Decoding of complex movies from a large retinal population

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Decoding of complex stimuli from the retinal activity remains an open challenge. To date, experiments have focused on decoding either a small number of discrete stimuli (e.g., decoding among several possible orientations of a drifting grating), or very low dimensional dynamical traces (e.g., of luminance in a full field flicker experiment). Here we stimulated a rat retina with a new class of synthetic stimuli, in which between 2 and 10 dark circular spots executed random dynamical motion on a square domain with no other constraints except for hard-core repulsion between the spots and reflection from the domain boundaries. The radius of the spots was $\sim 100\mu$m on the retina, somewhat smaller than the typical center of the ganglion cell receptive fields; to achieve good performance, the decoder would thus need to make use of the population code. We constructed separate decoders densely tiling all spatial locations in the stimulus. We then reconstructed the entire movie by decoding separately these local luminance traces from the spiking activity of ~ 100 neurons simultaneously recorded from a dense retinal patch. As a baseline, we trained linear decoders, whose performance was impacted by the substantial amounts of spontaneous activity in the rat retina. To mitigate this problem, we constructed nonlinear extensions to these decoders, which reached cross-validated correlation of $> 80\%$ in locations with good spatial coverage in the recorded population. This is achievable using biologically realistic sparse decoding kernels for each location; the resulting "decoding fields" of retinal ganglion cells are sharply localized, exhibit fine structure on a $\sim 50\mu$m scale, are collocated with the corresponding receptive field centers, and generalize across stimuli with different numbers of randomly moving spots. Decoding paradigms with rich dynamical stimuli can thus complement encoding studies to provide novel and practical insights into the organization of the neural code.

Additional detail

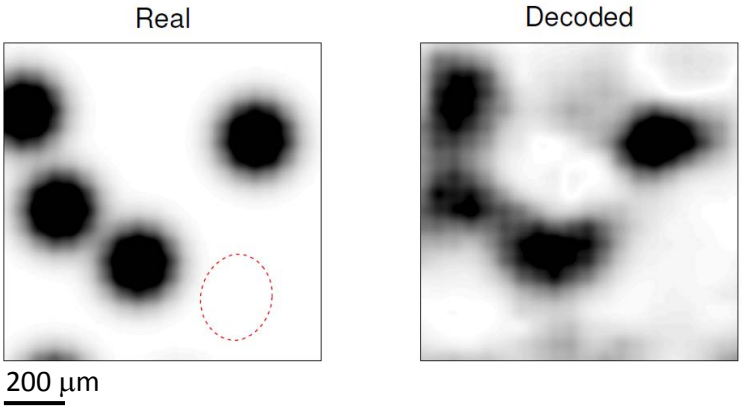

Figure 1: A zoom-in of the real (left) and reconstructed (right) single frame of the stimulus movie. Four randomly moving spots present in the stimulus are clearly distinguishable in the reconstructed frame. For reference, the average 1-std center contour of the ganglion cell receptive field is shown in the left panel (dashed line).

Studying the role of STN-DBS on Impulsivity using a spiking neuron network model of Basal Ganglia

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Abstract: Deep Brain Stimulation (DBS) of the excitatory basal ganglia nucleus, Sub Thalamic Nucleus (STN) is becoming the gold standard for the treatment of motor symptoms in advanced Parkinson's disease (PD). The effect of STN-DBS on cognition was found to be adverse and debatable with *Impulsivity* and premature responding being observed as the most common side effect. Iowa Gambling Task (IGT) captures one of the impulsivity features (premeditation) and resembles real life decision making scenario. Also, various experimental studies have reported controversial results on the performance (IGT score) of STN-DBS patients. So we built a 2D spiking network of basal ganglia (BG) to study the cognitive aspects of PD during medication and DBS while performing IGT. Key BG nuclei such as the Globus Pallidus externus (GPe) and Globus Pallidus internus (GPi) and STN were modeled as Izhikevich spiking neurons whereas the striatal output was modeled as Poisson train. The model was cast in reinforcement learning framework with the dopamine signal as reward prediction error. The model was tested on 3 conditions i.e., healthy controls, PD 'ON' and STN-DBS. We studied the effect of DBS on decision making (in terms of IGT score) by changing the electrode position (in STN) in the model. Our results show that changing the electrode's position and current spread independently leads to a critical change in performance levels. These results suggest that electrode position or current spread might be the probable reason for the observed controversial outcomes in STN-DBS patients. The model also shows that simulated PD 'ON' medication performed poorly compared to healthy controls as observed in experiments. This is one of the first models to use spiking neurons to test the effects of dopamine medications and STN DBS on complex decision making.

Keywords—Deep Brain Stimulation, Electrode, Iowa Gambling Task, Sub-Thalamic Nucleus.

Input to the brain during active sensation cannot be predicted from passive stimulation: Study of whisker system of awake, behaving mice

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Sensation is active. Animals gain information about their environment by active control of their sense organs. The aim of this study was to address a fundamental question in sensory neuroscience - what input do the sense organs provide to the brain during active natural behaviour?

To this end, we recorded extracellularly the activity of well-isolated, single whisker primary somatosensory neurons (PSNs) from awake, head-fixed mice as they explored an object with their whiskers. Simultaneously, we measured whisker movements and shape using high speed videography (1000 frames/s, total 1.5M frames). We extracted key sensory parameters (whisker angle, whisker curvature, whisker-object contact) using a semi-automatic, custom tracking algorithm.

We found that 90% of units responded to touch and/or to whisking. To determine the sensory parameters that drive the PSN response, we used a Generalised Linear Model (GLM) approach. We fitted GLMs to each unit and tested how accurately the response was predicted based on a variety of sensory inputs. Strikingly, we found that neural responses were often accurately described by a simple GLM , the key input to which was a rotational force (bending moment) on the whisker follicle (correlation coefficient between recorded and predicted response up to 0.91). Conversely, whisker angle was a poor predictor. This unexpected result is in contrast to previous descriptions of angle-encoding derived from passive stimulation in anaesthetised rodents. However, we were able to reconcile these observations by taking into account correlations between bending moment and whisker angle.

In conclusion, we have determined, in awake behaving animals, sensory features that play a major role in driving the activity of whisker primary somatosensory neurons. These features are different to those previously derived from work in the anaesthetised animals and thereby shed substantial new light on the nature of active sensation.

Title: Convergence of sleep and wake population activity distributions in prefrontal cortex over learning

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Summary The inference-by-sampling hypothesis proposes that neural population activity at each point in time represents a sample from an underlying probability distribution. One key prediction is that the distribution during "spontaneous" activity (representing the prior) and during evoked activity (representing the posterior) converge over repeated experience. Just such a convergence has been observed in small populations from ferret V1 over development. Unknown is the extent to which this hypothesis is a general computational principle for cortex: whether it can be observed during learning, or in higher-order cortices, or during ongoing behaviour.

We addressed these questions by analysing population activity from the prefrontal cortex of rats, learning rules in a Y-maze task. We focussed on sessions where the animal reached the learning criterion mid-session, allowing us to compare activity before and after learning. Our hypothesis was that the spontaneous activity in slow-wave sleep (SWS), in the absence of task-related stimuli and behaviour, constitutes the prior distribution.

We find that the distributions were conserved across all epochs (SWS pre- and post-session and during task behaviour), in that the same population states appeared in each, consistent with our interpretation of SWS activity as a prior. Crucially, we find that the task-evoked distribution after learning was more similar to the distribution in post-session than in pre-session SWS epochs, consistent with convergence of the posterior and prior distributions over learning. We also find that the similarity between behaviour and post-session SWS distributions was larger for rewarded trials, but did not converge for pre-learning unrewarded trials, suggesting the distributions were directly updated by learning. Our results are thus evidence that inference-by-sampling can be observed over the course of learning, and is a potential general computational principle of cortex.

Cellular mechanisms underlying behavioural state-dependent bidirectional modulation of motor cortex output

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Neuronal activity in primary motor cortex (M1) correlates with changes in behavioural state. However, the cellular mechanisms underpinning behavioural state-dependent changes in M1 output remain largely unresolved. Here we combined *in vivo* patch-clamp recordings, selective pharmacology, projection target mapping and computational modelling to investigate the membrane potential (V_m) dynamics of identified M1 layer 5B (L5B) pyramidal neurons in head-restrained mice during quiet wakefulness and self-paced, voluntary movement.

We show that changing behavioural state – from quiet wakefulness to movement – bidirectionally modulates (i.e. enhances or suppresses) M1 output via two opposing subthreshold mechanisms: 1) a global decrease in network-driven, slow large-amplitude V_m fluctuations, which reduced V_m variability, input sensitivity and firing rates in $L5B_{suppressed}$ neurons (quiet wakefulness: 6.3±3.9 Hz, movement: 2.8±2.5 Hz, $p<0.001$, n=17); and 2) a coincident increase in excitatory drive to a subpopulation of L5B neurons ($L5B_{enhanced}$) that depolarised mean V_m, increased input sensitivity and elevated firing rates (quiet: 5.7±3.8 Hz, movement: 12.9±7.4 Hz, $p<0.001$, n=24). The functional classification of L5B pyramidal neurons was not dependent on projection-class identity (pyramidal tract vs. intratelencephalic neurons), suggesting a fundamental organizing principle that transcends projection-type identity.

We next sought to identify the source of the increased excitatory input to $L5B_{enhanced}$ neurons during movement. We found that the movement-related tonic depolarization in $L5B_{enhanced}$ neurons was dependent on the interplay between ascending input from motor thalamus – which maintained V_m near to threshold – and noradrenergic input from the locus coeruleus. The behavioural state-dependent release of noradrenaline mediated a tonic depolarisation in V_m and selectively enhanced the signal-to-baseline ratio for information transmission in $L5B_{enhanced}$ neurons (SBR control: 1.1±0.2, SBR following noradrenergic receptor block: 0.3±0.2, p=0.006, n=6). Together, our findings provide a mechanism for how noradrenergic neuromodulation and network-driven input changes bidirectionally modulate M1 output during self-paced, voluntary movement.

Coarse grained analysis of patterned activity in a minimal neural network

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At the single cell level, neurons typically exhibit an all-or-nothing response, dependent on the summation of input currents they receive from the rest of the network. Due to far reaching processes, neurons can form connections with distant parts of the network, allowing for rapid communication across long distances.

Certain neural systems show computation through patterned activity; persistent localised activity, in the form of *bumps* has been linked to working memory, whilst the propagation of activity in the form of waves has been associated with binocular rivalry tasks. The assumption of infinitely fast synapses allows for the replacement of firing patterns with firing rates, resulting in a neural field model that is amenable to perturbative analysis. This description of the network averages out fluctuations in both space and time ignoring these small scale effects. Our aim is to perform analysis on a network that retains these small scale effects, but whose large scale effects can be predicted in an analogous way to neural field models.

We present analysis of a network of minimal three-state neurons whose transitions are probabilistic. By taking appropriate limits, we demonstrate the existence and compute stability of spatiotemporally patterned activity across the network. We then go on to show how coarse-grained analysis can be used to construct bifurcation diagrams for the network when these limits are relaxed and show how these can be used to reduce the complexity of the dynamics.

Ih current components functional significance highlighted by a new context utilization of the full trace method

Christophe B. Michel, Gilles Desmadryl, and Bruce P. Graham

A computational study of neuronal activity requires good identification of the ionic conductance parameters that shape the electrical excitability of the cellular membrane. Ideally, the conductances are pharmacologically isolated in order to identify their individual magnitude and time constant parameters. Unfortunately, in some cases, pharmacological tools do not exist and the biological discrimination of the effects of different conductances is impossible. This is the case, in particular, for the hyperpolarization activated cation current (Ih), known to be the resultant of fast and slow components [1][2] but without any information about their respective voltage dependent activation.

The aim of this study is, first, to test the ability of a known parameter identification algorithm, the full trace method, initially proposed for sodium current parameter identification [3], in extracting correct parameter values in the new context of two ionic conductance components and, second, by applying the algorithm on vestibular ganglion Ih current recordings, to highlight individually the role of both components, testing the identified Ih conductance models in a spiking neuron model.

In summary, we shown the full trace method is able to discriminate two populations of ionic currents much more accurately than a more classical method. This algorithm permitted the parameter identification of the mouse vestibular Ih current fast and slow components. We added the identified current models to a Hodgkin-Huxley type auditory neuron model [4], this showed first, the fast component induces the firing of only one rebound action potential after inhibitory stimulation whatever its duration or amplitude; second, the slow component induces firing of a number of rebound action potentials correlated to both stimulation duration or amplitude in control conditions and specializes to the stimulation amplitude in the presence of cAMP, an intracellular cyclic nucleotide that modulates Ih channel activity in the auditory pathway [2].

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Metabolic cost of action potentials in MNTB neurons is altered by activity-dependent NO modulation

Christophe B. Michel and Bruce P. Graham

The nervous system consumes a substantial proportion of the energy produced by the full body (Harris et al., 2012). Much of this energy consumption results from Na+ entering a neuron to produce action potentials (AP), which then needs to be pumped out again by the Na/K-ATPase, consuming ATP.

In parallel to metabolic requirements, a lot of control mechanisms act to tune ion channel activity to neuronal function. In particular, nitric oxide (NO) modulates target neuron excitability (Na+ channels) and switches the AP repolarization from Kv3 to Kv2 potassium channels (Steinert et al., 2011). This change also increases the neuronal maximal frequency firing in MNTB neurons in the auditory brainstem.

The aim of this work to is increase our understanding of the relationship between neuromodulation and the metabolic cost of neural activity. We have built a computational model of MNTB auditory brainstem neurons, taking account of their modulation by NO, and describing the glycolysis and mitochondrial activity in response to ATP demands from the Na/K-ATPase following an AP (Cloutier and Wellstead, 2010). Model outputs are compared between (1) the baseline (control) condition, (2) following increased NO levels, and (3) in other hypothetical conditions that allow examination of the contribution of particular ion channel types.

NO modulation reduces postsynaptic AP failures during high frequency stimulation, by potentiation of the Kv2 channels (Steinert et al., 2011). Our results show this is metabolically costly, but also that the parallel down-regulation of Na channels decreases the global metabolic cost. In addition, the model demonstrates that reduction of all ion channel densities can increase metabolic efficiency while still allowing AP generation.

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A whisker-based sequence discrimination task

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Making sense of the world requires integration of sensory patterns and sequences over time. For example, recognising a song or deciphering speech requires the identification and classification of a stream of vibrations. Interestingly, humans automatically learn unpredictable noise patterns even when not explicitly asked (Agus et al., 2010). Despite the central importance of sequence selectivity to sensory function, little is known about its substrates in the brain. To investigate, we developed a whisker-based sensory discrimination task in a go/no-go paradigm. First, we trained head-fixed mice to detect an 800 ms pseudo-random white noise sequence delivered to a single (C2) whisker. This sequence was composed of 8 x 100 ms 'syllables' of different amplitudes. Upon learning, a simple square wave vibration was added to serve as a no-go sequence. The no-go sequence was made progressively more complex until it became identical to the go stimulus apart from that the order of the syllables was scrambled. Mice were able to discriminate the two sequences with a success rate of 70%. We are currently performing an electrophysiological characterisation of S1 to locate the site and the potential cortical computations involved in sequence recognition.

Title: “The interplay of working memory and subcortical background oscillations”

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Abstract:

Working memory is responsible for the temporary manipulation and storage of information to support reasoning, learning and comprehension. During working memory tasks, modulation of different frequency band oscillations has been observed; however, a full explanation of this phenomenon is still needed. Background oscillations coming from subcortical structures drive a gating-like mechanism for working memory computations or states. It is also known that different frequency bands are associated with different computations carried out by working memory. Three well-known examples of this are: the storage of new information correlates positively with oscillations in the beta–gamma band, theta-band oscillations are directly linked to maintanance of information while ignoring irrelevant stimulations, and clearance of memory is associated with alpha-band oscillations. We propose a computational framework for the cerebral cortex that connects individual oscillatory bands to different working memory processes. The analysis is applied to cortex pyramidal neurons. By using point-neuron models, we investigate how different frequency bands act like a gate mechanism and how this mechanism enables different working memory computations to take place. For the simulations, we consider a population of both excitatory and inhibitory neurons. In order to have more realistic results, synaptic plasticity is also included. The effect of background oscillations is tested by delayed matching to sample task (DMS). DMS is a cognitive task which is mostly used in short-term memory studies to test loading, maintanance and clearance properties of the system. We show that flexible control of subcortical oscillations can drive working memory into different computations, and different responses will be obtained for different oscillation frequencies.

The carrot or the stick: opposite effects of rewards and punishments on human vigour

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Rewards and punishments play a major role in human motivation, decisions and learning. While the effects on decision making and learning have been well studied, motivation has been more elusive. A normative theoretical account based on reinforcement learning (Niv et al. 2005) has suggested that the rate of expected rewards should modulate movement vigour. As more rewards are available in the environment subjects should increase their movement vigour, an idea confirmed by experimental testing (Guitart-Masip et al. 2011). It was furthermore hypothesised that this modulation could be encoded through tonic dopamine levels in the basal ganglia, as supported by a recent finding that administering L-Dopa to subjects caused a specific increase in the effect of the reward rate on subjects' movement vigour (Beierholm et al. 2013).

Punishment in contrast has been hypothesised to have an opposite effect; larger rates of punishment should cause a subject to slow down to postpone future punishments (Cools et al. 2011), a modulation possibly encoded by tonic serotonin.

We presented subjects with an initial monetary endowment (£10) and instructed them to act fast in a perceptual odd-one-out task in order to avoid losing part of their endowment. The rate of potential punishment for slow responding fluctuated over time, creating a variable rate of punishment. Reaction times, the inverse of the effective vigour, were explained through a linear model that took account of several regressors including Potential Punishments, Rate of Punishment, Inter Trial Intervals etc.

We found that subject response times were modulated by the rate of punishment so that larger rates of punishment caused subjects to slow down, exactly opposite of the finding for providing rewards on the same task. These finding are in accordance with model predictions and provide further support for the idea of movement vigour being regulated through normative mechanisms.

Reliable and flexible receptive field development through unified pre- and postsynaptic STDP

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Abstract

While the expression locus of long-term synaptic plasticity has been debated for decades, there is increasing evidence that it is both pre- and postsynaptically expressed (Padamsey and Emptage, Philos Trans R Soc 2014). However, the functional role of this segregation remains poorly studied, and most plasticity models do not incorporate presynaptic expression. We introduce a novel phenomenological model of spike-timing-dependent plasticity (STDP) that unifies pre- and postsynaptic components. Our unified model captures the presynaptic aspects of STDP and the co-modification of short and long-term synaptic plasticity, consistent with a wide range of experimental results from rat visual cortex (Sjöström et al., Neuron 2001 and 2003). Functionally, this unified STDP rule develops receptive fields with improved reliability, as has been observed in rat auditory cortex *in-vivo* (Froemke et al., Nat Neuro 2013). In addition, this unified model enables fast relearning of previously stored information, in keeping with the memory savings theory (Ebbinghaus, Leipzig: Duncker & Humblot 1885), which refers to rapid relearning through hidden storage of forgotten but previously acquired memories, and suggests an explanation for visual cortex *in-vivo* structural plasticity results (Hofer et al., Nature 2008). Thus our work shows that unified pre- and postsynaptic STDP leads both to improved discriminability and more flexible learning.

Mind the Gap: A specific central auditory deficit in a mouse model of developmental disorder

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High temporal acuity of auditory processing underlies perception of speech and other rapidly varying sounds. A common measure of auditory temporal acuity in humans is the threshold of detection of brief gaps in noise. Gap-detection deficits, observed in human developmental disorders such as auditory processing disorder and autism, as well as being a common consequence of aging, are considered evidence for "sluggish'' auditory processing. Here we show, in a mouse model of developmental disorder, that deficits in auditory brain sensitivity to brief gaps in noise do not imply a general loss of central auditory temporal acuity. Extracellular recordings from auditory thalamic neurons in two of the three central auditory pathways, exhibit reduced responses following brief gaps in noise in affected animals, but normal responses to other sound stimuli including other rapidly changing sounds. Through experiments and the creation of a simple phenomenological model of central auditory intensity processing, we demonstrate that these stimulus-specific deficits arise from reduced neural population activity following noise offsets, not onsets. Moreover, the model allowed us to correctly predict additional stimulus-specific deficits which were validated in further experiments. Thus, a combination of in-vivo experiments and computational modelling reveals that dissociable sound-onset-sensitive and sound-offset-sensitive channels underlie auditory temporal processing, and suggests that developmental disorders specifically affect the sound-offset-sensitive channel.

Comparing Firing Properties of Two Interconnected Circuits to Understand Information Processing at Afferent Pathways

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Abstract
Thalamocortical circuits have been known to receive excitatory input via dentate nucleus of deep cerebellar nuclei (DCN) which receives the output from cerebellar cortex. Sensory evoked stimulation of cortico-pontine nuclei pathway stimulate the cerebellar granular layer thereby increasing the firing frequency of Purkinje cells resulting in inhibition of DCN. We modelled thalamocortical and cerebellar neuron firing properties with simple spiking models (Izhikevich, 2003; Naud et al., 2008) to understand the suppression of information to motor cortex (M1) arising due to cerebellar role in suppression of information to DCN (Molnar et al., 2004). In this study, we could reproduce firing properties of thalamocorticalrelay (TCR), inhibitory interneurons and thalamic reticular nucleus (TRN) of thalamic module and pyramidal, basket, non-basket cell and spiny-stellate cell populations of cortical module representing each cortical layer (Bhattacharya et al., 2014). We also reproduced firing properties of granule, Golgi, Purkinje, inferior olivary and deep cerebellar neurons in cerebellar cortex (Medini et al., 2014). Firing frequencies of these neurons matched electroresponsivenes of experimental data. Temporal coupling properties of firing rate matched previous studies (Nakamura et al., 2014) for both cerebellar and thalamocortical circuits. In this initial study, we matched firing properties of cerebellar circuits (Medini et al., 2014) as well as thalamocortical circuits (Bhattacharya et al., 2014). Further elaboration will help understanding timing and information processing in cerebellar cortex and its integration with thalamocortical circuits.

Keywords

Computational Neuroscience, Information Processing, Thalamocortical circuits, Cerebellum.

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A realistic model of neural ensembles reveals a harmonic connectivity structure underlying pitch processing

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Abstract

Pitch is a fundamental attribute of auditory sensation underlying the perception of complex sounds. However, understanding the neurophysiological mechanisms of pitch cortical processing is a challenging task. In this study we propose a novel approach for explaining neurocomputational aspects of pitch processing by combining a biophysical model of the peripheral auditory system with an ensemble model using realistic neural and synaptic parameters; for the first time to our knowledge.

The model consists of three stages. First, the model of the auditory periphery transforms the input stimuli into temporal patterns of auditory nerve activity. Second, an autocorrelation process generates a spectro-temporal representation of the activity. These two stages had been widely used in the literature and are supported by perceptual and neurophysiological data localising such processes in sub-cortical areas.

In the third step, the pre-cortical model response is processed by an ensemble of cortical populations parametrised by a preferred frequency value. These ensembles effectively integrate the signal into a stable representation of the perceived pitch, in resemblance with similar studies in perceptual integration of visual stimuli. The population model stems from a mean field approximation of a network of spiking neurons, further simplified such that the population dynamics are dominated by NMDA receptors. This simplification yields to a network architecture with recurrent self-excitations and effective inhibitory currents between populations.

In the current study we found that the optimal connectivity between ensembles naturally encodes a harmonic structure which is critical for the successful processing of the missing fundamental pitch of complex tones. Remarkably, our pilot results show that the trends of the gating variables of the populations seem to reproduce the N100m morphology of auditory evoked fields measured using MEG recordings; which has been directly associated to the perceived pitch.

Learning continuous time representations of tasks

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Abstract Animals are able to recognize which events or stimuli are important for their survival and which are not: they learn to properly react to specific inputs, by selecting not only the right actions but also in the right order and time. Reinforcement Learning (RL) algorithms are commonly used as a learning paradigm to explain *how* animals are able to respond in complex environments. In RL, the agent changes its behavior according to experience collected during the exploration of the world: action sequences are learnt given event-based state-transitions related to both the *what* and *when* of an animals' changing world. Animals however are continuously sampling the environment and have to learn both *what* and *when* themselves. To determine the *when* is problematic in RL, in particular when modeling reaction-times: observations either have to be sampled often, corresponding to many state-transitions (which is hard to learn), or at a coarse temporal resolution, at the expense of accurate reaction times.

In this work, a continuous time version of a biologically plausible neural RL model – AuGMEnT – is combined with an appropriate Basal Ganglia model of action-selection, such that it can learn fast, real-time responses in complex delayed reward tasks. AuGMEnT uses selective attention and neuromodulatory signals to learn sensory representations, and can efficiently solve non-linear RL problems, including working memory tasks, in a SARSA RL learning scheme. Our main contribution is that we generalize this biologically realistic architecture into continuous time. The action-selection model controls action execution, by keeping a selected action active for a minimal amount of time. The resulting framework models *time* as an intrinsic property of RL tasks, mapping to well-studied phenomena as reaction-times and the neural activity time-courses. Thus, this plausible neural RL model can learn to account for both *what* need to be done and *when* to do.

Estimation of the Phase Response Curve from Parkinsonian Tremor

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Abstract

Phase response curves (PRC), characterising the response of an oscillator to weak external perturbation, have been estimated from a broad range of biological oscillators, including single neurons. PRC estimates in turn provide an intuitive insight into how oscillatory systems become entrained and how they can be desynchronised. To date, PRC estimates have be constrained to theoretical neuronal models and experimental preparations (eg. *in vitro* slice recordings) where cycle variability is minimal and not comparable to levels of noise observed in seen in EEG or LFP recordings in whole animals. We aimed to develop a method which could recover the “population” PRC from experimental data, in order to provide novel predictions about the mechanisms of physiological coherence between neuronal populations and potential insights into suppression of pathological oscillations.

In view of recent interest in developing adaptive closed looped forms of neurostimulation for movement disorders we decided explore the application of PRC theory to the case of Parkinsonian tremor. Initial attempts to establish a causal effect of subthreshold Transcranial Magnetic Stimulation (TMS) applied to primary motor cortex on the filtered tremor phase were unsuccessful. We explored the possible explanations of this and demonstrate that assumptions made when estimating the PRC in a traditional setting such as a single neuron are not arbitrary when applied to the case of tremor PRC estimation. We go on to extract the PRC of Parkinsonian tremor using an iterative method which requires varying the definition of the tremor cycle and estimating the PRC at multiple peristimulus time samples. Justification for this method is supported by estimates of PRC from simulated single neuron data. We provide an approach to estimating confidence limits for tremor PRC and discuss the interpretational caveats introduced by tremor harmonics and the intrinsic variability of the tremor’s period.

Remote Associations in Hebbian Cell Assemblies

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We present a neurocomputational model to explore the neural circuitry that underlies cognitive processing of associative relationships. The Remote Associates Test (RAT) is widely used in experimental psychology to assess verbal creative thinking [1]. The test taker is given a list of word triplets (the cues) and instructed to find a fourth word (the target) that links the triplet. An example of a RAT item is the word triplet “fish, mine, rush” with the target word “gold”. Cue words presented separately usually elicit associations with numerous words, but since their combination triggers a thought of a specific word, it is said that the target word is remotely associated. Several studies have addressed the cognitive search process in RAT ([2, 3]), but without references to possible neural mechanisms.

Here, we propose an attractor neural network based on neurons and Hebbian cell assemblies (CAs) to explain these mechanisms. The activities of neurons in assemblies encode representations of words and define the network states. Transitions among the states are possible through hetero-associative synaptic connections between CAs. To simulate the phenomena observed in the RAT task, we introduce a minimal set of computational mechanisms in the network: global inhibition [4] and inhibition of return [5], inspired by a computational model of visual attention. Global inhibition regulates the activity of background cell assemblies which are addressed by the associative connections when a cue is presented to the network. Inhibition of return enables switching between various states of the network, which in turn allows for competition among potential target words. We present simulations of the search process in a space of associated concepts and analyse the dynamics of the network, in order to determine the conditions that allow the existence of remote associates.

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We present a novel method for modelling neural populations using population density techniques (PDTs). The vast majority of PDTs have been applied to leaky-integrate-and-fire neurons in the diffusion limit, i.e. input spikes have only a small effect on the post synaptic membrane potential. These techniques are then equivalent to Fokker-Planck equations.

Our method is an advance in the following respects:

- It applies to any (1D) neural model, and may well be extensible to higher dimensions.
- It makes no assumptions on the size or distribution of the synaptic efficacies.
- It can model input spike trains using non Markovian stochastic processes using a memory kernel, i.e. it moves beyond the Poisson or white noise approximation that is implicit in most current formulations of the technique. We provide an example of the gamma distribution.

We will show examples of neural circuits modelled with this technique that demonstrate that the state of individual neurons and that of the population may be related in non obvious ways. Whilst individual neurons may spike quasi-periodically at relatively modest rates, the population can demonstrate bursting. Experimentalists would experience this as a contrast between single unit recordings and local field potential behaviour. We believe that neural mass models would have difficulty to account for this contradictory behaviour.

We would be very interested in applying this technique to experimental multi-electrode array recordings.

A maze navigation task population rate model

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Abstract

During the 1940s Tolman performed maze experiments to understand how animals remember certain places. He proposed that the animals discover relationships between places and events as they explore the environment and suggested that exploration leads gradually to the formation of a cognitive map that enables the creation of detours and shortcuts. Later, the discovery of place cells by O'Keefe, for which he won a Nobel Prize (2014), gave evidence that such map structure could be formed in the brain. Nevertheless the underlying mechanisms of how animals learn to reach a goal location are yet not fully understood.

We present a model that tries to replicate such experiments using temporal difference (TD) learning in an actor-critic framework as in [1], but using rate rather than spiking neural activity because it allows us to systematically explore the relationship between parameters and experimental data [2]. In this model an animal navigates through a maze looking for a hidden platform that triggers a reward delivery. During navigation the information about the environment is given via place cells. Such information does not directly tell the animal where it is or where to go; however, reward information directly available at the goal is used by TD learning to ascertain where the greatest expectation of reward should be, and the temporal gradient information is used to learn appropriate expectation everywhere else. Thus, place cells give information about the environment to critic and actor cells, the former learn to predict expected future rewards whereas the latter choose the direction of motion of the animal. The model uses the error between the actual and expected reward to teach the synapses feeding both groups.

So far, our rate model has similar results as [1] and is computationally much cheaper which allows us to validate experiments via collaboration with Tobias Bast, School of Psychology, University of Nottingham.

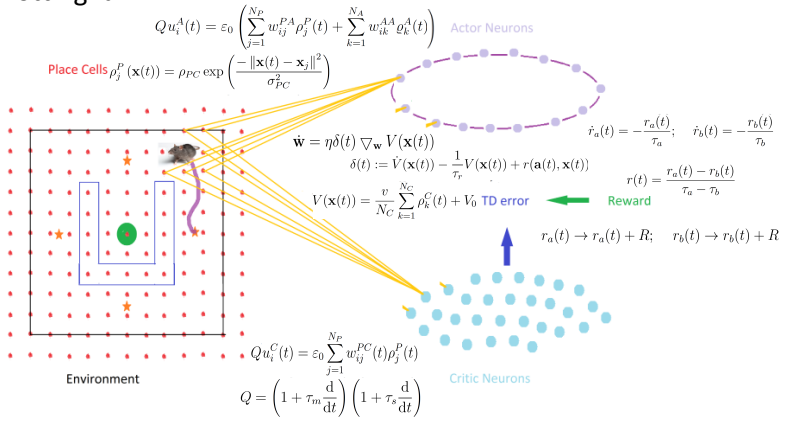

Figure 1. Model framework of the navigation task. Note the rate model for the actor (A) and critic (C) activity (u). During learning the synapses (w) are updated with the error (δ) between actual and expected reward. The value function (V) maximizes the cumulative future rewards (r).

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Action selection via partial synchronisation in a population model of the basal ganglia

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Action selection is one of the fundamental operations that a brain must perform. In the vertebrate brain there is evidence that a small, evolutionarily primitive, group of sub-cortical nuclei called the basal ganglia play a critical role in action selection [1]. Here we present a computational model for how mappings between actions and their associated movements may be learnt and stored, based on synchronisation between oscillatory neuronal populations and inspired by the hypothesised structure of the basal ganglia.

The model is organised in a hierarchical fashion. The lowest unit of consideration is a “micro-channel”, which comprises an excitatory and inhibitory pair of neuronal subpopulations (modelled according to the Wilson-Cowan equations). These subpopulations represent groups of neurons within the subthalamic nucleus (STN) and external globus pallidus (GPe) in the basal ganglia, respectively . A single micro-channel cannot generate oscillatory activity [2], but an inhibition-coupled pair of them can [3], with a frequency that depends on inhibition strength. We construct star-like networks of such pairs, and refer to each star as a “channel”, where the intrinsic frequencies of each pair vary smoothly across a channel. Synchronising the central element of each channel to a particular frequency, selects subsets of peripheral elements via partial synchronisation. We describe a mechanism by which associations between frequencies (actions) and micro-channel selections can be learned.

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An interface approach to planar neural fields: from spots to spirals

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Two dimensional neural field models with linear spike frequency adaptation ((1) and(2)) are known to support wide range of patterns of spatio temporal activity of the brain. These patterns include *spots*[3], associated with working memory, as well as more sophisticated self-sustained *spiral wave patterns* [2], usually linked to sleep-like states and pathological conditions such as hallucinations and epileptic seizures [1]. The model of integro-differential equations is

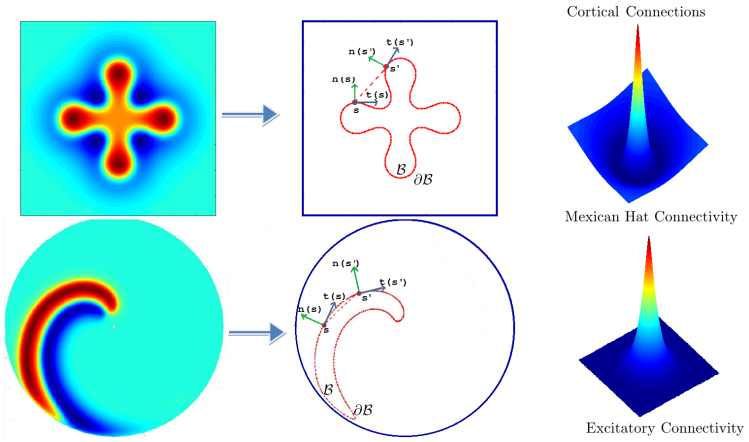
$$\frac{\partial u(\mathbf{x},t)}{\partial t} = -u(\mathbf{x},t) + \iint_{\mathcal{S}} w(|\mathbf{x}-\mathbf{x}'|) f(u(\mathbf{x}',t)-h) d\mathbf{x}' \; - a(\mathbf{x},t), \tag{1}$$

$$\tau \frac{\partial a(\mathbf{x},t)}{\partial t} = bu(\mathbf{x},t) - a(\mathbf{x},t), \tag{2}$$

where $\mathcal{S}$ is a disk of finite radius or a square domain. We are also concerned with similar neural field model to study the dynamics of *spiral wave* and *spot* solutions, despite for a Heaviside firing rate function.

The patterns in the integro-differential equation system are naturally defined by the interface between low and high states of neural activity, rather than the more computationally expensive space-time model. Dimensionally reduced system of equations can be derived using a recent *interface approach* [3], which leads a closed curve in two dimensional systems. Differentiating the level set $u(\mathbf{x},t) = h$ along the contour $\partial\mathcal{B}(t)$ allows us to obtain normal velocity, $c_n \equiv \mathbf{n} \cdot \dfrac{d\mathbf{r}}{dt} = \dfrac{\mathcal{F}(c_n)}{|\mathcal{F}(\mathbf{n})|}$, where $\mathbf{r}$ is a point on domain boundary. Using the Reynold's transport theorem, after dropping transients, we find the equation for interface dynamics in terms of line integrals:

$$\mathcal{F}(z(s,t) = \int_0^t dt' \, \eta(t') \oint_{\partial\Omega(t-t')} ds' \, w(|\mathbf{r}(s,t) - \mathbf{r}(s',t')|) z(s', t-t'). \tag{3}$$



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Slow irradiance increments scale activity and improve reliability across the early visual system

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Under natural viewing, the visual scene is characterised not only by local differences in luminance over space and time, but also by gradual, high amplitude, modulations in background light intensity (irradiance). Although humans perceive slow changes in irradiance, little is known about the neural circuits encoding and transmitting such information. We show here that slow irradiance ramps induce widespread increases in firing across neurones in the mouse visual thalamus (dLGN) and in the retina. This response originates with a particular retinal ganglion cell class (ipRGCs), but influences activity widely across the ganglion cell population. In both retina and dLGN, the additional spikes at high irradiance improve the reliability of responses to visual contrast (where present). In this way, graded increases in firing not only convey information about changing background light intensity but also represent a simple new mechanism for scaling resources available to vision and producing irradiance-dependent improvements in visual performance.

Travelling Wave and Bump Dynamics in a Spiking Neuronal Network

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As a result of modern imaging technologies, waves and bumps of neuronal activity have been experimentally verified at a variety of spatial scales in the cortex. Spatially localised bumps of activity are known to be involved in mechanisms of orientation tuning in the visual cortex, the rat head direction system, and working memory. In the turtle visual cortex, the presentation of stimuli has been shown to evoke propagating waves of activity. Also, mental processes including sleep and binocular rivalry are characterised through waves, as well as neurological disorders such as epilepsy and migraines.

In this poster we study existence and stability of coarse bumps and travelling waves in a bi-stable spiking neuronal network originally proposed by Laing and Chow [1]. The network consists of a set of N leaky Integrate-and-Fire neurons with a non-local lateral inhibition connectivity function,

$$\frac{dv_i(t)}{dt} = I - v_i(t) + \sum_{j,m} W_{ij}\alpha(t - t_j^m) - \sum_{i,m} \delta(t - t_i^m).$$

Direct numerical simulation show that the model displays a rich repertoire of emergent dynamics including: bumps, multi-bumps and travelling waves with variable number of threshold crossing. We make a continuum assumption and determine analytical solutions of waves in terms of firing times and wave speed, similarly to what was done by Osan et al [2]. The approach we use is semi-analytic, in the sense that we construct analytically well-posed boundary-value problems in the unknown firing times and speed, and then resort to numerical quadrature to compute integrals. We show that the analytical waves match the ones found in the discrete network, in the limit $N \to \infty$. We then study the bifurcation structure of such waves as the strength and timescale of post-synaptic input are varied simultaneously. Stability is analysed by perturbing firing times of the wave and deriving a corresponding Evans function. We provide numerical evidence that waves are robust under extrinsic noise in neuronal input and random neural connections.

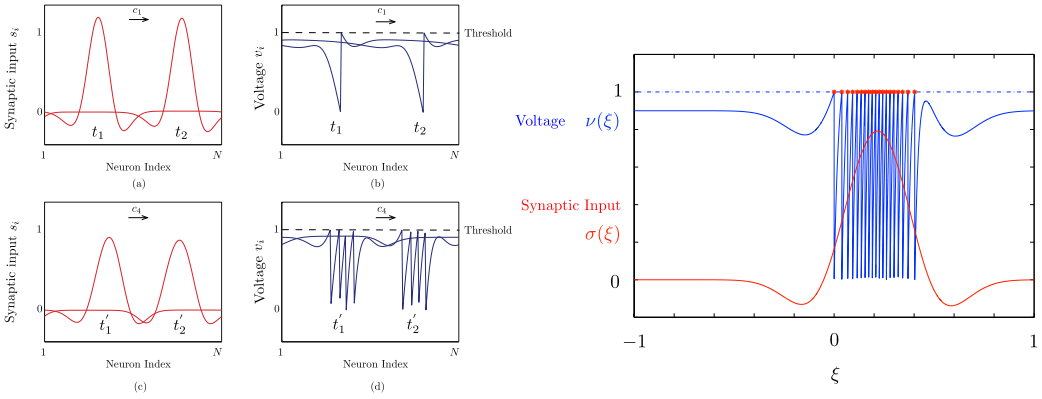

Figure 1: Left: Analytical solution of synaptic input and voltage profile for a single quad-spike pulse. Right: Solution for pulse with 20 threshold crossings in travelling wave co-ordinates. All waves can be fully depicted by wave speed c and a set of threshold crossing times $T_1, T_2, ..., T_M$

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Simulating the effect of parvalbumin expressing interneuron loss on LFP recorded *in vitro.*

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Parvalbumin-expressing, fast-spiking interneurons (PVINs) are a subset of GABAergic interneurons thought to provide the bulk of the inhibitory restraint in cortical circuits. They are particularly sensitive to injury and death caused by increased extracellular glutamate. Rat brain slices prepared using a schedule one protocol in regular ACSF have been shown to contain fewer PVINs and be more prone to the generation of epileptiform activity when incubated in a magnesium free artificial cerebral spinal fluid (ACSF-Mg_0) *in vitro*. In contrast, slices prepared using transcardiac perfusion of sucrose based (sACSF) demonstrate a more intact inhibitory microcircuit and are less likely to display epileptiform activity upon application of ACSF-Mg_0. Using a biologically plausible computational model of entorhinal cortex and the Virtual Electrode Recording Tool for EXtracellular potentials (VERTEX)[1] we will investigate the effect that the loss of PVINs has on the excitability of the network and the local field potentials (LFPs) recorded virtually. These will be compared with *in vitro* recordings of LFPs in rat entorhinal cortex prepared using regular ACSF and using sucrose based ACSF, which preserves the PVINs.

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Coarse-grained description of the spatio-temporal dynamics of network activity from experimentally verified single-neuron models and connectivity

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We combine experimentally verified models of neocortical-neuron voltage dynamics and network connectivity to derive a set of equations that describe the activity at a tissue scale. The resulting equations represent a neuronal field theory in which emergent properties at the coarse-grained level can be causally linked to the physiology of cellular and sub-cellular components. The description is mathematically tractable and can be elaborated to include further biophysical details such as multiple neuronal populations to capture the structure of the component microcircuits, synaptic dynamics and filtering as well as distance-dependent delays in signal propagation. For spatially homogeneous afferent drive the firing rate can be straightforwardly obtained together with the network response to weak spatio-temporal modulations of the afferents via a perturbative approach. For the spatially heterogeneous non-linear regime that the network is pushed into under stronger drive, we construct an iterative scheme that rapidly converges to the network firing-rate. The utility of the approach is illustrated using examples from the experimental literature.

Synaptic transmission of spike trains with arbitrary interspike intervals

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Short-term synaptic depression, caused by depletion of releasable neurotransmitter vesicles, modulates the strength of neuronal connections in an activity-dependent manner. Quantifying the statistics of this feature of synaptic transmission requires the development of stochastic models linking probabilistic neurotransmitter release with the spike-train statistics of the presynaptic population. A common approach has been to model the presynaptic spike train as either regular or a memory-less Poisson process - few analytical results are available that describe the behaviour of a depressing synapse when the afferent spike train has more complex, temporally correlated statistics.

Recently, we have derived a series of results that allow for the fraction of occupied release sites and the neurotransmitter release probability to be calculated for a presynaptic spike train with arbitrary interspike interval (ISI) statistics. The results take a particularly compact form when the presynaptic spike times are generated by a renewal process, i.e. when the ISIs are independent. This encompasses a broad range of models that are currently used for circuit and network analyses, including the class of integrate-and-fire models. Our approach also allows for the postsynaptic voltage mean and variance to be calculated, which in turn allows for an approximation of the firing rate of a neuron driven by depressing synapses from non-Poissonian presynaptic neurons.

These results will allow for the incorporation of more complex and physiologically relevant firing patterns into future analytic studies of neuronal circuits and networks.

Auditory-visual interactions at perceptual and cortical levels in mice

Thomas Deneux and Brice Bathellier

Although auditory responses have been reported in mouse primary visual cortex (V1), their computational and perceptual role in a multisensory context remains elusive. In particular, it is unclear whether specific multimodal information is channeled through these responses. To address these questions, we recorded neuronal populations in V1 using 2-photon imaging in awake, GCAMP6-transfected mice, during 2 sec drifting gratings and looming or receding visual and/or auditory stimuli.

Among 3,500 recorded V1 neurons, 25% responded to sounds. Although 7% of V1 neurons exhibited non-linear bimodal summation properties and appeared to signal specific combinations of bimodal stimuli, a large part of auditory responses were non-specific onset responses. Visual responses displayed clear stimulus specificity but much less at their onset than afterwards. Interestingly, auditory population responses correlated strongly with the non-specific onset visual responses. To assess the perceptual impact of this cross-modal activity, we trained mice to discriminate between the looming and receding disks in a head-fixed Lick/No lick protocol, first without sounds. Mice tended to lick on the onset of both visual stimuli, as predicted by the poor specificity of V1 onset responses, and learned to adjust their licking during the more specific phase of V1 responses (about 500 ms after onset). Introducing sounds in trained animals, with and without visual stimuli, resulted mainly in an increase of the first unspecific licking, reflecting the similarity of auditory and visual onset responses in V1, as we demonstrated using a simple computational model of the task.

Altogether our results show that specific information about the multimodal context is present in V1, but that the first order impact of auditory signals on mouse visual representation and on perception in a simple task is a boosting of stimulus onset saliency.

Reactivation and reinstatement of hippocampal cell assemblies

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The hippocampus plays an important role in the encoding, consolidation and retrieval of memories. Memory retrieval is believed to be mediated by the reinstatement of the patterns of neuronal activity that encoded the initial experience. To facilitate such reinstatement, neuronal activity patterns are thought to be consolidated by their reactivation in sleep, which predominantly occurs during hippocampal sharp-wave/ripples events (SWRs). However, a direct relation between the (sleep) reactivation of neuronal activity patterns and their subsequent (awake) reinstatement during memory retrieval has not been demonstrated.

According to the functional cell assembly hypothesis originally proposed by Hebb in 1949, memories are represented at the network level by the simultaneous activation of a group of neurons (=cell assembly) or by the sequential activity of a particular set of cell assemblies (=phase sequence). Despite the popularity of this hypothesis, there is no generally accepted method for the identification of cell assemblies from electrophysiological data.

Here, we use an unsupervised statistical method based on independent component analysis to identify neuronal assembly-patterns (defined as: *group of pyramidal neurons with activity coordinated within 30-ms time-frames*) from multi-unit recordings in the hippocampus of freely-moving mice. With this method we have been able to detect and track assembly-patterns with strong spatial tuning. We found that these patterns, which often involve neurons of both hemispheres, are reactivated during subsequent sleep and reinstated upon re-exposure to the same environment but not upon exposure to a different environment. Importantly, the strength with which assembly-patterns are reactivated predicts their subsequent reinstatement strength. We are now seeking to complement this first direct correlational evidence for a role of (sleep) reactivation on the (awake) reinstatement of assembly-patterns, with a causal test based upon the optogenetic silencing of hippocampal pyramidal neurons during on-line detected sleep SWRs (125-250 Hz).

Substance P release in the striatum allows for efficient switching between distinct actions in action sequences

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The striatum is the primary input nucleus for the basal ganglia, and receives glutamatergic afferents from the cortex. Under the hypothesis that basal ganglia perform action selection, these cortical afferents encode potential 'action requests'. It has previously been believed that selection of a particular action could be explained by mutual inhibition between GABAergic medium spiny neurons (MSNs) enforcing a ‘winner-takes-all’ outcome for the action channel of greatest salience. However, this account does not explain the ability of the striatum to perform clean, rapid switching between distinct actions that form part of a learned action sequence (Plenz, 2003, Trends in Neurosciences).

Substance P (SP) is a neuropeptide co-released with GABA in MSNs preferentially expressing D1 dopamine receptors. SP has a facilitatory effect on subsequent glutamatergic inputs to target MSNs, suggesting an additional co-operative function for the MSN network. Additionally, blocking the action of SP in the striatum is known to affect behavioural transitions. It has therefore been suggested that the release of SP may boost the effective salience of inputs to target MSNs and allow for rapid switching between actions in an action sequence.

The current research uses a computational model of a core GABAergic striatal microcircuit to show that switching between actions in a sequence takes place more efficiently in a model with patterned SP connectivity. Specifically, for an action sequence of the form A-B, the model shows a selection advantage for a structured projection scheme in which SP is released from MSNs encoding action A that project to MSNs representing action B. This supports the hypothesis that SP plays a role in action sequence generation and suggests that formation of directional SP projections may be part of action sequence automatisation.

Mapping the Functional Architecture of Vision

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Abstract

Genetic and imaging technologies, as applied to the zebrafish, are enabling a multitude of anatomical and functional landscapes to be studied. Our particular interest is the functional architecture underlying biological vision in vertebrates. We believe an integrative scientific approach involving the intersection of brain mapping, visual neuroscience and informatics makes one of the most captivating questions in science tractable in the zebrafish – *what does the eye tell the brain?*

Topographic organisation wherein neighbours in one space are neighbours in another space is a fundamental organisational feature of visual processing. Using a genetic indicator of synaptic function (synaptophysinGCaMP3) and confocal optical imaging in larval zebrafish, we have imaged en masse retinal ganglion cell (RGC) inputs to the optic tectum. Across a population of animals we have derived retino-tectal maps and estimated topographic precision for two distinct functional classes of visual encoding: direction- and orientation-selective motion detectors. Our findings suggest non-matching topographies associated with these two functional RGC classes that challenge our conceptual understanding of topographically organised circuits.

Mapping the anatomy and function of developing zebrafish larvae brains has considerable future potential. As a vertebrate model system its cost effectiveness, genetic amenability and the ease of optical imaging will make zebrafish brain mapping very accessible to a large new community of scientists. It will be a complex and technically demanding field requiring the coordinated interaction of many researchers with diverse scientific backgrounds: neurobiologists, physicists, biophysicists, neuroimaging scientists, theoretical neuroscientists, bioinformaticians, mathematicians and increasingly translational and behavioural scientists. Key to ongoing future success will be the successful collaboration between all associated disciplines and the translation of the wealth of approaches, methods and models to the zebrafish. We will present our work to increase its visibility and generate interest across a diverse audience to hopefully spark greater integrated and collaborative approaches.

Challenges in running a cortical microcircuit simulation on the SpiNNaker neuromorphic hardware platform.

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Abstract

This poster presents the challenges overcome in mapping a high-level description of a neural model in a language such as PyNN [1] into operational code running on a neuromorphic hardware, such as SpiNNaker [2]; as well as the challenges yet to be addressed. These include moving the data that represents the neural models onto the hardware itself, as well as making the executable code efficient enough, in time, energy, and memory consumption, to run the network in biological real-time given the restrictive nature of the hardware.

The cortical microcircuit model by Potjans and Diesmann[3] was translated from a provided PyNN description into a form which can be executed on the SpiNNaker platform. This includes setting up the network communication fabric and dividing up the problem so that it can run in parallel on the machine, and finally configuring the model executables to carry out the simulation itself.

Alongside the poster, we will present a demo which will show a live run of a scaled-down version of the cortical microcircuit. During the demo, we will show the active spikes generated by each layer of the microcircuit as they occur in the simulation. This will then show how the simulation appears to mirror the expected behaviour of the network as described in [3], as well as comparing the results to those obtained from the NEST simulator when running the same PyNN script.

Acknowledgments

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Large-scale analysis and visualisation of neuronal ion channel models

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Summary of work. The behaviour of neuronal circuits is mediated by underlying biophysical processes, namely ion channel dynamics[1]. Thus, a key component in describing the mechanisms by which these circuits function is through an understanding of how ion channel dynamics lead to interesting properties in single neurons and in networks. In the biophysical modelling literature, there is an abundance of published ion channel models used in simulated neurons, often also available on web archives like modelDB[2]. However, it can be quite difficult to determine which channel models are most appropriate for a specific neuronal simulation at hand. Their family relations, i.e., how an ion channel model was derived or inspired from another model, are often opaque, and assessing their similarity to each other and also to experimental data is time consuming. We have performed an exhaustive literature search to catalogue the presumed channel type, pedigree, and various other relevant information about existing ion channel models coded in the NEURON language. Additionally, we tested the physiological performance of each channel in standardised voltage clamp protocols from which we derived a benchmark similarity measure between model channels. We visualise family relations between various channels by creating genealogical trees and by using clustering methods. We then created a buffet-style database that lists all available reference information for each of the over 2000 available channel models. The database will bring order to the existing jungle of available ion channel models. It allows for maintenance, documentation, and easy access of currently existing models and, importantly, the integration and evaluation of new ion channel models in the future.

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Modeling a transient thalamocortical circuit (L5b-L4 loop) in the developing mouse neocortex.

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The brain is a complex network of 10^{11} neurons with 10^{14} synapses. Our understanding of how such networks develop is still limited. Novel genetic manipulations and optical techniques make it possible to create detailed connectivity maps at different times during development. However, it is nearly impossible to study the mechanisms underlying the slow transitions from one developmental stage to the next experimentally. Here we use computer models of developing circuits to study the synaptic plasticity rules that effect the changes in network connectivity. In particular, we focus on an early thalamocortical circuit between thalamic afferents, interneurons in layer 5b and spiny stellate neurons in layer 4 (L5b-L4 loop). Unpublished work from the lab has shown that this circuit is transient in nature and shortly after the L4 critical period for plasticity has ended (~postnatal day 9) synaptic connections between these cells are replaced by connections previously reported for the canonical cortical circuits (Anastasiades et al., in revision; Marques-Smith et al., submitted). The computer model of this developing circuit is composed of approximately 10,000 integrate-and-fire neurons. Each neuron is classified as one of four distinct cell types (PV+, SOM+, 5HT3R+, and PYR) and their firing properties have been matched to experimental recordings. After obtaining static models of the circuit at each of its stages in development, we tested distinct synaptic plasticity rules that may underpin the dynamic formation and destruction of these transient developmental circuits. Ultimately, this type of models may enable a targeted exploration of developing circuits and provide a framework for translational work and a bridge between experimental and theoretical neuroscience research.

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Frequency selectivity of neurons in the auditory system

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Frequency selectivity describes the ability to resolve the individual frequency components in sound, and is a fundamental feature of hearing. It is crucial for most auditory tasks such as identifying sounds, separating auditory objects, and understanding speech. The ability of the auditory system as a whole can be measured through the behaviour of a subject, whereas the ability of neurons, or populations of neurons, can be measured by observing their spiking activity. Traditionally the methods used to measure frequency selectivity perceptually and neurally are so different that results are incomparable. As a result the link between the two modalities is still poorly understood.

In an attempt to bridge the gap between the two approaches, we measured the frequency selectivity of single- and multi-units in the primary auditory cortex and midbrain of the guinea pig, using a model typically associated with behavioural measurements; the Power Spectrum model. The ability of midbrain neurons was found to match very closely with previous behavioural measurements in the guinea pig, as well as neural measurements made more peripherally using a significantly different approach. In contrast, units in the auditory cortex with a high characteristic frequency (CF) had better frequency selectivity, or sharper tuning, than the animal as a whole, and the preceding auditory brain regions. This would suggest that the ability to resolve frequency improves along the auditory system, but is then combined using sub-optimal coding to produce a perceptually poorer representation. Another possible explanation is that the Power Spectrum model, which assumes linearity, is not appropriate for measuring frequency selectivity in cortical neurons, or perhaps any auditory neurons. The question then arises, whether another model can perform better.

Frequency Selectivity of Cortical Adaptation: A comparative study in Humans and Guinea Pigs

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Electrophysiology of the central nervous system in humans is typically limited to non-invasive recordings of large populations of neurons. By using animal models we can increase the resolution of these recordings down to the single neuron level but it is not currently well understood how to directly relate the recordings of evoked potentials to firing behaviours at the single unit level, especially when comparing results between species.

Adaptation, the reduction in neural responses to repeated stimuli, is a ubiquitous phenomenon throughout human and animal sensory systems and is an important aspect of sensory neural coding. We have used this phenomenon, running comparable studies of adaptation in humans and in awake and anaesthetised guinea-pigs, to allow an inter-species comparison, a comparison of simultaneous recordings from multiple neural scales and an investigation into the effects of anaesthesia on population processing.

Pure tone adapter-probe sequences were presented and the resultant auditory evoked potential (AEP) amplitudes analysed, quantifying adaptation as the reduction in response size in the adapted probe compared to the unadapted response. The human EEG results suggest that adaptation progresses on two different timescales: rapid non-specific adaptation, with frequency tuning remaining unchanged over repeated tone presentations, and a second slower adaptation which sharpens the frequency specificity of AEPs. In comparison, under anaesthesia, guinea-pig EEG, LFP and multi-unit responses show only rapid non-specific adaptation and little or modest progressive sharpening of frequency selectivity. However, preliminary EEG recordings in awake guinea-pigs indicate that adaptation is substantially altered by anaesthesia.

Our results suggest, in both humans and guinea-pigs, adaptation contributes to refinement of the representation of frequency. However, qualitative differences in EEG responses are apparent across the two datasets. Future work will investigate the contributions of species differences and anaesthesia to adaptation in cortical AEPs and the underlying neural activity.

High Fidelity Large Scale Cortical Network Models of *In Vivo* Barrel Cortex.

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Devising physiologically relevant and biologically sound computational models of neuronal networks of the brain has proved to be an enduring challenge. The development of machine learning, statistical techniques, and advancements in computational paradigms have allowed for the study of firing statistics and connection possibilities of neural architecture. Most studies have focused on using models of uniform random sparse network architectures to fit experimental datasets of electrophysiological recordings *in vitro*. C. Tomm et al (2014) showed that computational models with varied degree distributions and synaptic weight correlations could provide a better fit to *in vitro* datasets. However, much less is known about neuronal circuit models of synaptic connectivity and transmission *in vivo*. Differences in intrinsic network dynamics, and in the activity levels of specific inhibitory and neuromodulatory cell populations heavily affect the deduced synaptic architecture. Using the fitting and parameter estimation procedures of C. Tomm et al (2014), we create biologically sound computational models that give rise to the experimental results of *in vivo* dataset by A. Pala et al (2014). They observed layer 2/3 of mouse barrel cortex characterizing synaptic connectivity and transmission of single-cell optogenetically stimulated glutamatergic neurons onto parvalbumin-expressing (PV) and somatostatin-expressing (Sst) GABAergic neurons.

Our computational models include ~5,000 integrate-and-fire neurons, each classified as glutamatergic excitatory, PV inhibitory, or Sst inhibitory, matching the experiment. By creating a model matching the observed results in the experimental research, we infer values for significant but hard-to-measure parameters underlying the neural networks *in vivo*, serving as a methodological framework for understanding the theoretical underpinnings of neural circuit architecture.

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Understanding the role of neuromodulation in the olfactory circuit of the fruit fly

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Abstract

The olfactory circuit of the fruit fly can learn to distinguish thousands of unique odours and store the valence of these odours presumably in the synaptic connections at later processing stages (Heisenberg M, Nature Rev Neurosci, 2003). Recent experiments have shown that the firing rates of a small set of neurons at the output of the olfactory circuit are correlated with learned approach or retreat behaviour in a T-maze reinforcement learning task (David Owald et al., under review, 2015; Aso Y et al. eLife, 2015). There is evidence that the learning process is gated by dopaminergic neurons (Waddell S, Curr. Opinion in Neurobiol, 2013). However the process by which dopamine helps encode the valence of an odour is still unclear. Here, we introduce a rate model of the fruit fly olfactory circuit to study dopamine mediated learning. Based on a previous model (Luo and Abbott, PNAS, 2006) and published firing rate responses to 110 different odours (Hallem et al., Cell, 2006), we introduce a reward modulated synaptic plasticity rule to provide a circuit level account of behavioural and electrophysiological data. We show that our model can reproduce the firing rates of output neurons that have been observed in reward based experiments. Our results suggest that a single output neuron can learn to decode the valence of a given odour with high specificity. We propose that the sparse coding used by the fly to store memories of odours is an efficient coding mechanism that enables output neurons to store the valance of an odour in a non-overlapping manner. The olfactory circuit of the fruit fly shares striking similarities with the olfactory bulb in mammals (Masse NY et al, Current Biology, 2009). Thus our work is a step towards a better understanding of how olfactory processing and reward modulated learning works across different species.

Feedforward inhibition and inhibitory synaptic plasticity generate sparse, selective, and background-invariant representations of auditory stimuli in a spiking model of zebra finch caudomedial nidopallium

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Pattern decorrelation and the separation of signal from noise are defining aspects of several sensory circuits. In a recent study of the zebra finch auditory stream, Schneider and Woolley (2013) reported a population of higher-order auditory cortex cells—broad spiking units of the caudomedial nidopallium (NCM)—that responded to specific sets of zebra finch songs and responded exclusively when the songs were played at intensities that permitted behavioural recognition against background noise. Here we describe a spiking model of the broad-spiking NCM cells (and accompanying circuit) that accurately replicates the sparse firing rates, selectivity patterns, and signal-to-noise dependences observed *in vivo*. Using leaky integrate-and-fire neurons as outputs and the electrophysiologically recorded primary auditory cortex trains from Schneider and Woolley (2013) as templates for input ensembles, we demonstrate that the implementation of inhibitory synaptic plasticity in a feedforward inhibitory module is sufficient to produce the selective, non-linear receptive fields necessary for cell-song specificity and behaviourally relevant firing patterns. Notably, the model recreates a linear increase in output firing rate as a function of the signal-to-noise ratio—but not of the input firing rate—in a manner that is consistent with both the biologically recorded NCM firing patterns and the behavioural variables relevant to signal extraction. We also describe preliminary evidence regarding multiple impinging signals (songs), dynamic thresholding, and the embedding of these feedforward modules in larger networks with lateral connectivity.

The effect of signal degradation on neuronal representations of speech in the auditory system

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Cochlear implants provide a degraded input to the auditory system. Despite this, cochlear implant users are able to discriminate speech sounds with a degree of accuracy comparable to that of normal hearing listeners in favourable listening conditions. The neural bases of this phenomenon is not well understood.

A set of vowel-consonant-vowel phoneme sequences, each produced by multiple talkers, were parametrically degraded using a noise vocoder. Single- and multi-unit neuronal responses were recorded in the inferior colliculus and auditory cortex of the guinea pig, and auditory nerve responses were generated using a computational model. The discriminability of these responses was quantified using a novel nearest neighbour classifier.

When envelope modulations were severely band-limited, classifier performance was qualitatively similar to that of human listeners for all brain regions. However, in the auditory nerve and the midbrain, the preservation of high rate envelope cues enabled the near perfect discrimination of speech tokens even for heavily spectrally degraded speech. High rate envelope cues do not appear to increase discriminability of cortical representations.

High rate envelope cues, represented up to the midbrain, are useful for discriminating speech tokens. However, qualitatively more consistent with perception, high rate envelope cues do not contribute to the discriminability of cortical neural responses. The optimal timescale of the neural code for discriminability also depends on the brain region and the degree of degradation of the stimuli.

Spatio-temporal Interactions Between Neuronal Assemblies

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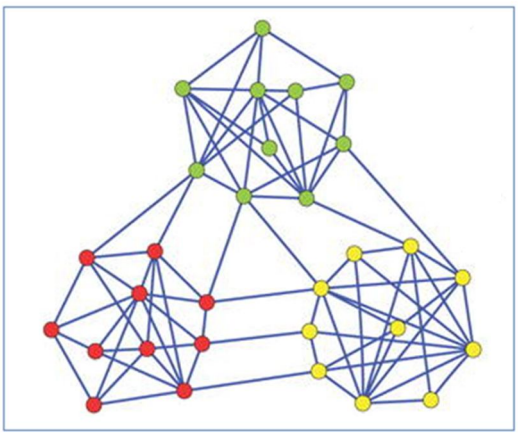
Polychronous neuronal groups (PNGs) are unique temporal patterns of neural activity in spiking neural networks, that emerge as units of reverberational memory. Small subsets of neurons that form PNGs, which are activated by specific time-locked patterns, can be strengthened to give rise to larger chains of spatio-temporal activity by spike timing dependent plasticity (STDP) rule.



In this work, we investigate the effects of modular network structures on polychronous neuronal group (PNG) formation. An example network topology to illustrate our motivation can be seen from the figure above. Networks with clustered architectures produce complex and patterned firing sequences, notwithstanding they have weak interconnections. In our simulation studies, we employed different parameter sets for each sub-population in order to simulate interactions between distinct neural circuits. Although our model is highly generic, it is representative in terms of functionality, thus giving insights on coordination among neural assemblies in a sense of PNG dynamics.

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** Figure is adapted from http://www.engineerdir.com/research/catalog/170/ web page given by researcher named Jianzhi Zhang.