity and visual stimulation by xenon strobe flash at 2.5 Hz during 5 minutes. All recordings were performed with a multiple glass-coated platinum-plated tungsten microelectrodes. Up to three distinct single units could be recorded simultaneously from the same site using waveshape spike sorting techniques [3]. The firing patterns are described by serial interval histograms, return maps and auto and crosscorrelograms. We will present results suggesting that PV depleted animals express a decreased ability to process information along parallel channels in the thalamo-cortical pathway. In conclusion, these new results are in agreement with our previous models [4] and extend further the key-role played by NRT in controlling the information processing of thalamo-cortical circuit.

Keywords: Parvalbumin, Thalamo-cortical networks, Extracellular recordings.

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The effect of prestimulus oscillatory dynamics on the performance of a cortical attractor network model in a simulated stimulus detection task

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Temporal variability in human perceptual capabilities has been a commonly reported phenomenon attributed to ongoing changes in the brain (VanRullen and Koch, 2003). In the presence of a continuous stream of information that sensory systems are exposed to, an important question about the nature of processing such sensory input arises. Based on rich experimental evidence it has been suggested that neuronal oscillations, which themselves display considerable variability at different time scales, contribute to the modulation of sensory information processing (Busch et al., 2009; Mathewson et al., 2009). Although the prestimulus cortical oscillatory activity, specifically the alpha rhythm accompanying the resting and baseline brain states, appear to be relevant in this regard, its modulatory role and the underlying causes remain rather elusive.

Since threshold stimulus detection task has been proven as a suitable approach to investigating oscillatory correlates of the prestimulus brain mechanisms mediating perceptual fluctuations (Linkenkaer-Hansen et al., 2004; Busch et al., 2009; Mathewson et al., 2009), we simulated such experimental paradigm with the use of a large-scale biophysically detailed (cortical layer 2/3) modular attractor network model (Lundqvist et al., 2006). To this end, we strongly relied on bistable mode of network's operation accompanied by oscillations in the synthesised local field potentials and inherent attractor dynamics with the mechanism of stimulus-triggered retrieval of activity patterns, stored in the recurrent connections. By default the network was in a non-coding ground state, functionally attributed to a so-called "idling" brain condition (Pfurtscheller et al., 1996), with alpha-like oscillations. In a hierarchical setup with two networks, one modelling a sensory area that processes sensory input and the other one referred to as an associative area that receives feed-forward projections from the lower network and simulates perceptual stimulus detection, we reproduced key experimental findings. In particular, we observed and studied the mechanisms of modulation of the network performance, both in terms of a detection rate and its latency, by prestimulus alpha power (Linkenkaer-Hansen et al., 2004; Mathewson et al., 2009) and phase (Busch et al., 2009; Mathewson et al., 2009; Drewes and VanRullen, 2011). Interestingly, depending on how we controlled the amplitude of alpha oscillations, by affecting either the excitatory or inhibitory drive in the network (within the excitatory-inhibitory loop), we verified seemingly conflicting experimental findings of positive (Linkenkaer-Hansen et al., 2004;) and negative correlations (Sauseng et al., 2009) between the alpha power and psychophysical performance. Hence, in line with recent electrophysiological studies in macaque monkeys (Bollimunta et al., 2011; Mo et al., 2011), our results support a hypothesis about different cortical origins and thus different nature of the oscillatory dynamics of the alpha rhythm, manifested in contrasting modulatory effects in stimulus detection tasks. In addition, the spatial extent of our model facilitated an investigation into the inter-area phase synchronisation conditions prior to stimulation conducive to its successful recognition. The modulation phenomena we identified could be tested experimentally in neuroimaging studies.

In conclusion, we have demonstrated that biophysically detailed hierarchical attractor networks provide a promising framework for reproducing and understanding the correlations between prestimulus oscillations and psychophysical performance in stimulus detection tasks. Since the alpha rhythm plays a dominant role in the modulatory prestimulus dynamics, our work can be linked to an ongoing discussion about the functional role of alpha activity in the brain. The reported results can be explained in the light of different hypotheses where alpha oscillations reflect idling (Pfurtscheller et al., 1996), active inhibition (Klimesch et al., 2007) or attention modulation (Mo et al., 2011).

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Stochastic pooling networks embedded in cortical networks of excitatory and inhibitory neurons

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Stochastic Pooling Networks (SPNs) are defined in [1], and form a useful model for understanding and explaining how naturally occurring encoding of stochastic processes can occur, due to the interaction of nonlinear lossy compression, random noise and redundancy. SPNs occur in systems ranging from macroscopic social networks to neuron populations and nanoscale electronics, and support various unexpected emergent features, such as suprathreshold stochastic resonance [2].

Previous work on suprathreshold stochastic resonance in populations of neurons has assumed very regular feedforward network topologies, e.g. [3, 4], and these networks are clearly identifiable as SPNs. Here we consider whether SPNs can be observed embedded within more complex neuronal networks with recurrent feedback synapses, such as models of cortical networks.

We address this question using the model of [5] as the 'embedding network' for our SPN. That cortical network model consists of sparsely connected pyramidal neurons and interneurons, and parameters are such that individual neurons fire at rates much lower an emergent population oscillation [5]. Since an SPN encodes an input random variable, we choose to study the hypothesis that learnt synaptic weights are stored in a distributed fashion in a network, so that weights can be 'selected for readout' from multiple neurons by 'signal spikes' arriving along axonal branches from a single upstream neuron. A single 'signal spike' activates synapses with the same weight on different SPN neurons, and if the weights, and other background synaptic input are strong enough, signal spikes can cause each SPN neuron to emit an action potential. Different upstream neurons activate different weight values in this model.

The 'pooling function' of the embedded SPN is formed simply by the total number of SPN neurons that spike in response to a signal spike. Due to noise, the total number of spikes is a conditional random variable that depends on the synaptic weight. The spike count can thus encode the analog weight value in a way that can be described as 'stochastic quantisation' [2] (since a discrete variable encodes an analog variable), or alternatively as a space-rate spike code that relies on noise [6].

In order to assess our hypothesis and the efficacy of our embedded SPN model, we simulated the network model of [5] where we have additionally embedded N SPN neurons, that receive 1000 random connections from the recurrent network, and therefore receive both excitatory and inhibitory spikes that act like a 'synaptic bombardment' [7] noise source. We assume there are many possible weights for signal synapses in the SPN, and based on simulations, we estimate how the probability of a spike in a single SPN neuron increases with synaptic weight. This allows us to calculate the correlation coefficient between signal synapse weight, and the SPN spike count output for varying N, under the assumption that the selected weight is a uniform random variable. We found that the encoding improves with SPN size and is optimal for moderate signal variance, which is consistent with existing studies of suprathreshold stochastic resonance [2].

Recent experimental evidence suggests the possibility that cortical neuronal may code certain information (e.g. stimulus orientation) in a randomly distributed manner throughout the dendritic tree, on all dendritic branches [8]. We therefore also consider the case where the embedded SPN consists of a single neuron with many dendritic branches, and each segment in the dendritic tree acts like a single neuron in the situation we first consider above. This idea is similar to the model of Poirazi *et. al* [9]. In this case, we assume a subset of synapses across the entire neuron are randomly selected by a signal spike, but unlike the distributed SPN, the pooling operation is the summation of the membrane potential within many dendritic branches prior to the soma. In our results, we compare this situation to the network SPN.

Keywords: stochastic pooling network, cortical connectivity, synaptic weight readout.

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Optically Mapping Electrical Activity in the Ganglion of the Leech Hyrudo Medicinalis

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We have used the newly developed voltage sensitive dye VF2.1.Cl to monitor the electrical activity of neurons in leech ganglia.The VF2.1.Cl dye detects voltage changes in neurons membrane by modulation of photo-induced electron transfer (PeT) from an electron donor through a synthetic molecular wire to a fluorophore [1]. These dyes give bigger responses than other voltage sensitive dyes and the optical changes occur with a faster kinetics. After staining an isolated leech ganglion we were able to monitor the electrical activity of almost 100 neurons in a ganglion, representing around 20–30% of all neurons in a ganglion. With this dye we were also able to monitor the slow changes of voltage membrane associated to the rhythmic activity of heart neurons (HE) and the associated interneurons. The time course of these optical traces and of electrical recordings obtained with conventional intracellular electrodes were very similar. When images were sampled at a frequency lower than 80 Hz the peak of the action potential (AP) could be missed and a truncated AP was recorded optically. In the absence of stimulation, the spontaneous activity was characterized by the firing of APs of several neurons at a frequency between 0.5 and 20 Hertz. Other neurons fired APs more irregularly and a much lower rate. By using these dyes we were able also to identify clusters of neurons electrically coupled, in agreement with previous electrophysiological observations. When mechanosnesory neurons were stimulated with an intracellular electrode it was possible to detect the overall changes of the electrical activity in the ganglion, therefore obtaining an accurate description of information processing occurring inside a ganglion.

Keywords: Voltage sensitive dye, Leech ganglion neurons, Electrical activity

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A novel mechanism for sparse and reliable stimulus coding in sensory cortices

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Many lines of evidence suggest that few spikes carry the relevant stimulus information at later stages of sensory processing. Neural mechanisms for the emergence of sparse sensory representations, however, remain unclear. Here we present a principle mechanism that introduces a temporally sparse code and, at the same time, increases reliability of the stimulus representation in spiking networks. It combines principles of signal propagation across successive network stages with the neuron-intrinsic mechanism of spike frequency adaptation. We show mathematically and in neural network simulations how a dense code at the peripheral stage translates into a temporal sparse code at the level of a cortical ensemble, which is embedded in a balanced network. At the same time, trial-by-trial variability of the population code is dynamically suppressed in response to stimulus changes by approximately 50% [1], matching experimental observations in sensory cortices [2]. We suggest that the same principle may underlie the prominent phenomenon of sparse coding in the insect mushroom body. Our results reveal a computational principle that relates spike frequency adaptation to temporal sparse coding and variability suppression in nervous systems.

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Estimation of the information pathway for a motor command generation in an insect brain based on the physiological data

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We report an approach to estimate the functional connection from the possible anatomical connections and physiological response of each neuron. Male silkmoth, Bombyx mori, is known for its programmed behavior for the pheromone orientation on the pheromone source detection [1]. The action command is generated in the premotor center, which is composed of the lateral accessory lobe (LAL) and the ventral protocerebrum (VPC). The morphology and the physiological response to the pheromone stimulus are obtained for main types of LAL-VPC neurons through the intensive electro-physiological and immunohistochemical experiments [2, 3, 4]. However, how the motor command is generated in LAL-VPC, or the information pathway in the network, is still unknown. Therefore, the purpose of this study is to investigate the functional connection in LAL-VPC to elucidate the mechanism of the motor command generation based on the detailed experimental data on each neuron.

LAL-VPC is located in each hemisphere, and is composed of five neuropile regions (inner LAL, outer LAL, .inner VPC, outer VPC and aiVPC) [5]. Each neuron sends its input and output terminals to some regions. Input is from the same side as soma, and output is sent to the same side for local interneurons (LIN) or to the opposite side for bilateral neurons (BLN). Descending neurons (DN) go outside of LAL-VPC to connect to the neck motoneuron for the steering motions. Fig. 1 is the schematic description of the structure, with a LIN, a BLN and a DN. Iwano et al.[5] listed 36 main neurons (LINs and BLNs) for the command generation. In addition, 7 types of DN are identified [3]. Therefore, we consider a network of 86 neurons for a pair of LAL-VPC, and estimate the connection strength between each neuron and regions. Morphology of each neuron restricts the possible connections. And we calculate the connection strength which can best reproduce the observed physiological response of each neuron, as an optimization problem. Sign (positive or negative) of the connection corresponds to excitatory or inhibitory synapse. From the experiments, LINs are supposed to be mostly excitatory, though some are inhibitory, while BLNs are supposed to be mainly inhibitory, though a pair of excitatory serotonin neurons is identified. Therefore, we also aim to investigate whether each neuron is excitatory or inhibitory from the optimal connection strength.

The main pathway is extracted from the obtained connection, both by the connection strength and by the neuron dynamics of the network simulation. Fig. 2 shows an example of obtained loop network to generate an alternating high and low activity (called flip-flop response) of some type of DN. The directed links in the figure indicate neurons, and the label on the link shows the response type of the neurons (brief activation: BA, brief inhibition: BI, long lasting activation: LLA, long lasting inhibition: LLI and flip-flop: FF), which is defined in Ref. [5].

Keywords: Functional Connection, Optimization, Insect Brain, Premotor Center, Odor Source Orientation.

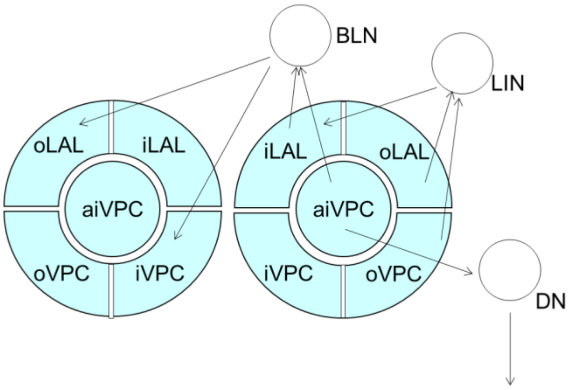

Figure 1: Structure of LAL-VPC.

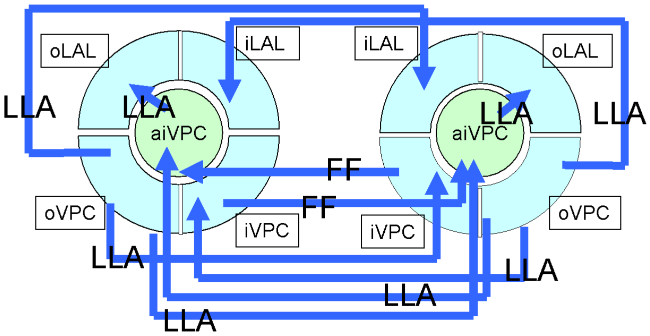

Figure 2: Loop network for the flip-flop activity of DN.

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Coding of temporally incoherent odour mixtures in the antennal lobe of honeybees

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Introduction In recent behavioural experiments with honeybees, *Apis mellifera*, we have found [1, 2] that the animals are able to distinguish coherent odour mixtures, where both odours arrive at the same time, from incoherent odour mixtures where the onset of one odour is delayed. Surprisingly this ability persisted down to an onset delay of only 6 ms. Moreover, the ability of bees to segregate the mixture components is facilitated in incoherent mixtures.

In this work we explore this surprising ability in a model of the honeybee antennal lobe (AL). We hypothesise that a winner-take-all inhibitory network of local neurons (LNs) in the AL could have a symmetry-breaking effect, such that the response pattern to an incoherent mixture is measurably different from the response pattern to the corresponding coherent mixture for an extended amount of time beyond odour onset.

The Model Figure 1A illustrates the general anatomy of the olfactory system of the honeybee as considered in our model and Figure 1B explains the circuit diagram of the model reduced to two glomeruli for clarity. In the full model we consider all 30 glomeruli for which responses to 16 odorants were reliably observed in [3], outlined in dark grey in Figure 1A. Both the projection neurons (PNs) and LNs are excited by olfactory receptor neurons (ORNs) and LNs inhibit the LNs as well as the PNs of all other glomeruli. The lateral inhibition between LNs is strong enough to lead to winner-take all responses in the population of LNs which then modify the response patterns of the PNs. ORNs are modelled as Poisson neurons, with response rates to specific odours reconstructed by matching the spike density functions of the model's PN responses to the glomerular activation patterns observed in imaging data [3]. PNs and LNs are modelled with conductance based models that were developed to reproduce the electrophysiological PN and LN response profiles observed previously [4].

Results Although we are still just at the beginning of this work we have already found that we (i) can approximate the experimentally observed response patterns in the AL model, (ii) the winner-take-all LN network does lead to different winners for different odours and, importantly, for different incoherent mixtures and (iii) the influence of the LN network leads to measurably different PN responses for different incoherent and the corresponding coherent mixtures. We tested the model on hexanol, octanol, their coherent mixture and temporally incoherent mixtures of these two chemicals. To analyse the results we calculated "template responses" to the individual odours and the coherent mixture as the average of PN spike density functions (SDFs) in all glomeruli in the interval from 100 to 200ms after odour onset. Figure 1C,D shows the correlation of the instantaneous PN SDF values of responses to incoherent mixtures with these response templates. We observe that the incoherent mixture with hexanol first is initially most similar to the response template of the coherent mixture, but eventually becomes more similar to the pure octanol response. The response to the octanol-first incoherent mixture is also initially more similar to the coherent mixture but then becomes more similar to the hexanol response pattern. This demonstrates that although the incoherent mixtures only had a microscopic delay of 10ms on this occasion, the responses are markedly different for the two incoherent mixtures and the coherent mixture for a macroscopic amount of time during the response. This difference could easily be exploited by the animals to recognise the incoherent mixtures against each other and against the coherent mixture.

Conclusion Odours are encountered by the bees in thin filaments in turbulent odour plumes. Odour mixtures emanating from the same odour source will arrive within the same filaments, i.e. as coherent mixtures, while odorants from separate odour sources that are mixed in the air would arrive in different filaments leading to incoherent mixtures. The ability of bees to distinguish incoherent and coherent mixtures could hence underlie a form of “odour object recognition” to help making sense of the complex odorant scene encountered by the animals.

In future work we will test our predictions in physiological experiments in the bee antennal lobe to confirm, falsify or further refine the model. We will perform more systematic explorations of the model to establish the extent of possible response characteristics depending on the model parameters and we will analyse the limitations of incoherent mixture perception given realistic constraints from the anatomy and physiology of the bee brain.

Keywords: Olfaction, Honeybee, Temporal Mixture Coding, Odour Object Recognition.

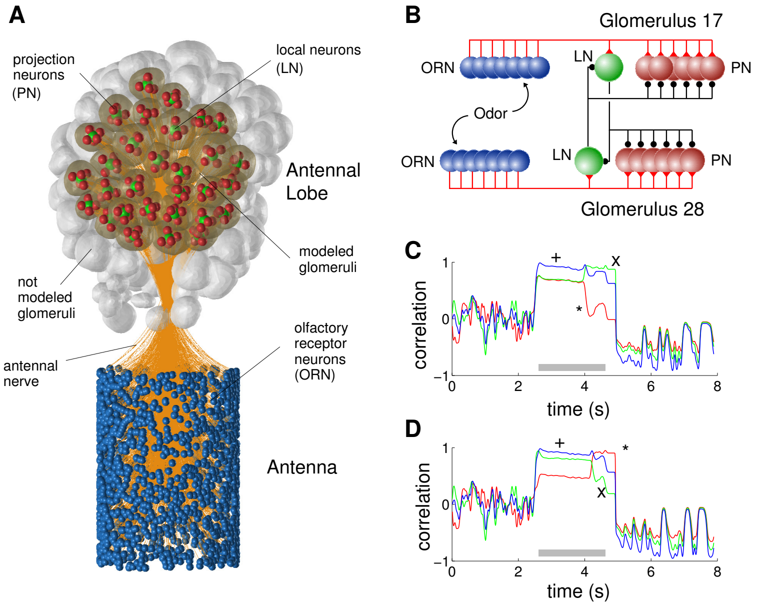

Figure 1: Model and initial results. A) Anatomy of the relevant structures considered in the model. B) Circuit diagram of the model exemplified for the two most active glomeruli for hexanol and octanol. C) Correlation of the PN responses to a hexanol-first incoherent mixture with 10ms delay to the response templates to hexanol alone (*), octanol alone (×) and the coherent mixture (+). D) correlation of the response to an octanol-first incoherent mixture to the three templates. The grey bars mark the presence of the stimulus at the ORNs.

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Discrimination of binary patterns by perceptrons with binary weights

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Information processing in neurons is understood incompletely, especially when neuronal inputs have indirect correlates with external stimuli as for example in the hippocampus. In such cases, researchers study neuronal responses to arbitrary input patterns. It is a challenging problem since for example hippocampal neurons have tens of thousands local inputs, synapses, that can be activated or not [6]. In the experiment, the most advanced techniques allow for selective activation of less than hundred synapses of a neuron [5]. In computer simulations, arbitrary spatio-temporal patterns of synaptic activation can be simulated. However, constraints on computational resources limit available samplings of patterns. That is why there is a growing interest to theoretical results on transformation of inputs in neurons.

Often, neurons process information as a part of a network that receives its inputs from another network. For example, the neurons in the hippocampal field CA1 process inputs from the hippocampal field CA3, among the others [1]. We studied how neurons process network inputs within short time windows. In the hippocampus, neocortex and other brain areas such time windows are the intervals when inhibition of neurons gets weak [2]. Intuitively, if an input pattern makes a target neuron spike then the target neuron should also spike in response to similar patterns - otherwise, neurons would be too sensitive to noise. On the other hand, neurons should discriminate between sufficiently different input patterns and spike selectively. Our main goal was to quantify how well neurons, in particularly in the hippocampus, discriminate patterns of spiking activity in input networks.

We modeled neurons with perceptrons. As a perceptron, the model neuron performs a linear classification of synaptic input patterns [7]. For example in hippocampal neurons, linear summation of inputs does occur to some extent [3]. There is a recent raise of interest to perceptron neuronal models [4, 9]. Most results are asymptotic with respect to the dimension of input vectors. Here, using combinatorial analysis, we complement them by some exact formulas.

In our study, we considered perceptrons with binary inputs and binary synaptic weights. Experimental findings support these assumptions in the case of CA1 principal cells. Binary inputs represent spiking activity in input neurons. If an input neuron spikes, the corresponding component of the input vector is equal to one, otherwise it is equal to zero. When an input neuron spikes, it activates its synapses with target neurons. If the neuronal excitation that results from the activation of synapses exceeds a threshold the target neuron spikes.

As a first step, we derived formulas for the case when all the neurons in the input network are connected with a target neuron. Then, we expanded our results to a general and more realistic case when some of them do not affect the target neuron. As an application of our main result, we provide a new hypothesis of how increased activity in the hippocampal field CA1 [8] may contribute to cognitive deficits in schizophrenia.

Keywords: perceptron, neuronal model, hippocampus

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The interplay between network topology and structural synaptic plasticity in a model of cortical sequence learning

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Models of cortical sequence learning and recognition that include timing variability have recently gained attention. For example, Byrnes *et. al* [1] model and simulate a spiking neuronal network that creates a sparse code and makes use of spike-timing dependent plasticity (STDP) in order to learn sequences with elements with variable duration.

In STDP, neurons modify (i.e., strengthen and weaken) their synaptic connections based on their relative spiking timing [2]. Recent experimental work, however, provides compelling evidence that structural plasticity, whereby synaptic connections between neurons can also form and disappear over timescales comparable to STDP, is a crucial component of learning [3]. Some researchers have theorised that a combination of reweighting of synaptic strength, and reconnection of synapses are both crucial to learning, but that reconnections are more important for longer term memory formation [4].

A recent model of cortical sequence learning, inference and prediction has explicitly incorporated the idea that structural plasticity may be more important than synaptic weight plasticity [5]. This model, that extends related theoretical work [6], also proposes a simple model of a cortical pyramidal cell where dendritic computation is crucial. Here, we study the influence of initial network topology in the so called 'temporal pooler' component of the model of [5], and investigate how the learning process changes the network topology over time. We also study how the model's performance depends on initial network topology, and whether the introduction of learning rules that enable synaptic weights to also be important for learning can improve performance.

Keywords: structural plasticity, cortical learning, adaptive complex network topology.

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Effectiveness of information transmission in the brain-like communication models

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The efficiency of information transmission by brain is one of the major interests that have been recently studied, both through data analysis and theoretical modeling [1, 2, 3]. Recent attempts to quantify information transmission have concentrated on treating neuronal communication process in the spirit of Shannon information theory. It was developed as a mathematical, probabilistic framework for quantifying information transmission in communication systems [4].

The fundamental concept of this theory is *mutual information*, which quantifies the information dependence of random variables or stochastic processes. If $\{X\}$ and $\{Z\}$ are input (e.g. stimuli) and output (e.g. observed reaction) stochastic processes, then mutual information between them is given as: $I(X;Z) := H(X) + H(Z) - H(X,Z)$, where $H(\cdot)$ are entropies [5]. Entropies of processes with unknown distributions (containing output process Z) have to be estimated and we accomplished it with Strong estimator [3, 6] as it is reliable and computationally fast. Maximal mutual information, called channel capacity, $C = \sup_{p_X} I(X;Y)$, reflects the upper bound on amount of information that can be communicated over the channel.

For neuron model we chose that proposed by Levy & Baxter [3, 7]. Our *brain-like* neural network model (Fig. 1) consists of number of paired *excitatory* E and *inhibitory* I neurons. Such two neurons constitute a *node* (E,I). Output of one neuron within a given node becomes input of the other one in the next discrete moment. Inhibitory neurons act to hold back activation of excitatory neurons they are paired with. Each node $(E,I)_i$ is connected with neighboring nodes $(E,I)_{i-1}$ and $(E,I)_{i+1}$ through output of neuron E_i. Other nodes can be connected through *long-range connections*. Some or all neurons E_i can be connected to the source of information, i.e a discrete, one-zero (*spike* or *no-spike*) stochastic process.

We search for maximal values of mutual information between input process $\{X\}$ and outputs of excitatory neurons $\{Z\}$s. We ran multiple simulations for architectures presented in Fig. 1. The information source parameters were as follows: *firing-rate* $0 \leq f_r \leq 1$ in steps of 0.05 and sequences of 1 000 000 bits were generated to reach high accuracy. Parameters associated with neurons were:

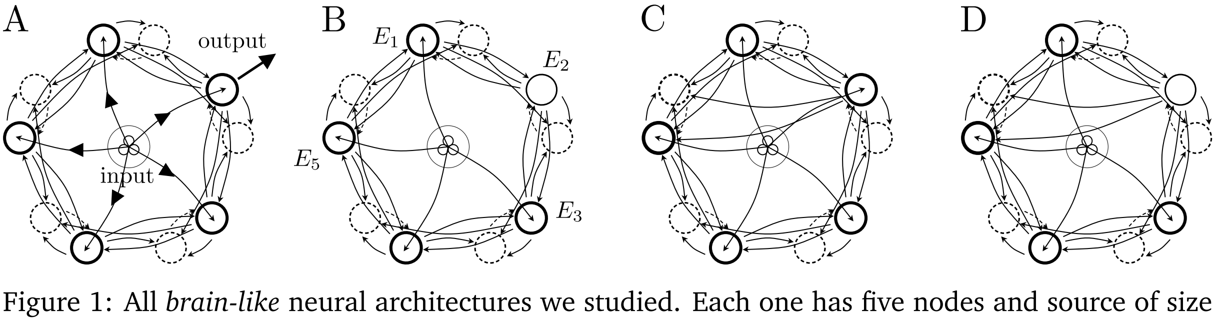

Figure 1: All *brain-like* neural architectures we studied. Each one has five nodes and source of size three. **A**, a *symmetric* case. **B**, E_2 has no access to the source of information. **C**, symmetric case with added *long-range* connection from E_2 to E_5. **D**, a combination of B and C.

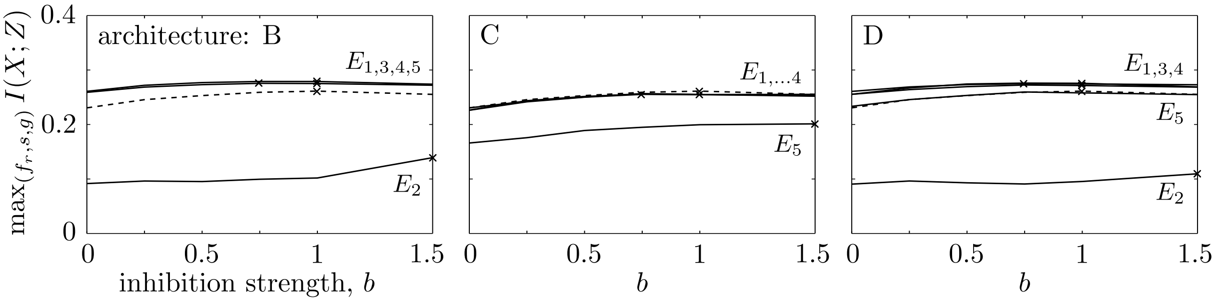

Figure 2: Mutual information between input process X and outputs of E neurons for architectures B, C, D (*symmetric* architecture result drawn with dashed line), maximized over: firing-rate f_r, synaptic success s and activation threshold g. Optimal values for each neuron marked with ×.

synaptic success $0 \leq s \leq 1$ in steps of 0.05, *activation threshold* $g \in \{0.2, 0.3, 0.5, 0.7, 0.9, 1, 1.2, 1.6\}$ and *amplitude fluctuations* were distributed uniformly on interval $[0;1]$. Neural network was parametrized with *inhibition strength* $b \in \{0, 1/4, 1/2, 3/4, 1, 3/2\}$ (relative to excitatory neurons strength).

Results are presented in Fig. 2. Most neurons reach the optimal information transmission around point where inhibition balances excitation, i.e. for $b = 1$. Generally, neurons are least efficient if there is no inhibition at all, i.e. for $b = 0$.

Efficiency of transmission of excitatory neuron lacking access to the source of information is decreased even by 62%, while other neurons efficiency rises by 7–13%, depending on inhibition strength. Long-range connection, if it originates from neuron having access to the source, brings 23–27% loss to target excitatory neuron transmission efficiency. If the connection originates from neuron without access to the source, the efficiency of target neuron is unchanged.

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Keywords: Brain-like network, Information transmission, Neuronal computation.

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Noise correlations in cortical networks

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Cortical activity exhibits correlated variability, frequently referred to as noise correlations. Correlation coefficients covering a wide range of values have been reported in many cortical areas. However little is known about its origin and data analysis based on recordings of cortical activity of awake, behaving animals performing non-trivial tasks are scarce. In the first part of my talk I will review recent theoretical [1] and numerical [2] work that we are doing to understand noise correlations in recurrent neural networks. In the second part, I will report results on noise correlation [3] obtained from data recorded as monkeys perform a perceptual decision-making task consisting in the detection of somatosensory stimuli.

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Calcium Activated Potassium Currents Contribute to High Fat Diet Induced Inhibition of POMC Neurons of the Mouse Hypothalamus

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Satiety signaling POMC neurons in the arcuate nucleus of the hypothalamus play a pivotal role in the regulation of energy homeostasis. While various endocrine and nutrient factors are defined and their acute physiological role and signaling mechanisms are increasingly well known, the effects of sustained extreme metabolic states and aging are less understood. However, defining diet and age associated changes in this network and elucidating their molecular mechanisms, is critical to the understanding of what makes the organism increasingly susceptible to metabolic disorders over its lifespan. Here we compared intrinsic electrophysiological characteristics of POMC neurons in mice on a normal chow diet (NCD) and mice on a high fat diet (HFD).

Using perforated patch clamp recordings, we showed that a HFD drastically modulates or rather impairs the intrinsic properties of anorexigenic POMC neurons. In HFD mice the resting membrane potential of POMC neurons was hyperpolarized, the action potential frequency was decreased, and the number of neurons with no spontaneous action potential firing increased. At the systemic level this is a dramatic reduction or even loss of an important satiety signal. Whole cell voltage clamp recordings revealed that the frequency of inhibitory postsynaptic currents (IPSCs) was significantly increased, while the excitatory input remained unchanged. Application of $GABA_A$ receptor blockers eliminated IPSCs completely, but neither $GABA_A$ nor $GABA_B$ receptor blockers restored the membrane potential and firing rate to control levels. The latter results indicate that the HFD induced hyperpolarization and decrease in firing rate could be caused by altered intrinsic properties. Our experiments showed, that an increase in free cytosolic Ca^{2+} leads to an activation of apamin-sensitive Ca^{2+} activated potassium currents that contribute to the reduced excitability of POMC neurons. We found three mechanisms that potentially contributed to the elevated intracellular Ca^{2+} levels: a) increase in voltage activated Ca^{2+} influx, b) decrease in the endogenous Ca^{2+} buffering, and c) decrease in the Ca^{2+} extrusion. Consistent with these cellular data, intracerebroventricular application of the SK channel blocker apamin into the left lateral ventricle caused a reduction of food intake in mice on HFD at a dose that was not effective in mice on NCD.

Keywords: Ca^{2+} handling, Hypothalamus, POMC neurons.

Nonparametric estimation of interspike interval distribution and its characteristics

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We address the problem of non-parametric estimation of the probability density function and some recently proposed measures of statistical dispersion of positive continuous random variables, which statistically describe the distribution of the interspike intervals in neuronal activity records.

Although standard deviation is used ubiquitously for quantification of variability, such approach has limitations. The dispersion of the probability distribution can be understood in different points of view: as “spread” with respect to the expected value, “evenness” (“randomness”) or “smoothness”. Although the probability density function, or its estimate provide a complete view, quantitative methods are needed in order to compare different models or experimental results.

We apply the maximum penalized likelihood estimation of the probability density function proposed by Good and Gaskins [1] and present a complete methodology how to estimate the probability density function of the interspike intervals and dispersion measures with a single algorithm, [2].

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Fano Factor Estimation

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Fano factor (FF) is one of the most widely used measures of variability of spike trains. It is defined as

$$\mathrm{FF} = \lim_{t\to\infty} \mathrm{FF}_t = \lim_{t\to\infty} \frac{\mathrm{Var}(N_t)}{\mathrm{E}(N_t)},$$

where N_t denotes the number of spikes in time interval of length t. Its standard estimator, $\widehat{\mathrm{FF}}$, is the ratio of sample variance and sample mean of spike counts observed in window of fixed length, t, [1]. These counts are obtained either from n (short) independent spike trains or from a single (long) spike train, which is divided into n intervals of length t. It is known that $\widehat{\mathrm{FF}}$ is strongly biased for small t in both cases, therefore the window should be chosen large enough to reduce this bias. However, in estimating from single spike train increasing of t causes decrease of the number of intervals with spike counts, which leads to larger variance of $\widehat{\mathrm{FF}}$. Thus the question of optimal t arises. In this work we study Fano factor and its estimation for renewal processes with focus on this issue.

We investigate the dependence of FF_t on t and the effect of refractory period on this dependence. Both, relative and absolute refractory period, cause an initial decrease of FF_t, which can lead to nonmonocity of corresponding curves. Because of this effect, $\widehat{\mathrm{FF}}$ for small values of t does not reflect the true value of FF. This is illustrated for gamma and inverse Gaussian probability distributions of interspike intervals.

Finally, we derive an approximate asymptotic formula for mean square error (MSE) of $\widehat{\mathrm{FF}}$ when Fano factor is estimated from n independent spike trains. Using simulations we show that this formula can also be used in the situation with single spike train to find t which minimizes MSE. However, the length of the window which minimizes MSE is not always in practice suitable, as for FF near one it can be extremely short and has to be increased.

Keywords: Fano factor, renewal process, mean square error.

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Novelty detection and jamming avoidance share common computational mechanisms in pulse gymnotiforms

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Electric fish explore their environment using an electric organ discharge. The electric field is modified by the presence of nearby objects allowing the fish to identify different object attributes related to their impedance, shape, position in the electric field, size and distance. This study is focused on the electro-sensory electromotor cycle of *Gymnotus omarorum*.

These fish show a characteristic electromotor behavior unit consisting of transient reductions of the interval between electric organ discharges followed by a slow relaxation phase. This type of pacemaker responses is triggered either by sensory signals or skeleton-motor commands [1]. This basic behavior is part of more complex behaviors specifically related to changes of electro-sensory images of the environment: a) the novelty response and b) the jamming avoidance displays [2]. Novelty responses occur when the presence of a novel object modifies the self-generated electric field. Since each EOD generates an electric image, a novelty response causes an increase in the frames per second rate, allowing the fish to explore such object with larger time resolution. Jamming avoidance displays are triggered by allo-generated electro-sensory signals either preceding or coincident with the EOD. These displays tend to maintain the mutual information between self-generated electro-sensory signals recorded at the skin and the brain in the presence of jamming [3].

The aim of this study was to further investigate the sensitive periods of the EOD cycle in which changes in local or global stimuli provoke transient reductions of the pacemaker interval and the electro-sensory mechanisms involved in detecting the changes in stimulus that trigger this behavioral unit.

First, we investigated in behavioral experiments how an interference signal cause changes in the pacemaker rate. We applied global (head to tail) or local (with a dipole near the skin) 0.1-1ms electric stimuli to water. As expected, onset and offset of stimuli coincident with the EOD provoke novelty responses. To further investigate the phase of the stimuli involved in triggering such response the short stimuli (0.1 ms) was slowly varied (0.1-1 per second) over the EOD and the EOD interval. When sweeping the late phase of the waveform it easily provoked novelty responses. When the stimuli swept intermediate phases of the inter EOD interval no responses were obtained but when the stimuli approached the next EOD transient reductions of the pacemaker interval were also observed. Phase locked stimuli at long delays (close to the next EOD) caused oscillating changes of the cophase, suggesting that there is the change of the stimulus, rather than its steady presence, the cause of transient accelerations of the pacemaker. These data are coherent with previous modeling [4, 5].

Second, to investigate the sensory mechanisms involved in the detection of stimulus variation we recorded units and field potentials in the freely moving animals while applying electrical stimuli to the receptive field of the explored ELL zone. We found that changes in the stimuli applied at the time of the EOD (thus mimicking the appearance or disappearance of an object) cause relatively large field potentials ("novelty potentials"). With the stimulus polarity that increases the main slope of the EOD waveform, these potentials occur at about 12-14 ms after the EOD only in the next interval after the modified image. With the other polarity it occurs at a phase of 14-20 ms in the next 4 or 5 intervals following the image change. Interestingly, when we elicited the jamming avoidance displays by applying a global stimuli (mimicking the presence of a second fish), or even placing another fish in the neighborhood of the implanted one, similar field potentials occurred previously to the EOD transient accelerations.

Our data suggests that the novelty responses and the jamming avoidance displays share common sensory mechanisms at the electro-sensory lobe. Interestingly, the single "novelty potential" occurs about the time of transition between the silent and the active period of pyramidal neurons (see companion abstract), suggesting that this potential may be the expression of a descending control signal, phase locked with the EOD.

Keywords: electro-sensory system, unitary recording in freely moving fish, jamming avoidance, novelty responses

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Response Properties of First- and Second-Order Neurons in the Olfactory Systems of a Moth and a Frog

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The first two neural layers of the olfactory systems of insects and vertebrates are similarly organized. The first-order sensory neurons, the olfactory receptor neurons (ORNs), principally located in the insect antennae and the vertebrate main olfactory epithelium, project their axons in the primary olfactory centre in the brain – the insect antennal lobe and the vertebrate olfactory bulb. There, they make synapses with local neurons and second-order output neurons – the insect projection neurons (PNs) and the vertebrate mitral cells (MCs).

In recent years we have studied experimentally [1, 2, 3] and theoretically [4, 5] various aspects of the stimulus-response relationships of these two neuron types. They present a number of intriguing response properties with their high (or low) sensitivity and small (or wide) dynamic range. To study these properties and analyse how the spiking response reflects quantitatively the intensitive and temporal features of the olfactory stimuli we have used a comparative approach based on insect and vertebrate neurons. For insects (a moth), we have analysed ORNs and PNs responding to the main component of its sex pheromone (a hydrocarbon molecule), and for vertebrates (a frog), the ORNs and MCs responding to four ‘ordinary’ odorants (anisole, camphor, isoamylacetate and limonene).

Spike trains were recorded with electrophysiological techniques adapted to the four preparations and odorants were applied as square pulses of different concentrations. Methods were developed to analyse quantitatively these spike trains in both neuron types and in both groups. Beyond clarifying the respective merits and limits of these methods (e. g. spike counts in fixed time window, kernel-estimated firing rates, instantaneous firing rates etc.), their broad application revealed the multidimensional nature of spike trains.

Clear differences between groups appeared in the response patterns. The most apparent was the often triphasic response of frog ORNs, contrasting with the monophasic response of moth ORNs, and the bi- or triphasic response of moth PNs. In order to facilitate the comparisons, in all cases we focused on the properties of the first phase (called here ‘response’ for short).

We showed that the responses of both neuron types in both groups present similar properties. For example the response latencies decrease exponentially with the dose whereas the peak response frequencies increase according to sigmoid Hill functions. The parameters describing these responses (for example threshold, dose at mid-maximum frequency, maximum frequency, Hill coefficient for frequencies) are different in different neurons. However, they follow the same statistical distributions (normal or lognormal). This large variability was expected for frog generalist neurons but less for moth specialist neurons. Finally, the main differences between moth and frog neurons were found to be quantitative. For example the response frequencies, the dynamic ranges and the increase of sensitivity of second- with respect to first-order neurons are higher in the moth than in the frog.

These results provide reference data to develop models of single neurons [4], neuron populations [5] and neural networks [6, 7], and to understand the environmental features that controlled their evolution [8].

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A model of Trial-to-Trial Variability in Monkey Motor Cortex

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Whether the strong variability in cortical spike trains is noise or important for computation remains an open question. Time resolved analyses have recently shown that the trial-to-trial variability is modulated over the course of experimental trials and can depend on the experimental condition [1, 2]. One hypothesis that can explain such modulations is that of an ongoing background activity of a network onto which the activities of individual neurons are superimposed [3]. We use spike train statistics to investigate this hypothesis. Similar to [4], we assume a division of the neuronal variability into a part that is due to relatively slow changes in network state and one that arises from the neurons intrinsic properties. Further we show that time resolved parallel analysis of the Fano Factor (FF) and squared Coefficient of Variation (CV^2) can be used to quantify these individual components of the count variance [5]. We use extracellular recordings from the motor cortices of two monkeys performing a delayed center out reach task (data previously published [6]) to show that the CV^2 is only weakly modulated over time (see also [7, 8]) and can be used as an indicator for a neuron's intrinsic variability. We then present a gamma process model where the average rates and regularity parameters ($1/CV^2$) are fitted to the dataset. The FFs can then be matched by adding varying amounts of backround rate to the individual trials. This model then captures the FF modulations observed in the data and can be used to further investigate the interactions between ongoing activity and task related processes.

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Keywords: variability, motor cortex, monkey

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Dependency problems in neuronal network modeling

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The understanding of the neuronal code is important to know the structure of the neuronal network. Mathematical models may help to this aim. Indeed, there exist several mathematical models for the description of the dynamics of the membrane potential of a single neuron. Furthermore, mathematical tools for their study have been developed during past decades [1, 2, 4, 5]. Mathematical models for the description of small networks, extending single neuron models, exist in the literature [3, 6]. However, their study presents several mathematical problems and simulations or numerical approaches are often necessary [7].

Here we focus on some of these difficulties and we develop some specific mathematical tools to study two network models characterized by the leaky integrate and fire structure. We assume that the inter-times between successive spikes of each single neuron are independent identically distributed random variables. On the contrary the inter-spike intervals of two or more neurons are dependent. We look for the dependence properties of the spike trains generated by different neurons. Due to the difficulty of the problem, we limit our study to the case of two neurons, but the proposed methods may be extended to larger networks.

In the first model, we consider two neurons whose membrane potential evolves according to an integrate and fire Wiener model. Each membrane potential evolves independently from the other, until the time when one of them attains a threshold value. When that neuron releases a spike, its membrane potential is reset to its resting value and its evolution restarts anew. At the same time, the membrane potential of the other neuron has a jump of constant amplitude. Then, the dynamics of both neurons pursue independently until one of them reaches again its boundary, producing a jump in the membrane potential of the other. The study of the coupling of the inter-spike intervals of the two connected neurons presents new problems with respect to single neuron models. Here we discuss them and we present some analytical result on the coupling properties of the spike trains for the case of two neurons modeled through jump diffusion processes, when the diffusion is a Brownian motion.

The second model describes the membrane potential evolution of two neurons through a bivariate Ornstein-Uhlenbeck process characterized by correlated noise. The spike mechanism is analogous to that of the one-dimensional Leaky Integrate and Fire models for single neuron (cf. [8]). For this process, we determine numerically the joint distribution of the first passage time through a two dimensional boundary.

The developed tools are not yet sufficient for a complete study of the dependence properties of the two considered models, but they represent a first step toward the study of the spike trains. To attain this goal, we should generalize our method to the case of arbitrary couples of spike epochs of the considered neurons.

Keywords: Leaky integrate and fire model, Jump process, First passage time.

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Spike-triggered covariance revisited

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Neurons in sensory systems are often exquisitely tuned to specific stimulus features. Thus, a first step in the characterization of their input–output transformation is to identify which aspects of the stimulus affect a neuron's activity level and which do not. As the space of possible stimuli is typically high-dimensional, an exhaustive exploration of all candidate stimuli appears impractical. But fortunately for neuroscientists, individual neurons often seem to be remarkably selective, and only care about subspaces of low dimensionality. The identification of such low-dimensional spaces of relevant stimuli and their distinction from the larger irrelevant space is a crucial challenge in sensory neuroscience.

In the simplest scenario, an analysis may aim at identifying a single relevant dimension in stimulus space, corresponding to a particular stimulus feature. This is suited, for example, for neurons whose response properties are well captured by their receptive fields. A standard technique for assessing the receptive field from electrophysiological experiments is to measure the spike-triggered average (STA) under stimulation with a broad-band signal, typically white noise.

In many cases, however, a single stimulus feature is insufficient to describe a neuron's response characteristics. If the cell is sensitive to several features and pools them in a nonlinear fashion, its stimulus–response relation may not be well captured by just the receptive field. For these reasons, spike-triggered covariance (STC) analysis has emerged as a popular extension of the STA. In STC analysis, the stimulus segments that precede a spike are characterized through a principal component analysis, which allows the extraction of multiple relevant stimulus dimensions. The basic idea is to detect differences in variance between the distribution of spike-producing stimulus segments and the prior distribution of all stimulus segments. The method is based on the construction and diagonalization of the spike-triggered covariance matrix C. Irrelevant stimulus dimensions are identified as the eigenvectors of C whose eigenvalues are equal to the prior stimulus variance. The eigenvalues of relevant stimulus directions, in contrast, differ from the prior variance.

The statistics of the applied stimulus play an important role for applying STA and STC analysis. In neurons whose firing probability depends on a single stimulus direction, the STA provides a consistent and unbiased estimator of the relevant direction when the probability distribution of all applied stimuli displays spherical symmetry [1]. This condition states that all stimulus segments that have the same magnitude (i.e. the same Euclidean norm) must also have the same probability of occurrence.

Surprisingly, the requirements concerning the stimulus distribution are more restrictive for STC analysis, where stimuli need to follow not just a spherically symmetric, but a Gaussian distribution to guarantee that the analysis provides a consistent estimator of the relevant stimulus space [2]. Given the otherwise tight analogy between STA and STC analysis, this difference appears puzzling. For STA analysis, the requirement of a spherically symmetric stimulus distribution is best understood in a geometric picture of why the technique works [1]. The insight and intuition supplied by the geometric proof thus calls for a similar perspective on STC analysis.

Here, we provide such a geometric derivation for STC analysis, leading to a simple proof of why the technique works, that is, of the consistency of the method [3]. The geometric approach highlights the importance of spherical symmetry also for STC analysis and suggests a simple modification of the procedure that makes it applicable to stimulus ensembles with general spherical symmetry, not necessarily Gaussian. In the modified method, irrelevant stimulus directions are identified as the eigenvectors of C whose eigenvalues appear in the spectrum as a baseline of degenerate values. An examination of the symmetry properties of the space of spike-triggering stimuli reveals that irrelevant directions span a subspace where the matrix C is highly symmetric, actually proportional to the identity matrix. Therefore, the irrelevant subspace is a highly degenerate eigenspace of C. For non-Gaussian stimuli, the numerical value of the degenerate eigenvalues cannot be predicted in advance, since it may vary with the stimulus distribution and the input–output transformation implemented by the cell. In the extended method, hence, irrelevant directions can no longer be identified by the magnitude of their eigenvalue. Degeneracy, however, typically suffices to distinguish them. Relevant directions, in consequence, are flagged by eigenvalues popping out as outliers from the degenerate spectrum.

By means of a simple linear transformation, the new approach can be extended to arbitrary elliptic stimulus distributions, containing correlations between different stimulus components. To facilitate identification of relevant stimulus dimensions also when analyzing finite data sets, we finally introduce a new statistical test that assesses the significance of relevant stimulus dimensions. The extended method widens the applicability of spike-triggered covariance analysis, allowing the experimenter to choose the stimulus from a larger class of statistical distributions, and thereby, to better select the stimuli that drive cells most efficiently.

Keywords: covariance analysis, receptive field, linear-nonlinear model.

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Ideal observer in the stochastic interpolation model of the auditory brainstem

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The precision of timing of action potentials reached the most expressed form in the neural circuits of the auditory pathway. The task of spatial hearing requires the neural network to be able to distinguish time difference of tens of microseconds. The particular mechanisms of neural coding differ in various animal species. It has been experimentally shown that *temporal code* (in the form of spike latency) is used in some invertebrates [1] while *topographic code* is used in some birds (in the form of *delay lines* [2]). The code used in mammals is a matter of controversy since no clear evidence for delay lines was shown. Moreover experiments on small mammals show that the *interaural time difference* tuning curves of the critical binaural neurons are shifted so that the slope part of the curve covers physiological range of the animal [3]. This type of so-called *slope code*, encodes particular value of azimuth into particular value of firing rate. We model the stochastic circuit, which uses this coding scheme and ask how the noise present in the spiking mechanism influences the overall time, which the circuit needs for reliable estimate of the sound source azimuth. For measuring this time we use ideal observer methodology [4] and estimate the time needed by single binaural neuron to reach the perceptual decision, see Figure 1. This figure shows a perceptual decision measure in dependence on the standard deviation of the spike time, for short called the jitter, which is a noise inherent in the neural circuit.

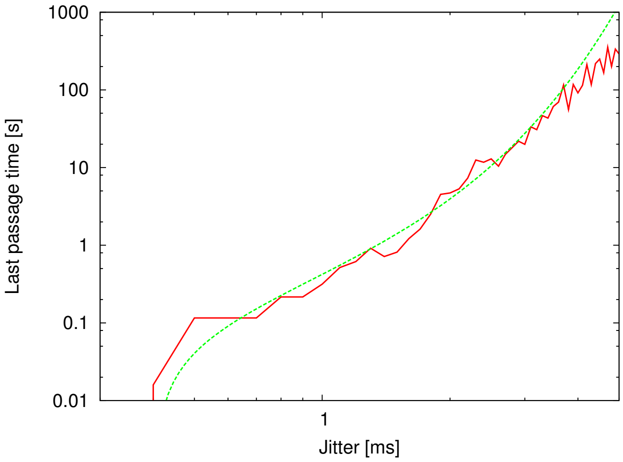

Figure 1: **The jitter value determines the time needed for the perceptual decision.** Parameters of the exponential function were fitted (dotted line) to the last passage time dependency on the spike timing jitter values obtained by the computer simulation of the mammalian sound location neural circuit (solid line).

Parallelism further helps to lower the noise. We have discussed in [4] that in comparison to only single neuron, sensory neural processing is faster when several neurons of the same nucleus are used. The parallelism in the auditory pathway is ubiquitous, from periphery up to higher processing relays, and the parallel fibers also converge on higher order neurons. For example the level of noise is lowered due to convergence in avian nucleus magnocellularis [5]. The conditions for both enlargement and diminution of jitter due to convergence are given in [6].

The desirable effect is lowering the spike timing jitter. Optimal level of the jitter must exist, since zero jitter would not allow the stochastic neural computation (and is not possible in the real biological system anyway) and high values of jitter peturb the incoming signal so its decoding is no more possible. The jitter level attained by given neurons is one of the key parameters influencing the performance of the sound location circuit as a whole, therefore its values in the mammalian circuit are worth of close investigation.

It is known from the human psychophysics that the just noticeable difference of azimuth accuracy in the mid line is $\pm 2^\circ$. The variable shown in Figure 1 (the last passage time) in dependence on the jitter values denotes how long time does the simulated azimuth accuracy take before it enters (lastly passages into) the $\pm 2^\circ$ reference interval mentioned above. This way we relate the neural computation and its code to human perception.

Keywords: auditory brainstem, ideal observer, medial superior olive, stochastic interpolation model, sound location neural circuit, sound source azimuth

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Synchronization of stochastic neuronal networks

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Synchronization is an universal phenomenon in networks of coupled neuronal units and induces a large scaled coherent rhythmic spiking. I will concentrate in my talk on the influence of noise in the dynamics, on effects of network-disorder and network-correlations on the neural activity, and on modifications arising from a delayed interactions between the stochastic neurons. For all these topics paradigmatic models for phases of the neurons are introduced and will be investigated. Outgoing from the stochastic dynamics of the ensemble of neurons, I formulate nonlinear balance equations for the mean phases and study them by bifurcation theory. In dependence on noise intensity, strength of disorder and of correlations and mean delay time conditions for synchronizations are elaborated. Computer simulations support the findings, but show also the limitations of the made approximations in certain cases as will be discussed in the talk.

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Order patterns networks (ORPAN) – Concept and applications

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Complex networks provide an excellent framework for studying the function of the human brain on a variety of scales, from the interaction of single neurons to the activation of large cortical areas. Plenty of studies have recently shown the merit of a graph-theoretical approach to better understand brain functions [1]. A basic problem for this approach is that estimating functional networks from measured signals of brain activity is far from being trivial, especially if the data is non-stationary and noisy, as is often the case with physiological recordings. In particular, two decisions have to be made : First, one has to decide which measure to use for estimating the functional connectivity between the individual components of the network (nodes). The choice defines the nature of the dynamic interactions considered as a functional connection. Usually this step gives a real valued all-to-all functional connectivity matrix between all nodes. Second, a threshold has to be applied to convert the real-valued similarity matrix into a binary matrix representing the functional graph. Thresholding is necessary to distinguish true functional relationships between nodes from links that appear only by chance.

Here we introduce an efficient method to estimate time evolving functional networks from multivariate data. The concept we employ are order patterns, which provide a symbolic representation of a real valued time series that represents the local rank structure of a given time series. Order patterns have been shown to be suitable for short and non-stationary data [2]. An advantage of this approach is that it replaces the notion of similarity by that of identity in defining a functional link between two nodes, abolishing the need to decide for a threshold that classifies the (correlation) values as *high enough* to be considered as a functional link; a step that is prone to arbitrary choices.

We demonstrate the potentials of this approach with model data as well as experimental data from an electrophysiological study on language processing.

Keywords: functional networks, network reconstruction, order patterns, EEG/ERP

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Inferring nonstationary input activities from non-Poisson firing of a neuron

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The cerebral cortex has been classified according to the cytoarchitectonics, reflecting the structure and organization of cortical tissue. The cytoarchitectonically divided areas were found to have the different functions. Recently, we collected neuronal signals recorded from individual cortical areas and investigated their non-Poisson irregularity. It turned out that neuronal firing irregularity does not vary significantly in time for each neuron but varies among neurons in a manner strongly correlated to cortical functions; neuronal firing patterns are regular in motor areas, random in the visual areas, and bursty in the prefrontal area [1]. Because spikes are originally determined by the signals that have been delivered to individual neurons, it may be possible to inquire into the input signals that have generated such firing patterns. Though problems of estimating inputs from output signals are generally ill-posed, a large number of randomly arriving input spikes make it possible to extract some information from an output spike train; a number of irregular synaptic inputs result in uncorrelated fluctuations with means and amplitudes that can be translated into the activities of presynaptic excitatory and inhibitory neuronal populations. Mathematical methods of estimating inputs from output firing pattern have been developed on the assumption that presynaptic neuronal activities are constant over time [2]. We proposed tracking temporal variations in input parameters comprising the mean and the amplitude of uncorrelated fluctuations [3]. I first review the methods for gauging the non-Poisson irregularity from a spike train [4], and then, discuss the method of transforming the information of firing patterns back to the activities of presynaptic excitatory and inhibitory neuron populations.

Keywords: neuronal firing pattern, non-Poisson, estimating inputs.

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Slope-based suprathreshold stochastic resonance in populations of phasic neurons due to intrinsic ion channel noise

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Ion channel noise can non-trivially affect spiking patterns [1]. However, whether channel noise can give rise to noise-enhanced neural processing [2] is unclear, as it has received relatively little attention in this context compared with synaptic noise. An exception is recent simulations [3] of a population of Hodgkin-Huxley models. This work revealed that a noise-enhancing effect called suprathreshold stochastic resonance (SSR) [4] can be observed in the population model, solely due to channel noise, as modelled by Markov-chain techniques that track the state of every channel.

We have therefore investigated (i) whether other forms of such stochastic facilitation [2] can be observed due to ion-channel noise models; and (ii) whether new efficient stochastic differential equation (SDE) approximations to channel noise [5] are accurate for such simulations. Specifically, we replaced current noise with channel noise in a model of phasically firing neurons that exhibits a noise-enhancing effect called slope-based stochastic resonance (SBSR), i.e. noise enables firing in response to slowly varying inputs [6]. We found that SBSR persists for a broad range of patch areas.

However, our main result is to show that SSR and SBSR can be combined to form a new noise-enhanced coding effect due that we label ‘slope-based suprathreshold stochastic resonance.’ This result suggests intrinsic channel noise might be exploited in-vivo to enable phasic population responses to robustly encode slowly varying signals. Although our study used channel noise, the same effect would likely be observed with synaptic or injected current noise.

Keywords: Phasic neuron, ion channel noise, slope encoding.

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Analysis of non-renewal spiking in neuron models with adaptation

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Spike-frequency adaptation is a common feature of many neurons and has a large impact on sensory information processing. Spike-triggered adaptation currents lead to an intricate neuronal dynamics with a stationary firing statistics that cannot be described by a renewal model. This is most prominently revealed by negative correlations between interspike intervals, which have been frequently measured in adapting neurons, both in experiments and model simulations. The link between adaptation and non-renewal spiking statistics, such as the serial correlation coefficient of interspike intervals (ISIs), is, however, still poorly understood theoretically. In my talk, I will present a theoretical analysis of simple models with adaptation that can be solved analytical. In particular, expressions for the ISI distribution, the serial correlation coefficient, and the power spectrum will be derived, which explain many of the observed non-renewal features. For the supra-threshold regime (limit cycle spiking), I will demonstrate how weak-noise approximation techniques can be used to calculate the stationary statistics for arbitrary adaptation strength and arbitrary time constants. In particular, perturbation theory is used to study how deviations from the limit cycle due to noise propagate from spike to spike. Moreover, the Fokker-Planck equation can be solved in the neighborhood of the limit cycle, which yields the stationary voltage distribution as well as the distribution of the adaptation current upon firing events. Finally, I address the problem of serial correlations in neurons operating in the subthreshold regime. To this end, an escape rate approch based on a Markovian dynamics of a discrete adaptation variable yields an exactly solvable case providing a theory for negative ISI correlations in fluctuation-driven neurons.

(Leaky) Integrate and Fire models can be coincidence detectors

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Integrate and Fire models, as well as Leaky Integrate and Fire models, are generally considered a good and simple tool to describe the membrane potential dynamics of a single neuron. Their use to investigate the neural code has helped the interpretation of many features, such as the role of noise in signal transmission. They can qualitatevily reproduce experimental data and, in some instances, fit the observations quantitatively.

Despite their success, their study was mainly qualitative up to recent years. The development of statistical techniques for the estimation of their parameters is quite recent. Furthermore it is mainly focused on the parameters appearing in the drift and diffusion coefficients. The estimation of the firing threshold value presents difficulties. Indeed, the observation of experimental intracellular recordings shows that the membrane potential may cross the threshold level several times before an action potential is generated.

This fact suggests changing the spiking mechanism typical of (Leaky) Integrate-and-Fire models. Here we do not identify the spike time with the first passage time of the process describing the membrane potential dynamics through a threshold. We study a modified version of the (Leaky) Integrate-and-Fire neuron model where a spike is generated whenever the membrane potential remains without interruptions above the threshold level within a period of time after crossing. Hence the firing time is not defined by an instantaneous crossing of the level, but depends on the behavior of the membrane potential on a prescribed window.

The proposed spiking mechanism enhances the range of behaviors of the modeled neuron. Contrary to the (Leaky) Integrate-and-fire models, the neuron with the new firing definition behaves both as an integrator and as a coincidence detector, depending on the width of the introduced window.

Keywords: Leaky Integrate and Fire model, Threshold mechanism, Integrator, Detector.

Transmission efficiency in the brain-like neuronal networks. Information and energetic aspects

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Biological systems evolve as compromises and many of them can be expressed in terms of energy efficiency [1, 2]. Inspired by brain network architecture we analyze the communication channels composed of the main brain ingredients. We study the information-energetic transmission efficiency of such neuronal networks. The Shannon Information Theory is applied and the fundamental concept of this theory, Mutual Information between input and output signals is estimated with high accuracy. The entropy estimator is that of high quality proposed in [3] and the encoded information were of 10^6 bits long to reach high accuracy. The model of neuron considered is that in the spirit of probabilistic approach proposed by [1] and further explored in [4].

The network constitutes from *nodes* each of them being a pair *excitatory* neuron and corresponding *inhibitory* one. The nodes are distributed uniformly over the circle (Fig. 1). Each node is connected with neighboring nodes and additionally the nodes can be connected through *long-range connections*. Source signals are modeled by Bernoulli process (*spike* or *no-spike*) and they can support excitatory neurons only. We study a variety of complementary architectures (Fig. 1). The following parameters affect the effectiveness of this communication system: Source parameter – firing rate f_r, entropy h; Neuron parameters – synaptic failure s, threshold activation g, inhibitory level of dumping b, number of synapses l; Network parameters – size r, number of nodes n. We assume that most energy is consumed by spikes. Thus, with Mutual Information for a given neuron denoted by MI, we analyze the information-energetic formula:

$$\Lambda(b) = \max_{g} \left(\frac{\max_{(s,f_r)} MI(s,f_r,b,g)}{\vartheta(s^0, f_r^0)} \right),$$

where $\vartheta(s,f_r)$ is equal to $s \cdot (n f_r + b f_I + \sum_w f_w)$, $s \cdot (b f_I + \sum_w f_w)$, $s \cdot \sum_w f_w$ for with- and without access to the source and for inhibitor, respectively. $\vartheta(s^0, f_r^0)$ are the values maximizing MI. The denominator is proportional to the number of spikes actually used to transfer information. The role of inhibitors, long-range connections and size-delay effects are studied and information-energetic optimal parameters are determined.

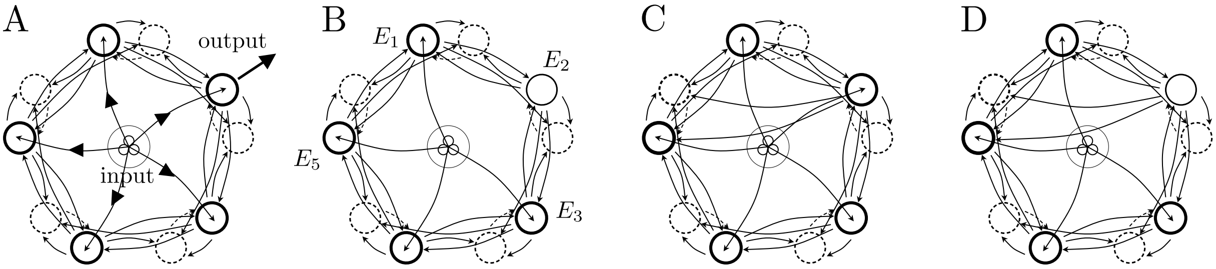

Figure 1: *Brain-like* neural architectures we studied. Each one has five nodes and source of size $l = 3$. **A**, a *symmetric* case. **B**, E_2 has no access to the source of information. **C**, symmetric case with added *long-range* connection from E_2 to E_5. **D**, a combination of B and C.

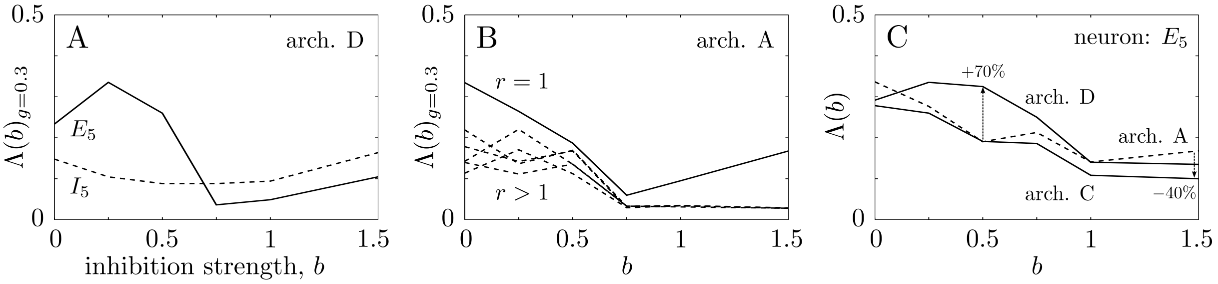

Figure 2: **A**, illustration of inhibition influence. **B**, size effects. **C**, long-range connection role.

Inhibitors influence: Parameter b, being a ratio of inhibitory neurons' strength in relation to excitatory neurons' strength, affects every signal that I neuron sends forward. If $b = 0$, then amplitude of every inhibition signal is reset to zero as if I neurons had completely no effect on the structure's behavior. The bigger the b is, the more potent inhibition signals are in relation to excitatory ones. If $b = 1$ then both types of neurons react with the same strength. It turned out that inhibitors can strength the effectiveness of transmission even by 50 percent (Fig. 2A).

Size effects: The most important effect of the size increase is a delay in transferring the information. Therefore it was expected that the transmission is most efficient for smaller size, i.e. for $r = 1$ (r is radius of the circle) but surprisingly further increase of the size ($r = 2, 3, 4$) does not change effectiveness significantly (Fig. 2B). We also observe that a two times increase of the size can cause even three times decrease of the information-energetic efficiency.

Long-range connections role: We observe that long-range connection can lead to improve target neuron's information-energetic efficiency significantly (even by 70 percent) if the neuron starting it has no access to the source of the stimuli. If the connection originates from neuron that has such access, it can bring a 40 percent loss to the target neuron's efficiency (Fig. 2C) – however this connection increases the efficiencies of starting neuron and neurons neighboring target neuron by up to 24 percent.

Conclusions: Our research shows, both through qualitative and quantitative results, that the brain-like networks significantly improve the information-energetic transmission efficiency.

Acknowledgments: This paper has been supported by NCN grant N N519 646540.

Keywords: Neuronal Communication, Brain-like Network, Shannon Theory.

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Identification of noisy response latency in presence of a background signal

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In many biological systems, an applied input (stimulation) has an impact on the output (response). If the response can only be observed on top of an un-distinguishable background signal, the estimation of the response can be highly unreliable, unless the background signal is accounted for in the analysis [1].
Such estimation becomes even more unreliable if there is a delay in the response to the stimulus. In fact, if the background activity is ignored, however small it is compared to the response activity, and however large is the delay, the estimate of the time delay will go to zero for any reasonable estimator when increasing the number of observations [2].

Here we propose non-parametric and parametric estimators for the time delay and the response latency, defined as the inter-time between the onset of an input and the output. These estimators are compared on simulated data. Theoretical results on the response latency are also presented.

This problem is described in the context of information transfer within a neural system, more specifically on spike trains from single neurons. However, the proposed technique can be applied to other biological system where one is interested in the estimation of the response to a stimulus.

Keywords: Response latency, background signal, point processes.

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Modeling the Relations between Neuronal Membrane Potentials, Ion Currents and Ion Channel Dynamics

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`http://www.uni-marburg.de/fb20/physiologie/ags/braun`

Different types of modeling approaches are used for the examination of neural coding and brain dynamics. The physiologically most realistic modeling strategy is the Hodgkin-Huxley type approach [1]. Unfortunately, when facing larger scale problems the original Hodgkin-Huxley (HH)-type algorithms soon become unhandy and even have been considered as “computationally prohibitive” [2]. Accordingly, a diversity of simplified approaches has been developed, especially in the biophysics community, like the widely used Fitzhugh-Nagumo model. With such simplifications, however, the direct relation of the models’ variables and control parameters to the physiological mechanisms are often sacrificed.

By contrast, our simplifications of the original HH equations have been introduced with focus on actually most relevant experimental and clinical measures [3]. As an example, the complicated and unhandy equations for the calculation of voltage dependent rate constants in the original HH-model have been omitted. Voltage dependencies of (in-)activation time constants can anyhow by neglected. The precise shape of an action potential, nowadays, is of minor interest. Especially, in agreement with conventional presentation of experimental data, the steady state voltage-dependencies of the ionic conductances can be given by easy adjustable Boltzmann functions. Nevertheless, whenever it is required, ion channel rate constants can be considered. These interdependencies, again, can be implemented in a simpler and easy adjustable way, i.e. by single exponential curves with unit values at the half activation voltage of the Boltzmann function.

The figure illustrates these relations, noteworthy, by means of teaching tools (`www.clabs.de`) that are widely used in medical and other life-science faculties. While the original equations, especially for the rate constants, are difficult to interpret, all curves of the actual version are reflecting actual measures as they are described in conventional physiology textbooks. The same strategy of simplified but physiologically justified simulations has been used for the implementation of a conductance based HH-type model of a chemical synapse. In this case, the focus was laid on clinically relevant drug effects [4]. In any case, the most important point is that the model is adjusted to the specific task and refers to the physiologically and/or clinically relevant measures. Hodgkin and Huxley, 60 years ago (`www.cnsorg.org/hodgkin-huxley60`), have provided an explanation for action potential generation and conduction in the squid giant axon with exceptional success, However, the main reason for the enormous impact of their work in neurophysiology and beyond was the introduction of a revolutionary new concept that turned out to be physiologically appropriate and extraordinarily flexible for successful adjustment to other tasks, allowing simplifications where possible and extensions whenever required.

For the K^+-channel, additionally the relations between the sigmoid activation curve and accordingly adjusted exponential voltage dependencies of transition rates between open and closed states are shown (d). Black dots indicate the relative open times (p) at different voltages (V) as obtained from 40 ms simulations runs as shown by only a few examples in (e). The exponential curves of opening and closing probabilities p_o and p_c (given per ms) are implemented symmetrically to the half activation potential of the sigmoid activation curve with $a = 0.11$ and $b = (-)0.035$.

Keywords: Hodgkin-Huxley-model, Boltzmann function, transition rate.

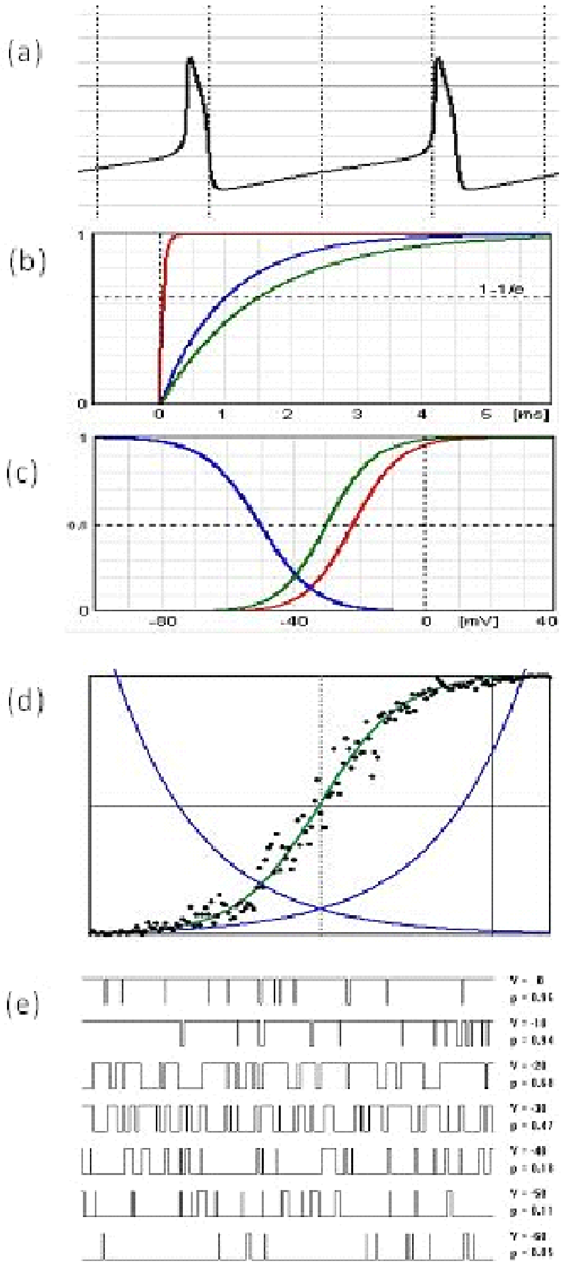

Figure 1: The model generates action potentials (a) on the basis of different first order time delays (b) and sigmoid voltage dependencies (c) of fast Na^+-channel activation followed by Na^+-inactivation and slower K^+-channel activation. For numerical values see [3] or `www.clabs.de`.

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Understanding disordered topography of auditory cortex through natural sound statistics

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Recent imaging techniques have revealed a qualitative difference between primary sensory cortices. As neighbouring neurons of the primary visual cortex (V1) specifically respond to light stimuli presented at similarly localized areas of the eye field, its principal topography, called retinotopy, is smooth. By contrast, the topography of the primary auditory cortex (A1), the tonotopy, is disordered [1]. This discrepancy appears to be inconsistent with the canonical model of the neocortex.

We hypothesize that V1 and A1 still use a common coding strategy and that it produces the dissimilar topographies by adapting to their inputs of contrastive statistics. Adaptation to natural image statistics has successfully explained the response properties of V1 neurons [2] and even their smooth topography [3], whereas this line of research has been limited to A1. We focused on how their natural inputs statistically differ: natural images show only local correlations, while natural sounds typically exhibit correlations between distant frequencies. Learning of the non-local statistics might result in topography dissimilar to that of V1.

To test the hypothesis, we used natural sounds as the input to a model that has been previously proposed for the smooth topography of V1, topographic independent component analysis [3], whose input was originally natural images. Learning of natural images, as reported, resulted in a smooth topography similar to V1, whereas the same algorithm applied to natural sounds exhibited a more disordered topography due to natural sound statistics that have distant correlations. This A1 model adapted to natural sounds predicted that the disorder might not be totally random: frequency selectivities of neighbouring neurons would be biased toward being harmonic. Furthermore, non-linear responses similar to pitch selectivity were found in the model's second layer, which originally modelled the complex cells of V1. These results suggest that V1 and A1 exhibit dissimilar topographies owing to the difference of inputs, even though they share an adaptive coding strategy.
Keywords: Tonotopy, Primary auditory cortex, Topographic independent component analysis.

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Analysis of synaptic action in stochastic interpolation model of the auditory brainstem

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Background: Mammals are able to localize sound sources with high accuracy. There exist multiple mechanisms of sound azimuth perception in neural circuits of various animals [4]. All the mechanisms must use one neuron as coincidence detector. In previous work, the model of the first binaural neuron as a stochastic coincidence detector has been introduced [5]. The neural fiber delay line is not the only way, how is the brainstem neural circuit computation implemented. Another plausible way of neural computation is the stochastic interpolation mechanism realized by the synaptic circuitry [6].

We describe in detail selected synaptic characteristics of the first binaural neuron. This neuron is in mammals in the nucleus of the medial superior olive. This is the first neuron from the periphery receiving post-synaptic potentials from both sides.

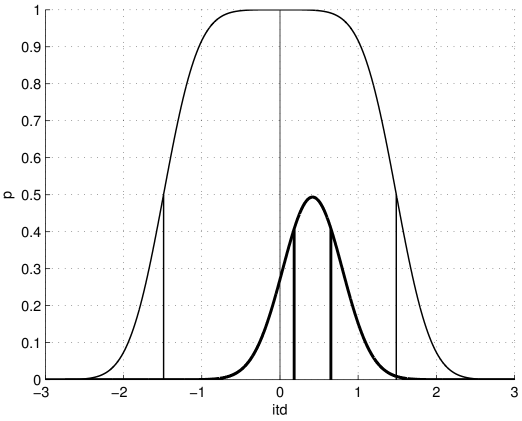

Figure 1: **Spike generation in dependence on the time delay.**
The narrower curve (thick line) shows the firing probability in a full model with both excitation and inhibition. The broader bell-shaped curve (thin line) shows the output in response to the excitatory input only (with the inhibition disconnected, in analogy to animal experiments abolishing inhibition). Vertical lines show the widths of time windows used for the coincidence detection. The parameters of the neuron model are described in the text. Note that both axes are shown in normalized, dimensionless arbitrary units.

Model: In the presented model, summation of synaptic potentials is expressed in analytical form using formulas for the time course of excitatory and inhibitory post-synaptic potentials, we call them activations for short. The model neuron is the generalized perfect integrate-and-fire model. When the sum of the post-synaptic potentials exceeds the threshold, neuron fires an action potential and its membrane potential is reset back to the resting state. The time range during which the action potential is generated is calculated using inversion function of the time course of the sum of all the activations.

Several formulas describing synaptic activations exist, namely alpha-function, double exponential and kinetic model, ordered from the simplest to the most complex. The double exponential proved to be the most suitable for our calculations with the inversion function, therefore we use it. In the full description of the model circuit, both excitations and inhibitions are used.

Results: We use typical parameter values based on the fitting and exploration of experimental data [4, 7]. The rise times (leading edges) last typically in order of one millisecond. This compares well with typical maximum interaural time difference, which is for example in gerbil about 330 μs [4]. We express the threshold height normalized by the maximum activation amplitude. This way we have no free parameter left. Both the deterministic and stochastic analytical calculations with the model show that the neural computing with post-synaptic potentials is essential for the mechanisms implemented by this neural circuit. Figure 1 shows comparison of the full model with the model with excitation only. This figure well compares to experimental results discussed in [1, 4].

Conclusions: The model is consistent with data acquired in electro-physiological experiments [1]. An analytical calculation using the Laplace transform was used to obtain similar activation curves [3]. Calculation with delays gives comparable results obtained with the use of the concept of neuronal arithmetic [2, 6].

Keywords: Medial superior olive, Stochastic interpolation model, Excitatory and inhibitory post-synaptic potentials.

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Very Slow Synchronization and Variability of Interspike Intervals in a Globally Coupled Neuronal Oscillators

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Abstract

Using the three-dimensional Bonhoeffer-van der Pol (BVP) equations, the dynamics of globally coupled neuronal oscillators is examined. There are interesting phenomena such as very slow phase-locked oscillations (compared with the inherent period of each uncoupled neuronal oscillator) and the death of all oscillations. We show that this slow synchronization is mainly caused by the existence of "fast" oscillators. The variability of interspike intervals (ISI's) and noise effects on the spiking are also studied.

Introduction

In order to clarify how the spiking and biological rhythm are regulated in a network of neurons, a population of globally coupled neuronal oscillators was studied [1] using the Hodgkin-Huxley (HH) equations [2] as a model of single neuronal oscillator. In this coupled system, it was shown that the neuronal oscillators presented a very slow phase-locked or synchronized oscillation compared with the inherent period of each uncoupled neuronal oscillator. The generation mechanism of these phenomena, however, has not been clarified yet.

In this study, a population of globally coupled neuronal oscillators is analyzed using the three-dimensional BVP equations [3, 4] which are much simpler single neuron model than the HH equations. Similarly to the case of the HH equations, there are interesting phenomena such as very slow phase-locked oscillation and the death of all oscillators. We investigate the generation mechanism of these global oscillations.

A population of globally coupled neuronal oscillators

Let us consider a population of the extended (three-dimensional) BVP oscillators globally coupled through a common buffer (a mean field) [1, 5]:

$$\frac{dx_i}{dt} = x_i - \frac{{x_i}^3}{3} - y_i - z_i + I_{\mathrm{ext}} + D(w - x_i), \tag{1a}$$

$$\frac{dy_i}{dt} = \eta(x_i - ay_i), \tag{1b}$$

$$\frac{dz_i}{dt} = \varepsilon_i(x_i - bz_i), \quad \varepsilon_i \ll 1, \tag{1c}$$

$$\frac{dw}{dt} = \frac{D'}{N}\sum_{i=1}^{N}(x_i - w), \quad (i = 1, \ldots, N) \tag{1d}$$

where x_i corresponds to the membrane potential and y_i is the refractory (or inhibitory) variable of the i-th neuron. z_i also denotes a refractory variable, but its dynamics is supposed to be much slower than that of y_i. The variable w denotes the mean field of the neuronal population, and the parameters D and D' (for the sake of simplicity, we suppose $D \equiv D'$ hereafter) denote the coupling strength between each neuron and the mean field.

When $D = 0$ in eq. (1), this system becomes a population of uncoupled BVP oscillators. Because the slow variable z_i is added to the original (two-dimensional) BVP equations [6] (or FitzHugh-Nagumo (FHN) equations [7]), we can see peculiar phenomena such as chaos and very slow spiking in the single neuron model [4].

Local stability of the equilibrium point and slow synchronization

If the coupling coefficient D is large enough, the population of oscillators show synchronizations or phase-locked oscillations. The ISI or the period of such synchronized oscillations is around the single oscillator's inherent period at first, but it grows up abruptly for the increase of D. If D is increased further, the slow phase-locked oscillation terminates and the equilibrium point becomes stable through the Hopf bifurcation. Therefore, we suspect that the "local" stability of the equilibrium point has a certain relevance to the slow synchronized oscillation, although the synchronized oscillation is a "global" behavior. Although the size of the Jacobian matrix of eq. (1) at the equilibrium point is very large: $(3N + 1) \times (3N + 1)$, the analysis of its eigenvalues can be reduced to that of lower dimensional matrices[5]. From this analysis, we found the fact that "fast" oscillators are important for the emergence of very slow synchronization.

Variability of interspike intervals and noise effects

In the presence of noise, the single (three-dimensional) BVP neuronal model shows various interesting behavior such as noise-induced acceleration and deceleration and various ISI's variability. We also study the noise effects on the synchronization and the ISI variability in the globally coupled neuronal population.

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Structural phase transition in the neural networks

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We consider a model for a neural network, which is a stochastic process on a random graph. The neurons are represented by the "integrate-and-fire" processes. The structure of the graph is determined by the probabilities of the connections, and it depends on the activity of the network. We investigate the dependence between the initial level of sparseness of the connections and the dynamics of activation in the network. We find a critical window for the level of sparseness which yields optimal (in some sense) performance of a network.

Keywords: Integrate-and-fire neurons, Random graphs, Phase transition.

Network Inference with Stochastic Hidden Units

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A good deal of recent work has dealt with the problem of inferring the connections in a network from a record of the activity of its units. In particular, attention has focused on statistical modeling of neural networks based on recorded spike trains[1]. However, this work has assumed that data are available from all the units in the network, a condition that never applies in actual experiments. Here we lay a foundation for treating more realistic situations by developing learning algorithms for networks of binary stochastic units containing "hidden" in addition to "visible" units. For Gibbs equilibrium networks, with symmetric connection matrices, this problem is solved by the classic Boltzmann learning algorithm. For the more general case of asymmetric connection matrices, this problem was also solved many years ago ("back-propagation in time") for networks of continuous-valued units. However, learning in networks of stochastic binary units with arbitrary connection matrices has not been treated previously. We derive an algorithm for this case here.

In the network model we consider, units can take on the values ±1 and are updated synchronously according to the stochastic rule

$$P[S_i(t+1)|\mathbf{S}(t)] = \tfrac{1}{2}[1 + S_i(t+1)\tanh H_i(t)], \quad H_i(t) = \sum_j J_{ij} S_j(t) = \sum_j J_{ij} s_j(t) + \sum_b J_{ib}\sigma_b(t). \tag{1}$$

The likelihood of a history of the system is $P[\mathbf{S}] = \prod_{ti} P[S_i(t+1)|\mathbf{S}(t)]$. We denote the N_v visible units by s_i and the N_h hidden ones by σ_i: $\mathbf{S} = (\mathbf{s}, \boldsymbol{\sigma})$. The likelihood of a history of the visible units s is obtained by marginalizing out the hidden units, and the learning rules are found by gradient ascent on the resulting log likelihood $\log P[\mathbf{s}] = \log \sum_{\boldsymbol{\sigma}} P[\mathbf{s}, \boldsymbol{\sigma}]$. They have the form

$$\Delta J_{ij} \propto \frac{\partial \log P[\mathbf{s}]}{\partial J_{ij}} = \sum_t \sum_{\boldsymbol{\sigma}} [S_i(t+1) - \tanh H_i(t)] S_j(t) P[\boldsymbol{\sigma}|\mathbf{s}]. \tag{2}$$

The weight $P[\boldsymbol{\sigma}|\mathbf{s}] = P[\mathbf{s}, \boldsymbol{\sigma}]/P[\mathbf{s}]$ in this average is like a Boltzmann weight for a statistical-mechanical problem for the hidden units with an energy $E_{\mathbf{s}}[\boldsymbol{\sigma}] = -\log P[\mathbf{s}, \boldsymbol{\sigma}]$ and partition function $P[\mathbf{s}] = \sum_{\boldsymbol{\sigma}} P[\mathbf{s}, \boldsymbol{\sigma}]$. If there are no hidden-to-hidden connections, $P[\mathbf{s}, \boldsymbol{\sigma}]$ factorizes into a product of independent factors for each time step in the data. In this case, the statistical-mechanical problem to be solved for each time step has N_h variables. In the general case, $P[\mathbf{s}, \boldsymbol{\sigma}]$ does not factor, and the problem to be solved has $N_h T$ variables $\sigma_i(t)$, where T is the number of time steps in the data. The energy $E_{\mathbf{s}}[\boldsymbol{\sigma}]$ contains terms describing "external fields" acting on each $\sigma_i(t)$ from the visible data $s_j(t \pm 1)$ at both the previous and subsequent time steps, terms which couple each $\sigma_i(t)$ with all $\sigma_j(t \pm 1)$, and nonlinear couplings among the different σ_i at each t. With knowledge of the normalizing denominator $P[\mathbf{s}]$ (the partition function of this auxiliary statistical mechanical problem), the averages in (2) can be evaluated. This constitutes the exact algorithm for finding the couplings J_{ij}. The evaluation can be done exactly for small N_h and T; for large systems and/or data records one can resort to Monte Carlo simulations.

One can develop a mean field theory for this problem, valid for large, densely connected networks, based on a free energy $F_{\mathbf{s}}[\mathbf{m}]$ which is a function of "magnetizations" $m_i = \langle \sigma_i \rangle$. It has the form

$F_\mathbf{s}[\mathbf{m}] = E_\mathbf{s}[\mathbf{m}] - S[\mathbf{m}]$, where $S[\mathbf{m}]$ is a sum of single-unit entropies $-((1+m_a)/2)\log((1+m_a)/2) - ((1-m_a)/2)\log((1-m_a)/2)$ for units with constrained magnetization m_a. Minimizing $F_\mathbf{s}[\mathbf{m}]$ leads to coupled mean-field equations

$$\begin{aligned}\tanh^{-1} m_a(t) &= \sum_j J_{aj} s_j(t-1) + \sum_b J_{ab} m_b(t-1) \\ &+ \sum_j [s_j(t+1) - \tanh H_j(t)] J_{ja} + \sum_b [m_b(t+1) - \tanh H_b(t)] J_{ba} \end{aligned} \tag{3}$$

(where now $\sigma_b(t)$ is replaced by $m_b(t)$ in the expression for $H_i(t)$ in (1)) for the $m_a(t)$. There are many ($N_h T$) of these equations, but they can be solved much more quickly than running Monte Carlo simulations for $N_h T$ units. They have a simple interpretation: The first line is just the input to unit a from the visible and hidden units, respectively, at the preceding time step. The second line had the form of back-propagated errors from visible and hidden units at the following time step. The combined effect of these influences determines the appropriate target on the hidden units to be used in the learning rule (2). This result is a generalization of an old formulation of back-propagation learning for conventional networks with a single hidden layer in terms of such "internal representations"[2].

Keywords: networks, inference, stochastic dynamics.

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Computational investigation of Glutamate-AMPA interaction in synaptic transmission

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The excitatory postsynaptic response, following presynaptic activity, is the mechanism that neurons use to transfer the information coded in the spike sequence of the presynaptic neuron to the postsynaptic one in the brain. Because of this key role all the elements present in the synaptic structure, which are thought to give a contribution in shaping the postsynaptic excitatory response, is object of very attentive experimental and computational investigation. In this framework, mathematical models and computer simulations are providing valuable information that could not be obtained experimentally due to technical limitations.

To clarify the mechanisms involved in stochastic variability of postsynaptic excitatory response, in previous papers we proposed a model of excitatory synapse based on a detailed geometrical description of the synaptic structure. The model was based on Brownian motion of Glutamate (GLUT) molecules in the synaptic cleft, described by Langevin Equations in a discretized form with a very fine time step ($40femtoseconds$) and on a detailed description of their binding to post-synaptic AMPA and NMDA receptors although only the AMPA response was simulated since,in normal conditions, NMDA are blocked by $Mg\hat{+}+$ ions [6, 7, 8, 9]. Herein, we present an update of the model based on new values of the model parameters obtained by more recent experimental findings [1, 2, 3, 4, 5]. In a recent report we studied the effect of AMPARs trafficking on the shape of the miniature Excitatory Post Synaptic Currents (mEPSCs) produced by AMPARs activation demonstrating the possibility to define an inferior limit for the binding probability between the molecules of GLUT and receptor binding site[9].

In the present work, we present a series of computational experiments intended to study the effect of the the position of the binging site by using a better description of the 3D structure and dimension of the AMPA receptors and by considering that they are elements protruding from the PSD [5]. The presence of filaments in the synaptic cleft, connecting the pre and postsynaptic cells and located around the PSD area, is also considered. Moreover, the decreasing of the Excitatory Post Synaptic response with the increasing of the eccentricity of the position of the releasing vesicle with respect to the center of the Active Zone (AZ), is studied by the space distribution of number of collisions of GLUT molecules on receptor binding sites. At last, the dynamics of the binding process has been studied by means of the description of the inter-collision times among single Glut molecules and the binding sites of the several AMPA receptors which they *visit* without success until till the final binding occurs (see Figure 1).

Keywords: Glutamate Synaptic Response; Synaptic Parameters; Computer Simulation

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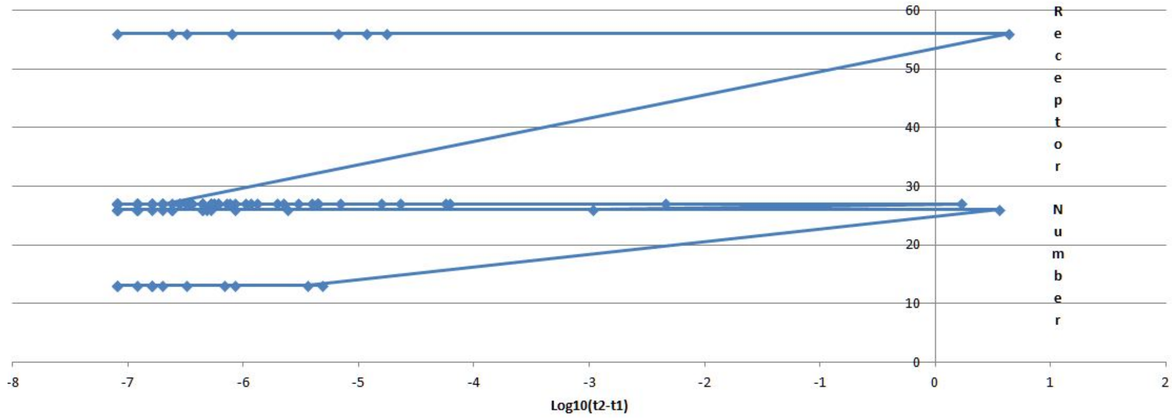

Figure 1: Sequence of time intervals between successive impacts of a GLUT molecule on the binding sites of AMPA receptors, which terminate with a successful binding. Four different receptor sites were visited. First impact occurred after 190.349398720μs on receptor 13. After it passed through receptors 26 and 27 before binding on receptor 56 at time=199.963628560μs. Main simulation parameters: Releasing position on AZ, $x0 = 90nm$; Released Molecules=775; Binding Probability=0.0136; AMPARs Number=55; NMDARs Number=13. The horizontal axis shows the values of the decimal logarithm of the time differences between two successive impacts.

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Efficient coding beyond the retina

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The principle of efficient coding [1] is that sensory systems take advantage of the statistical regularities of the natural environment to focus their limited resources on aspects of stimuli that are unpredictable. This is a powerful framework for understanding retinal design principles. Whether it is also applicable to cortical visual processing is less clear, as there is no "bottleneck" comparable to the optic nerve, and much redundancy has already been removed by the retina. Here, we present 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. This convergence motivates a more detailed psychophysical study of sensitivity to image statistics, which in turn suggests a hypothesis about natural image statistics.

The starting point is a recent analysis of high-order correlations in natural images [2]. This study showed that for natural images, high-order correlations in certain specific spatial configurations are informative, while high-order correlations in other spatial configurations are not, as they can be accurately guessed from lower-order ones. To determine the relevance of this dichotomy for visual processing, we construct artificial images (visual textures) composed either of informative or uninformative correlations. We find that the informative correlations are visually salient, while the uninformative correlations are nearly indistinguishable from random.

To understand the physiological origin of these perceptual signals, we recorded from single neurons in the visual cortex (V1 and V2) of the macaque. Overall, we found that neuronal responses mirror the psychophysical findings: many neurons respond differentially to the informative statistics; few respond to the uninformative ones. Laminar analysis showed that the differential responses to high-order correlations first become prominent in the supragranular layers of V1. The sensitivity to high-order statistics increases further in V2, and exceeds 80 % in its supra- and infragranular layers. These findings indicate that selective sensitivity to high-order correlations arises as the result of intracortical processing in V1, and is further enhanced in V2.

Motivated by these findings, we undertook a further analysis of human sensitivity to local image statistics of low and high order [3]. We focused on image statistics that characterize 2x2 neighborhoods in binary images; this is a 10-dimensional space. We find that human visual sensitivity to these image statistics is highly selective, and that interactions between image statistics are well-described by an ellipsoidal isodiscrimination surface. The shape and slant of this ellipsoid is consistent across observers. We hypothesize that the directions of peak sensitivity – which are not the mathematically "natural" directions – correspond to the statistics that are most informative about natural images.

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Event-related potentials associated to decision-making in emotionally-primed Ultimatum Game

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Decision-making is considered the most essential phase in volitional act. This is supposed to occur in the temporal window that follows sensory processes and before the motor response confirming that a decision was made. Let us consider a scenario where one party, the "proposer", offers how to split a finite resource (e.g., a sum of money). If the other party, the "responder", accepts the deal, the resource is distributed according to the proposal, and if he rejects, both parties get nothing. This kind of situation is similar to an iterative implementation of the the Ultimatum Game (UG) [1], which is originally a one-shot bargaining game with no communication and no negotiation. Continuous EEG was recorded using 60 scalp Ag/AgCl active electrodes mounted on a headcap and referenced to the linked earlobes. Event-related potentials (ERPs) from scalp electrodes were recorded during the whole decision-making process. We observed two distinct components at most electrode sites during both conditions of UG. The first component is an early positive wave with a peak latency of about 200 *ms*, identified as 'P200'. The second component is a negative wave peaking at about 350 *ms*, identified as Feedback-Related Negarivity, 'FRN'. P200 was peaking with the same latency for proposer and responder decision-making. In the responder condition we observed an additional positive component, occurring after P200, visible along all midline sites, but with amplitude larger at frontal site (FCz). The latency of FRN was bigger in proposer *vs.* responder condition at all sites, but in responder condition the amplitude of the wave was similar at all frontal sites. In the proposer condition at right frontal sites (F2 and F4) the amplitude of this wave was smaller than at left frontal sites (F1 and F3). These results suggest different coding of decision-making for proposers and responders and extend previous results [2]. In UG the proposer has to store a specific value in the in short-term memory buffer and, then, engage retrieval processes to enable his offer after the instruction.

Keywords: P200, Feedback-Related Negativity, Lateralization.

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Synthetic and elemental coding of the pineapple “accord” and its components

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A fascinating property of the sense of smell is that odor mixtures often have distinctive emergent qualities, and their individual components are consequently difficult to identify. Here, we make the hypothesis that the emergence of a new quality of an odor mixture is initiated from the peripheral olfactory mucosa. In order to test our hypothesis, “the blending mixture perception” was studied in the Rat at the peripheral and behavioral level.

To this aim, single olfactory receptor neurons (ORN) responses were electrophsiologically recorded in response to (1) the binary ethyl maltol (Emalt) + ethyl isobutyrate (Eiso) mixture from which emerge the pineapple fragrance and (2) each of the molecules. Amplitude of the ORNs responses was plotted as a function of concentrations and the curve obtained for the mixture showed a clear dominance of Eiso or a suppressive or a amplifying effect of Emaltol regarding the response to Eiso when used alone; these 3 effects being equally observed. For the behavioral study, animals were submitted to a conditioned odor aversion (COA) paradigm consisting of the association between Emalt or Eiso (conditioned stimuli) and the administration of a gastric malaise (0.15M Lithium chloride *i.p.* injection). The conditioned aversion to Emalt or Eiso was assessed by presenting successive discriminative two-bottle tests during which the animals had to choose between the conditioned odor versus the mixture Emalt+Eiso.

The results showed that animals conditioned to Eiso showed a clear aversion to the mixture suggesting an elemental strategy that corresponds to the detection of one component of a mixture in order to avoid it. By contrast the animals conditioned to Emalt failed to develop a clear aversion to Emalt thus rendering the absence of conditioned Emalt+Eiso aversion difficult to interpret. Our results obtained at the cellular level showed that the pineapple “accord” induced a remarkable ratio of synergy which may sign an “accord” specificity.

At the behavioral level, our data suggest that animals developed an elemental strategy coding thus rendering possible the detection of the Eiso in the pineapple “accord”. The status of Emalt needs to be précised using other types of conditioning which will use rather reinforcement. As a conclusion even in “accord” the different components can present different status regarding discriminative processes.

Keywords: Odor coding, odor mixture, conditioned odor aversion, behavior

Representational capacity of neural codes in the cortex

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The coding of sensory stimuli in the neural response is a fundamental property of neural systems that impacts many of its properties. The coding scheme also determines how many different stimuli a population of neurons can represent. Although the coding of single stimuli has been studied extensively, coding of multiple stimuli has been studied far less. Here we study the representational capacity in the visual system when stimulus pairs are represented simultaneously. We assume that the response to the individual stimuli is given, and that the neurons interacts non-linearly to form the response to the pair. Using a Bayesian read-out we find that using a linear sum leads to a smaller capacity, than a maximum-like interaction. Thus non-linear interaction improve coding capacity. The results provide a novel interpretation for the non-linear interaction observed experimentally.

Dynamics of axon fasciculation and its consequences for ephaptic coupling

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During neural development, the growing axons frequently fasciculate, i.e. form bundles of parallel axons. In the basic process leading to fasciculation, an advancing growth cone encounters the shaft of another axon, attaches to it and follows it. Fasciculation is crucial for setting up correct connectivity in various parts of the nervous system.

In addition to its role in guiding axon growth, fasciculation also influences neural activity. In tightly packed bundles, the electric field arising from an action potential traveling in one of the axons significantly affects the transmembrane voltage in the other axons. Such ephaptic coupling has been experimentally shown to result in synchronized propagation of spikes within the bundle and in changes in conduction velocity in the individual axons. It has been predicted that ephaptic coupling may also trigger action potentials in inactive axons, leading to spreading of electric activity across the bundle.

Our study is motivated by the biology of the mammalian olfactory system, in which axon fasciculation plays an essential role. The nasal epithelium contains about 10^6 olfactory sensory neurons, which belong to approximately 1000 distinct types. The axons progressively fasciculate in the olfactory nerve and on the surface of the olfactory bulb; axons of each type type finally converge into a specific glomerulus in the bulb. Type-specific axon-axon interactions are presumed to play a key role in the fasciculation process. The axonal type is defined by which odorant receptor protein is expressed in the neuron. It has been shown, however, that the expression of specific types of cell adhesion molecules is strongly correlated with this axonal type.

We have developed a mathematical model of fasciculation in a population of growing axons with adhesive interactions. The axons are represented as directed random walks in two spatial dimensions; each random walker (growth cone) interacts with the trails (axon shafts) of other random walkers. In the simplest version of the model [1], all axons belong to the same type and have strong adhesive interactions, so each newly growing axon encountering an existing fascicle will join the fascicle and never detach. We introduce a turnover of axons (corresponding to adult neurogenesis in the olfactory epithelium) and study the resulting slow dynamics of axon fascicles. In the general version of the model [2], we introduce axons of multiple types, with type-specific interactions and the possibility of detachment of axons from fascicles. The resulting dynamics leads to fasciculation patterns for which we compute quantities such as the distribution of fascicle sizes, the increase of mean fascicle size in the direction of growth, and the purity of fascicles according to axon type.

There are indirect experimental indications [3] that ephaptic coupling between axons of olfactory sensory neurons leads to significant modifications of their electric activity. Ephaptic coupling in fascicles of these axons has been analyzed computationally by Bokil et al. [4], who predicted that additional action potentials are triggered especially within fascicles of small and intermediate size. The overall effect of ephaptic coupling in this system is therefore expected to depend sensitively on the detailed pattern of axon fasciculation.

We use the axon configurations generated by our fasciculation model to evaluate the effects of ephaptic coupling in a population of fasciculating axons. Based on the analysis of Bokil et al. [4], we trigger additional action potentials when the ratio of the number of active axons to the the total

number of axons in a given fascicle exceeds a critical value. We discuss the parameter ranges in which ephaptic coupling leads to a nontrivial spreading of the sensory electric activity. For configurations with 2 types of axons (carrying distinct sensory information), we evaluate the degree of cross-activation between the two axon types; such cross-talk is expected to be detrimental to efficient neural processing in the olfactory bulb.

Keywords: axon guidance, random walk, ephaptic coupling

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