Poster (Session D) Zodiac Room

(D1) Risk-sensitivity in motor learning

Alaa Ahmed (University of Colorado, Boulder)

Not all movement errors are created equal. For example, compare a 5 cm error in foot placement when approaching the edge of a curb, to the same error approaching the edge of a cliff. One would likely avoid the cliff edge more than the edge of the curb. Thus, movement planning would be risk-sensitive and depend on the subjective value of an error, rather than its actual value. Interestingly, models of movement adaptation have traditionally assumed that adaptation is proportional to movement error1. In recent years the notion of proportionality been challenged2,3. However, the role of risk-sensitivity, which emerges from a distortion between the subjective and actual value of an error, has not been investigated in movement adaptation. Here we quantified adaptation in a unique cliff-like virtual environment that was stable, but only within certain limits, to influence the subjective value associated with a given movement error.

Seated subjects (N=9) made reaching movements to a target directly ahead of them while grasping the handle of a robotic arm. Feedback was presented on a monitor at eye-level. The protocol consisted of: 50 no-force trials, 200 in a viscous curl-field (stable condition), 450 in an identical curl-field with a cliff-like region of instability (unstable condition), and 50 no-force. Curl-field gains varied from trial to trial and were biased to the left. During the unstable condition, curl-field dynamics were maintained but rightward errors greater than 2.5cm were penalized, with a line indicating edge of the boundary. In the first 50 trials of the unstable condition a strong rightward force was applied if the cursor crossed the cliff. After these 50 trials, this force was de-activated leaving only an audiovisual warning should the subject cross the boundary. Importantly, because most movement errors were less than 2.5 cm, subjects were merely alerted to the presence of the cliff. To adapt subjects must produce a force towards the instability. We hypothesized that errors closer to the edge would be penalized more heavily than errors of the same magnitude that occurred when the instability was not present. This would lead to *reduced* adaptation to the stronger gains.

Adaptation was calculated in both conditions using previously developed methods2. Movement error was similar across conditions ($P > 0.1027$). Adaptation to the strongest perturbation was greater in the stable compared to the unstable condition ($P = 0.0050$), but similar for the remaining gains. Model results corroborate these findings. Sensitivity, fit using a state-space model2, was larger in the stable compared to the unstable condition only for the largest gains ($P < 0.01$), and similar for all others ($P > 0.123$). This asymmetry suggests that subjects were responding to the fact that over-compensation was penalized only for rightward errors. These results imply that movement adaptation is risk-sensitive. It is not solely dependent on movement error, but can be modulated by the subjective value associated with the error. In other words, we may not simply learn from our mistakes, we may learn from the value of our mistakes.

(D2) OpenfMRI.org: An open data-sharing project for cognitive neuroscience

Deana Barch (Washington University), Russell Poldrack, Anthony Wagner, Tor Wager, and Jason Mitchell

The goal of the the OpenfMRI project is to provide an openly accessible, broad, and highly usable repository of raw functional magnetic resonance imaging (fMRI) data, as well as providing a resource to all researchers in the field who wish to share their own data. The project is developing a new infrastructure for the broad dissemination of raw data within the field of cognitive neuroscience, which will multiply the value of current investments in this research by making the data and results much more widely available. To date the repository has made available data from 12 complete fMRI studies (totaling 220 individual subjects), with an additional set of studies planned to be released in the next year. The openfmri.org web site will soon be integrated with an XNAT data management system as its back end, and this XNAT instance will perform data processing via the Lonestar cluster at the Texas Advanced Computing Center, which will allow high-throughput analysis of very large datasets and testing of multiple processing pipelines. The data processing pipeline code is openly available from GitHub. The OpenfMRI database is now federated via the Neuroscience Information Framework, and datasets shared via the site are linked out from the PubMed entry for the appropriate publication. The data are already being used by other researchers (e.g., they will be the primary datasets for the 2012 Brainhack event in Leipzig), and in the first 6 months of the new web site more than 60 datasets have been downloaded by researchers. In the future, we plan to introduce additional features including the ability to download intermediate processed data, and the ability to view analysis results directly from the main web site.

(D3) Mechanisms controlling spatial gradients of cAMP in neurons

Kim Blackwell (George Mason University) and Ted Abel

The ability of neurons to differentially respond to specific temporal and spatial patterns of stimulation underlies the storage of memory and information in neural circuits. Signal transduction pathways are critical for information storage; and alterations in key signaling molecules, such as the cAMP-dependent protein kinase (PKA) signaling pathway, modify both hippocampus-dependent learning and late-phase long-term potentiation (L-LTP). cAMP is generated at the plasma membrane by adenylyl cyclase and degraded by phosphodiesterases distributed throughout the neuron. The rapid diffusion of cAMP impairs its spatial specificity, but rapid degradation by phosphodiesterase could help shape microdomains of cAMP. For example, in dissociated hippocampal cultures expressing the FRET sensor Epac1camps, we observed steady-state dendrosomatic cAMP gradients following bath application of NMDA, isoproterenol (a $-adrenergic receptor agonist), or forskolin (a nonselective activator of adenylyl cyclase). In addition, pre-treatment of neurons by isoproterenol decreased the cAMP response to NMDA. Both of these responses were abolished by inhibition of phosphodiesterase type 4 activity and overexpression of PKA reduced the cAMP response, suggesting PKA phosphorylation of phosphodiesterase type 4 is a potent negative feedback loop controlling cAMP. To investigate the effectiveness of this feedback loop or whether other mechanisms underlie these observations, we constructed a spatial model of a CA1 pyramidal neuron soma and proximal dendrite in NeuroRD, a multicompartmental stochastic reaction-diffusion simulator. To the reactions pathways from Kim et al. (2011), we added cAMP binding to Epac1camps in order to quantitatively compare simulated and experimental FRET signals. Simulations demonstrate that a lower concentration of phosphodiesterase type 4 in the soma compared to dendrites is required to reproduce the observed dendrosomatic cAMP gradients. A critical parameter is the rate at which PKA phosphorylates phosphodiesterase, because fast phosphorylation of phosphodiesterase limits cAMP elevation and PKA activity in response to a $-adrenergic receptor activation through a fast negative feedback loop. Even with a slow rate of PKA, simulations demonstrate that the enhanced phosphodiesterase activity produced by PKA phosphorylation is not sufficient to limit the subsequent cAMP response to NMDA stimulation, in part because adenylyl cyclase is synergistically activated by the GsGTP produced by $-adrenergic receptor stimulation. This suggests that upstream reactions, such as desensitization of the $-adrenergic receptor, enhanced GTPase activity, or switching of $-adrenergic receptor coupling from the Gs to Gi subtype of G protein is required for pretreatment with isoproterenol to limit the subsequent response to NMDA stimulation.

(D4) Gamma rhythms, theta rhythms, and baths of inhibition
Christoph Borgers (Tufts University) and Nancy Kopell (Boston University)

In experimental work in the Moghaddam lab (University of Pittsburgh), GABAA-receptor-mediated synaptic transmission in rat prefrontal cortex is disrupted by injection of the drug FG-7142, a partial inverse agonist of GABAA-receptors. There are unexpected effects on both pyramidal cell firing frequencies and rhythms:

1. The mean firing frequency of pyramidal cells does not appear to be affected immediately, but gradually falls during one or two hours following the injection. This is unexpected because FG-7142 weakens inhibition.

2. Gamma power increases significantly immediately following the injection. This is unexpected because GABAA-receptor-mediated inhibition, which is down-regulated by FG-7142, is thought to underlie gamma rhythms. During one or two hours following the injection, gamma power gradually falls, while power in lower frequencies, in particular the theta range, increases.

We present simulations of a model network demonstrating that these effects could arise robustly if the dominating effect of FG-7142 were the down-regulation of an "inhibitory bath" affecting pyramidal cells, PV+ basket cells (thought to be crucial for gamma rhythmogenesis), and LTS cells (thought to be important for theta rhythmogenesis). Such an inhibitory bath might arise from yet another class of interneurons, perhaps for instance CCK+ basket cells. In the model, the immediate rise in gamma power is the effect of the down-regulation of the inhibitory bath, and the gradual changes over one or two hours result from the gradual re-emergence of the inhibitory bath as the drug is cleared.

(D5) Investigating phase-dependent pattern generator robustness
Hillel Chiel (Case Western Reserve University) and Peter Thomas

(D6) CRCNS data sharing: NeuroML database for multiscale models in neuroscience

Sharon Crook (Arizona State University)

The complexity of problems associated with structure and function in neuroscience requires the integration of remarkably diverse data about the nervous system at multiple levels and scales. One approach to understanding these data is to perform theoretical and computational studies using multiscale neuroscience models. The goal of the NeuroML project is to develop a structured, declarative language for describing complex neuronal and neuronal network models that facilitates scientific reproducibility, data and model archiving and exchange, simulation software development and interoperability, model database creation, and model publication. This international, collaborative initiative focuses on the key objects that need to be exchanged among existing software applications, such as descriptions of neuronal morphology, ion channels, synaptic mechanisms, and network structure. This modular approach brings additional benefits: not only can entire models be published and exchanged, but each individual object--such as a specific potassium channel or excitatory synapse--can be shared and re-implemented in a different model. The use of XML as a definition language provides the transparency, portability and extensibility required in these efforts, and also brings an infrastructure of established tools for efficient software and database development. The goal of this project is to take advantage of this infrastructure and provide a stream-lined set of tools for the computational neuroscience community to share, find, view, and test NeuroML models and their components. Here we present progress toward the development of a database for multiscale models in neuroscience that are described using NeuroML.

(D7) Computationally modeling the impact of end-organ structure on neural responses in Tactile Afferents

Gregory Gerling (University of Virginia), Ellen Lumpin, Daine Lesniak, Kara Marshall and Scott Wellnitz

The long-term goal of this research is to understand how end-organ morphology influences neural responses in mammalian touch receptors. Of the cutaneous somatosensory afferents that underlie our sense of touch, the slowly adapting type I (SAI) afferent responds to a robust range of indentation with well-defined receptive fields, making it vital to everyday tasks involving shape and texture discrimination. SAI responses originate from tree-like afferents that branch repeatedly to terminate in a few to dozens of Merkel cell-neurite complexes. Signals from these complexes are converted to action potentials (spikes) at spike initiation zones, which are nodes of Ranvier proximal to Merkel cells. These spikes integrate along the branching structure to produce SAI responses, which vary greatly between afferents. In our initial analysis of this variation, we found that the total number of Merkel cells does not correlate with firing rate differences, which is perplexing given that the transduction elements of the SAI are believed to lie at Merkel cell-neurite complexes. *In light of this result, we hypothesize that variation in the grouping of Merkel cell-neurite complexes to each spike initiation zone accounts for differences in firing properties between SAI afferents.*

To test this hypothesis, we construct computational models of an SAI afferent combining finite element analysis, fitted functions, probabilistic noise distributions and differential equations. These techniques allow modeling the transformation of indentation to strain energy density by skin, of strain energy density to membrane current by receptor transduction, and of current to spike times by spike initiation. In particular, combining models of spike initiation and receptor current in a reconfigurable network allows for simulating changes in SAI spiking corresponding to changes in Merkel-cell number, Merkel-cell grouping to spike initiation zones, and interactions between spike initiation zones.

Computational experiments are performed to 1) determine if variation in the grouping of Merkel cell-neurite complexes can explain how SAI afferents with identical Merkel-cell counts generate different firing rates, 2) determine if the same grouping principles combined with variation in the number of spike initiation zones explains how SAI afferents with fewer Merkel cells can generate higher firing rates than SAI afferents with more Merkel cells, and 3) verify the impact of grouping over a wide range of Merkel-cell counts.

Initial results suggest that the grouping of Merkel cells per spike initiation zone can explain differences in firing rates between SAI afferents. When the number of Merkel cells is held constant, firing rates increase with the size of the largest Merkel-cell group, and to a lesser degree, with the size of the second largest Merkel-cell group. Although our results suggest that SAI firing rate increases with Merkel-cell count, they demonstrate that this effect is obscured by the larger impact of Merkel-cell grouping.

(D8) Anatomical distributions of activation patterns in fMRI

Polina Golland (MIT)

(D9) Inter-subject functional connectivity hyperalignment of neural representational spaces.

J Swaroop Guntupalli (Dartmouth College), Michael Hanke, Peter Ramadge, and James Haxby

Multivariate encoding & decoding models of cortical responses from fMRI are usually subject-specific due to inadequate alignment of the underlying representational spaces using anatomical features. Our proposed method of alignment called hyperalignment aligns representational spaces across subjects into a common high-dimensional space using Procrustean algorithm. We showed that this common space is valid across brains and across a wide range of stimuli and cognitive states (Haxby et al. 2011). Hyperalignment is limited, however, insofar as it relies on time-locked stimulation and time-locked cognitive states as the basis for alignment. Here we present a new method, 'connectivity hyperalignment,' which aligns voxel spaces based on common patterns of functional connectivity of voxels to other brain regions rather than on common, time-locked responses. We derived the alignment parameters using the fMRI data from 20 subjects while they watched the movie Raiders of the Lost Ark. We used different halves of the movie for different subjects to derive connectivity profiles of voxels in the ventral temporal cortex to spherical seeds across the whole-brain. These connectivity profiles are used to derive the hyperalignment parameters. Hyperalignment parameters are then applied to data from categorical-perception experiments in the same subjects. Between-subject classification (BSC) accuracy using data in common space was 59.1% (chance accuracy:14.3%) for face & object categories and 63.2% for animal species (chance accuracy: 16.7%) which are both significantly higher than using anatomically-aligned data (face & object: 52.5%; animal species: 45.7%) and are equivalent to within-subject accuracy (face & object: 58.7%; animal species: 61.3%).BSC of movie time segments from one movie-half was performed using data in the common space derived based on the other movie-half and anatomically-aligned data. BSC accuracy using our method (54.9%) clearly outperformed anatomical alignment (36.8%; chance<1%). We also computed the between-subject, between-voxel correlation of connectivity vectors from the test movie half to evaluate how this method improves functional connectivity across subjects. Between-subject correlation of connectivity vectors averaged over all pairs of subjects, all voxels in the ventral temporal cortex, and two movie halves is 0.55 for connectivity-hyperaligned data and 0.38 for anatomically aligned data. These results demonstrate that the voxel connectivity-profiles can predict their response-profiles well enough to extract fine-scale visual object information, and these connectivity spaces are shared across subjects, and our method of connectivity hyperalignment aligns common information patterns and their functional connectivity vectors with the rest of the brain. Moreover, our method, by virtue of using connectivity instead of stimulus-locked responses, can afford models of areas that do not respond to external stimuli in a consistent manner, namely those areas in the default-intrinsic system that play a central role in social cognition.

(D10) A computational framework for understanding decision making through integration of basic learning rules

Ramon Huerta (University of California San Diego), Brian Smith, and Maxim Bazhenov

Both nonassociative and associative learning rules modify neural circuits. However, it remains unclear how these forms of plasticity interact to produce realistic behaviors. Here we show that integration of these simpler learning rules into a model of decision making can be used to produce realistic accounts of learning behavior. We use as a model both nonassociative (unsupervised) and associative (supervised) conditioning of olfactory learning in the honey bee. For both types of learning, honey bees frequently show a fairly abrupt increase in response after a number of conditioning trials. The occurrence of this abrupt change appears at different presentation trials for associative and nonassociative conditioning. We report here on a simple but comprehensive model that integrates the abrupt switch in decision making and the different time scales involved in both types of learning. To study this switch-like behavior, we developed a model of the areas of the honey bee brain known to process olfactory information, and we then integrated reinforcement into the model. We then tested the model with data from an artificial gas sensor array using metaloxide gas sensor arrays. We found that a smooth change of the synaptic weights can result in an abrupt increase in performance; the interaction of unsupervised and supervised learning rules was critical for producing the behavioral switch. Furthermore, in order to replicate the experiments, unsupervised learning must operate at a much slower time scale than supervised mechanisms. The results show that an integrated set of supervised and unsupervised learning rules implemented using fan-out connectivities together with neural inhibition can replicate the time scales of unsupervised and supervised learning, the nonlinearity in the decision making process and fluctuations of the behavior around transitions points.

(D11) Functional connectivity and representation of respiration in the cerebellar cortico nuclear pathway

Dieter Jaeger (Emory University), Ying Cao, Selva Maran, and Detlef Heck

Spiking of cerebellar nuclear (CN) neurons, the cerebellar output signal, is modulated by inhibitory inputs from cerebellar cortical Purkinje cells (PCs) and excitatory input from mossy fiber collaterals. However, little is known how CN activity is shaped by its population of inputs in awake animals, and how intrinsic dynamic properties of CN neurons contribute to synaptic integration. We addressed this issue in the framework of rhythmic motor behavior, specifically breathing, which is represented by spike modulation in PC activity. We simultaneously recorded single unit CN neurons and PCs in the vermis of awake, head fixed mice while monitoring respiratory movements. Spontaneous spike activity ranged from 8 to 50 Hz in CN neurons and from 40 to more than 100 Hz in PCs. The simple spike activity of PCs and the spike activity in their postsynaptic CN neurons were found to be significantly modulated in relation to respiratory movements. Cross-correlation analysis at high temporal resolution (5 ms) revealed no or weak correlations between spike firing and respiratory behavior. By contrast, firing rates averaged over time windows of 100 ms and 500 ms duration showed strong rhythmic correlations with respiratory movements in 6 out of 8 FN neurons and 4 out of 8 PCs. We also observed slow rate correlations between simultaneously recorded pairs of CN neurons and PCs and between simultaneously recorded pairs of PCs. Slow rate correlations between pairs of PCs were higher for sagittally aligned pairs. These relations were modeled using a full morphological compartmental model of a CN neuron with active properties tuned to replicate in vitro CN activity. We constructed 500 artificial PC spike trains as gamma distributed processes closely mirroring the spiking properties of PC recordings. The behavior associated rhythmic modulation were estimated from a peri-event time histogram of PC spiking and the average event modulation was convolved with the baseline firing rate at the timing of recorded breaths. We then manipulated the amount of covariance between the PC inputs given to the model to examine how CN neuron modulation will be controlled by PC input at the population level. Using a particle swarm optimization algorithm we found a 20% correlation in PC inputs was necessary to simulate the observed modulation depth in CN activity. Our results suggested that the representation of behavior and the neuronal interactions within the cerebellum are based on spike rate modulations rather than on precise timing of action potentials, and that to explain robust behavioral modulation of CN activity a substantial degree of phase-locked co-modulation in populations of PCs is required.

(D12) Network analysis reveals information flow between the human amygdala and orbitofrontal cortex during decision-making

Rick Jenison (University of Wisconsin-Madison), and Antonio Rangel

To make effective decisions, values must be assigned to the different options under consideration prior to making a choice. There are potentially a number of areas in the brain implicated in the computation of economic valuation. A critical open question concerns the direction of information flow between these different areas, specifically between the amygdala and orbitofrontal cortex (OFC). Our studies were carried out in four patients undergoing diagnosis and, later, surgical treatment for pharmacologically intractable epilepsy. Participant-patients undergo implantation of intracranial electrodes for periods of up to two weeks, after which electrodes are surgically removed and the seizure focus removed. Participant-patients are awake and alert during recording sessions. We recorded from eight macrocontacts on bilateral electrodes implanted directly in the amygdala nuclei for which we have high resolution MRI to precisely identify where the contacts were positioned. Additionally 256 epipial macrocontacts were recorded simultaneously from the surface of the brain, which included coverage of the fusiform gyrus (FG), parahippocampal gyrus (PHG), lingual gyrus (LG), ventromedial prefrontal cortex (vmPFC) and dorsolateral prefrontal cortex (dlPFC).

We previously examined the coding of value in single-unit activity in the human amygdala during decision-making experiments (Jenison et al., 2011). In this study we examined the contribution of the amygdala to network dynamics of value-related neural activity in other areas of the brain while patient-participants evaluated appetitive and aversive food items. Local field potentials (LFPs) provide a source of subthreshold integrative information not available in spike trains, and can therefore provide a complementary study of value coding. We observed covariation of averaged evoked responses with item ratings in the amygdala around 250 ms following the onset of the stimulus, which paralleled the time course observed in our previous single-unit recordings. We performed a Granger causal connectivity analysis (Seth, 2010) to estimate the direction of influence between areas of the brain implicated in the computation of value. Time-domain causal networks were constructed and causal flow was estimated to identify causal sinks and sources. These analyses show a flow of information from the temporal lobe and amygdala to the OFC, suggesting that the amygdala provides a strong causal source during value-based decision-making.

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(D13) Collaboration on high-resolution maps of synapses on hippocampal neurons
William Kath (Northwestern University), Stephen Smith, Stefan Remy, and Nelson Spruston

This US-German Collaborative Research in Computational Neuroscience project combines patch-clamp electrophysiology, two-photon imaging and uncaging, array tomography and computational modeling to investigate synaptic integration and dendritic computation in hippocampal neurons. We will present the results of initial experiments showing that strongly and weakly excitable dendrites can be easily distinguished from one another, and that strong dendritic spikes are more resistant to inhibition than weak dendritic spikes. We will also present simulations of synaptic integration in spines on the dendrites of CA1 pyramidal neurons demonstrating the major factors influencing spine electrical compartmentalization.

(D14) Spike sorting for spatially dense high channel count extracellular recordings
Nancy Kopell (Boston University) Ed Boyden and Chrisoph Borgers (Tufts University)

High channel count electrical recordings from spatially dense extracellular neural probes have the potential to increase our understanding of neuronal network dynamics, but require new methods of data analysis to be of practical use in neuroscience. Teasing apart network dynamics using these data (e.g., using measures of association and spike pattern classification) requires automated spike sorting with very low error rates. In particular, we are interested in the network dynamics related to oscillations within and across cortical layers, which will be facilitated by identifying many layer-localized single units. Importantly, for usage in conjunction with causal technologies such as optogenetic perturbation, the algorithms must be able to run in effectively real time, a major constraint on the computational complexity of the resulting algorithm.

The accuracy of spike sorting is fundamentally limited as the problem is underdetermined. The most common techniques confront this limit by using either manual or automated clustering techniques on individual spikes in a feature space (e.g., of waveform shapes). But very low error rates are difficult to achieve with these techniques, and manual clustering, probably the most popular technique, does not scale well to systems with very high channel counts. Accordingly, we have developed a spike sorting approach for the case of spatially dense high channel count extracellular recordings, first applying a well-established source separation technique called Independent Components Analysis (ICA) to continuous recordings, and then pursuing further analysis on putative single units which are well separated from noise and other units. We evaluate the ICA components for spiking activity using a conservative thresholding procedure on the components, only keeping putative single units that are well separated.

We have performed robustness testing on this algorithm using simulated data that encompasses many of the realistic variations and noisinesses of natural neural data, including spatial non-linearities in spike shape from individual cells. We find that the algorithm returns false positive single units at an average rate of 5% for a wide variety of simulated datasets. The number of single units isolated by our algorithm increases with detector density, suggesting that this low error, automated approach will perform optimally for high density neural probes. Further, this algorithm is parallelizable, making it appropriate for the kind of real-time analysis that is critical for closed-loop optogenetic perturbation of online recorded neural activity patterns.

(D15) New tools for the mechanistic dissection of neural networks: a robotic system for automated whole-cell patch clamping in vivo and optimized molecular reagents for multi-pathway optogenetic control
Nancy Kopell (Boston University) Ed Boyden and Chrisoph Borgers (Tufts University)

In vitro preparations have played a key role in the development of detailed biophysical models of the genesis of neural rhythms and of their computational properties. However, such models ultimately need to be validated in vivo, as they depend upon, and influence, global network states and behavior. Unfortunately, this has been traditionally a very difficult process, both painstaking and requiring high skill. We speculated that it might be possible to automate the steps leading to the establishment of whole-cell patch clamping in vivo, an approach which would greatly expand the availability of this technique, would increase throughput, allowing new kinds of systematic investigations, and could also allow the practical pursuit of multiple simultaneous recordings.

We developed an algorithm, composed of specific actions performed in response to defined electrophysiological events that, implemented in a simple robotic module, attached to a conventional in vivo patch clamp system, allows high-yield automated patch clamping of cells *in vivo*. Our "autopatching" robot can detect and record from neurons in the anesthetized living mouse brain in whole-cell mode. We validated the performance of our robot in both the cortex and hippocampus, acquiring high-quality recordings at varying depths, and are currently working on a multi-channel version of it capable of recording multiple neurons simultaneously in the live brain.

In addition to performing high-quality recordings, the ability to precisely perturb specific network elements is crucial to validating, refining, or disproving biophysical models of, and to assessing the functional role of specific neurons in emergent patterns of, neural network activity. Optogenetic reagents have emerged as an effective strategy for controlling the activity of genetically defined cell populations with exquisite temporal specificity, but it has been difficult to simultaneously drive two spatially overlapping sets of targets. Such a tool would be important for studying how one set of neuron gates or modulates the function of a second, or for studying how two sets of neurons jointly influence a third. Accordingly, our laboratory has developed a pair of channelrhodopsins with well separated activation spectra, suitable for performing multi-color activation of two sets of neurons. We are investigating the use of these novel reagents for the study of how multiple similar vs. distinct cell populations coexisting within a circuit work together to generate neural rhythms.

(D16) Sparse incomplete representations by the granule cells of the olfactory bulb
Alexei Koulakov (Cold Spring Harbor Laboratory)

Mitral/tufted cells of the olfactory bulb receive odorant information from receptor neurons and transmit this information to the cortex. The most abundant cell type in the olfactory bulb is the population of inhibitory interneurons called granule cells that form unusual dendrodendritic synapses with the mitral cells. Granule cells is continuously generated throughout the lifetime of the organism by the population of progenitor/stem cells located in the subventricular zone. Despite these complex processes, granule cells do not project out of the olfactory bulb. Here we propose that granule cells form sparse incomplete representation of olfactory stimuli. The errors of these representations are transmitted to the olfactory cortex by the principal neurons of the olfactory bulb. We explore the possible mechanisms of learning by the granule cells and compare these results with experimental data.

(D17) The temporal extent of shape information in the human visual system
Gabriel Kreiman (Children's Hospital, Harvard University), and Jedediah Singer

Humans can recognize objects and scenes in a glimpse while maintaining stable and continuous representations, suggesting rapid integration of visual information. Here we investigated the time course over which shape information is integrated by presenting subjects with asynchronous image fragments. We found that temporal asynchronies of 30 milliseconds can impair visual recognition, but considerable temporal integration persists even with 100 milliseconds of asynchrony

(D18) Advanced stimuli to probe electrosensory processing and memory in Mormyrid fish
Todd Leen (Oregon Health & Science University), Patrick Roberts, and Nathan Sawtell

The mormyrid senses its environment by emitting an electric organ discharge and detecting, via electroreceptors on the skin, the perturbations that nearby objects cause in the electric field. A combination of in vivo, in vitro, and computational studies shows that mormyrid electrosensory lobe (ELL) acts as an adaptive filter; it builds predictions of expected electrosensory input and subtracts the predictions from actual sensory input allowing novel behaviorally-relevant signals to be processed more effectively.

Experimenters have been unable to present the system with precisely-controlled, complex spatial-temporal stimuli — previous research used one or two simple dipole sources placed in the water. We are developing and refining a computer-controlled system that generates skin surface fields with specified spatial-temporal profile. Control voltages sent to a printed circuit board array of Ag-AgCl electrodes project sequences of field patterns onto the skin to simulate objects, or test specific hypotheses about central processing. To predict the skin potential resulting from electrode control voltages, we use finite element models together with measurements of the potential at the skin (provided by an array of fine, Ag-AgCl wires). The skin potential measurements are used to correct the model for errors in fish geometry and inhomogeneous tissue conductivities. Supporting software includes GUI control of the hardware interface, model calibration and error-correction algorithms, receptive field estimation (using random control voltages and a reverse-correlation procedure), and frame and movie generation.

We have developed an adaptive spatial-temporal model of ELL neural circuitry that demonstrates the effects of spike-timing dependent synaptic plasticity at the synapse from parallel fibers onto medium ganglion (MG) cells. Changes in the spatial pattern of stimulus lead to an adaptive response in medium ganglion and efferent cells that depends on stimulus history. We conclude that synaptic plasticity at the parallel fiber synapses onto MG cells is sufficient to explain changes in efferent responses.

Our new stimulus system will facilitate tests of hypotheses suggested by the models and by earlier experimental work. As an early test we report on field potentials in early processing of ELL, and their correspondence with electrical patterns on the skin.

(D19) Propagation of uncertainty information during perceptual decisions
Wei Ji Ma (Baylor College of Medicine), Andreas Tolias

Understanding how neural populations perform computations is a central quest in systems neuroscience. A population of sensory neurons responding to a stimulus is commonly thought of as representing a point estimate of that stimulus. Recent psychophysical studies, however, indicate that this view is incomplete. These studies used perceptual tasks in which optimal performance requires the observer to take into account sensory uncertainty on a trial-to-trial basis, and found that human observers are near-optimal. This phenomenon, formalized using the framework of Bayesian inference, suggests that along with the representation of a stimulus comes a representation of its uncertainty, and that this uncertainty information is utilized by the brain. We study how populations of neurons encode and propagate sensory uncertainty information for use in perceptual decision-making. We designed a visual task in which observers classify ambiguous stimuli in the presence of sensory uncertainty. Optimal performance requires observers to combine two types of uncertainty information on a trial-to-trial basis. We show that humans and monkeys perform this task in a near-optimal manner, and how near-optimal behavior can be achieved by a biologically plausible neural network.

(D20) Text, neuroimaging, and memory: unified models of corpora and cognition
Jeremy Manning (Princeton University), Kenneth Norman, David Blei

Topic modeling algorithms are unsupervised statistical methods for decoding latent topics that pervade a collection of documents, where each topic is defined as a probability distribution over words in the vocabulary (e.g. Blei et al., 2003). A word's K-dimensional topic vector reflects the weights assigned to that word by each of K topics. In this way, a word's topic vector defines its position in meaning space, where each dimension of meaning space is a topic.

Here we present a method for using a topic model trained on a large text corpus to decode topic vectors from neural activity recorded during a memory experiment. In the first phase of the experiment, participants in a functional magnetic resonance imaging (fMRI) scanner are asked to think about the properties of each word in a long list; each word is presented several times. Data from this phase of the experiment are used to calibrate a model that decodes topic vectors from the blood oxygen level dependent (BOLD) response. In the second phase of the experiment, participants study and recall shorter lists comprised of the same items.

Whereas the overt rehearsal procedure (Rundus & Atkinson, 1970) has participants narrate their rehearsals as they study a list of words, our approach allows us to track participants' positions in meaning space by decoding topic vectors from their BOLD activity as they study and recall words in the experiment. In this way, our approach allows us to covertly gain insights into participants' strategies and into the neural mechanisms underlying episodic memory encoding and retrieval.

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(D21) The incorporation of new information into prefrontal cortical activity after learning new tasks

Ethan Meyers (MIT), Xue-Lian Qi, and Christos Constantinidis

Humans and nonhuman primates have the ability to learn complex new tasks. This ability requires that new information is integrated into neural systems that already support other behaviors. To study how task learning changes neural representations, we analyzed single unit recordings from the prefrontal cortex (PFC), a brain region important for task acquisition and working memory, before and after monkeys learned to perform two new behavioral tasks. A population decoding analysis of the PFC firing rate activity revealed that there was a large increase in task-relevant information, and smaller changes in stimulus-related information, after training. This new information was contained in dynamic patterns of neural activity, with many individual neurons containing the new task-relevant information for only a short period of time in each trial in the midst of other large firing rate modulations. Additionally, examining data from dorsal and ventral PFC separately revealed that stimulus information could only be decoded with high accuracy from dorsal PFC, while task-relevant information was distributed throughout both areas. These findings help reconcile the controversy about whether PFC is innately specialized to process particular types of information, or whether its responses are completely determined by task demands, by showing there is both regional specialization within PFC that was present before training, as well as more widespread task-relevant information that is a direct result of learning new tasks. The results also show that new information is incorporated into PFC through the emergence of a small population of highly selective neurons that overlay new signals on top of patterns of activity that contain information about previously encoded variables, which gives new insight into how information is coded in neural activity.

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(D22) CRCNS: Adaptive perceptual-motor feedback for the analysis of complex scenes

Cynthia Moss (University of Maryland), Timothy Horiuchi

Our project brings together behavioral, neurobiological, and computational studies of adaptive audiomotor integration in the echolocating bat, an animal that can negotiate a complex auditory world in complete darkness. For the echolocating bat, spatial perception of the environment builds upon its active production of sounds that reflect from objects. Perception by sonar draws upon functionally connected neural structures that play different roles in parsing, grouping and tracking auditory objects over time. The midbrain superior colliculus (SC) is implicated in target selection, attention, and the control of gaze. Previous research on the SC in visually-dominant animals has revealed shared neural control over attention and premotor commands to shift gaze. The SC of the echolocating bat shows specializations for acoustic orienting by sonar, including 3-D spatial auditory response profiles and pre-motor activity coupled to sonar call production. Here we report on studies of adaptive changes in head and pinna position, sonar vocalizations, responses to natural and artificial sounds in the SC of the echolocating bat, and related modeling efforts.

In experimental work, we have used high speed video recordings to localize the head and pinna positions of an echolocating bat engaged in an insect tracking task, a wideband microphone array to reconstruct the bat's sonar beam pattern of the bat engaged in spatial tasks, and neural recordings to natural and artificial sound sequences. Our behavioral studies reveal the bat's adaptive changes in pinna/head position and the width of the sonar beam pattern in response to abrupt changes in target velocity, and frequency-dependent directional adjustments of the sonar beam pattern in the presence of distracters. Our neural recordings from the SC of the awake, restrained bat have focused on the spectro-temporal responses to playbacks of natural echolocation call sequences and systematic manipulation of stimulus elements in these sequences. We constructed spectro-temporal receptive fields (STRF) for auditory neurons in the SC and found several trends. First, we discovered neuronal response latencies to auditory stimulation. Short latency responses occurred within 15 milliseconds of the stimulus, while longer latency responses occurred between 40-60 milliseconds after sound presentation. Furthermore, the responses at short latency tended to be excitatory, whereas longer latency responses can be both excitatory and inhibitory. These results suggest that the activity of SC neurons is modulated on two time scales, and possibly by different circuit phenomenon. Our computational modeling efforts have focused on this balance of excitation and inhibition in shaping auditory responses in the SC. Our initial computational model for the bat SC is based on the primate SC models by Arai and Keller (2005) and Trappenberg et al. (2001) that center on the interaction of locally-interconnected SC neurons (locally-excitatory and distally-inhibitory) and the disinhibition pathway via the substantia nigra. With this SC model, we are seeking to explain neural data in the bat, describe the control of head movements, and hypothesize its role in temporally coordinating and modulating echolocation vocalizations. The combined efforts of our experimental and modeling techniques will provide a new perspective on sensorimotor integration in the SC, and how multiple motor actions are coordinated for orienting behaviors.

(D23) Model of hippocampal-amygdala interaction: Implications for PTSD

Catherine Myers (UMDNJ-New Jersey Medical School, and DVA NJHCS)

The hippocampal region, amygdala, and ventromedial prefrontal cortex (vmPFC) typically show structural and/or functional abnormalities in post-traumatic stress disorder (PTSD), but it is not known to what extent these abnormalities represent aspects of a common pathway to PTSD, or each represent different nodes of dysfunction resulting in a common PTSD pathology. In this project, we are working to develop computational models of the brain abnormalities observed in patients with PTSD, to explore how different types of simulated dysfunction might give rise to the learning abnormalities observed in patients with the disorder. At the same time, we are collecting empirical data on hippocampal-dependent and –independent learning and generalization in patients with PTSD symptoms, to provide data to test and constrain the model.

In the last funding period, we completed a study (n=100) of veterans with varying degrees of PTSD symptoms, subdivided into three symptom clusters: re-experiencing symptoms (such as intrusive and recurrent thoughts and images), avoidance symptoms (such as avoiding reminders of the traumatic event), and arousal symptoms (such as hypervigilance). Our important new finding (pilot results reported last year) was that different patterns of learning were associated with different symptom clusters. Specifically, hippocampal-dependent generalization was associated primarily with re-experiencing symptoms, learning to obtain a cognitive reward was associated primarily with arousal symptoms, and learning to avoid a cognitive punisher was associated primarily with avoidance symptoms. These behavioral data suggest that different learning biases, and putatively different brain substrates, could contribute independently to different types of PTSD symptoms. We have begun to apply computational modeling to simulate these data, focusing initially on the reward and punishment learning data.

Specifically, we have applied a reinforcement learning model to individual subject data on the reward and punishment learning task. The model included four free parameters learning rate, perceived strength of reward outcome, perceived strength of punishment outcome and gain ("inverse temperature"), the degree to which actions are biased by past expectations vs. the tendency to explore new responses). Maximum estimation techniques were used to determine the unique combination of estimated parameter values that best fit each individual's behavioral performance. We observed significantly greater estimated learning rate and/or gain (the degree to which actions are based on prior expectations vs. exploration of new responses) in veterans with more severe PTSD avoidance symptoms – and this relationship did not hold with respect to other PTSD symptom clusters (re-experiencing or arousal symptoms) or to overall severity of PTSD symptoms.

Because the gain parameter in reinforcement learning models has been associated with activity of ventrostriatal dopamine signals, these results suggest possible brain mechanisms that could underlie the development, expression, and maintenance of pathological avoidance in patients with PTSD. Understanding these mechanisms may suggest possible new avenues for therapy; specifically, different avenues of therapy may be optimal for patients displaying different severity of symptom clusters, reflecting different underlying nodes of dysfunction.

(D24) Modeling acquisition and extinction of conditioned fear associations in amygdale circuits
Satish Nair (University of Missouri), Gregory Quirk, and Denis Pare

The overall objective of the proposed cross-disciplinary research is to use an integrated computational-experimental approach to study the acquisition and extinction of conditioned auditory fear associations in the neural components of the fear circuit of mammals (amygdala, prefrontal cortex, and the hippocampus). The long-term goal of this study is to study pathologies, such as anxiety disorders, that are thought to arise from deficits in the fear circuit, and assist in the development of medications.

Specific Aim 1: To investigate the underlying mechanisms of learning and neuroplasticity in the amygdala related to the acquisition and extinction of conditioned fear using a biologically realistic computational model, and to test model predictions in experiments.

Specific Aim 2: To investigate the mechanisms involved in the regulation of amygdala-dependent conditioning and extinction fear memory by the ventromedial prefrontal cortex, using a biologically realistic computational model, and to test model predictions in experiments.

The following structures were modeled using the Hogkin-Huxley formulation: lateral amygdala (LA), basal amygdala (BA), inter-calated cells (ITC), central amygdala (Ce), and the prelimbic cortex (PL). Hebbian plasticity was implemented in excitatory AMPA and inhibitory GABA receptor-mediated synapses to model learning. The occurrence of synaptic potentiation vs. depression was determined by intracellular calcium levels, according to the calcium control hypothesis.

(D25) Higher order maximum entropy models for cortical networks
Bruno Olshausen (UC Berkeley), Urs Koster, Jascha Sohl-Dickstein and Charles Gray

(D26) How does V1 encode dynamic natural scenes?
Bruno Olshausen (UC Berkeley), Urs Koster, Amir Khosrowshahi, Ian Stevenson and Charles Gray

(D27) Plastic effects of transcranial electric stimulation

Lucas Parra (City University of New York--CCNY)

Transcranial electric stimulation in humans can lead to electric fields of at most 1V/m on the cortical surface. This may polarize cell membranes by a fraction of a milivolt. While these intensities seem very small, there are a number of in vitro experiments explaining the basic mechanisms by which such low-amplitude electric fields may nevertheless acutely alter neuronal activity, both at the single cell and at the network level. However, the long-term plastic effects which have been repeatedly observed clinically are less well understood.

In humans, both enhancing and suppressing effects have been founds with constant-current stimulation of either polarity. Some studies argue that depolarizing currents enhance glutamaergic or NMDA dependent Hebbian-type plasticit while other studies have invoked homeostatic plasticity. Lasting effects on synaptic efficacy have only recently been found in vitro. These studies demonstrate that very specific conditions on network activity are required in addition to weak-field stimulation in order to observe lasting changes in synaptic efficacy.

In human EEG we observed that a short 25 minute stimulation with slow-oscillating fields applied at the beginning of the night can have lasting effects on decay of slow-wave activity in the course of the night. A detailed multi-scale computational model supports the hypothesis that field-induced cell polarization results in an increase of firing rate and that this accelerates synaptic downscaling, which in turn result in an acceleration of slow-wave decay during transcranial stimulation. To better understand the cellular mechanisms of fields on synaptic plasticity and adaptation we are now performing slice experiment in rat hippocampus. We are evaluating the effects of constant current weak-field stimulation on carbachol-induced gamma activity. We have already observed adaptation effects in the order of seconds. We are also exploring the effects of fields on long-term plasticity (LTP) using a classic tetanus-induced LTP protocol.

(D28) Reinforcement learning in multi-dimensional action spaces

Bijan Pesaran (New York University) and Nathaniel Daw

Decisions can be carried out in an abstract representation common to both effectors or may depend on the effector signaling the choice. To distinguish between these alternatives, we continue to examine behavioral representations and neuronal representations in a series of interlinked experiments using humans and non-human primates.

In the non-human primate study, we extend our previous work that considered spiking activity in two regions of the posterior parietal cortex (PPC). Our goal has been to study representations guiding looking and reaching as subjects make decisions for each effector, eye and hand. We have previously found neurons in two subdivisions of PPC, area LIP and PRR, encode values for reaches as well as saccades. We now examine recordings of local field potential (LFP) activity and its relation to spiking. LFP activity reflects the activity of populations of neurons near the recording electrode and has been argued is more similar to the BOLD signal acquired using fMRI than is spiking activity. We find that LFP activity in both area LIP and PRR mirrors the properties of neurons in these areas and encodes the rewards earned by subjects for different movements. Interestingly, the reward selectivity is present as increased in gamma frequency band (30-90Hz) activity as well as decreases in beta frequency band (10-30 Hz) activity. The results of spike-field coherence within ad between area LIP and PRR indicate that while gamma band activity is a property of activity within each area, that the beta frequency band activity is a signature of long-range circuits. Specifically, we find the activity of a population of neurons in LIP is coherently active with LFP activity in PRR only in the beta frequency band and not in the gamma frequency band. The same is true for the spiking activity of a population of PRR neurons and LFP activity in area LIP. Examining the timing of choice selectivity in the spiking activity of PRR neurons and LIP neurons reveals that the long-range coherent neurons are choice selective significantly before the neurons that do not exhibit long-rang coherent patterns of activity. These results indicate that decisions are made by subpopulations of neurons that participate in beta frequency band activity patterns across a distributed network of areas in the posterior parietal cortex.

In our human work, we have extended our earlier work carried out in non-human primates by examining how humans learn to choose actions in high-dimensional spaces in a new set of experiments. First, we used fMRI to probe effector-specific valuation using bimanual choice tasks that required either separate or conjoined motion of the hands to earn reward. This gives a bigger picture view on the networks supporting such choices. In separable conditions, posterior parietal areas (consistent with the non-human primate studies) and also areas of supplemental motor cortex appear to be involved in effector-specific valuation and choice. In conjoined conditions, the latter areas are differentially coupled with value-related areas of ventromedial prefrontal cortex, suggesting a model in which top-down control from more abstract valuation centers is recruited to solve the coordination case. In a second series of studies, we have examined tasks in which the “curse of dimensionality” over actions arises when multiple actions are performed sequentially rather than (as in the other studies) simultaneously. These studies demonstrate that to solve the sequential choice problem subjects employ multiple, behaviorally and neurally differentiable strategies. The balance between these is disrupted in certain patient groups. We have also shown that by manipulating aspects of the reward statistics, we can affect which strategy healthy subjects use to solve the problem, in a shift in many ways analogous to the conjoint vs separate distinction from the multi-effector learning studies.

(D29) Computing motion-dependent proprioceptive feedback using a forward dynamics musculoskeletal model of cat hindlimb: Role of muscle history-dependent properties

Boris Prilutsky (Georgia Institute of Technology), Alexander Klishko, Sergey Markin, Natalia Shevtsova, Ilya Rybak, and Michel Lemay

Our long-term goal has been to develop a comprehensive neuromusculoskeletal model of the spinal control of locomotion by combining a CPG model (Rybak et al 2006) with a musculoskeletal model of cat hindlimbs generating realistic motion-dependent afferent signals (Prilutsky et al 2007) to better understand the mechanisms of locomotor recovery after spinal cord injury. Since motion-dependent afferent signals are considered critical for recovery of locomotion after spinal cord injury (Rossignol 2006; Markin et al 2010; Lemay et al 2011) and direct recordings of afferent activity can provide information about only selected muscle afferents, it is critical to develop a computational model that can accurately predict signals from the muscle spindle and Golgi tendon organ afferents whose activity is a function of muscle fascicle length-velocity and tendon force, respectively (Prochazka 1999). The aim of this study was to investigate how history dependent muscle properties (such as dynamic force enhancement and depression, static force enhancement and depression, and force-velocity relation, e.g. Zatsiorsky, Prilutsky, 2012) affect time-profiles of muscle fascicle length and tendon force (and thus afferent feedback) while the muscle undergoes a stretch-shortening cycle, an essential element of muscle locomotor action. A generic Hill-type muscle model was used which consisted of the contractile component with force-length and force-velocity relations, the passive parallel and serial elastic components with known force-length relations. In addition, the muscle history-dependent properties were incorporated in the model. Integrating equations of muscle contraction dynamics with initial conditions and known muscle activation as input, yielded muscle length- and force-time histories. Muscle model parameters (slack length and parameters of the force-length relations, maximum muscle force, etc.) were identified by minimizing the difference between the measured and simulated fascicle length in soleus and gastrocnemius muscles during locomotion. Conducted simulations of the stretch shortening cycle with the model demonstrated a critical role of the force-velocity relation in reproducing realistic force-time histories. Specifically, the model reproduced realistic force profiles best when the double-hyperbolic force-velocity relationship (Edman, 1988) was used. We conclude that accounting for history dependent muscle properties and the realistic muscle force-velocity relation are important for accurate simulations of activity from muscle length- and force-sensitive afferents.

(D30) Afferent specificity, inhibitory subtypes and astrocytic glutamate transporters influence orientation selectivity: A computational study in mouse primary visual cortex

Dipanjan Roy (Technical University Berlin), Konstantin Mergenthaler, Jeremy Petravicz, Caroline Runyan, Nathan Wilson, Mriganka Sur, and Klaus Obermayer

One of the most prominent stimulus specific output features that gets encoded in the primary visual cortex (V1) is orientation selectivity and tuning. Several recent in-vivo experimental studies on mouse visual cortex have found that inhibitory cells of all subtypes are broadly tuned for orientation [1, 2], contrasting the findings of many other studies in higher mammals and rodents, which have shown the existence of inhibitory neurons that are as sharply tuned as excitatory neurons [3, 4]. Two very critical questions naturally emerge as a result of these diverging findings: (1) How similar are the output response such as orientation selectivity compare with that in previously described species? (2) What is the synaptic and network mechanism behind the sharpening of orientation selectivity in the mouse visual cortex?

Here, we investigate the above questions in a computational framework with a recurrent network model of rodent primary visual cortex. Subsequently, We make an attempt to identify physiologically relevant network parameters that provides the best fit to the data.
The synapses with and without astrocytic modulation are incorporated independently in a recurrent network model of rodent primary visual cortex adapted from a previously described map model in [5] and consists of an excitatory and inhibitory populations with orientation tuning organized in a ”salt-and-pepper” manner. Further, for synapses without astrocyte mediated mechanisms we incorporate differential afferent input to inhibitory cells motivated from new experimental findings of differential output responses of soma-targeting subtypes [4]. Layer 2/3 excitatory cells are connected preferentially to neighboring cells with similar orientation tuning based on recent studies [2]. Network simulation reveals combined feedforward drive with precise fine scale lateral excitation and inhibition predicts a range of orientation tuning for both excitatory and inhibitory populations placed in layer 2/3 of primary visual cortex. For the astrocyte mediated synaptic mechanism, detailed models with several conformational receptor stages were incorporated for NMDA and AMPA receptors. Theses receptors are driven by a bi-exponential glutamate concentration, with a decay constant which is modified by astrocytic glutamate uptake and which increases by a drug of TBOA-concentration [6]. Furthermore, the decay constant is selectively varied for the excitatory to excitatory and excitatory to inhibitory synapses motivated by the their difference in geometry and receptor concentration.
Synaptic mechanism with the differentiated increase in decay times for both connections can lead to enhanced response at preferred orientation and broadening of tuning for neurons as observed in other species [7].
In order to further constrain our network parameters we estimate the p-values using Kolmogorov-Smirnov test over the entire range of recurrent excitation and inhibition values. Based on the estimated p-Values we infer that there are several points in different operational regimes of this network under sensory drive which commensurate well with several recent experimental observations. In particular, there are several points in the recurrent regime of this network which give indistinguishable OSI distributions, an operational regime, where network parameters most likely generate sharp orientation tuning particularly within orientation representations with diverse local neighborhoods.

(D31) Biophysically accurate non-classical and inhibitory interneuron properties in a sparse coding network

Christopher Rozell (Georgia Institute of Technology)

Neurons in the primary visual cortex exhibit a baffling array of tuning properties, often unaccountable by the classical linear feedforward model. Specifically, excitatory neurons display a number of nonlinear effects collectively known as non-classical receptive field (nCRF) effects [1], and inhibitory neurons have diverse orientation tuning properties [2]. Furthermore, excitatory cells outnumber inhibitory cells by a ratio of 9:1 [3], yet the excitatory and inhibitory drives are balanced.

Efficient coding models of early vision have been shown to be able to explain key features of linear filtering properties [4] and some single cell nonlinear effects [5]. However, population statistics of nonlinear properties have not been studied in these models. In addition, inhibitory cells were not typically modeled.

Here we demonstrate that many of the aforementioned excitatory cell and inhibitory cell properties emerge naturally from a network that implements sparse coding. To be specific, several nCRF effects including surround suppression, contrast invariant orientation tuning, and cross orientation suppression emerge in the excitatory cell population as a result of sparse coding strategy; the excitatory to inhibitory cell ratio could be understood largely as a result of the overcompletness of representation; moreover, a subpopulation of inhibitory interneurons exhibit orientation tuning due to sparse recurrent connections with the principal cells; another subpopulation displays untuned properties due to low rank connectivity patterns. We also demonstrate that the network exhibits balanced excitation and inhibition, as a result of the receptive field structure.

We simulated a population of 2048 excitatory neurons with graded response described by the dynamics of locally competitive algorithm (LCA; [6]), which converges to the sparse coding representation at steady state. Inhibitory interneurons were described by linear units. The low rank and sparse recurrent connectivity pattern was a result of low rank plus sparse decomposition [7] of the LCA connectivity matrix. Non-classical receptive field effects were studied by presenting bar and drifting grating stimuli to the simulated network. Receptive fields of the inhibitory cells were mapped by sparse dots patterns.

(D32) Investigating the relationship between spikes and instantaneous LFP phase through the use of spike encoding models

Kyle Rupp (Johns Hopkins University), Marc Schieber, and Nitish Thakor

It is believed that the spiking of a neuron may be related to the surrounding local field potential (LFP), though this relationship is poorly understood. Recent research has shown that the instantaneous phase in the beta band of the LFP can help explain the firing patterns of neurons. Spike encoding models provide a convenient means of exploring the relationship between a feature of interest and the firing profile of a neuron. Here we used point process generalized linear models to investigate the effect of the instantaneous phase of the LFP beta band on the probability of a neuron firing.

The data used here consisted of 69 neurons recorded from primary motor, premotor, and somatosensory cortices of a macacque monkey during a reach-to-grasp task. Instantaneous phase was calculated by taking the Hilbert transform of the bandpass filtered (10-45 Hz) LFP signal. Two models of spiking probability were built and compared for each neuron, where one model incorporated firing history and instantaneous LFP phase and the other incorporated only firing history. The predictive power was calculated for each of the 2 models. Additionally, the ratio of the log likelihoods for each model was calculated, and a log ratio test was performed to generate a p-value for each neuron. We found that incorporating instantaneous phase information had the effect of increasing the predictive power for the population of neurons ($p = 1.8 \times 10^{-4}$, paired t-test). The log ratio test showed that the model improved significantly for 44 of the 69 neurons (63.8%). Together, these results indicate that the inclusion of instantaneous LFP phase information improves the spike encoding models, suggesting a significant relationship between phase and spike timing.

(D33) Direction selectivity in parietal cortex before and after visual categorization training

Arup Sarma (University of Chicago), Xiao-Jing Wang, and David Freedman

Recent studies have shown that neuronal activity in the lateral intraparietal (LIP) area can reflect the learned category membership of stimuli during a motion categorization task. However, relatively little is known about how category-representations in LIP develop during learning. The primary goal of this project is to understand how visual representations in LIP are influenced by the category-learning process by recording from LIP before and after categorization training.

One monkey was initially trained to perform a delayed match to sample (DMS) task using 360° of random-dot motion directions as sample and test stimuli. During the DMS task, the monkey indicated (by releasing a lever) whether a test stimulus showed the same motion-direction as a previously presented sample stimulus. 8 sample directions were used during neuronal recordings. The monkey correctly identified matching stimuli and +/-75° non-matching stimuli with >90% accuracy. The monkey was subsequently trained on a delayed match to category (DMC) task using the same stimuli where he indicated whether sample and test stimuli were in the same category, as defined by an arbitrary category boundary.

We recorded 92 LIP neurons during Delayed Match-To-Sample (DMS) task performance. A majority of neurons were direction selective (one-way ANOVA comparing 8 sample directions, $P<0.01$) during the sample epoch (64/92). While prior studies in LIP during a motion-categorization task found strong, and often sustained, category selectivity during the delay period, few cells were direction selective during the delay epoch of the DMS task (15/92). During the test epoch, neurons primarily showed selectivity for test direction (40/92). Recordings in the same monkey after categorization training will more directly reveal how visual representations in LIP change due to learning categories.

Our results indicate that LIP shows strong direction selectivity for currently-viewed stimuli during the DMS task, but not during the subsequent memory-delay period. This suggests that short-term memory representations of motion direction in LIP may vary depending on task demands. While the DMS task can be solved by simply detecting repetition of stimuli, the DMC task requires an additional abstract categorization process and cannot be solved by repetition detection. Thus, one possibility is that more abstract tasks could produce persistent activity and selectivity in LIP during working memory. Meanwhile, short term memory in tasks which only require knowledge of stimulus identity may be encoded through mechanisms other than persistent firing.

(D34) Force measurements on locusts during visually-evoked collision avoidance maneuvers

Sergy Shkarayev (University of Arizona)

The collision avoidance behavior of the locust, *Schistocerca americana*, in response to simulated approaching objects, also called looming stimuli, was investigated in a low speed wind tunnel. The insects were mounted using a sting on a sensitive six-component microbalance custom-designed for the experiments. Forces and moments were measured as a function of time during the simulated approach and interpreted in the context of collision avoidance behaviors. The looming stimulus was presented from the side on a white screen positioned on the sidewall of the tunnel. The stimuli effectively evoked robust and discernible collision avoidance responses in the form of changes in aerodynamic forces and moments as a function of time.

Locusts responded to the stimulus in the initial stages of looming by attempting to either (a) fly over it, (b) fly under it, or (c) steer around it. These behaviors appeared in the form of increases or decreases in lift, thrust and side forces. The steering away tendencies caused rolling and yawing moments. In the later stages of looming, just before the stimulus ended, the insects tended to respond with a behavior that seemed to represent a last ditch effort to avoid the collision and named ‘glide’ by various researchers. This maneuver was characterized by a sudden drop in lift and thrust for a brief period during which the locust would lose height quickly in order to avoid the simulated object. This was usually followed by a sharp rise in lift and thrust, as well as side forces in some cases. The type of avoidance response exhibited by the locusts was generally insensitive to mass although the heaviest locust tested exhibited a mild tendency to move sideways and roll towards the stimulus just before the collision.

The trajectories of the looming stimulus were varied in order to see its effect on the locusts’ collision avoidance behaviors. It was observed that for the looming stimulus presented from below, locusts generally tried to fly upwards without resorting to ‘glide’ maneuvers. When the stimulus was presented from the top towards the locust, it resorted to a long ‘glide’-like maneuver triggered around the end of the stimulus.

Locusts increased noticeably their wing flapping in response to the looming stimulus causing an increase in average lift and thrust. Interestingly a 5% - 10% concurrent increase in the wing-beat frequency was recorded, most likely one of the reasons for the increase in lift and thrust.

(D35) Memory and prediction in cerebral cortex, basal ganglia and cerebellum
Robert Scheidt (Marquette University), Nicole MG Salowitz, Aaron Suminski

If memory is to improve fitness for survival, it must shape future actions to satisfy shifting environmental demands. We used functional MR imaging (FMRI), a robotic device and systems identification techniques to examine neural correlates of predictive compensation for spring-like loads during goal-directed wrist movements. Although load changed unpredictably from one trial to the next, people nevertheless used sensorimotor memories from recent movements to predict and compensate upcoming loads. Prediction enabled subjects to adapt performance so that the task was accomplished with minimum effort. Population analyses of functional images revealed a distributed, bilateral network of cortical and subcortical activity supporting predictive load compensation. Importantly, the results reflect active engagement of three adaptive mechanisms known to contribute to motor learning [1-2]. Cortical regions (including prefrontal, parietal and hippocampal cortices) exhibited trial-by-trial fluctuations in BOLD signal consistent with storage and recall of sensorimotor memories or "states" (working memory) [3-4] assumed to be formed using some form of Hebbian learning. Bilateral activations in associative regions of the striatum were correlated with error costs and load predictions consistent with reinforcement learning [5] and prospective scaling of previously learned motor programs [6]. Activity in cerebellar cortex and its output pathways was consistent with supervised learning and the predictive compensation for tool use (eg. direct adaptive control of limb movement [7]). Predictive activity in the red nuclei and centromedian thalamus suggest a mechanisms for recursive prediction updating, which can also predict multi-rate adaptations previously observed in more deterministic environments [8]. Analysis of single subject images found that predictive activity was as likely to be observed in multiple neural systems as in just one. Thus, predictive compensation in the presence of environmental uncertainty is mediated by multiple, distributed, adaptive mechanisms spanning cortical and subcortical structures.

(D36) LFP spectral estimates improve predictive power of neuronal point process encoding models
Ryan Smith (Johns Hopkins University), Nitish Thakor, and Marc Schieber

Neuronal encoding models attempt to explain variability in spiking behavior as a combination of a number of observed parameters. Although many models have begun accounting for this variation as a function of experimental parameters, few have fully exploited the information contained in the local field potential (LFP) that is often recorded simultaneously. In this study, we investigate the impact of instantaneous LFP spectral power on the variability of local spiking activity recorded from a macacque monkey performing a reach-to-grasp task. The use of point process generalized linear encoding models of neuronal spiking provides a convenient means for the incorporation of the continuous-valued LFP signal without sacrificing resolution in the prediction of spiking behavior.
Spike encoding models were constructed from neurons (N = 71) recorded from floating microwire arrays implanted in primary motor, premotor and somatosensory cortices. Estimates of spectral power of the LFP signal were calculated at multiple electrodes from each array in frequency bands spanning 5-13 Hz, 14-22 Hz, 25-40 Hz and 75-100 Hz. The spiking activity of each neuron was modeled as a function of its own recent spiking activity as well as the estimates of LFP spectral power recorded from the same electrode array. For comparison, each neuron's activity was also separately modeled solely as a function of its own spiking history. Likelihood ratio tests indicated that the inclusion of LFP power significantly improved ($p < 0.05$) model fit in 62 neurons (87.3%). Similarly, the inclusion of these features resulted in a significant increase ($p < 0.005$) in the predictive power of the neurons. These results indicate that LFP spectral information could play an important role in modeling neuronal variability during a motor task.

(D37) US-German Collaboration: How dynamic is encoding? State-dependent feature-selectivity in thalamo-cortical circuits of the rat whisker system
Garrett Stanley (Georgia Tech/Emory), and Cornelius Schwarz

The dynamic association of computations performed by almost identical repetitive microcircuits across neocortex is the basis for the generation of highly flexible 'states' that give rise to vastly different behaviors. The key to reaching an understanding of cortical processing, therefore, is to study how it adapts signal processing to these different states. It is generally believed that the relevant mechanism for adaptive processing lies in interactions of thalamo-cortical loops, and in view of the repetitive outlay across neocortex may generalize across states. Therefore, our project compares thalamo-cortical coding in bottom-up (sensory driven), top-down (cognitive), and vigilance related states. The rat tactile whisker system is a model system that offers a broad knowledge base of connectivity and neuronal processing and a superior accessibility of thalamo-cortical representations. The specific aims of our project are to 1) assess feature selectivity of thalamic and cortical neurons in range of states using encoding models, based on white noise analysis, and 2) study behavioral tasks with different perceptual equirements to assess whether behavioral discriminability is correlated with (and thus possibly caused by) the ability to dynamically adjust feature selectivity. Thus far, we have developed some of the computational tools based on spike-triggered analysis, using simulation and data from the anesthetized rat. In parallel, we have developed the behavioral framework necessary to integrate the work across the two laboratories. We will present preliminary work on both the acute and behavioral sides of the project.

(D38) Neural and computational models of spatio-temporally varying natural scenes
Garrett Stanley (Georgia Tech/Emory), Jose-Manuel Alonso, and Michael Black

As we move through our visual environment, the spatial and temporal pattern of light that enters our eyes is arises from the illumination of the scene, the properties of objects within the environment, their motion relative to each other, and our own motion relative to the external world. From the perspective of the computer vision community, an important challenge exists in inferring the motion of the external environment (or "optical flow") from sequences of 2D images. From the perspective of the neuroscience community, quantifying the distributed neural representation of luminance and motion in the early visual pathway is a critical step in understanding how scene information is extracted and prepared for processing in higher visual centers. In our collaborative project, our goal was to synthesize these two distinct problems to serve both efforts. In response to natural scene movies, we show that neurons in the visual thalamus exhibit synchrony that is modulated by the properties of the scene. We report that the occurrence of synchronous firing of cat thalamic cells with highly overlapping receptive fields is strongly sensitive to the orientation and the direction of motion of the visual stimulus. We show that this stimulus selectivity is robust, remaining relatively unchanged under different contrasts and temporal frequencies (stimulus velocities). Computational modeling suggests that the nonlinearity of spike generation at cortex might be regulated by thalamic synchrony, ultimately shaping the cortical selectivity for orientation and direction, and that thalamic synchrony is a good predictor of motion in the scene. Finally, we have developed naturalistic, but artificially synthesized, natural scene datasets that capture the statistical properties associated with natural scenes while providing ground-truth knowledge of important scene properties such as optical flow. Most recently, we have developed a new data set, derived from a 3D animated film, which allows us to render scenes under conditions of varying complexity and evaluate where existing flow algorithms fail. Our final goal will be to provide a comprehensive analysis of the population response of thalamic neurons to the synthesized scenes that directly links population synchrony to ground-truth elements of the scene structure and motion.

(D39) Preclinical antidepressant and antipsychostimulant properties of a novel monoamine transporter inhibitor identified via structure-based virtual screening

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The purpose of the study was to discover and preclinically test antidepressant, anxiolytic or antipsychostimulant therapeutic lead compounds of novel molecular scaffold with affinity for the plasma membrane monoamine transporters (MATs). A three-dimensional computer model of the dopamine transporter was created and used to screen a structural library of small molecule compounds. Those predicted from the model to show high affinity were tested in vitro at the human dopamine, norepinephrine and serotonin transporters via displacement of a high affinity radiolabeled cocaine analog. Assays were also conducted that measured inhibition of cellular uptake of the appropriate [^{3}H]-monoamine neurotransmitter. Compounds displaying affinity for at least one of the three monoamine transporters were tested in mice in the conditioned place preference (CPP), locomotion, tail suspension test (TST) and forced swim test (FST) paradigms. When warranted, dopamine levels in the nucleus accumbens (NAc, the “reward” center of the brain) were assessed via microdialysis in response to the compound. The lead compound coded MI-4 displayed high nM / low uM binding affinities at all three MATs. Mice receiving cocaine (10 mg/kg, i.p.) spent significantly more time in the CPP drug-paired chamber. MI-4 (10 mg/kg, i.p.) reduced cocaine's effect by half, but did not exhibit rewarding effects when administered alone. MI-4 displayed minimal effects on locomotion and NAc dopamine levels, and dose-dependently reduced TST and FST immobility similar to that seen with classic antidepressants. MI-4 was found to be the ifenprodil analog and NMDA antagonist RO-25-6981. While antidepressant properties have been associated with NMDA antagonists, the additional ability of this drug class to antagonize the rewarding effects of cocaine is not established. The findings suggest that monoamine transporter computational model-based virtual screening of large databases of molecules is a viable method of identifying antidepressant and antipsychostimulant lead compounds of unique scaffold.

(D40) Limited role of intraglomerular inhibition in shaping responses to dynamic olfactory input

Matt Wachowiak (University of Utah), and Erik Sherwood

Odorant-evoked activity in the mammalian olfactory bulb (OB) is dynamically shaped by odor-sampling behavior, with individual sniffs eliciting bursts of activity across OB neuron populations. Mitral/tufted cells (MCs) – the principal OB output neurons – generally maintain sniff-driven patterning even at high (>5 Hz) sniff frequencies, while olfactory receptor neuron (ORN) inputs attenuate and show less patterning. Here, we investigate the glomerular circuitry that shapes inhalation-driven dynamics in MCs. First, we constructed a computational model of a glomerular circuit, including an external tufted (ET), PG, and mitral cell, each as a single-compartment, Hodgkin-Huxley-style model, and modeled MC responses to sensory input using different connectivities between these cell types. As input to the model we used signals derived from ORN recordings imaged from awake, naturally-sniffing rats. Results from these simulations suggest that synaptic depression and ET cell bursting can strengthen MC patterning, but that recurrent and feedforward inhibition have limited roles in shaping the temporal dynamics of MC responses. To confirm this result experimentally, we tested the effect of suppressing glomerular inhibition in vivo using optogenetics. We injected a Cre-dependent virus containing the proton pump Archaerhodopsin into the dorsal OB of GAD2-Cre mice, targeting GAD65+ periglomerular (PG) interneurons. After three weeks, we obtained extracellular recordings from MCs below the infected region while controlling sniffing in the anesthetized animal and using light stimulation to suppress PG cell-mediated inhibition. The most prominent effect of optical stimulation was an increase in odorant-evoked MC peak firing rates; however, there was little change in fine-scale temporal dynamics. Together, these results suggest that inhibition from glomerular interneurons may affect MC excitability but may not be critical in determining their temporal response patterns. Instead, feedforward excitation from ET cells may largely shape the temporal structure of MC responses and serve to maintain MC sniff patterning.

(D41) Internal model estimation for closed-loop brain-computer interfaces

Byron Yu (Carnegie Mellon University) and Aaron Batista

The motor system successfully plans and executes sophisticated movements despite sensory feedback delays and motor plant dynamics that change over time. Behavioral studies suggest that internal models are central in motor planning and control, but neural correlates thereof have thus far been limited, especially of a full internal model of the plant. Leveraging brain-computer interface (BCI) experiments as a window into this motor control loop, we developed a probabilistic framework to extract the subject's internal forward model and to infer the subject's internal estimates of the prosthetic plant state.

BCI provides us the unique opportunity to design task goals, to define prosthetic plant dynamics as linear and low-dimensional, to observe all relevant sensory feedback, and to monitor the activity of all neurons that drive the plant. While we are also interested in the engineering goal of developing assistive BCI systems, our immediate goal is developing a statistical framework for basic scientific studies of the neural basis of motor control and learning. We studied cursor-based BCI control by a Rhesus monkey implanted with a 96- electrode array in motor cortex. We found that recorded neural commands were consistent with a strategy requiring a forward model to predict upcoming cursor positions. Our

probabilistic framework estimates that forward model, allowing us to extract the subject's internal predictions of cursor state. Recorded neural movement commands were more consistent with aiming from these internal state estimates than from actual cursor positions. Extracted forward models explained roughly 75% of the subject's aiming errors and revealed that the subject often believed the BCI cursor was moving straight to the target, even when the actual cursor did not. Motor adaptation is driven by such differences between expected and actual consequences of neural control, and we believe this approach will yield insight into mechanisms that drive internal model formation and adaptation.

(D42) From flows to surfaces: Toward a model of cortical surface inference

Steven Zucker (Yale University), Daniel Holtmann-Rice, Roland Fleming and Romain Vergne

One of the most important functions of vision is to estimate the 3D shape of objects in our environment. Many different cues (e.g. disparities, shading, texture) provide information about shape, but how the visual system estimates shape is poorly understood. It is well understood, however, that the (early) visual system is organized around orientation. Here we present evidence that crucial information is extracted from the way local image orientation signals vary continuously across the surface of an object ('orientation flows'), and that these flows provide the foundation for surface inferences. To start, striking regularities in the flows emerge when computer renderings of shaded and textured objects are represented in a (superficial-layer) V1 fashion. These orientation flows change when illumination and texture patterns change, leading to a number of psychophysical predictions. A model of shape inference from shading flows reveals how surface and light source properties emerge from the flows, and the geometry of the model could be learned by the visual system. Together these findings suggest that the visual estimation of shape from shading, highlights and texture may have more in common than previously thought, and that orientation fields could act as a 'common currency' for the visual estimation of shape.