

**Local-Area
Systems & Theoretical
Neuroscience Day**

July 8, 2008

UCL

Programme

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1. Anatomical and physiological constraints limit the applicability of a classical circuit model for V1 simple cells

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A surprisingly small number of studies have addressed the fundamental question to what extent the anatomical properties of macaque visual cortex can explain the physiological characteristics of simple cells in layer 4C. Based on well-established anatomical data, we created a realistic computational model of the thalamocortical pathway in macaque to determine whether the classical Hubel and Wiesel model for constructing orientation-tuned simple cells from LGN inputs can account for the physiological properties observed in extracellular studies of the primary visual cortex (V1).

Some of the major anatomical constraints, taken from the literature, in our model are the extent of the axonal arborisation of LGN axons in cortical layer 4C (for P-cells, 0.2 mm diameter on average, for M cells 0.6 mm on average and 1.2 mm maximum), the spread of horizontal connections in layer 4C (projections up to 3-4 mm in upper 4C alpha), the spread of the dendritic field of spiny stellate neurons in layer 4C (maximum 0.2-0.25 mm diameter) the variation in cortical magnification factor as a function of eccentricity (E) in V1, the variation in the density of LGN neurons with E, and the number of LGN P and M cells that project to a single layer 4C neuron (on the order of 10-30). The major physiological constraints in the model are the classical receptive field (CRF) sizes of V1 and LGN neurons measured with patches of drifting sinusoidal gratings, the extra-classical surround suppression in the LGN, the orientation tuning bandwidth and the spatial frequency preference and bandwidth in V1.

The model was built and tested within a flexible framework that allowed it to operate on arbitrary time-varying binocular achromatic visual stimuli. It consisted of networks of tens to hundreds of thousands of neurons, depending on E and size of visual field being tested, and included Poisson or conductance-driven integrate-and-fire spiking mechanisms.

We found that for E between 2-8 deg, RFs of average or greater size are anatomically implausible under the classical Hubel and Wiesel model. In particular, assuming RFs are built from M LGN afferents, direct feedforward connections can account only for CRF sizes up to about 1.5 deg at E=8 deg and up to about 0.5 deg at E=2 deg, whereas physiological RF sizes ranging from 0.5 to 3 deg are common. For P-cell afferents, the validity of the classical model is almost completely abolished. By including lateral projections within layer 4C, we found that a more realistic range of CRF sizes could be explained.

2. Understanding pitch perception as a multi-scale hierarchical generative process

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Pitch is a salient unitary percept derived from the periodicities in a sound signal. Modelling the neural processing of the pitch is essential for understanding the perceptual phenomenology in music and the prosody in speech. However, in order to study the temporal dynamics of pitch, we need to invoke a wide range of time scales over which the perceptual information is integrated; and none of the existing approaches could account for the balance between temporal integration and temporal resolution windows in pitch perception.

Another major challenge for modelling is to relate the perception of pitch to neurophysiological data. Functional brain-imaging studies strongly suggest that there is some form of hierarchical processing in the auditory system, starting in subcortical structures. Moreover, there is also an increasing dispersion of responses, which are longer in cortex; and no attempt has yet been made to explain these latencies. The goal of this work is to develop the most compact neurocomputational formulation possible consistent with these evidences.

In this study, we introduce the novel idea that top-down activity within a hierarchical processing architecture is critical for understanding the temporal dynamics of pitch in a unified model. We present a simplified model of neural ensembles responses, which explains the stimulus-dependent time scales of temporal resolution and integration in pitch perception. We demonstrate that this model is an extension of autocorrelation models of pitch. We also show that the model is similar to a hierarchical generative process in which higher cortical levels predict the response in lower levels and modulate them via feedback connections. The model also explains the latency of the pitch onset response in cortex; and is consistent with other recent neurophysiological data.

In addition, we specifically conducted a psychoacoustic experiment to assess the temporal resolution of the auditory system. The experiment was conducted independently to the model development and subsequently used to successfully test the model predictions.

The simulation results show that this model provides for the first time a unified account of perceptual results in a range of challenging studies. Although highly idealized, the model significantly advances the identification of basic elements in the processing of the pitch over time, and provides a novel account of the role of feedback connections in the auditory system

3. Directional selectivity in basal dendrites of cortical pyramidal neurons

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Dendritic integration is thought to be strongly dependent on the spatiotemporal pattern of synaptic input. Indeed, it has been shown that highly synchronous inputs delivered to a spatially restricted segment of a dendrite can produce local dendritic spikes, while temporally distributed input does not. However, it is not known if such extreme degrees of spatiotemporal synchrony exist in vivo, nor whether more

asynchronous input patterns can be distinguished from each other. We have therefore tested whether the dendritic response to a particular spatial pattern of asynchronous synaptic inputs is sensitive to the temporal sequence of their activation. We have made whole-cell recordings from layer 2/3 pyramidal cells and activated synaptic input onto the basal dendrites using 2-photon glutamate uncaging in acute slices of the rat somatosensory cortex. We found that sequential activation of synapses along a basal dendritic branch, from the end of the dendrite towards the soma, produces a significantly larger somatic voltage change than activation in the reverse order. This effect is dependent on the membrane potential, and on both the spatial and the temporal distribution of the activated synapses. Furthermore, we find that NMDA receptor activation is essential for the observed directional selectivity, and compartmental modelling shows that this can be explained by a combination of passive cable properties and NMDA receptor kinetics. We conclude that basal dendrites of layer 2/3 cortical neurons can detect the sequence of synaptic activation, and suggest that this may be an important property of dendrites for information coding and processing.

4. Stimulus contrast modulates lateral connectivity in visual cortex

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An extensive network of lateral connections exists within primary visual cortex (V1), yet little is known about its functional contributions because of difficulties in measuring connectivity. One hypothesis is that the spatial extent of the lateral input to each cell is modified by the level of contrast in the visual stimulus. This hypothesis is supported by the well-characterized reduction in spatial summation of individual cells with increasing stimulus contrast.

We measured V1 lateral connectivity during spontaneous activity and with different stimulus contrasts. We recorded local field potentials (LFP) and spikes across a 10x10 electrode array in anesthetized monkeys and cats. We assessed connectivity by computing the average LFP waveforms across the entire array, triggered by spikes at a given reference electrode.

We find that both LFP amplitude and time-to-peak depend on the location of the reference spikes: 1) the amplitude falls with distance in an exponential fashion and 2) the time delay increases linearly with distance, with a speed of 0.2-0.4 m/s. This speed of propagation is consistent with measurements in horizontal connections within V1 and strongly suggests that the strength of correlations between the LFP and spikes measures lateral connectivity.

Stimulus contrast strongly modulates the spatial extent of V1 lateral connectivity. When transitioning from low to high contrast, the rate of spatial decay of the spike-triggered LFP amplitude away from spikes is greatly reduced (5 fold in cats, 3 fold in monkeys). These data are consistent with the reduction of spatial summation with increasing contrast, and show that the spatial footprint of the lateral connectivity is greatly reduced for high vs. low contrast stimuli.

We conclude that the influence of lateral connectivity on cortical responses is not constant but rather is modulated by the sensory input, being stronger when sensory stimulation is weak and strongest when the stimuli are absent.

5. Gap junctions and emergent rhythms

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Gap junction coupling is ubiquitous in the brain, particularly between the dendritic trees of inhibitory interneurons. Such direct non-synaptic interaction allows for direct electrical communication between cells. Unlike spike-time driven synaptic neural network models, which are event based, any model with gap junctions must necessarily involve a single neuron model that can represent the shape of an action potential. Indeed, not only do neurons communicating via gaps feel super-threshold spikes, but they also experience, and respond to, sub-threshold voltage signals. In this presentation we show that the so-called *absolute* integrate-and-fire model is ideally suited to such studies. At the single neuron level voltage traces for the model may be obtained in closed form, and are shown to mimic those of fast-spiking inhibitory neurons. Interestingly in the presence of a slow spike adaptation current the model is shown to support periodic bursting oscillations. For both tonic and bursting modes the phase response curve can be calculated in closed form. At the network level we focus on global gap junction coupling and show how to analyze the asynchronous firing state in large networks. Importantly, we are able to determine the emergence of non-trivial network rhythms due to strong coupling instabilities. To illustrate the use of our theoretical techniques (particularly the phase-density formalism used to determine stability) we focus on a spike adaptation induced transition from asynchronous tonic activity to synchronous bursting in a gap-junction coupled network.

6. Explicit representation of the posterior and it's evolution in time in a human estimation task

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When driving in traffic, our perception provides snapshots of different parts of the surrounding world at different instances in time (e.g. traffic ahead and behind). This sensory information has to be combined requiring us to estimate how the surroundings may have changed in absence of new sensory information. It is an open question what internal representations and computations are used (and which should be used) to achieve this, which we address here computationally and experimentally. Here, we show that humans estimating the position of an occluded moving object, retain second-order information about the estimate's posterior probability distribution and evolve their estimate's uncertainty over time in a way that is consistent with an explicit representation of the posterior. We carried out a psychophysics experiment to address this question (6 subjects, 1200 trials each). Subjects observed a particle moving away in a random direction on a linear trajectory (at one of two different velocities). After 200 ms the object vanished and continues moving for $T=200-900$ ms. After this time the radial position of particle is shown (to eliminate bias of the position estimation task by uncertainty about the time passed) and subjects had to indicate the angular position of the particle and their perceived uncertainty ("error bars") about their estimate. Subjects gained reward if the particle was within error bars or lost points reward if not. Reward increased as error bars were made smaller and vice versa. At the end of each trial subjects received feedback about the particle position and the score achieved. We found that, subjects estimate's of the position was related to a subject specific level of uncertainty. Moreover, as the time in which the object moved invisibly increased subject's uncertainty scaled as a square root power-law of time ($\sigma = T^{0.54 \pm 0.03}$). This scaling is consistent with an explicit representation of the estimate in terms of a probability distribution updated in time by a stochastic partial differential equation of the Fokker-Planck type. However, subject's actual sensory estimation error (thus their performance and not their belief about their performance) scaled linearly with time ($\sigma = T^{0.95 \pm 0.08}$, yet subjects did not correct the way they estimated how their uncertainty evolved over time (N=1200 trials). This suggesting that

human's may use a fairly generic model of how the unobserved world changes: in the form of random additive noise. This is appealing from a computational perspective as it allows to retain the Bayesian framework in a straightforward manner by updating the relevant probability distributions to the same instant in time using stochastic calculus.

7. Analysis of visual motion: evidence for post initiation processing in a simple perceptual task

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A decision is a commitment to a proposition or plan of action, based on evidence, prior knowledge and expected costs and benefits. In many instances, decisions are based on a stream of evidence in time. In this case, there are, in effect, two decisions: when to terminate the process and a choice. The link between choice and termination time is often apparent in the tradeoff between speed and accuracy. This statement masks a subtle but important distinction: Termination of the decision process is an internal event that must then give rise to an overt behaviour. This gap between decision- and reaction-time, termed 'non-decision' time, is poorly understood. We hypothesized that the motor system might exploit this gap in time by dissociating action initiation from action specification.

In the current study, we investigated whether humans can process sensory information available after a decision has been reached and prior to movement initiation, and how any post initiation processing (PIP) is incorporated into an ongoing action. Most choice-reaction time studies require subjects to make rapid, ballistic movements to indicate their choice. For example, in the direction-of-motion paradigm, monkeys and humans typically register their decisions by making saccadic eye movements to a left or right choice target. Saccadic eye movements are truly ballistic; once initiated, they are fully specified. Thus there is no opportunity to revise a decision. Here, human subjects were asked to judge the direction of moving random dots (left and rightward motion in which we control the coherence, and hence difficulty) and to reach to one of the two targets (left and right) based on their decision. The advantage of this setup was that it uses arm movements to indicate decisions which, unlike saccadic eye movements, can be modified during execution.

Crucially, in our experiment, on movement initiation the random dots were extinguished. We found that the visual information arriving between the decision and movement initiation could update the decision online and was reflected in altered hand trajectories. We examined the probability and timing of such updating of decisions as a function of both the motion coherence and whether the initial decision was correct or incorrect. We extend the theoretical framework developed for the initial decision, that of accumulation of noisy evidence to a decision 'bound' (drift diffusion model) to incorporate updating of the decision after an initial decision has been made.

8. Analysis 2D pattern motion through the eyes of a fly

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The nervous system selectively integrates an enormous amount of sensory inputs to generate behaviour that aids the survival of an animal. One example is of a fly controlling its flight using the visual information of its environment. It does with a relatively simple neural system while mammalian system would need to sample a large population of neurons to perform the same task reliably. Previous studies have looked at how the direction of motion of a pattern is used to control yaw. We ask the question: how does the fly realize the direction of motion of a 2D pattern?

Flies are known to have elementary motion detectors (EMDs) that detect visual motion between pairs of eye facets in the compound eye. Due to the geometric arrangement of the eye facets the information regarding motion is constrained along certain directions. Little is known about how information along different directions is then integrated to control flight. We recorded the response of the H1 neuron, the activity of which is involved in yaw control, and determined its direction tuning curves to different plaids (overlapping sine wave gratings moving in different directions). Observing how neurons deal with the information from each of the plaid components can tell us about its directional integrating properties. The experimental results show that the tuning width across the different plaids is similar.

We built a model based on the known structure of the fly visual system. It consists of EMDs tuned to different directions (as constrained by the geometry of the compound eye) with a sigmoid input non-linear function, a weighting of the EMD responses, summation at H1 and an output non-linear function. We fitted the model to the recorded response to different plaids. We find that the sigmoid input non-linear function is a crucial component involved in predicting the response of the neuron. As an independent check, we compared the contrast tuning response predicted by the model to the actual response and found a similar trend, which other models fail to predict. Using the model fitting exercise, we were able to determine the tuning width of EMDs and the non-linear function operating on their outputs. We conclude that by having a sigmoid input non-linearity at the EMDs, the fly visual system can effectively compute the direction of motion of a 2D pattern.

9. Feature binding in the feedback layers of area V2

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The visual representation of an object is distributed amongst multiple, functionally specialized areas of the cerebral cortex. When several objects are represented simultaneously, what mechanism preserves the identity of a single object as its features are progressively separated at higher levels of processing? We address this question—known as the ‘binding problem’—by examining combinatorial feature-selectivity of neurons in area V2 of the anaesthetized macaque monkey. We find that dual selectivity for chromatic and spatiotemporal attributes is common enough in the superficial and deep layers that receive feedback connections from higher areas, but disproportionately sparse within the middle layers (4 & 3) that relay ascending signals. In other words, for example, the neurons in V2 relaying motion information to area V5 are not colour-sensitive, and the colour-selective neurons in V2 communicating with area V4 are not direction-selective. Neurons that do combine colour and direction sensitivity are found in layers that do not send output to higher centres such as V4 and V5, but do receive feedback from them.

How does this arrangement promote binding? Firstly, because cortical feedback pathways are the likely conduit for top-down attentional modulations. Secondly, because in terms of cognitive modelling, attention is instrumental in binding by acting to select one single object for higher representation, and filtering

out competing objects. We propose that dual-selective neurons perform a ‘bridging’ function, mediating the transfer of feedback-induced bias between feature dimensions. Hence, for instance, if attention were directed toward a particular colour, only dual neurons tuned to that colour, and to the motion direction physically coupled to it in the visual stimulus, would show feedback enhancement. This modulatory effect on activity could then be propagated through V2 (by translaminar & transcolumar intrinsic connections) in order that the selected feature combination be reflected in the pattern of activity across unimodal output neurons in layer 3. And, subsequently, across their fields of influence in higher level areas—such that representations of a single attended object come to dominate in multiple feature maps, as envisaged by the ‘integrated competition’ model of attention. In short, we postulate that the bridging function of dual-tuned neurons in V2 acts to unify the outcome of parallel object-selective processes taking place along specialised visual pathways diverging from V2.

10. When noisy means cardinal: visual biases for cardinal orientations revealed by degrading stimulus identity

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According to Bayesian theory, the influence of “a priori” biases on perception should be greatest when certainty about stimulus likelihood is least. These biases are thought to have evolved because certain types of stimulus are encountered more frequently than others. For example, our environment is particularly rich in perfectly horizontal and vertical things. Degrading information about stimulus orientation may shift perception toward a priori biases. We tested this hypothesis by asking observers to align a pointer with the average orientation of a briefly displayed array of Gabor patches. Unbeknownst to the observers, each patch’s orientation was drawn from a Gaussian distribution with near-horizontal (i.e. $0^\circ \pm 2^\circ$ or $0^\circ \pm 14^\circ$) or near-vertical mean (i.e. $90^\circ \pm 2^\circ$ or $90^\circ \pm 14^\circ$), and one of two possible standard deviations: $\sigma = 2^\circ$ or $\sigma = 14^\circ$. On average, responses elicited by the larger standard deviation were closer to the cardinal orientations. In particular, our results indicate a predisposition for seeing things as being perfectly horizontal or vertical. More generally, our results demonstrate that visual biases can be revealed by statistically degrading stimulus identity.

11. Attention resolves the effects of a computational bottleneck: modelling binding, precueing, and task-driven bias

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As William James famously said, “everyone knows what attention is”, and indeed we all have introspective access to the effects (and frustrations) of attentional selection. But attempts to delineate exactly why the brain needs to selectively filter incoming information, and what the mechanisms and effects of selection are, have floundered in a sea of heterogeneous effects. We have previously proposed a new probabilistic computational framework that unifies a number of attentional effects under a single normative description of the resource that is limited, why it is limited, and how attention helps [1].

Our framework is grounded in the Helmholtzian notion that perception requires an inverse inference from neural firing to the features in the world that caused it. Multiple sources of noise and ill-posedness make this inference poorly constrained, and the optimal approach is to compute posterior belief distributions over features according to Bayes rule. There is much evidence for Bayesian optimality in tasks involving

a single object, but in cluttered natural scenes the resources required to represent the full posterior grow exponentially in the number of correlated features. We therefore suggest that a fundamental, computational resource limitation is the ability to represent joint distributions over large numbers of features, and that the brain makes approximations that neglect some of the correlations. Attention then consists of a ‘hypothesis’ that takes the mathematical form of an extra prior, but can be thought of as making a proposal about which location, or feature value, is of interest. The brain approximates the product of the true posterior and this extra attentional hypothesis, such that the approximation is more accurate in the proposed region. The attentional hypothesis can be driven by top-down cues or bottom-up salience computations, but also dynamically evolves towards a better match between itself and the true posterior as measured by an approximated partition function. This dynamic evolution towards ‘true’ proposals allows attention to reveal correlations not explicitly represented in the approximation, as it settles on co-occurring feature values that have a high correlation in the true posterior.

Here we illustrate this framework by implementing analogues of three top-down attentional paradigms in a simple model, which consists of an array of feature maps connected to an output layer via a local weight matrix. Noisy observations are drawn from this generative model, and we compute the posterior belief both with the appropriate attentional hypothesis and without. Performance on pre-cueing, task-driven bias, and binding tasks is simulated by mapping the posterior to a perceptual decision, and reveals the predicted attentional benefits. For pre-cueing, this approach has much in common with previous treatments of attention as a prior over locations of interest [2]. However, it also encompasses paradigms that are semantically or technically unsuited to such a treatment, and explicitly considers the case of multiple objects and thus the binding problem. We also consider possible anatomical implications of the framework.

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12. Understanding color categories, color constancy, color induction, and lightness perception from information theory

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I explore an understanding of colour appearance predicated on the brain’s mapping sensory inputs into discrete categories conveying the maximum bits of Shannon information about the input. Under sufficiently high (but not infinite) signal-to-noise ratio, when an input ensemble contains the usually large dynamic range, an information maximizing mapping from the contrast-gain-controlled photoreceptor inputs to, e.g., six, categories typically carves the input space into regions that correspond to the perception of white, black, red, green, blue, and yellow colour categories. This input-to-category mapping corresponds to another mapping from surface reflectance to category of colour appearance. Illumination changes that sufficiently preserve signal-to-noise can alter the input-to-category mapping but leave the reflectance-to-category mapping almost unchanged, achieving colour constancy. This hypothesis of informationally optimal colour boundaries, when applied to small input ensembles made of inputs from a single or a part of a scene, can account for various colour illusions in particular color induction, and, under achromatic inputs, typical phenomena in lightness perception. It does not at present accommodate the spatial configuration factors that influence colour/lightness appearance.

13. How to maximize your reward rate

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When making decisions, there is always a tradeoff between speed and accuracy. Fast decisions have the potential for high reward rates (that is, more reward per unit time), but generally lead to lower accuracy. Slow decisions raise accuracy, but decrease reward rates. How do we find a happy medium? In general this is a hard question, especially in an uncertain world in which data is noisy, partially observed, and unreliable.

Here we address this question in a simplified task in which subjects have to decide whether a set of dots is moving to the right or left. Although simple, this task contains the key elements of almost all decision-making: the longer one stares at the dots, the more likely one is to be correct, but if one stares too long the reward rate becomes unacceptably low.

The most standard framework for analyzing this task is the diffusion-to-bound model (Palmer et al., 2005). Here we present a more rigorous framework based on dynamic programming. This allows us to do several things that the diffusion-to-bound model can't: determine optimal policies in the presence of nuisance parameters, compute full posterior probabilities over rewards, and explore how the prior probability that the dots are moving to the right affects behavior.

To apply this framework to the moving dot task, we generate spike trains that mimic those produced by motion sensitive brain area MT in response to moving dots, and calculate the optimal strategy of an ideal observer looking at those spike trains. Given the optimal strategy, we then ask two questions: do animals follow it in behavioral tasks, and does the next area after MT, LIP, properly integrate the MT spikes?

14. Implicit jumps in perceptual processes cause expansion of perceived duration; pauses cause contraction

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Sensory input can distort our perception of time. For instance, a visual stimulus containing high temporal frequencies or fast motion will on average seem to last longer than a stimulus with low temporal frequencies or slow motion, even when the physical duration is the same.

We show that this and several similar phenomena may be explained by assuming that sensory input is used in a probabilistic manner to aid time estimation. Since natural visual (or auditory) scenes evolve according to well-defined temporal statistics, observations of natural stimuli can be used to provide probabilistic constraints on elapsed time. Unnatural stimuli, such as those described above, can therefore distort time perception.

A key prediction of this framework is that implicit “jumps” or “pauses” in perceptual processes should expand or contract, respectively, their perceived duration. We present data from a new psychophysical experiment that tests this prediction in the setting of linear motion. A linearly translating box was caused to jump or pause in its motion, whilst hidden behind an occluder. Subjects judged the duration of the motion to be longer (for jumps) and shorter (for pauses) than the veridical duration of the motion. This result is in agreement with the theoretically derived prediction.

15. Rephasing of CA3 gamma oscillations by mossy fiber input in vitro

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During gamma oscillations, firing rates of principal cells and interneurons in a network are periodically modulated at 30–100 Hz, resulting in field potential oscillations.

The coherent periodic firing of interneurons imposes alternating epochs of high and low excitability on the principal cells in the network. If input to a network arrives at a random phase relative to ongoing oscillation this variable inhibitory tone may compromise the reliability of the network response. Alternatively, periodic input may be able to entrain local oscillatory circuitry, thereby controlling the relative phase of input and inhibition.

The dentate gyrus and CA3 region both act as gamma generators in vivo and the CA3 region receives strong input from dentate gyrus via the mossy fibres. Entrainment of CA3 gamma by the dentate gyrus could significantly affect signal propagation between these regions.

One approach to studying coupling between oscillators is to experimentally measure their phase response curves (PRCs) and then consider the entrainment properties using the theory of pulse coupled oscillators.

Although it is an oversimplification to consider the spatially extended CA3 region as a single oscillator or the output from the dentate gyrus on a gamma cycle as a single pulse, these methods provide a tool for experimentally investigating coupling between the dentate and CA3 gamma oscillators.

We have measured the phase response of carbachol induced gamma oscillations in the CA3 region in vitro to mossy fiber stimulation.

At low stimulation intensities the rephasing is type 1 by winding number; the new phase after stimulation varies through a whole cycle as the phase of stimulation is varied over a whole cycle. At stronger stimulation intensities the rephasing becomes type 0 by winding number with the new phase after stimulation only varying over a small range as the phase of stimulation is varied over a full cycle.

In the weak stimulation regime, the phase response curve has a region of stimulation phase in which mossy fiber input delays the oscillation and a region in which it advances the oscillation. This shape of PRC allows a pulse coupled oscillator to entrain 1:1 with a periodic input of either higher or lower frequency. Our experimentally measured PRCs predict that for inputs at similar frequency to unforced CA3 gamma, entrainment will occur at a phase such that mossy fiber input arrives while local inhibition in CA3 is weak. Entrainment of gamma oscillations in CA3 by mossy fiber input may therefore facilitate signal propagation between dentate gyrus and CA3.

16. Encoding self-motion at individual central synapses

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The synapse is the fundamental element of neuronal communication. However, how sensory stimuli are represented at the level of single synapses, and how much information the activity at a single central synapse contains about a sensory stimulus has not been determined. Here we address these questions by taking advantage of cerebellar granule cells (GCs) as they provide an ideal model system for two reasons. First, they receive on average only 4 excitatory inputs from mossy fibres (MFs), making it possible to

distinguish single inputs. Second, MF-GC synapses in the flocculus receive prominent vestibular input, which constitutes a well-defined sensory stimulus with a low dimensional stimulus space.

To characterise the representation of vestibular stimuli at the MF-GC synapse, we performed in vivo whole-cell voltage-clamp recordings at -70 mV from GCs in the cerebellar flocculus of ketamine/xylazine anaesthetised mice. In the absence of vestibular stimulation, vestibular-sensitive GCs showed spontaneously occurring excitatory postsynaptic currents (EPSCs) with an average frequency of 13.0 ± 2.4 Hz. Vestibular stimulation resulted in a bidirectional modulation of EPSC frequency, which correlated linearly with the angular velocity, rather than position or acceleration. A lack of synaptic short-term dynamics over the observed frequencies ensured that the velocity representation was linear not only in terms of frequency, but also in terms of excitatory charge transfer at the GC membrane. In a subset of cells distinct inputs could be reliably distinguished based on their EPSC amplitude. In those cases, only a subset of inputs was modulated by vestibular stimulation while the remaining inputs were insensitive to horizontal rotation, suggesting that despite receiving very few inputs GCs can have multi-dimensional and/or multi-modal receptive fields. Using a Bayesian approach we examined the capacity of GC EPSC trains to report the stimulus velocity that evoked it, in order to estimate the size of the population of MF inputs/GCs to reach a behaviourally relevant resolution. While activity in a single GC could report the presence and direction of movement, the error in the stimulus reconstruction was large. However, with increasing GC number the velocity estimates improved in accuracy and reliability in a logarithmic fashion, and an ensemble of as few as 100 GCs, i.e. less than 400 synapses, provided an accuracy of $4.8^\circ/\text{s}$, approaching the psychophysical limit. Thus the representation of angular velocity requires synaptic signals that are distributed over many tens of GCs but that within an individual cell may be integrated with other stimulus features.

17. Modelling spatiotemporal interactions in direction selective V1 neurons

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The spatiotemporal interactions underlying direction selectivity in V1 neurons remain obscure. Recent work using a type of 2D white noise stimulus has revealed intriguing patterns in the resulting 2D sequential interaction maps from direction selective neurons in macaque V1 (Livingstone and Conway, *J Neurophysiol*, 89:2743-2759, 2003). Suppressing and facilitatory subregions in interaction maps may be elongated along the axis of preferred orientation of the neuron or symmetric and round, with no elongation. Elongated subregions were often asymmetric, with facilitatory interactions more extensive than suppressive ones. Elongation was correlated with direction tuning bandwidth, i.e. narrowly-tuned cells had more elongated interactions. We examined the shapes of 2D interaction maps and the associated direction tuning curves obtained with models of direction selective (DS) V1 cells. We tested how parameters that affect direction tuning width contribute to the shapes of 2D interaction maps.

We used two spatiotemporal filter-based models of DS V1 cells, a motion energy model and a Reichardt detector. The motion energy model generated interaction maps with symmetrical elongated facilitatory and suppressive subregions. Decreasing the window of integration of the spatial filter broadened direction tuning and eliminated subregion elongation in the maps. The Reichardt detector model also showed round, symmetric suppressive and facilitatory map subregions. Decreasing the distance between detectors narrowed direction tuning, but did not elongate map subregions. Neither of these models generated asymmetry in the extent of facilitatory vs. suppressive interactions. To further investigate the neural circuitry underlying the shapes of 2D interaction maps, we are developing a network model with spiking inhibitory and excitatory V1 neurons with realistic LGN inputs. This model will allow us to test how network connectivity patterns and non-linearities associated with biophysical mechanisms, including synaptic dynamics, dendritic integration and somatic spiking, shape the 2D interaction maps. This will shed light not only on the generation of experimentally observed map shapes, but also reveal how DS

receptive fields are built. Support: The Wellcome Trust.

18. Investigating cortical spiking dynamics in vivo using simultaneous intracellular and multiunit recordings.

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In primary sensory areas, repeated sensory stimuli are known to trigger variable spiking responses. It is unclear if this variability is a result of intrinsic noise or is actually encoding information (e.g. due to additional input from brain areas other than the afferent pathway). We have addressed this question using a bottom-up approach: studying the effect of small perturbations on the cortical network during a repeated stimulus. Theoretical analysis and simulations using highly recurrent network connectivity based on the mammalian cortex show that the effect of small perturbations can grow very rapidly and interfere with the effect of the driving incoming input from the whisker. We demonstrate that one can quantify this effect by measuring the mean increase in the firing rate of an average neuron in response to a single synaptic input. If the mean increase is sufficiently large, then perturbations grow, which can preclude precisely repeatable spike trains. To address this question experimentally, we have used in vivo patch-clamp recordings from cortical pyramidal neurons in the barrel cortex of anesthetized rats. We find that a perturbation consisting of a single extra spike leads to 25 extra and missing spikes in the network. Using theoretical calculations and modelling, we show that the mean increase in firing rate provides a quantitative lower bound on the precision at which spike timing can carry information. To validate these predictions, we are making simultaneous patch-clamp recordings from layer 2/3 pyramidal neurons and from multiple units using an extracellular multisite recording silicon probe. We stimulate the primary whisker of the barrel with a dynamic stimulus and assessed the reproducibility of spike trains. We then introduce a perturbation by injecting depolarizing or hyperpolarizing current into the patched neuron during the whisker stimulation and observe the evolution of activity in the network recorded with the extracellular probe. These experiments allow us to link the spiking of single neurons with precisely timed activity in tens of recurrently connected cells in order to validate and improve our models of the effects of noise on cortical dynamics.

19. Slow Rise Times of IPSPs Activated by Ivy Cells

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To date, 17, classes of inhibitory interneurons, including the newly characterised Ivy cell (Fuentealba et al, in press), have been described in the CA1 region of the hippocampus.

Dual sharp electrode, or whole cell recordings were used to study and compare the inhibitory postsynaptic potentials (IPSPs) elicited by 3 different subclasses of interneurons in postsynaptic hippocampal CA1 pyramidal cells.

The 10-90% rise times of IPSPs elicited by Ivy cells were significantly slower than those of bistratified or basket cell IPSPs. Although the spike duration of Ivy cells was significantly longer than those of basket or bistratified cells, the spike duration was not long enough to account for this difference in rise times.

Nor could it be explained by dendritic filtering, as bistratified and Ivy cells both target dendritic regions of pyramidal cells, or by a significant jitter in the onset latencies of quantal components of the IPSPs.

To determine whether the slow rise times could be due to the involvement of different postsynaptic GABAA receptors, IPSPs elicited by proximally targeting basket cells and dendrite-preferring bistratified and Ivy cells were challenged with benzodiazepine site ligands. The amplitudes of basket and Ivy cell IPSPs, unlike bistratified cell IPSPs, were significantly enhanced by zolpidem and by Etomidate, suggesting these synapses utilise GABAA receptors containing alpha 1, 2 or 3 and beta 2 or beta3 subunits respectively. These data suggest that the slow rise times of Ivy cell IPSPs are not due to GABAA receptors with unusually slow kinetics, to presynaptic spike duration or conduction jitter, or to dendritic filtering. It remains to be determined whether it could be due to longer diffusion distances of GABA.

20. Characterizing neural dependencies with Poisson copula models

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The activities of individual neurons in cortex and many other areas of the brain are often well described by Poisson distributions. Unfortunately, there is no simple joint Poisson distribution that can incorporate statistical dependencies (e.g., correlations) between neurons. For this reason, neural population coding models often either assume that the individual neurons are independent, or transform the joint activity mathematically to continuous quantities and model them using a multivariate distribution that naturally encodes dependency, such as the multivariate Gaussian. However, these solutions are sometimes poorly suited to describing neural population responses, failing to match either the marginal distributions of individual neurons or the detailed form of their dependencies. Here we develop a joint model for neural population responses using copulas, which allow Poisson marginal distributions to be combined into a joint distribution that can exhibit various kinds of dependency.

Copulas are mathematical objects that specify a joint distribution's dependency structure separately from its marginal structure [1]. Copulas provide a principled way to quantify non-linear dependencies that go beyond correlation coefficients, in a manner that is independent of rescaling of individual variables.

Here we present some results on constructing joint distributions for the activity of pairs of neurons by choosing the marginals to be Poisson distributed, selecting an appropriate parametric family of copulas, and fitting the model parameters (of both the marginals and the copula) using Maximum Likelihood estimation. Different copula families are able to capture dependencies of different kinds (e.g., dependencies limited to the lower or upper tails of the distribution, or negative dependencies). The selection of an appropriate parametric family for the copula distribution can be addressed by cross-validation.

Acknowledgments

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21. Odor-quality perception and its representation in the olfactory bulb

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Understanding how patterns of neuronal activity contribute to odor perception will shed light on how external information is translated by the nervous system. Previously, large-scale lesioning of the nasal epithelium or the main olfactory bulb (OB) has been reported to produce only mild deficits in odor detection and discrimination. This has led to the idea that much of the glomerular activity within the OB is redundant and that odor processing can be achieved with a limited amount of sensory input. Here we have combined behavioural experiments and in vivo imaging to directly examine the relationship between OB activity and odor perception in mice with disrupted olfactory representations.

Water-deprived mice (C57BL/6J, P30-70) were trained to discriminate a monomolecular rewarded odor (S+) from an unrewarded odor (S-) using a go/no-go behavioural paradigm. Subsequently, under pentobarbitone anesthesia (1.1mg/g b.w.), S+ and S- odor - evoked activity on the dorsal surface of the OB was recorded using standard intrinsic-signal imaging. Mice then received a nasal flush of either ZnSO₄ (8.4%) to partially ablate sensory input, or NaCl (9%, sham treatment). Three to five days later, mice were assessed on discrimination of an unfamiliar odor pair and then on recognition of the pre-treatment S+ and S- odors. Mice were then re-anesthetised and a second imaging session was carried out to assess the representation of S+ and S- odors.

We find that ZnSO₄ - treated mice required significantly more trials to discriminate rewarded unfamiliar odors accurately ($\geq 80\%$ correct) than sham treated mice (336 ± 39.9 , $n = 5$ mice vs 166.6 ± 44.4 trials, $n = 6$ mice; $p < 0.05$). Both groups however demonstrated equivalent discrimination accuracy scores after 340 trials ($90.7 \pm 3.7\%$, vs $91.7 \pm 5.9\%$; $p > 0.05$) and showed no difference in their mean discrimination times ($p > 0.05$). For unrewarded familiar odorants, ZnSO₄-treated mice showed significantly poorer recognition than sham mice (71 ± 7.4 vs $90 \pm 2.8\%$, $p < 0.05$) and an initially significant discrimination deficit of rewarded familiar odorants (71.1 ± 7.3 vs $89.8 \pm 2.2\%$ $p < 0.05$; first 20 trials). Comparison of pre- and post-treatment imaging data revealed that the integrity of glomerular-activity patterns observed in the second session correlated with the ability to recognize S+ and S- odors ($r = 0.74$, $p < 0.05$, $n = 13$ mice).

In contrast to previous lesion studies, our data show that perceived odor quality and the ability to distinguish odorants depends critically upon the number and integrity of functional input channels to the OB.

22. Adaptive Optimal Control Approaches to Sensorimotor Learning

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Recently it has been shown that it is possible to explain a wide range of motor psychophysical findings on the basis of stochastic optimal feedback control. Here we extend the optimal control framework to allow for adaptive responses to environmental changes. In order to compute an optimal action an optimal feedback controller requires an internal model F of the dynamics of the environment such that consecutive states x and the motor command u are connected by $x_{t+1} = F(x_t, u)$. In learning experiments this transition function can depend on additional parameters a_t that change over time, so that $x_{t+1} = F(a_t, x_t, u)$, e.g. changing loads attached to the arm etc. From a theoretical point of view, the adaptive control problem has to learn to solve two problems: The first is the structural learning problem that is learning the structure of the task $F(\cdot)$, e.g. the class of visuomotor rotation or gain changes. The second is the parametric learning problem, that is finding the unknown parameters a_t , such as the particular setting of a rotation or gain.

In order to test experimentally for structural learning we exposed human subjects to a task with a fixed structure $F(\cdot)$ which can have different parameterisations a_t . Importantly the parameters for the task change randomly between blocks of trials making the task impossible to learn, although it is possible for subjects to learn the structure which remains fixed over the trials. In one of the experiments, we exposed subjects to randomly varying 3d rotations where the rotation angle was drawn from a uniform distribution $[-60^\circ, +60^\circ]$ every four trials. One group of subjects exclusively experienced random rotations around the vertical and the other group around the horizontal axes. Later in the experiment we introduced blocks of probe trials with rotations around either axis that were identical for both groups. Interestingly, both groups reacted very differently to the same trials. They showed structure-specific facilitation, variability patterns and exploration strategies. Once the structure of the environmental change is known, optimal adaptive routines can be established to respond to them. These parametric adaptive responses can be computed (approximately) by adaptive optimal control methods. We tested such an adaptive linear quadratic control model in a visuomotor rotation experiment where the rotation angle changed randomly every trial so that subjects had to adapt online in order to hit the targets. The model's predicted adaptive behaviour was consistent with the experimentally observed kinematics and variability patterns.

23. Binomial analysis accounting for functional differences between neocortical synaptic connections

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The simple binomial model of synaptic release considers a connection as made of a number of release sites (n), each with an identical, but independent probability (p) of releasing transmitter upon spike arrival, resulting either in a failure of transmission, or a quantal postsynaptic response (q) (del Castillo and Katz, 1954). This model predicts specific relationships between the statistics of the resulting postsynaptic response amplitudes.

Synaptic connections were studied using dual sharp microelectrode recordings in slices of adult rat and cat neocortex and recorded cells filled with biocytin. Current injections elicited trains of action potentials in the presynaptic cell and excitatory postsynaptic potentials (EPSPs) were recorded in the postsynaptic cell. By varying the amplitude and shape of the injected current, a range of presynaptic firing patterns was elicited, allowing the statistics and dynamics of the EPSP amplitude fluctuations to be studied.

When connections involving different classes of neurones were compared, inherent differences in the relationships linking their statistics of release were revealed (Bremaud et al., 2007). Most strikingly, the variability in amplitude for a given mean EPSP amplitude differed.

To explore these differences further, methods exploiting the statistical relations predicted by the simple binomial model were employed and the binomial parameters n , p and q estimated. Significant differences between these parameter estimates were found when different classes of connection were compared.

The simple binomial model assumes uniform p and q across all n release sites (at any one time). To

determine whether our analysis would be meaningful if more complex schemes were to underlie release, Monte Carlo simulations of models in which p and q varied across release sites were also run.

More complex models could generate significant shifts in parameter estimates, but the scale of these shifts was smaller than the experimentally obtained differences between connection classes. The parameters obtained were concluded to be acceptable estimates of n , mean p and mean q , and to demonstrate that each connection class employs a different combination of these parameters to achieve a given synaptic strength.

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24. An oscillatory interference model of grid cell firing

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Medial entorhinal grid cell firing can be modelled as the result of interfering sub-threshold membrane potential oscillations (Burgess, Barry, O'Keefe, Hippocampus, 2007). This model makes two kinds of prediction: temporal and structural. Temporal predictions include that the intrinsic firing frequency of grid cells exceeds the EEG theta frequency by an amount that increases with running speed and decreases with the spatial scale of the grid-like firing pattern. Structural predictions include that the grid-like firing pattern is associated to the environment via connections from place cells, which in turn receive inputs from putative 'boundary vector cells' tuned to respond when at a specific distance from an environmental boundary along a specific allocentric direction. We investigate these predictions in electrophysiological recordings from freely-moving rats. Our results generally support the model, constrain its future development, and highlight the question of the potentially differential functional roles of the different cell layers in medial entorhinal cortex.

25. Temporal edge detection in human auditory cortex

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Auditory environments are constantly fluctuating. These fluctuations are due in part to the oscillatory nature of many acoustic sources and in part to the dynamics of their appearance and disappearance from the auditory scene. Presumably, one of the first stages of detecting these onset and offset events, that are superimposed on the already changing input entering a listener's ears, is the extraction of auditory temporal edges. The process of deriving a temporal edge depends on the statistical properties of the stimulus before and after the transition. In some cases, edges are detected as a violation of a previously acquired representation of the scene, for example when an ongoing auditory object, against some background, disappears or changes its properties. This is the kind of processing that is tapped by the much used MMN paradigm. However, the opposite side of the coin—the processes by which auditory cortex detects the emergence of regularity out of 'disorder', such as when an auditory source appears out of an ongoing random background, is also an 'edge detection' task but has been much less explored. We use magnetoencephalography (MEG) to measure early auditory cortical responses to

transitions between constant tones, regularly alternating, and randomly alternating tone-pip sequences. Such transitions embody key characteristics of natural auditory temporal edges. Our data demonstrate that the temporal dynamics and response polarity of the neural temporal-edge-detection processes depend in specific ways on the generalized nature of the edge (the context preceding and following the transition) and suggest that distinct neural substrates in core and non-core auditory cortex are recruited depending on the kind of computation (discovery of a violation of regularity, vs. the detection of a new regularity) required to extract the edge from the ongoing fluctuating input entering a listener's ears

26. What impairs information coding in the Basal Ganglia in Parkinson's disease?

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Recordings from deep brain stimulation electrodes in the basal ganglia of patients with Parkinson's disease (PD) have shown that chronic dopamine loss is accompanied by increased beta frequency (13-30 Hz) oscillations at the single-cell and neuronal population levels. These oscillations are stronger when patients are off dopamine replacement medication than when they are on medication. Additionally, when on medication, the oscillations decrease even further when patients initiate movements. This suggests that the increased oscillations in the basal ganglia networks may be related to the movement deficits seen in the patients. How these excessive beta oscillations impact information processing in these circuits is unknown, but behavioral deficits might be due to decreased information coding capacity. To address this hypothesis, we recorded single-neuron activity from multiple sites in the external globus pallidus (GP) of control rats and 6-OHDA-lesioned rats, the latter of which is a PD model that shows exaggerated beta oscillations after chronic dopamine loss. We then characterized the effects of these oscillations on the network entropy, a measure of information coding capacity, by comparing entropy between neural ensemble activity in lesioned and normal animals.

Dopamine loss was associated with significant reductions in the firing rates of GP neurons and significant increases in single-cell beta oscillations and synchronized beta activity. We have used a logistic regression model to examine the relative effects of firing rate, oscillations and synchrony on the entropy in the network. The reduction in firing rates had the largest effect on entropy (86.3% decrease), the increased oscillations the second largest effect (11.9% decrease), and the excessive synchrony the smallest effect (1.8% decrease), at least for pairs of simultaneously-recorded GP neurons. However, effects of synchrony are likely to be higher when larger populations of neurons are considered rather than pairs. We are currently developing a model of the network effects of synchrony, at the population level, so its effects can be more directly compared to firing rates and oscillations. The results suggest that the excessive beta oscillations seen in basal ganglia circuits in PD may lead to a decrease in the entropy of these networks. However, the results also emphasize the importance of changes in firing rates in the Parkinsonian state.

27. Adaptive processing of interaural level differences

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Adaptation phenomena have been reported in all sensory systems and can provide valuable insight into mechanisms of sensory coding. To examine how the mammalian auditory system adapts to the statistics of binaural spatial cues and how adaptation at the neuronal level may translate into perceptual phenomena we recorded from neurons in the inferior colliculus of anaesthetized ferrets and carried out behavioural experiments in human listeners using almost identical stimuli. Stimuli consisted of a combination of dynamic adaptors and static test stimuli. The adaptors consisted of five seconds long sequences of broadband noise with dynamically varying interaural level differences (ILDs). The ILD values of the adaptor were drawn randomly from a Gaussian distribution and changed every 5ms. Each test stimulus consisted of a 100ms long noise burst with a static ILD and was presented immediately after the adaptor.

Employing reverse-correlation we characterized each neuron's activity during adaptation in terms of a linear filter and a nonlinear gain function. Responses to the static test ILD were used to obtain more traditional ILD-response functions. During behavioural experiments human listeners were required to lateralize the static test ILDs in a two-alternative forced choice task.

Neuronal adaptation to changes in the mean or variance of the distribution from which ILD values were chosen was closely matched by the perceptual effects observed in human listeners. Filter shape mostly remained constant across different means and ILD-response functions shifted in the direction of the mean of the adaptor's distribution. Parallel changes were observed in human perception as lateralization was biased away from the mean of the adaptor. Decreasing the variance of the adaptor's distribution was associated with an increase in neuronal gain and steeper ILD-response functions. The psychophysical experiments provided evidence for a perceptual correlate of this increase in neuronal sensitivity as lateralization thresholds improved with decreasing variance of the adaptor.

28. Lighting up the world of neural signalling with photostimulation

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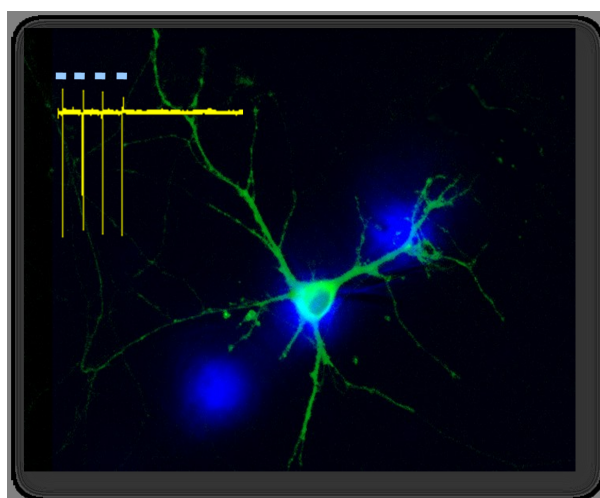
The field of neural coding has relied on electrical techniques such as patch clamping and microelectrodes for both stimulation and recording. There are of course other methods such as sensory interaction in animals. But until recently it has not been possible to target the stimulation of specific neurons with light in the way that calcium imaging has lit up field of neural recording. However, it is now possible to encode specific cells with light sensitive ion channels and stimulate action potentials at will.

The dominant light sensitive channel used at present is the channelrhodopsin-2 which originates from the eye of a motile swamp microalgae called *Chlamydomonas reinhardtii*. It can be readily transfectable into neurons via standard techniques and AAV viri are now available which can express it in vivo with ample potential for cell targeting promoters. To date, it has been expressed in cell culture, *C. Elegans*, rodents, and there is now discussion about its potential for prosthetics and clinical trials in humans.

In cells expressing sufficient levels of ChR2, and stimulated with sufficient light, it is possible to generate

action potentials at will. This can be done by stimulating individual action potentials with individual pulses of light, or by generating responses as a result of a broad temporal illumination. Light requirement is high, and it takes around 2-5 nJ of light stimulation per action potential. This response is poor compared to rhodopsin due to the lack of dedicated optical architectures found in dedicated cells such as rods and cones. In addition, as the channel is basically a passive system, there is no amplification such as the G-protein linked cascade in most visual systems.

In this presentation we highlight our own work in developing prosthetic retina strategies using this technique. We will describe the equipment we have developed to stimulate multiple neurons and neuron substructures simultaneously. This can be seen in Figure 1 where a neuron has been stimulated with 3 targeted spots of light. Individual pulses create individual action potentials. We will discuss the efficacy of signal transfer to the neurons, and spatial and temporal frequency limitations. Finally we will discuss the future directions of the technique.



29. Postsynaptic activity-dependent modulation of unitary IPSPs by specific presynaptic cannabinoid receptors in rat neocortex

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Endogenous cannabinoids (CB) can serve as retrograde modulators and their receptors are expressed in a subset of neocortical interneurons. The aim of the present study was to investigate the modulation of inhibition by CB receptors in two populations of interneurons. Dual whole-cell recordings combined with biocytin labelling were performed in acute slices of rat neocortex (postnatal day 17-22). Layer II/III accommodating multipolar and bitufted interneurons were recorded simultaneously with postsynaptic pyramidal cells. The axons of multipolar interneurons projected horizontally within layer II/III, while the axons of bitufted interneurons were more vertically oriented, spanning layers V to I. Unitary IPSPs elicited in postsynaptic pyramidal cells by multipolar and bitufted interneurons were reduced by the CB receptor agonist anandamide. Depolarisation-induced suppression of inhibition (DSI) was evident in the IPSPs activated by both proximally targeting multipolar and dendrite-preferring bitufted interneurons. Unitary IPSP amplitudes were reduced by approximately 50% compared with control recordings in both populations, accompanied by an increase in the proportion of apparent failures of transmission. Following addition of the selective CB1 receptor antagonist AM-251, these effects were blocked in the multipolar

interneurones; however bitufted cell IPSPs remained depressed. We propose that another type of CB receptor is involved here. Our data suggest postsynaptic activity-dependent interneurone-specific and selective insertion of presynaptic CB receptors that differentially modulate inhibition in layer II/III of the neocortex.

30. Role of feedback connections: A Bayesian inference model

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There exists substantial evidence, including recently published papers, showing V1/V2 cortical activity responding to illusory contours (eg. Kanizsa's triangle). This means V1 is representing information which correlates with the visual perception but which does not arise from the ordinary feedforward paths (retina and LGN). The same evidence strongly suggests this response is driven by feedback connections from higher-level areas. On the other hand, several authors have emphasized the important role played by feedback connections in visual perception and have suggested hierarchical Bayesian inference as a plausible underlying interpretation (Rao & Ballard, 1997; Friston, 2003; Lee & Mumford, 2003; Murray et al., 2004; Olshausen & Field, 2005; Sillito et al., 2006). The proposed model aims at providing a functional interpretation of the illusory contour phenomenon, and more generally, of the role of feedback connections in visual perception, under the perspective of a Bayesian inference framework. More precisely, we attempt to implement a feedback model based on the Bayesian Belief propagation algorithm, taking as a startpoint a well-known feedforward cortex-based object recognition model (HMAX model - see Riesenhuber & Poggio, 1999; Cadieu et al., 2007).

31. Monte carlo map seeking circuits

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The Map Seeking Circuit of Arathorn [1] is a biologically inspired mechanism which offers a generic solution to the complex task of estimating chains of image transformations by proposing a model for the forward/backward projections in the neural circuitry of the brain. For the majority of object recognition problems, the consideration of all the possible combinations for a non-trivial number of transformations introduces a combinatorial explosion in computational complexity. The MSC has a layered architecture representing different parameters to be explored and implements an ordered sequence of comparisons of transformed images using forward/backward superimpositions at each layer in an iterative process. The entire search space is given uniform weighting initially and the mechanism operates by culling unlikely combinations considering one parameter at a time. Although the search is partitioned into 1D sub-spaces, the superimpositions allow several likely combinations of the parameters in the sequence to be taken into account at once, allowing a combinatorial dimension to the search. The complexity in this scheme, therefore, grows additively as the number of different parameters in the sequence is increased rather than exponentially as an initial expectation from the nature of the problem.

In this work, we first provide a statistical interpretation of the MSC in a Bayesian framework. The superimpositions in this scheme are explained as marginalisations that remove the effect of all the other parameters except for one at a time. Then we introduce Monte Carlo Map Seeking Circuits (MC-MSC) that improve the performance of the MSC by representing the likelihoods of the parameters by a set of samples which are initially placed at fixed intervals and keep only the 'important' characteristics of the likelihoods as the iterations proceed for an accurate estimation of marginalisations. A major drawback

of the dimensionality reduction through marginalisations is that of ‘collusions’, i.e. combinations of patterns create new illusory patterns in the superimpositions, in the presence of clutter as might be expected for practical problems. This is addressed by adopting a serial/parallel search scheme inspired by the biological visual search in the form of a ‘queuing’ procedure. Our preliminary results illustrate the performance of MC-MSD and ‘queuing’ (79% correct detection rate for 135 cases – cluttered input image with similar objects present) in comparison to fully parallel MSD (21% success rate) scheme in the case of translation, rotation, and scaling parameter search.

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32. Resonance in subthalamo-cortical circuits in Parkinson’s disease

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Neuronal activity within and across the cortex and basal ganglia often synchronizes at ~ 20 Hz in patients with Parkinson’s disease and is linked to impaired movement. Defining how activities in spatially distributed brain regions overtly synchronize in narrow frequency bands is critical for understanding disease processes. To address this, we studied cortical responses to electrical stimulation of the subthalamic nucleus, a key basal ganglia structure, in parkinsonian patients. We stimulated at various frequencies between 5 and 30 Hz. By fitting a damped oscillator function to the cortical response obtained during 5 Hz stimulation in patients off dopaminergic therapy we found that the natural frequency of the subthalamo-cortical circuit is around 20 Hz. When the system was forced at this frequency by stimulation of the subthalamic nucleus at 20 Hz, the undamped amplitude of the cortical response increased ($3.1 \pm 0.7 \mu\text{V}$ and $1.8 \pm 0.1 \mu\text{V}$ with stimulation at 20 Hz and 5 Hz, $p = 0.0053$) due to resonance phenomena. Restoration of dopaminergic input by treatment with the dopamine prodrug, levodopa, increased the damping factor of oscillations by 30 % (0.18 ± 0.01 and 0.14 ± 0.01 on and off levodopa, $p = 0.001$), thereby limiting resonance phenomena. Our results show that the basal ganglia – cortical network has a tendency to resonate at ~ 20 Hz in parkinsonian patients. This resonance phenomenon underlies the propagation and amplification of activities synchronized around this critical frequency. Crucially, dopamine acts to increase damping and thereby limit resonance in the basal ganglia – cortical network.

33. The affect of facial expression on decision making

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When appraising information in order to make a decision, we are strongly influenced by how that in-

formation is presented. For example, it has been shown that subjects are more likely to choose a given option if it is presented in terms of gains, rather than losses. Since humans are highly social creatures, and most real-world decisions are made within a social context, one would also expect social cues to influence decision making. To investigate how social and utilitarian cues interact during decision-making, we tested participants on a guessing game in which they were asked to choose one of two faces (one smiling, one angry or sad) on each trial. They were told that one face had a higher probability of a 'win' than the other, and to try and determine through trial and error which face that was. After making the choice, participants were told whether they had won or lost on that trial, and this information was shown along with the face they had chosen. One face led to a win 40% of the time, the other 60%. After every block the probabilities changed, and the probabilities were balanced across facial expressions.

We compared participants' responses to an ideal-observer model that predicted the optimal response on any given trial based on the evidence available. Participants' performance deviated significantly from that of the ideal observer, demonstrating a bias towards selecting the smiling face. By fitting additional model parameters, we found that this bias consists of both a prior bias towards the smiling face, and a tendency to overweight positive outcomes associated with it. Positive outcomes associated with sad or angry faces were systematically underweighted.

These results are in accordance with previous imaging studies. Smiling faces have been shown to act as positive reinforcers, activating OFC, thought to represent the reward value of stimuli. Since lesions of OFC cause reliable deficits in extinction and reversal tasks, OFC has a clear role in guiding decision-making behaviour. Conversely, there is evidence that viewing sad or angry facial expressions elicits activity in ACC, an area associated with error detection. This suggests that sad or angry faces are taken as an indication of disapproval, encouraging a change in behaviour. By modifying our task for use with fMRI we hope to extend these findings. Specifically we will examine instances where a subject should have chosen an angry face (based on the available utilitarian evidence) but chooses a smiling face instead. Thus we hope to elucidate the neural basis of conflict between social and utilitarian cues in decision-making.

34. Networks for integrating sensory evidence and value in the human brain

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In Bayesian models of perceptual decisions, a belief distribution over the stimulus is combined with the value of each outcome to yield a choice that maximises expected value. Psychophysical data demonstrates that value is integrated with an estimate of internal uncertainty to optimally guide perceptual decisions (Whiteley & Sahani, 2008). How this integration is implemented by the human brain is unknown.

We measured fMRI BOLD responses while inducing shifts in perceptual decision criteria through asymmetric value. We used a blend of house and face images in order to generate a full psychometric function between objects with known stimulus-selective activation profiles in inferior temporal cortex. Subjects were not informed of the image continuum, and were simply asked to categorise stimuli as either faces or houses. Asymmetric monetary losses were imposed for incorrect face and house decisions, varying on a trial-by-trial basis. This design allowed us to ask how value and uncertainty interact to alter people's perceptual decisions, and how these variables are encoded and integrated in the brain.

Behavioural results indicated shifts in the point of subjective equality as a result of asymmetric costs, as predicted by a Bayesian integration of value with sensory uncertainty. Functional imaging showed

stimulus-selective activations in bilateral FFA and PPA that correlated with choice probability for faces and houses, respectively. However, activity in these regions was invariant to increases in stimulus-specific value. Instead, both types of asymmetric value trials (face and house) revealed consistent activations in left inferior frontal sulcus, anterior thalamus and posterior parietal cortex (PPC). In contrast, a stimulus uncertainty regressor derived from psychophysical data showed positive correlations with activity in anterior insula and paracingulate, consistent with previous reports (Grinband et al., 2006). A preliminary analysis suggested that the interaction of uncertainty and value is expressed in a modulation of activity in PPC.

Together, these data point to a theoretical framework in which value and uncertainty are integrated within dissociable prefrontal and cortico-thalamic networks at a late stage of a perceptual decision hierarchy. This post-sensory integration of value in perceptual decisions may be adaptively advantageous, allowing action selection to be flexible in its usage of sensory evidence in different reward contexts.

35. Mixed Mode Oscillations and Canards in networks of piece-wise linear neural oscillations with gap junctions coupling

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A piece-wise linear model of the Fitz Hugh-Nagumo model that supports a Canard solution will be presented. Periodic orbits (both small and large amplitude) are obtained in closed form; For globally gap junctions coupled networks we show further how to study network solutions describing synchronous states. Importantly we will be able to analyse stability in the strong coupling regime. We need this analysis to explore the existence of Mixed Mode Oscillations and their dependence on system parameters; At the end, the importance of such Mixed Mode Oscillations in generating brain rhythms will be discussed.

36. Level response changes in IC: adaptation or instantaneous non-linearity?

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Recent work has demonstrated that the responses of non-linear systems can appear sensitive to changes in the stimulus statistics, even when the parameters of the underlying system remain constant. A Reichardt motion detector, for example, exhibits a form of dynamic gain control closely resembling the apparently adaptive behaviour of the H1 neuron in the fly visual system. In the auditory domain, neurons in the inferior colliculus (IC) of anaesthetised guinea pigs have been shown to adapt their response characteristics to the sound-level distribution of an amplitude-modulated noise stimulus. Specifically, the rate-level functions of these neurons change in a way that improves the population coding accuracy around the most commonly occurring stimulus sound levels. We asked whether, and to what extent, this stimulus adaptation in IC could be explained as an inherent effect of an essentially unadaptive but nonlinear system being probed with varying stimuli (as has been suggested for H1), or whether it is a

consequence of more slowly-acting adaptive processes in the system.

Following the former hypothesis, we first extended a parametric model originally proposed to characterize the responses of A1 neurons to short amplitude transients, so as to model the responses measured in the IC experiments. The longest membrane time constants in the model are on the order of 10 ms, much shorter than the duration of individual sound-level stimuli in the experiments (50 ms). Nevertheless, we found that for appropriate parameter settings, the rate-level functions obtained from the model were indeed sensitive to stimulus statistics, and in a way that closely resembled several key characteristics of the changes observed in IC. We then returned to the original data to quantify the relative contributions of the instantaneous effect of changes in the probe stimuli on the one hand and long term adaptive effects on the other. This analysis revealed a continuum of response characteristics: While instantaneous effects failed to account substantially for the observed changes in a majority of cells, we also found several cells for which the model provides a reasonable explanation as well as cases where cell responses seemed to be determined by both instantaneous and long-term adaptive effects.

Thus, although an established non-linear level-response model has the potential to reproduce the experimental findings, this mechanism alone does not provide a sufficient explanation. Firstly, we want to extend our simple model to incorporate slower adaptive processes. Secondly, we are going to apply our current analysis to similar data from IC neurons in the domain of interaural time differences.

37. Neural-mass modelling of spontaneous brain function

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Introduction There is a growing interest in the investigation of spontaneous brain function (SBF) using fMRI as a potential tool for exploring healthy brain function as well as for development of disease biomarkers.

A pair of features of SBF clearly stands out: Firstly, coherent spontaneous low-frequency (0.01-0.1 Hz) activity fluctuations (SLF) [1], and secondly, SLF coherence for specific large-scale networks of brain regions. We speak about functional connectivity (FC) between these regions.

Use of neural mass model to explore the possible mechanisms of SBF was adopted by Honey [2]. In our study we utilise less computationally demanding model allowing us to observe the behaviour for range of parameter settings. Two phenomena we focus on are FC agreement with underlying anatomical structural connectivity (SC) and frequency of SLF.

Materials and methods We use a connection matrix of macaque cerebral cortex comprising of 47 visual, sensory and motor areas linked by 505 pathways identified by anatomical tracing studies [3]. We diverge from Honey by employing a classical neural-mass model for the dynamics, connecting 47 Wilson-Cowan type with modules by excitatory-to-excitatory coupling employing sigmoidal firing rate function (model implemented in MATLAB, sampling rate 10 kHz, two different measures of FC, namely Pearson's correlation and transfer entropy [5] have been used).

Results We demonstrate that high FC/SC agreement depends critically on parameter settings of the model. In SLF investigation, spectrum of band-limited power signal did indeed show power in low-frequencies but not uniquely in the 0.01-0.1 Hz range as reported in fMRI and LFP studies [1], [4].

Discussion and conclusion The dependence of FC/SC agreement on model parameters outlines important consequences for studies of this type. Still, our model does not so far fully mimic the in vivo observed temporal scale low-frequency fluctuations which to our best knowledge have not been explicitly computationally modelled so far. Our next aim is to analyse the effect of heterogeneity in temporal scales of modules and non-binary connectivity matrix and to implement the between-module transmission delays. The ultimate goal is being able to make testable predictions on individual's resting state fMRI BOLD signal pattern using individual's DTI.

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38. What can place and grid cells tell us about the metric structure of the cognitive map?

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The neural encoding of place in mammals is supported by a network of structures in the limbic system including hippocampus and entorhinal cortex. Hippocampal neurons, called place cells, exhibit spatially localized firing fields and are collectively thought to form a map-like representation, the so-called “cognitive map.” More recently, it has been found that neurons in entorhinal cortex, afferent to the place cells, have multiple firing fields arranged in a spatially regular grid-like array. These “grid cells” may provide metric information to the place cells, and thus study of the properties of grids can shed light on the underlying metric structure of the cognitive map. In particular, the grid cells open up the opportunity to explore the encoding of complex, three dimensional spaces.

There are various forms of three-dimensional encoding that the cognitive map could theoretically incorporate, ranging from a completely flat representation containing no height information at all, through intermediates (e.g. contour map, slice map) to a fully three-dimensional, volumetric map. I will present data from our preliminary investigations into encoding of a partially three-dimensional space, the helical maze. On the helical maze, place cells show a sensitivity to height but grid cells, surprisingly, do not. This dissociation between place and grid cells will be explained in terms of a hypothesized modulation (by height) of the grid cell inputs to place cells. It suggests that the vertical dimension may be encoded differently from the horizontal ones, a possibility that is currently under investigation in a homogeneous, volumetric maze.

39. Selectivity for grasp in local field potential and single neuron activity recorded simultaneously from M1 and F5 in the awake macaque monkey

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The selectivity for object-specific grasp by local field potentials (LFPs) was investigated in two awake macaque monkeys trained to observe, reach out, grasp and hold one of six objects presented in a pseu-

dorandom order. Simultaneous, multiple electrode recordings were made from the hand representations of primary motor cortex (M1) and ventral premotor cortex (area F5). LFP activity was well developed during the observation and hold periods of the task, especially in the beta frequency range (15-30 Hz). Selectivity of LFP activity for upcoming grasp was rare in the observation period, but common during stable grasp. The majority of M1 (90/92) and F5 (81/97) sites showed selectivity at least one frequency, which was maximal in the beta range but also present at higher frequencies (30-50 Hz). When the LFP power associated with grasp of a specific object was large in the beta frequency range it was usually of low power in the higher 30-50 Hz range, and vice-versa. Simple hook grips involving flexion of one or more fingers were associated with large beta power, while more complex grips involving the thumb (e.g. precision grip) were associated with small beta power. At many M1 sites there was a highly significant inverse relationship between the tuning of spikes (including those of identified pyramidal tract neurons) and beta range LFP for different grasps, whereas a positive correlation was found at higher frequencies. High levels of beta LFP and low pyramidal cell spike rate may reflect a common mechanism used to control motor set during different types of grasp.

40. Modularisation through the lense of Shaping

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An important solution to the problem of acquiring temporally and structurally rich and complex cognitive capabilities is modularization, or divide and conquer. We, and indeed other species, are able to learn simple elements and recombine them in multifarious ways in order to address sophisticated challenges. However, despite some important suggestions, most computational models have focused on uniform, rather than modularized learning, that is, taking on the full complexity of tasks starting from a naive state. Not only does this make learning of a single problem more difficult, but it also fails to generate sub-solutions that can be re-used later. Evidence for the nature and importance of modularity comes from the behavioral procedures used for training subjects to solve complex tasks. Subjects are shaped, i.e., are led step-by-step to acquire elemental sub-components before being presented with full tasks.

Previously, we used a computational model to elucidate shaping's substantial beneficial effects on learning. We demonstrated this in a hierarchical, conditional one-back memory-based cognitive task called 12-AX, which we continue to employ here. However, in that study, we solved by hand one of the critical problems in making shaping work, namely the allocation mechanism that creates new network resources for each stage of shaping. Here, we explore algorithmic replacements for this homunculus which are based on ideas about the cortical and subcortical processing of surprise. Changes in tasks over the course of shaping can be detected based on sudden increases in the observed error (a form of unexpected uncertainty); this provides a signal that new resources should be allocated. We show that a mechanisms based on this can allow shaping to work well for standard learning; in certain cases such as reversal learning can even out perform the manual allocation previously employed.

41. Clustered connections within the intrinsic circuitry of extrastriate area V5/MT in the rhesus macaque

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The middle temporal (V5/MT) visual area of the macaque monkey is specialized for visual motion and binocular depth. From single unit studies, V5/MT has been proposed to have a columnar organization for direction of motion (Albright et al, J Neurophysiol 51:16-31, 1984) and a clustered organization for binocular disparity (DeAngelis et al, J Neurosci 19:1398-415, 1999). Although connections to and from V5/MT to cortical and subcortical areas have been identified anatomically, the intrinsic columnar organization has been difficult to define anatomically in the rhesus macaque. Using small tracer injections into area V5/MT, we have revealed a clustered pattern of intrinsic connections within area V5/MT.

In anaesthetized macaques (Sufentanil, i.v., and 0.3-0.5% Isoflurane), we recorded neuronal activity with a tungsten electrode attached to a glass capillary tube containing the tracer, Cholera Toxin subunit b (CTb, 1% low salt soln, List Biological Labs). V5/MT was identified based on stereotaxy, sequences of grey and white matter on approach, and receptive field properties (e.g. size and direction tuning). We pressure injected 50-100nl of CTb at neurophysiologically identified sites within V5/MT in three animals. After 48-72 hours, animals were perfused and the tissue processed. Parasagittal sections were stained with SMI-32 antibody and Gallyas to confirm the location of V5/MT, and were histologically examined for CTb labelled cells. Labelled cells were drawn and analysed using Neurolucida (Microbrightfield Ltd).

Labelled cells were found within layers 2, 3, 4 and 6, extending throughout most of the dorso-lateral extent of V5/MT (12 mm), with a clear gap between superior and inferior layers. In the latero-medial axis, labelled cells were found up to 2 mm on either side of the tracer injection. Inspecting the parasagittal sections, we found a clustered pattern of labelled cells on both sides of the injection site and in sections medial and lateral to the injection site. We observed between 1-3 such clusters in most sections. We also analysed the pattern of label quantitatively in two hemispheres from two monkeys. We carried out a Fourier analysis and an autocorrelation analysis on the density of labelled cells along layer 6 and layers 2-4, separately within each section. The analysis confirmed clusters of labelled cells at 1-2 mm intervals. We conclude that V5/MT has a distinct local circuitry of connections, both within the superior layers and in layer 6.

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42. Chopper responses to amplitude-modulated tones: stochastic mode-locking theory and observed spiking patterns?

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Responses to amplitude-modulated pure tones have been used extensively to assess temporal properties of neurons across the auditory system. The synchronisation to the modulation frequency has mostly been measured by an index called vector strength. This index is based on the distribution of spikes along the

period of modulation. One obtains a low value when the spikes occur evenly across the period and a high value when they are sharply distributed around a single time. In the ventral cochlear nucleus, chopper units have been found to show band-pass temporal responses at high sound pressure level and low-pass temporal responses at low level. However, the fine structure of the responses remains uncharacterised.

Here, we show that data obtained from chopper neurons in response to amplitude-modulated tone exhibit more complex synchronised discharge patterns, reminiscent of mode-locked states. These responses can be organised around an Arnol'd tongue structure of a periodically forced model accounting for the sub-threshold properties of the T-multipolar cells. Numerical simulations of a stochastic version of this integrate-and-fire model give response patterns similar to the one observed experimentally. Thus, the results tend to show that care should be taken when considering the temporal properties of a neuron only on the basis of its vector strength.

43. Random networks exhibit instantaneous correlations of excitation and inhibition as observed in cortex

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Cortical neurons are driven by both excitatory and inhibitory sources, and an increasing amount of evidence suggests that this excitation and inhibition is tightly balanced. Can such a balance be explained by simple, static mechanisms, as predicted by models of random networks? A recent *in vivo*-study (Okun & Lampl, *Nat. Neurosci.* 11, 535-537, 2008) found almost instantaneous correlations of excitation and inhibition in pairs of cortical neurons, seemingly contradicting random models and calling for continuous control with millisecond precision. Motivated by insights from mean-field theory, we investigated the question whether the dynamics observed in cortex are compatible with simple models of random networks.

We simulated a minimal model of an unstructured cortical column consisting of two populations, one excitatory and one inhibitory, and excitatory input from an external source. We chose the quadratic integrate-and-fire neuron model with conductance-based synaptic dynamics. Neurons were connected randomly with 10% connection probability and synaptic strengths were chosen within a physiologically realistic range.

When the model network was left without external input apart from brief bursts of variable strengths, we observed excitatory and inhibitory dynamics similar to those reported in the *in vivo*-study.

Specifically, both the size of the cross-correlations and the time-lag between excitation and inhibition were in close agreement with experimental values. In our model network, as in cortex, inhibition lags excitation by several milliseconds when measured via the position of the peak in the cross-correlogram. We find that the position of this peak is insensitive to the size of the synaptic time constants, while the width of the cross-correlation increases with increasing synaptic time constants.

Our results demonstrate that instantaneous correlations of excitation and inhibition in cortical networks do not require precisely timed control mechanisms. Rather than invalidating models of random networks, as previously suggested, recent data obtained from intracellular pair-wise recordings *in vivo* provide additional support to the notion that simple random models can capture essential aspects of cortical dynamics. Since entirely random networks do not support functional roles, our results highlight the fact that precise timing does not constitute evidence for temporal coding mechanisms.

44. Stimulus-specific adaptation occurs in neurons of the medial but not ventral auditory thalamus

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Neurons in the primary auditory cortex respond more strongly to a rarely presented "deviant" tone than to the same tone when it is common, or "standard" (Ulanovsky, Las and Nelken, 2003; Ulanovsky, Las, Farkas and Nelken, 2004). This phenomenon, called "stimulus-specific adaptation" (SSA), has been proposed as a possible single-neuron correlate of the mismatch negativity (MMN), a cortical evoked potential associated with stimulus novelty. Previous studies in cat have suggested that SSA is absent from single neurons in the auditory thalamus (Ulanovsky et al. 2003, Ulanovsky et al. 2004); however, these reports did not differentiate between the auditory thalamic subdivisions. To explore the possibility of thalamic SSA more completely, we recorded extracellularly from 30 single units and 22 multiunit clusters in the ventral, medial, and dorsal subdivisions of the mouse auditory thalamus, while presenting the anaesthetised animals with sequences of standard and deviant tones. As in the cat studies, standard and deviant tone frequencies were separated by no more than 0.5 octaves, and evoked similar responses in most neurons. Using stimulation rates of 1.25 - 2.5 stimuli/s, we found SSA in neurons in the medial subdivision of the mouse auditory thalamus, but not in the ventral subdivision. The median neuronal stimulus-specific adaptation index (defined as in Ulanovsky et al. 2003) was significantly greater than zero in the medial subdivision at all stimulation rates tested (sign-rank test, $p < 0.05$), but was not significantly different from zero in the ventral or dorsal subdivisions for any of the tested stimulation rates. A smaller sample from the dorsal subdivision ($N = 13$ dorsal, compared to 20 medial and 19 ventral) also showed no significant SSA. Our results indicate that SSA does occur in the auditory thalamus, but only in the medial subdivision. Together with related findings of SSA in neurons of the "belt" regions of the inferior colliculus (Perez-Gonzalez, Malmierca and Covey, 2005), the results suggest that SSA is either a general property of some neurons in the non-lemniscal auditory system, or a cortical phenomenon that influences subcortical auditory processing only within the non-lemniscal pathway.

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45. Simultaneous magnetoencephalography and subthalamic local field potential recordings in Parkinson patients

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Insight into how brain structures interact is critical for understanding the principles of brain function and may lead to better diagnosis and therapy. To study interactions between the cortex and deep brain

structures (basal ganglia and the thalamus) we recorded, simultaneously, local field potentials (LFPs) from deep brain stimulation (DBS) electrodes and magnetoencephalographic (MEG) signals from the cerebral cortex (CTF 275 channel system) from Parkinson's disease (PD) patients with bilateral DBS electrodes in the subthalamic nucleus (STN).

High-amplitude artefacts in the MEG, originating from slight movements of ferromagnetic parts of the electrode, pose a challenge to conventional analysis methods. However, we developed several methods capable of extracting physiologically meaningful patterns from the data.

We studied the patterns of coherence and directed coherence at rest between STN-LFP and MEG. Coherence patterns observed between 5 and 45 Hz varied in their topography between subjects. This variability can possibly be related to phenotypic differences among our patients.

We also examined movement-related spectral changes in STN and cortical sensorimotor areas. Our preliminary results show that task related changes at either cortical or STN level can influence the partner structure, offering an explanation of why neuromodulation at either level may potentially be effective.

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46. Octopamine and state-dependent coding properties of optic-flow processing cells in the blowfly visual system

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How is visual information processing related to the mode of locomotion? We may expect the state of locomotion, e.g. walking or flying, to impose different requirements on information processing regarding bandwidth, control system time constants and energy expenditure. We have explored the effects of Octopamine (OA) receptor activity, a putative component of the flight state, on information processing in the blowfly, *C. vicina*. OA is an invertebrate neurotransmitter, neuromodulator and neurohormone associated with "fight or flight" responses in many species. OA haemolymph levels are elevated during flight in the cricket and locust, and the highest density of OA receptors is found in the optic lobes in the locust. We recorded extracellularly from spiking V1 and V2 cells, which belong to a population of motion-sensitive cells in the fly lobula plate. Both are most sensitive to vertical motion presented in the ipsilateral visual field and receive weaker input from the contralateral eye. We used periodic gratings to determine the directional tuning curves at specific locations in the cells' receptive fields. The OA agonist chlordimeform (CDM) was applied, at a concentration of $2.6\mu M$, high enough to significantly elevate the spontaneous spike rates of the cells. CDM increased the V1 cell spontaneous spike rate by a factor of 2.9, from 10.4 ± 4.3 Hz to 27.0 ± 6.4 Hz, and the V2 cell activity by a factor of 2.3, from 7.3 ± 3.4 Hz to 16.4 ± 5.6 Hz. CDM also elevated the information rate at which the direction of motion is encoded in both cells. We present increases over time windows sufficiently long to ensure significant non-zero increases. The V1 cell's information rate was boosted by 55% over a 50ms window. The V2 information rate was increased by 24% over a 100ms window. Gains in the modulation depth of the directional tuning curve were offset by simultaneous increase of the response variabilities. The elevated spontaneous activity, however, allows both neurons to express more information about motion in the anti-preferred direction. CDM also decreased the mean response delay of the V2 cell by 6.0% from 23.4ms to 22.0ms, and that of the V1 cell by 4.4% from 21.4ms to 20.45ms. Our findings suggest that OA adapts the system to the higher dynamic range of stimuli during flight as opposed to walking by i) shortening the neural response delay, ii) elevating the spontaneous activity for a more efficient use of the negative response range and iii) increasing the modulation depth of the directional tuning curve. The higher efficiency in neural processing is reflected by an increase of the information rate for coding directional motion and comes at the expense of an increased metabolic cost.

47. The opposite of crowding revealed using classification images

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When a peripherally viewed stimulus is presented with flankers, observers' discrimination thresholds usually increase. We wondered whether a change in the locus of information accrual accompanied these performance deficits and employed psychophysical reverse correlation to find out. Surrounding the target with a vertical grating caused a slight elongation and a rotation in the decision templates for orientation identification. We also found that the contrast required to maintain criterion performance in this condition was actually lower than it was in a target-alone condition. However, this facilitation decreased with practice, due to perceptual learning in the target-alone condition. Unlike the surround, individual flanks elevated contrast thresholds, but decision templates were similar with both of these contexts. The rotation of decision templates (off-orientation looking) suggests that performance is limited by additive internal noise. We speculate that this noise can be reduced when the target is easily segregated from its surround.

48. Neural correlates of visual afterimages

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Human visual perception of prolonged, static stimuli has been extensively investigated psychophysically, and yet the underlying neuronal activity remains largely unknown. Consider two simple examples. An image stabilised on the retina will be perceived to fade over the time course of several seconds. Conversely, following fixation of an image for several seconds, its removal will leave the subject with the perception of a negative afterimage. Along with a host of more elaborate visual aftereffects (including illusory figural, motion and contingent aftereffects), these phenomena can yield important clues to both the circuitry and functional activity at multiple stages of visual processing. However, a direct investigation of neuronal responses in this context is lacking.

We recorded extracellularly from the LGN and V1 in the anaesthetised, paralysed macaque, presenting both optimal sinusoidal gratings ("preferred") and the opposite contrast gratings ("anti-preferred") for varying amounts of time (1 to 64 s), followed by mean gray epochs.

In the LGN, P-cells showed a strong response which decayed exponentially (mean τ of ~ 20 s) to both onset of the preferred stimulus and the offset of the anti-preferred stimulus. Indeed, after repeated presentation of the anti-preferred grating over the course of several minutes, cells responded as strongly to the mean gray screen at stimulus offset as they had previously to the onset of the preferred stimulus. The build-up and decay of these after-responses was well fit by a simple exponentially adapting model. M-cells showed a different pattern of activity. In response to the preferred stimulus, they showed a strong response with both sustained and decaying components. However, the after-response at anti-preferred stimulus offset was always much less than the response to the preferred stimulus. We hypothesise the existence of an adapting element which is specific to the circuitry of the P-pathway.

In V1, we recorded the responses of orientation-tuned cells and found a strikingly different pattern of behaviour. Relative response amplitudes were somewhat scattered, with some cells responding more to the preferred stimulus, and others to the anti-preferred stimulus offset. However, after-response time constants were generally much shorter than those recorded in the LGN. The average response to anti-preferred stimulus offset decayed to baseline with τ of 1.3 s. Thus a second important question about visual pathway circuitry emerges: where and what is the gating mechanism which cuts short

after-responses in V1 relative to the activity in LGN?

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49. Effects of I_h on electrophysiological and synaptic properties of interneurons of the CA2 region of the adult rat hippocampus

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The CA2 subfield, if considered at all, has been seen as a transitional zone between CA1 and CA3. It is, however, the only CA region receiving direct input from the supramammillary body, indicating a role for this subfield in the generation of theta rhythms. Moreover, its direct inputs from entorhinal cortex and amygdala can directly activate CA1 independently of the CA3 subfield and in parallel with the trisynaptic pathway. In addition, CA2 is resistant to temporal lobe epilepsy, but exhibits particular interneuronal loss early in the onset of schizophrenia. The most thoroughly studied CA2 interneurons, the basket and bistratified cells, display striking features that are quite distinct from those of their equivalents in CA1, ie. spiny horizontal dendrites, a pronounced "sag", indicative of I_h , in response to hyperpolarising current injection and they receive facilitating EPSPs from neighbouring pyramidal cells. Dual intracellular recordings were performed in CA2 to investigate the contribution made by I_h to the electrophysiological and synaptic properties of these cells. The "sag" seen during negative current injection in CA2 interneurons was completely blocked after 25 min exposure to the I_h blocker ZD7288 and hyperpolarised the cells, resulting in an increase in spike threshold. ZD7288 produced only a small decrease in the amplitude and an increase in the duration of EPSPs, and however no change in paired pulse ratios. CA2 interneurons also presented a higher level of spontaneous synaptic activity after application of ZD7288.

50. 3D current flow in a large scale model of the cochlea and the effect of mutations on sound transduction

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Sound perception is facilitated by mechano-electrical transduction in the hair cells, sensory cells of the cochlea of the inner ear. The transduction is brought about by the sound-induced potassium influx, which induces changes in membrane potential facilitating neuronal encoding of incoming sound.

Here we present a large scale computational model of potassium circulation in the cochlea. The cochlea is in the model split longitudinally into 300 sections and each section divided into 6 compartments (scala media, inner hair cell (IHC), outer hair cell (OHC), extracellular space near IHCs, extracellular space near OHCs and stria vascularis). This semi-cellular network is described as an equivalent three-dimensional electrical circuit of resistors, capacitors and batteries and the flow of potassium ions is treated as electrical current. The sound-induced potassium influx into hair cells is represented by variable resistors realistically reflecting the cochlear macromechanics. The MATLAB simulations describe the dependence of the electrical potentials of hair cells, governing sensitivity and frequency selectivity of transduction process, on the frequency of sound.

As the model is based on the molecular potassium circuits in the cochlea it allows the assessment of how do mutations in the potassium-transport related genes affect the electrical properties of hair cells and

thus the sound transduction. The model was used to analyse the role of mutations in gap junctions, the most common cause of deafness, and potassium transporters, also known to be involved in some hearing impairments. The simulations indicate that reduced conductivity due to these mutations decreases the hair cells electrical potentials at high frequencies, compromising the sensitivity and frequency selectivity. Thus, gap junctions related forms of deafness can be explained by a decreased recirculation of potassium ions in the cochlea. This computational-based approach could serve as *in silico* platform for understanding the effect of gene mutations on the function of the cochlea.

51. Learning in the Context of Change-based Inference

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We have recently investigated a new way of conceptualizing the inferential capacities of non-linear recurrent networks in terms of the change in a statistic of the population activity over the time since a stimulus is presented. Evaluating change allows inferences to be fast, relatively insensitive to noise, and, in suitable cases, invariant to irrelevant dimensions of the stimulus. We proved the technique in the context of the bisection task, which is a popular psychophysical testbed for visual hyperacuity, using recurrent weights whose values were determined by hand.

One central observation was that a wide range of structurally different sets of recurrent weights supports near-optimal behaviour. This suggests that a learning algorithm could work well. Here, we show the power of using backpropagation-through-time algorithm (BPTT) to learn weight matrices to solve the task, where we evaluated the change in the location of the centre of mass (in visual space) of the network over the course of one, discrete, iteration. We directly imposed the obvious prior constraint of translation invariance.

BPTT was readily able to find many appropriate sets of recurrent weights that perform near-optimally; different initial conditions lead to different weights. This breadth demonstrates the benefits of an appropriate computational representation of the task. We are presently analyzing how the network performs this inference in a highly non-linear regime, far from equilibrium.

52. How do we perceive regularity in textures?

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We measured the just-noticeable difference (JND) in orientation variance between two textures (Fig. 1) as we varied the baseline (pedestal) variance present in both textures. JND's first fell as pedestal variance increased and then rose, producing a 'dipper' function similar to those previously reported for contrast, blur, and orientation-contrast discriminations. We show that a dipper function (both facilitation and masking) is predicted on purely statistical grounds by a noisy variance-discrimination mechanism. However, for two out of three observers, the dipper function was significantly better fit when the mechanism was made incapable of discriminating between small sample variances. We speculate that a threshold non-linearity like this prevents the visual system from including its intrinsic noise in texture representations, and suggest that similar thresholds prevent the visibility of other artifacts that sensory coding would otherwise introduce, such as blur.

53. Optimal control predicts human performance on objects with internal degrees of freedom

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Humans regularly interact with objects with internal degrees of freedom from carrying a cup of coffee to folding a shirt. While objects with no internal degrees of freedom can be regarded as a fixed extension of our limbs, non-rigid objects pose a more complex control problem. In recent years stochastic optimal feedback control has emerged as a framework for human motor coordination. Optimal control has been used to explain average movement trajectories as well as trial-by-trial variability in a wide range of motor behaviours, such as obstacle avoidance and bimanual coordination. In this study, we investigated whether the optimal control framework can be extended to object manipulation with internal degrees of freedom and whether it can account for the complex behaviour necessary to control such objects. We used a virtual reality set-up together with a vBOT robotic interface to simulate the dynamics of a virtual object attached to the subject's hand (for details see Koerding et al., 2004). Subjects started with both hand and object aligned in the starting position and were required to move both the hand and object to the target position within a certain time window that was reduced during training down to 0.8 - 1.2 s. As a prototypical object with internal degrees of freedom, the object was simulated as a damped mass, attached to the hand by a spring. However, we created six different complex dynamic objects by introducing anisotropies for the mass, viscosity and spring constant matrices (such as x-y dependencies and a velocity-dependent rotational force field applied to the mass). Subjects ($n = 6$) learned to control the six different mass-spring objects until they achieved 25% correct trials. Positional data and forces were recorded at 1000 Hz and the last 25 successful trials were analysed. We used an optimal control model based on the model proposed by Todorov & Jordan (2002) and included the dynamics of the different mass-spring-damper systems. Our optimal control model predicted complex hand trajectories such as loops and s-shaped curves, which deviate substantially from the straight hand paths seen during normal reaching movements. Experimental performance of subjects was well fit explaining 83 - 97% of the variance in all conditions. The results suggest that the framework of optimal control can be extended to manipulation of objects with internal degrees of freedom and underline the generality of the optimal control framework as a theory of motor coordination.

54. A Model of a CA3 Hippocampal Neuron Incorporating Channelrhodopsin-2 Light Gated Ion Channels

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The possibility of use of light sensitive proteins, such as channelrhodopsin-2 (ChR2), for the excitation of neurons is opening up a new field in neuroscience. The activation of genetically-encoded ChR2 molecules depolarizes neurons in response to blue light. These ion channels spontaneously close down after about ten milliseconds. In order to simulate the generation of action potentials in these cells we have developed a Matlab code based on the CA3 Hippocampal neuron models available in the open literature [Traub

et.al. (1991), Migliore et.al. (1995)] and our models for the ChR2 photo-current kinetics [Nikolic et.al. (2008)]. The results of simulations are compared with our experimental results. Very precise patterns of action potentials can be created using this tool, however there is currently an upper limit of how fast the cells can be driven with this current, which is around 40Hz. Our model allows us to get a better insight into the dynamics of the action potentials generated by light and to identify possible improvements in the stimulation patterns.

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Nikolic, K. et.al. (2008), submitted to Biophys. J.

55. When is foveal 'crowding' abnormal?

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Clinical tests of visual acuity (VA) that employ multiple, neighbouring optotypes assume that visual 'crowding' at the fovea is negligible. Findings from recent studies suggest that crowding effects can affect high contrast acuity thresholds at the fovea. The absence of data to describe the distribution of crowding effects within 'normal' vision makes it difficult to establish when a measured reduction in VA (with crowding) can no longer be considered to be within the normal range and is therefore indicative of abnormal development or pathology. The aim of this study was to quantify the effects of crowding on VA in the normal population. We measured acuity thresholds, with and without crowding, in central vision (i.e. at the fovea and at 1°, 1.5°, and 2°) in eighty normal subjects with the age range of 29.3 ± 10.7 years. The statistical distribution of the differences between the two measures of VA shows significant crowding effects at the fovea that increase linearly with eccentricity and provides a useful template to identify those subjects that show abnormal sensitivity to crowding.

56. Sensory coding by spatial patterns of cerebellar Purkinje cell complex spikes

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Climbing-fiber-evoked complex spikes in cerebellar Purkinje cells tend to be locally synchronized. What is the role of this synchrony in the encoding and processing of sensory information within the olivocerebellar cortical circuit? We used in vivo two-photon calcium imaging, together with an information-theoretic data analysis technique, to investigate this question. Our results showed that spontaneous synchrony falls off over hundreds of microns mediolaterally between individual Purkinje cells. The synchrony we observed was increased following administration of harmaline, in accord with an olivary source. We were able to elicit calcium transients in cerebellar region Crus IIa by peri-oral stimulation, observing that a periodic train of airpuff stimuli resulted in entrainment of calcium transients. Periodic sensory

stimulation also resulted in a transient modulation of synchrony following stimulus onset. Conjecturing that this stimulus-dependent synchrony might be the signature of a spatial pattern population code, we analysed the information content of the complex spike population code, as reflected by calcium events, about stimulus timing. We found that spatial patterns of calcium events from up to seven cells provided on average 59% more information than that available by counting the number of events across the pool. The olivocerebellar feedback circuit thus may act to correct sensory error on a signal represented by, rather than single-neuron responses, the spatial pattern of activity in a local pool of climbing fibers.

57. Phasical activation of serotonin dorsal raphe neurons by nociceptive stimuli

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Serotonin neurons play a central role in a variety of behavioural and cognitive functions, particularly in processing aversive stimuli. It has been suggested that serotonergic dorsal raphe neurons may encode a prediction error rule for aversive stimuli and act as an opponent system to the midbrain dopamine system, which encodes a prediction error rule for appetitive stimuli. We examined the hypothesis whether nociceptive footshocks phasically activate neurochemically-identified serotonin neurons in the dorsal raphe nuclei.

In the past, serotonin neurons were typically identified by their physiological properties: Serotonin neurons fire in a slow clock-like pattern and have broad action potentials. Recent studies using juxtacellular labelling demonstrated that not all of these presumed serotonin neurons were 5HT-positive. Therefore, we combined electrophysiological recording and the juxtacellular labelling method to identify the neurons. We recorded from neurons within the dorsal raphe nuclei in anaesthetised rats. During the recording nociceptive footshocks were administered, and then the individual neurons were labelled juxtacellularly, and then identified by immunohistochemistry.

Results showed a variety of different neurons within the dorsal raphe nuclei, which can be grouped due to their electrophysiological and histological properties. Group I consists of 5-HT-positive cells with typical clock-like firing that were phasically activated by the footshocks. A second group included 5-HT-positive neurons that were either inhibited or showed no reaction to the footshocks. A majority of these showed stereotypic bursting pattern. The last group contains 5-HT negative neurons, which showed ambiguous reactions to the administration of nociceptive stimuli.

This study gives evidence that at least some serotonergic dorsal raphe neurons are phasically activated by nociceptive stimuli.

58. Increased sensitivity to positive feedback in stochastic sequence learning in medicated patients with Parkinson's disease

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OBJECTIVES: A growing body of evidence suggests that dopamine plays a key role in reinforcement learning. Animal studies have shown that phasic bursts of dopamine neurons are observed after reward, whereas the firing of dopamine neurons drops below baseline after choices that do not result in reward. Therefore, disruption of the midbrain dopamine system as in Parkinson's disease (PD) may lead to deficits on tasks that require learning from positive and negative feedback. Previous studies have shown that in a probabilistic selection task and a transitive inference task, learning from positive or negative feedback is differentially affected by PD and the dopaminergic medication used to treat it. However, previous studies have not directly examined these effects during learning, but rather have shown deficits after learning during transfer. The aim of the present study was to examine stochastic sequence learning in PD patients.

METHODS: A group of medicated PD patients and age-matched healthy controls were assessed. Participants were required to learn sequences of four button presses, where each button press was performed either with the left or right index fingers. We used six sequences in the task, each of which had two left and two right button presses. After each button press, participants received feedback whether or not it had been correct. Importantly, the feedback was noisy (85% correct feedback). Thus, on 15% of the trials, even if the participants had pressed the correct buttons, the feedback informed them that they were incorrect. Their task was to use this 'noisy' feedback to learn the correct sequence of button presses and then repeat it eight times. After participants had executed the sequence correctly eight times, a new sequence was introduced and the participants once again had to learn the new sequence by trial and error. We used a randomized block design with eight blocks in total.

RESULTS: Both medicated PD patients and age-matched controls were biased to preferentially learn from positive feedback relative to negative feedback. Although the medicated PD group required more trials to learn the sequences they showed an enhanced learning effect from positive feedback relative to the control group.

CONCLUSION: Our finding that medicated patients with PD showed increased sensitivity to positive feedback in stochastic sequence learning, may reflect a dopamine 'overdosing' effect in the fronto-striatal circuits which are less affected in PD. Future assessment of stochastic learning in PD patients in the "off" medication state would be of interest.

59. A visual search asymmetry for bandlimited Gaussian curvature

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Search asymmetry is a litmus test for basic visual features. The letter Q is thought to contain a basic feature because i) it can be found quickly, no matter how many Os it is hiding amongst and ii) it is much harder to find an O amongst Qs. When two orthogonal Gabor patterns have the same spatial frequency, their sum can be found quickly, just like the letter Q. This sum is often called a plaid and it contains regions of both high and low Gaussian curvature, which are thought to automatically attract attention. I can now confirm that 4-cycle/degree Gabors do not pop-out from plaids of the same frequency. This result supports the notion that these plaids contain a basic visual feature. However, 2-cycle/degree Gabors do pop-out from 2-cycle/degree plaids. Do 2-cycle/degree Gabors contain a basic visual feature that is absent from 2-cycle/degree plaids?

60. Spiking neural network simulation: hybrid system integration with the Parker-Sochacki method

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Mathematical neuron models can be described as hybrid discrete/continuous systems, with the continuous part of the system being expressed as differential equations (Brette et al., 2007). The Parker-Sochacki (PS) method is a new technique for the numerical integration of differential equations that works by iteratively computing the Maclaurin series for each variable in a system of polynomial equations.

We applied the Parker-Sochacki method to two neuron models: the Izhikevich ‘simple’ model and a Hodgkin-Huxley (HH) type neuron. The Izhikevich model (Izhikevich, 2003, 2007) is a two variable, phenomenological neuron model, featuring a quadratic membrane potential and a linear recovery variable. The Izhikevich model neuron is capable of a rich dynamic repertoire; it is the simplest model capable of spiking, bursting, and being either an integrator or a resonator (Izhikevich, 2007). Since the model equations are polynomial, the PS method can be applied directly here. We show that effective adaptive error control can be achieved by locally adapting the solution order without employing adaptive stepsize control. Using this approach, we develop an adaptive-order solution algorithm for the Izhikevich model that solves for exact (floating point) spike times despite using large fixed time steps. Exact synaptic event times are also accommodated.

HH models feature equations that are not polynomial. Taking the HH model from (Brette et al., 2007) as an example, we show how to employ variable substitutions to arrive at a system solvable using the PS method. Furthermore, we demonstrate that equations featuring rational functions and compositions thereof are also solvable using the PS method. The solution algorithm features adaptive order processing and exact synaptic event times.

Benchmark simulations test our PS algorithms against the Bulirsch-Stoer (BS) and 4th-order Runge-Kutta (RK) methods. The Izhikevich network model is based on Benchmark 1 from Brette et al., (2007). It features 4000 cells (80% excitatory, 20% inhibitory) randomly (2%) connected via conductance-based synapses. Using a quantitative measure of accuracy, and taking performance as accuracy/CPU time, the PS method performs 2.6 times better than RK and 22.1 times better than BS.

The HH model benchmark simulations expose a single neuron to sequences of synaptic inputs recorded during Izhikevich model simulations. Using a similar quantitative measure of performance, the PS method performs 71.3 times better than RK and 9.6 times better than BS here.

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61. Dendrodendritic junctions and their effect on network rhythms.

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Dendrites are the main site for synaptic input to neurons. They are usually considered as pure post-synaptic elements that serve as a spatio-temporal filter for the synaptic input to the soma. This is not the whole story however, as dendrodendritic junctions have been shown to be prominent in some brain areas, for example the olivocerebellar system [Zeeuw et al., 1997] and the olfactory bulb [Christie and Westbrook, 2006]. These junctions mean that the dendrites of cells function as both post and pre-synaptic elements simultaneously. Here we consider a network of gap-junction coupled passive dendrites, each possessing an active spiking soma. Specifically we model a dendrite with the cable equation and

a soma with the piece-wise linear models, so that the network model is analytically tractable. These piece-wise linear models are capable of capturing both Type I and Type II behaviour. The dendrites are modelled as a chain of passive compartments on which a gap-junction is placed.

Earlier work by Nadim and Golowasch has already uncovered the effect of changing cable diameter on signal transmission between dendrites with gap-junctions [Nadim and Golowasch, 2006]. Here we focus on the emergent network rhythms resulting from information flow both to and from an active soma in a network with gap junctions between dendrites.

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62. Interpreting Neural Dynamics in the Brain with Partial Directed Coherence

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Monosynaptic projections from the hippocampus to medial prefrontal cortex (mPFC) are thought to be involved in regulating working memory. The neural dynamics of this connectivity were compared in vivo under control conditions and after kainic acid (KA) administration, using partial directed coherence analysis (PDC).

PDC is a statistical technique based on autoregressive modeling of multivariate time series in conjunction with the concept of Granger Causality and provides clues to directional connectivity and magnitude of information flow between neuronal ensembles. Hippocampal and mPFC local field potentials (LFPs) were recorded in isoflurane-anaesthetised rats with a 16-wire micro-electrode array and an 8-wire micro-electrode bundle respectively. Separate groups of rats were administered KA or received no drug treatment. PDC was applied to LFP data in animals with confirmed dorsal hippocampal and mPFC placements.

In the control group, PDC detected a stronger flow of information from lateral to medial hippocampal sites and from mPFC to the hippocampus. KA disrupted this directionality in the hippocampus, but did not alter directionality between mPFC and the hippocampus. These results suggest that a significant flow of information also occurs in the mPFC-to-hippocampus direction, and that acute-elevated neuronal activity, induced by KA administration, does not disrupt this inter-regional connectivity.

63. The neural correlates of a three-element alignment task: visuospatial interpolation in the absence of explicit local orientation cues

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There is a wealth of literature on the role of relatively short-range interactions between low-level orientation-tuned filters in the perception of discontinuous contours. However, little is known about how spatial information is integrated across more distant regions of the visual field in the absence of explicit local orientation cues, a process referred to here as visuospatial interpolation. One possibility is that the relative position of stimulus elements is encoded in the form of covert oculomotor plans in the eye movement control networks. To examine this hypothesis we used high field functional magnetic resonance imaging to study brain activity while observers either judged the alignment of three Gabor patches by a process of visual interpolation, or discriminated the orientation of the individual patches. Compared to the orientation discrimination, the interpolation task did not evoke activity in areas associated with eye movement control; instead, activity was restricted to a region that coincides with previous reports of the lateral occipital complex, an area implicated in the perception of form and illusory contours. In contrast, the orientation task, which involves visuospatial processing but no interpolation across space, evoked activations that included caudal regions of the intraparietal sulcus, an area characterised by sensitivity to surface orientation and object rotations. These results do not support a role for a covert oculomotor strategy during spatial interpolation, but instead, hint at a possible commonality between the processing of discontinuous contours and the encoding of relative position during an interpolation task.

64. The influence of the reactivity of the electrode-brain interface in therapeutic deep brain stimulation

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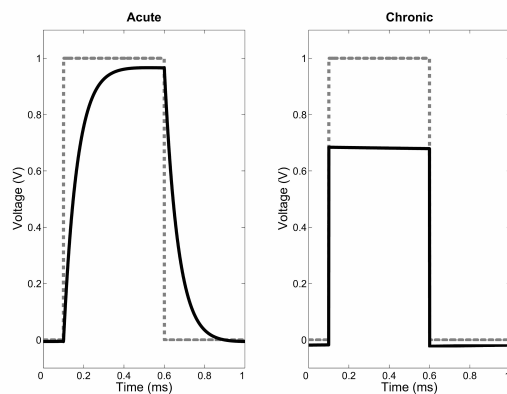
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Deep brain stimulation (DBS) is a therapy for treating a number of neurological and psychiatric disorders. The treatment involves the implantation of quadripolar electrodes into condition-specific targets in the human brain and injecting electrical pulses across a depth electrode brain interface (EBI). In our previous work (Yousif et al., 2007; Yousif et al., 2008) using a static finite element method (FEM) model solving the Laplace equation, it was revealed that the resistance of the depth EBI which changes over time post-implantation, has a significant effect on the electric field induced in the surrounding neural tissue. In the present study, we extend our previous EBI model to look at the influence of frequency dependent reactivity of the EBI on the time-varying induced potential distribution, by using an approach which combines a complex FEM model with Fourier analysis. The main finding of the present study is that, once the electric pulses pass through the peri-electrode space the pulse waveform is distorted, and this distortion is different with changing biophysical properties of the EBI over distinct post-implantation stages. In particular during the acute stage, the interface of lower reactivity behaves similarly to a

low-pass filter, and distorts the fast rise and fall of the square pulse; whereas in the chronic stage the stimulating amplitude of the square pulse is reduced $>30\%$ by the interface of higher reactivity, and this amplitude slightly falls off during the plateau phase of the waveform (Figure). This indicates that the reactivity of the EBI significantly influences the stimulus waveform in the time domain. In conjunction with our previous studies, we conclude that to make accurate predictions of the stimulation-induced current distribution in the human brain using FEM structural models, both the resistive and reactive components of the EBI need to be taken into account.

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The voltage waveform in the tissue (solid black line) is distorted from the original waveform (dashed grey line), but in a strikingly different way in acute and chronic post-implant stages.

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