Abstracts for Poster Presentations

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Real-time, closed-loop experiments can uncover causal relationships between specific neural activity and behavior. An important advance in realizing this is the marked point process filtering framework which utilizes the mark or the waveform features of unsorted spikes, to construct a relationship between these features and behavior, which we call the encoding model. This is a dynamic relationship, because learning changes coding properties of individual neurons, and electrodes can physically move during the experiment, changing waveform characteristics. We introduce a sequential, Bayesian encoding model which allows incorporation of new information on the fly to adapt the model in real time, for experiments which can be segmented into multiple, unequal length epochs where encoding followed by decoding, occur. In the encoding phase, behavior and marks are observed simultaneously to construct updates to the encoding model, while in the decoding phase, only the marks are observed, and we decode the corresponding behavior. Model parameter posteriors are obtained during encoding using Gibbs sampling, with posterior of the previous epoch being incorporated as a prior to the current epoch. The priors reflect how certain we are about model parameter values, and we may relate the width of the prior to the notion of how quickly receptive fields and recording quality changes in a unit of time. If the full behavior is sampled at each epoch, and conjugate priors are chosen, this leads to an analytically tractable sequential encoding model. However, in practice, behavioral repertoire is only partially sampled in each epoch, yet we show that the model is still approximately conjugate, and we present computationally tractable numerical approximations for solving the model. A possible application of this framework is to the decoding of the contents of hippocampal ripples in rats exploring a maze. During physical exploration, we observe the marks and positions at which they occur, to update the encoding model, which is employed to decode contents of ripples when rats stop moving, and switch back to updating the model once the rat starts to move again.

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Analysis of hydra neural network during locomotion

The hydra is representative of the most primitive nervous systems. In turns out that it possesses the complex behavior of the neural network during locomotion. This cnidarian offers a convenient preparation for calcium imaging because it is possible to record from almost all neurons in the nervous system simultaneously. In this work we present the preliminary analysis of the neural network dynamics of hydra during behavior revealed by calcium imaging. We discuss the potential biophysical mechanisms of found patterns of activity using neural network simulations. In particular, we concentrate on role of gap junction and synaptic communication between neurons for activity propagation. Studying the dynamics of the hydra neural network provides the unique opportunity of understanding

the most basic rules of how nervous system computes and organize neural activity patterns to form behavior.

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Theta and gamma rhythm generation in a model network of fast-spiking striatal interneurons

Theta (4-10 Hz) and gamma (40-90 Hz) oscillations in the striatum manifest during behaviorally relevant time points in movement, reward, and decision making tasks, as does their cross-frequency coupling. Fast-spiking interneurons (FSIs) in striatum strongly inhibit the medium spiny neurons (MSNs) that make up 95% of striatal cells; therefore, they have a powerful influence in patterning striatal activity. These FSIs communicate with one another using both GABA synapses and dendro-dendritic gap junctions, and therefore have a synchronized network within the striatum that is likely to be involved in producing behaviorally relevant rhythms. Because FSIs can act in synchrony and have such a strong influence on MSNs, the FSI network could change the state of the striatal network as a whole by producing rhythms in unison in response to certain properties of the input it receives from cortex. This suggests that FSIs and their rhythms may play a vital role in informational routing in the striatum by integrating input streams to produce a unified result, allowing the computation of a decision. To simulate rhythm generation by FSIs, we used a dynamical system of 100 model fast-spiking interneurons, each of which was a two-compartment Hodgkin-Huxley neuron with a D-type slowly-inactivating potassium current (D-current). We found that these neurons burst at 5 Hz when stimulated tonically, with spikes within a burst occurring at 75 Hz. These frequencies are determined by the time constants of the potassium currents within the cell. Additionally, we found that a network of these FSIs can produce either a theta rhythm, a gamma rhythm, or both, depending on the conductances of the gap junctions and inhibitory synapses between the individual cells. Because dopamine increases gap junction conductance as well as excitability of the FSIs, the rhythmic regime of this network can be altered by differences in dopaminergic tone. Our findings shed light on the role of cognitive rhythms and dopamine in informational routing and decision making in the striatum.

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Pain is a multidimensional experience that includes sensory and affective components. Human imaging studies have identified patterns of activities within key neocortical areas that can encode different pain experiences, but it remains unclear how pain can also be encoded reliably at the level of individual neurons or populations of neurons within a discrete brain region. The primary somatosensory cortex (S1) has been thought to be important in the sensory-discriminative aspect of the pain, yet the anterior cingulate cortex (ACC) is known

to play a crucial role in the affective-motivational experience of pain.

To date most pain studies have focused on spinal or peripheral pathways. However, a complete understanding of pain mechanisms requires the physiological study of neocortex. Using in vivo ensemble neuronal recordings from the rat S1 and ACC, we investigate neural codes for acute thermal pain at both single-cell and population levels. To detect the onset of acute thermal pain signals, we propose a latent state-space framework to decipher the sorted or unsorted S1 and ACC ensemble spike activities. Specifically, decoding is formulated as a change-point detection problem. The state space analysis allows us to uncover a latent state process that drives the observed ensemble spike activity, and to further detect the "neuronal threshold" for acute thermal pain on a single-trial basis. Our results suggest an optimal decoding strategy for decoding acute thermal pain signals may be based on combined evidence from S1 and ACC population codes.

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Predictive coding in area V4: dynamic discrimination of partially occluded shapes

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The primate visual system has an exquisite ability to recognize objects in natural scenes even though most objects appear partially occluded. The robustness of shape discrimination in the brain has yet to be matched in computer vision. How the brain recognizes partially occluded shapes, therefore, is an important question. Recent experimental results from primate area V4, an intermediate visual cortical area in the shape processing pathway, suggest that feedback from higher cortical areas such as prefrontal cortex (PFC) may play an important role in delayed emergence of robust shape selective signals in V4, when animals are engaged in discriminating partially occluded shapes.

In order to understand such dynamic discrimination of partially occluded shapes in V4, we implement hierarchical predictive coding. Predictive coding has been hypothesized to be a method of efficient coding in various sensory systems, and has successfully reproduced responses in early visual areas [1]. Here, we propose that higher cortical areas make predictions on V4 activities, which are represented as feedback signals to V4. Our two-layer model, composed of distinct neuronal populations of V4 and a representative higher cortical area PFC, assumes hierarchical Bayesian inference and obtains the optimal representation of V4 and PFC activities by maximizing the posterior probability of the neuronal responses given the input shape stimulus. We propose that the probabilistic inference occurs in two steps; initially, the V4 responses are inferred solely by the bottom-up sensory signals. However, later in time, the V4 neurons receive feedback prediction signals

from the higher cortices, which reshape the probability distribution of V4 responses. Our model successfully reproduces the response characteristics of V4 and PFC measured in experiments. In other words, we found that inclusion of the feedback predictions results in decreased dependence of shape selectivity on the occlusion level, thus maintaining robust shape discrimination.

In conclusion, our results suggest that robust shape discrimination in presence of partial occlusion is achieved in V4 by interactive feedforward-feedback computation, and the feedback signals in V4 can be explained in the predictive coding framework.

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Parameter estimation for conductance-based models: A comparison of approaches

Conductance-based models that accurately capture the dynamics of different cell types within a network are powerful tools for exploring the role that specific ionic currents play in network activity. However, such models contain many parameters and determining appropriate parameter values based on electrophysiological data remains a significant challenge. The traditional parameter estimation approach requires data from a series of voltage-clamp experiments in which current traces are recorded after isolating a single ionic current pharmacologically or through other means. This type of voltage-clamp data is typically not available for all the cell types in a given network; instead the only data available may be voltage traces from current-clamp recordings. Fitting a Hodgkin-Huxley-type model to current-clamp data is difficult because many of the dynamical variables of the model (i.e. the gating variables representing the opening and closing of ion channels) are not measured directly. In this scenario, modelers often resort to hand-tuning models by visually comparing simulated voltage traces to the data and choosing parameter values that appear to give the desired behavior. Alternatively, one can attempt to infer parameter values in a more automated fashion by employing a parameter estimation algorithm. A variety of algorithms have been developed that differ in certain aspects of their implementation, such as the strategy used to search parameter space, the objective function used to compare the model and data, or the way in which the objective function is optimized. In this poster, we compare the ability of several approachesincluding regression, genetic algorithms, and data assimilationto infer parameter values based on simulated voltage traces from Hodgkin-Huxley-type models. We then assess the performance of these algorithms on current-clamp data from neurons in the suprachiasmatic nucleus, the master circadian pacemaker in mammals.

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Analyzing Neural Activity using Lenz-Ising Models and associated Hopfield Networks

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We present here a novel method for finding and extracting salient low-dimensional representations of the dynamics of populations of spiking neurons. This is a classical problem in data analysis of parallel spike trains, and quite a number of approaches to detect and classify recurring spatiotemporal patterns (STP) of neural population activity were proposed [1, 2].

Yet, most published methods so far assume a noiseless scenario and either focus on synchrony detection and / or seek to classify exactly recurring STP in neuronal activity [3, 4]. Given the usually high variability of population responses to stimuli, the re-occurrence of such exactly repeating STP becomes more and more unlikely with increasing population size, though. Assuming that despite this variability, network activity is not random per se (under the well-supported hypothesis that the population has to code information about stimuli in some form of STP [5]), a much more plausible situation is that some underlying STP appears in several "corrupted" variants differing in a few missing or excess spikes (characterized by a low Hamming distance to a true, underlying STP). The proposed method is robust to this variability in the signal and able to extract the underlying recurring patterns, even for seldomly occurring STP and large population sizes (¿ 100 cells).

The proposed method [6, 7] first fits a maximum entropy Lenz-Ising model [8] to windowed, binned spiking data using minimum probability flow parameter estimation [9] and then employs the associated Hopfield network [10] to cluster and classify the raw patterns using the Hopfield memories. This addresses the hard problem unsupervised clustering and classification of very high-dimensional noisy binary data and can not only be applied to spiking activity, but rather any noisy binary data and has furthermore be shown to be a powerful tool for image de-noising and compression [11].

We furthermore model the sequence of occurring STP (labeled Hopfield memories, see [7]) as a Markov process, we can perform a state space analysis of the system. Tracing paths of low entropy in the associated Markov graph, we are able to extract low-dimensional representations of stereotypical neural population activity (which might be associated to a stimulus).

We demonstrate the approach on data, specifically one data set obtained in rat barrel cortex [12] using our free available open source software [13] and show that it is able to

extract a remarkably low-dimensional, yet accurate representation of network activity observed during the experiment.

Sampling from the obtained Lenz-Ising model using an MCMC method (Swendsen-Wang) should furthermore allow us to shed more light on the question of how much of the total correlation in network activity can actually [14, 15] be explained by a pairwise maximum entropy model. This is work in progress, joint with V. Itskov, Penn State University.

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Structure in neural population recordings: interesting or epiphenomenal?

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The ability to simultaneously record large number of neurons has given rise to hypotheses that consider the population response as the central object of analysis. Often these analyses find some set of patterns in the data: examples include low-dimensional dynamical systems [1] , linear readouts with simpler tuning than is seen at the level of single neurons [2], and other population structures. These structures are relied upon to support different scientific hypotheses; however, we lack the necessary statistical testing methods to validate such population structures. In particular, here we develop a test of epiphenomenon: are these population structures non-trivial, interesting findings in the data, or are they simply a direct consequence of simpler, lower-order primary features that we already assume exist in the data? For example, should we expect to observe low-dimensional dynamical structure due to the temporal smoothness of neural firing rates? Traditional permutation tests (shuffling controls) are inadequate to answer these questions, leaving room for doubt in many population-level studies.

Here, we introduce methods based on Fisher randomization and maximum entropy to generate random surrogate datasets that have the same first and second order features as a given dataset across times (temporal smoothness), neurons (signal correlations), and conditions (tuning). The reference distribution found from these surrogates allows a test of epiphenomenon (H0: population structure exists to the extent expected by the primary features) vs. interesting structure (H1: population structure exists beyond the extent expected by the primary features). As a first application, we used this method to validate the hypothesis that motor cortical responses have low- dimensional dynamical structure. Our results show significant dynamical structure in the motor cortical population responses beyond what is expected from the temporal smoothness of firing rates, neural correlations, and tuning of single neurons alone, providing statistical support to recent findings [1].

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Spectral analysis of local field potential.

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Oscillations often provide us with information of the origin. For instance, electrical oscillations measured by electroencephalograms and electrocardiograms afford clues to cognitive disorders and cardiac dysfunction, respectively. Here we devise a Bayesian algorithm that may be applicable to the problems of inferring the origin from oscillating signals. To understand the working of the algorithm, we first consider inferring coins from the sound spectra of their collision. By devising a Bayesian learning algorithm, we reveal that optimizing the inference naturally leads the machine to select frequencies at which individual coins exhibit specific peaks in their sound spectra, indicating that inferences can be efficiently made by detecting the resonance sounds inherent in different coins. The machine has achieved a high performance of greater than 90% in correctly inferring single coins. In the present contribution, we report the result obtained by applying the Bayesian learning algorithm to the inference of the layer location of the local field potential (LFP). The machine has also achieved a high performance and we shall discuss the problem specific to the LFP and the possibility of biological application of this spectral analysis.

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Spike-frequency adaptation optimizes the tradeoff between efficiency and accuracy in a predictive coding model

Networks of neurons are tasked with performing computations on their inputs, and relaying this information to downstream networks. The accuracy of the representations they produce can be critical for downstream processing. However, neural networks don't have unlimited resources with which to operate, putting constraints on the quality of representations that can be achieved. Using a top-down approach, we build a neural code that seeks to minimize its representation error and its metabolic costs [1]. In doing so, we obtain a neural network that is E/I balanced and whose neurons are subject to spike-frequency adaptation. This framework allows one to investigate and make predictions about the structure of neural networks as well as the roles that specific biophysical mechanisms may

have in neural computation.

We use this approach to investigate encoding and decoding in a model of orientation discrimination. While spike-frequency adaptation leads to efficient and biologically realistic spiking activity, it also produces a variable population code that is dependent on recent spiking history. This can lead to drastic changes in the neural tuning curves that depend on the statistics of the preceding stimuli. Despite those changes, an accurate representation can still be obtained without having to adjust the decoder because the global network activity adjusts itself through balanced, recurrent connectivity. These results predict that population code variability isn't simply due to noise, rather, it is a consequence of the cost/accuracy tradeoff inherent in the neural code.

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The hippocampal recurrent neural network model for replay, reverse replay, and preplay

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In hippocampus, firing sequences of place cells corresponding to spatial pathways are often replayed after the experience. Moreover, it has been also found that those firing sequences are sometimes replayed in the reverse direction (reverse replay), and already observed before the experience of the pathway (preplay). These experimental findings imply that there are preexisting spontaneous firing sequences in hippocampal recurrent network which are utilized for coding spatial pathways, and they has to be replayed bidirectionally. We developed a recurrent network model that maintain bidirectional spontaneous firing sequences under the short-term and long-term synaptic plasticity, and also modeled dendritic computing in pyramidal neurons that helps the acquisition of place fields by selectively gating and potentiating sensory inputs based on firing sequences of the recurrent network. We show the basic properties of our recurrent network model and dendritic computing model, and how the combination of them realizes preplay-based acquisition of place fields.

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Observing firing rates of neurons and the level of synchrony between them is a common technique to draw conclusions on the micro-circuitry of the neuronal network they are embedded in, and on the input they receive from other stages of the nervous system. These questions are obviously of great importance for understanding the nature of neural coding. Using a very simple model network of leaky integrate and fire neurons that receive a mixture of common and independent inputs, we show that separating a synchrony code from a

firing rate code from measurements of average spike counts and spike-spike synchrony is mathematically impossible.

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Deep neural networks have performed well in various practical applications such as visual image classification and acoustic modeling. Developments of the gradient descent method have provided essential contributions to training of these deep networks. In particular, for training multi-layer networks, the natural gradient is superior to other methods such as second-order optimization because it can avoid or alleviate the plateau phenomena where learning becomes very slow. However, the main drawback of the natural gradient method is the high computational cost for the Riemannian metric of parameter space and its inverse.

In this presentation, we propose two types of efficient methods to realize natural gradient learning in multi-layer networks. First, we focus on score matching divergence, which is an alternative to Kullback-Leibler divergence for unnormalized statistical models, and introduce its Riemannian metric. By using the score matching metric, we derive an adaptive natural gradient algorithm that can avoid computation of normalization constant and inversion of the metric. Second, by using reparametrization of weight vectors, we propose a novel metric, which requires much less computational cost to invert it. Experimental results in multi-layer neural networks demonstrate that both proposed methods can avoid the plateau phenomenon and accelerate the convergence of learning.

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On the Spike Train Variability Characterized by Variance-to-Mean Power Relationship

We propose a statistical framework for modeling the non-Poisson variability of spike trains observed in a wide range of brain regions. Central to our approach is the assumption that the variance and the mean of ISIs are related by a power function characterized by two parameters: the scale factor and exponent. This single assumption allows the variability of spike trains to have an arbitrary scale and various dependencies on the firing rate in the spike count statistics, as well as in the interval statistics, depending on the two parameters of the power function.

On the basis of this statistical assumption, we show that the power laws with various exponents emerges in a stochastic leaky integrate-and-fire model and in a conductance-based neuron model with excitatory and inhibitory synaptic inputs, depending on the input regimes and the ratio between excitation and inhibition. We also discuss based on this result that the conventional assumption of proportional relationship between the spike count mean and variance could lead to the wrong conclusion regarding the variability of neural responses. Finally, we propose a statistical model for spike trains that exhibits the

variance-to-mean power relationship, and a maximum likelihood method is developed for inferring the parameters from rate-modulated spike trains.

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A hippocampal-entorhinal microcircuit model for adaptive communication through theta and gamma rhythms in a memory-based navigation task.

Neural rhythm plays an important role in communication between different cortical areas. Such a communication is not constant in time, but dynamically changed depending on demands of memory-consolidation, memory recall, and so forth. Gamma and theta rhythms in hippocampus and entorhinal cortex (EC) are critical for memory-based navigation task. A recent study (Yamamoto, et al., 2014, Neuron) has shown that coherence of these rhythms is dynamically changed during a T-maze task in which a rat is required to choose one of arms depending on the previous choice. They have found that neural activities in EC3 locked with theta rhythm is selectively higher in a test trial than in sample trial and also found that gamma synchrony between hippocampus and entorhinal cortex which only occurs around a decision point is necessary for the correct choice. Blocking this connection reduces success rate to chance level. This study implies that information of previous choice is transported through the gamma synchrony in dynamic way. What mechanism, however, underlies such a dynamic and flexible communications remains unclear.

For understanding this mechanism in microcircuit level, in this study, we model a local neural circuit including pyramidal neurons and some types of inhibitory neurons. This model network has three sub networks corresponding to CA1 and entorhinal cortices (EC3 and EC5) with input from CA3 to CA1 and that from a thalamus nucleus (reuniens). We assume that working memory of the previous choice is stored in EC3 and/or EC5 neurons as persistent activities and the decision is triggered by medial PFC via reuniens. By this model, we analyze the functional role of theta and gamma rhythms and conditions of each type of neurons under which the synchronization occurs in appropriate timing. We found that persistent activity with locked to theta rhythm is triggered by non-linear interactions of inputs from CA3 and EC3 to CA1 through CA1-EC5-EC3 loop. Because CA3 input encodes spatial information, this theta rhythm is generated in specific location on the maze. We also found that gamma synchronization that transfers the information stored in entorhinal cortices to CA1 is generated by interaction between feed-back and feed-forward inhibitions with triggered by reuniens. These results implies different roles of theta and gamma rhythm: theta-locked activity stores information in longer time scale (during a trial) and gamma synchronization triggered by the thalamus input controls more detailed timing to transfer the stored information.

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Comparison of MEG and fMRI signals during movie viewing

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Naturalistic stimuli, such as movies, provide a useful tool to study brain processes in experimental settings that mimic everyday life. Despite the complexity of the stimulus, previous studies with functional magnetic resonance imaging (fMRI) and recently with magneto- and electroencephalography (MEG/EEG), have shown that movies can generate consistent brain activity across the subjects time-locked to the movie.

As the origins of fMRI and MEG signals are different, they provide complementary views of brain function by reflecting hemodynamics and direct electromagnetic activity, respectively. Here we compared fMRI and MEG signals during movie viewing to find out how the hemodynamic and electromagnetic activity are represented in the brain under complex naturalistic stimulus. We showed a 15-minute black-and-white movie (At Land by Maya Deren, 1944) twice to eight subjects during MEG and fMRI recordings in separate sessions.

As the signal-to-noise-ratio of unaveraged trials is inherently poor especially in MEG, we needed advanced machine learning methods to find consistent signals from highly noisy and complex data sets. Here we applied a spatial filtering scheme based on multi-set canonical correlation analysis (MCCA) that maximizes the intersubject correlation and provides mutually orthogonal time-courses for each subject. The resulting signal components were compared to fMRI time series. We show the results of the comparison between fMRI and MEG signals, together with intra-modality analysis.

Despite the differences in the neurophysiological origins of MEG and fMRI signals, our results show evidence of similarities between the fMRI and the MEG signals. We also demonstrate that our methodological approach to find consistency in noisy and complex data was feasible to discover task-relevant brain activity.

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Imaging activity of motor cortical neurons in freely behaving mice performing a skilled motor task

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The first step toward understanding how neural circuitry activities generate behaviors involves monitoring large populations of neurons in a local network while a freely behaving animal performs a task. Here we use calcium imaging with the integrated miniature microscope to study the neural dynamics of hundreds of motor cortical neurons while mice perform a single seed grasping behavior. Our custom written preprocessing method for analyzing calcium imaging data will be presented, including automatic denoising, movement correction, ROI identification and signal extraction. The extracted calcium transient traces of individual neurons allow us to compare the spatial, temporal and sequential patterns of cortical activities in different conditions: resting state, successful trials, and failed trials. Furthermore, chronic imaging experiments allow us to examine the activity patterns during behavioral sessions across multiple days. The variability and stability of the spatial temporal neural patterns between successful and failed trials will be presented and discussed.

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Internally-generated dynamics in a simple inhibition-dominated neural network model

Abstract: Large-scale simultaneous neural recordings have enabled significant breakthroughs in understanding how neural activity reflects external stimuli, but the internally-generated dynamics that emerge in the absence of stimuli are still not well understood. For example, spontaneous sequences have been observed in both cortical and hippocampal networks (Luczak et al., 2007; Stark et al., 2015), and patterned motor activity arises from central pattern generator circuits (CPGs) (Marder and Bucher, 2001); however, the mechanisms underlying this pattern generation remains unclear. One common feature of all these networks, though, is an abundance of inhibition, which has led to the idea that cortical circuits may function similarly to CPGs (Yuste et al., 2005). To further explain the source of these internally-generated dynamics, we must tease apart the influence of many potential biological factors that may shape this activity. These range from single cell properties, such as intrinsic rhythmicity, to network-level properties, such as the structure of connectivity. In this presentation, we narrow our focus to the role of network connectivity alone by studying a new inhibition-dominated model, Combinatorial Threshold-Linear Networks (CTLN), with simple neurons but complex connectivity dictated by a directed graph. CTLN has

the potential to be an ideal toy model because it is simple enough to be mathematically tractable (we prove new theorems), yet complicated enough to exhibit rich behavior and provide reasonable (first) approximations to a range of observed neural phenomena, such as multistability, fast sequences, slower "cell assembly" sequences, and complex rhythms.

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Selecting Basis Sets for Event-Related Potentials

We focus on Event-Related Potentials, which generally involve EEG waveforms with only one or a few oscillations. The traditional approach to modeling ERPs involves averaging values at each time point to produce an estimate of the true waveform. To test a hypothesis about amplitude differences, for example, an average is again taken - this time over an arbitrarily-defined window. However, a combination of landmark-based reparameterization and current statistical techniques for working with longitudinal data can allow for more natural testing of a wider set of possible hypotheses. These procedures can also produce visualizations of data that reflect both the natural hierarchy in which ERP data is collected and the scientific hypotheses of interest.

The approach begins with the statement of a scientific hypothesis. This hypothesis is then translated into an appropriate basis set that will yield meaningful coefficients relative to the problem of interest. This is a non-trivial step that is best achieved through communication between neuroscientists and statisticians. The basis set can then be viewed as a generalized (non-polynomial) spline, which can be fit using Generalized Linear Modeling techniques into a Hierarchical, or Mixed Effects, framework and are equivalent to Regression Spline Mixed Models.

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Title: Emergence of spontaneous fluctuations in spiking neuron networks

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Spontaneous fluctuations in neuronal firing activity is widely observed in neural networks in vivo as well as in vitro. In the recent studies, it was proposed that a rich variety of temporal dynamics in neuronal firing can be utilized for working memory and motor control in the brain. Thus it is important to comprehend the mechanism by which spontaneous fluctuations appear. When considering an isolated network of neurons, the firing rates remains constant if the interactions among neurons are weak. However, if the interactions are strong, the network may exhibit non-stationary fluctuation in the firing rates even in the absence of external inputs. The critical interaction strength for the emergence of

fluctuations may depend greatly on the network structure in which neurons are connected Here we prove that we can predict whether fluctuations may emerge in a network, given information about the interactions between neurons. Furthermore, we develop a method of reallocating connections among neurons so that fluctuations may be either impeded or impelled in a network. Accordingly we found that reciprocal connections and clustering tends to facilitate spontaneous fluctuations in the firing activity.

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A useful task for a neural network to perform is to "replay a sequential activity pattern that it generated in the recent past. Such an ability could, for example, allow an organism to immediately recreate a reward-yielding motor sequence or to store information about a once-occurring stimulus into long-term memory by replaying the evoked neural activity sequence many times. Indeed, sequential replay is observed in in vivo neocortical dynamics. In a simple model winner-take-all network we explore how fast, activation-dependent increases in the excitability of neural ensembles could allow sequential replay to occur. Unlike the typically invoked spike-timing-dependent plasticity (STDP) learning rule, which due to its incremental effect modifies network dynamics quite slowly, excitability changes might occur much faster, due, for example, to rapid changes in local network states that persist over timescales of working memory. We show that for certain connectivity patterns such excitability changes, despite being effectively nonassociative, can bias the network towards replaying a combinatorially large number of possible sequences, and that in combination with slower learning rules, this replay can cause a novel stimulus-evoked activity sequence to become "embedded into the network after a single stimulus presentation. Next, we analyze the replay capacity of several networks with different recurrent architectures, and we show through an information theoretic analysis that the information contained in a neural activity sequence about a past stimulus increases as the network connectivity "aligns with the prior distribution over stimulus transitions. Finally, we discuss a general theoretical framework for interpreting our results that bridges both the working memory for and the planning of sequences. In this framework, information about a sequence is contained in steady, spatially distributed inputs to a set of ensembles, and the physical generation of the sequence arises through an interaction of this spatial input with the temporal dynamics conferred by the inter-ensemble connectivity structure.

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Rhythmic oscillations are ubiquitous in the nervous system, span a multitude of frequencies, and play important functional roles in cognition and motor behavior in both health and disease. A prominent rhythmic pattern is the hippocampal theta oscillations (4 - 10 Hz), which is evident in the rodent brain during motor activity and REM sleep , and provides a basis for temporal coding of spatial information and episodic memory.

The generation of hippocampal theta oscillations involves the interplay of various mechanisms including a septal pacemaker, circuit interactions, and the intrinsic properties of single neurons. Several neuron types including hippocampal pyramidal cells (PYR) exhibit subthreshold theta-band resonance: a peak in the voltage amplitude response to oscillatory current inputs at a preferred (resonant) frequency. These findings suggest that subthreshold resonance may underlie network theta oscillations. However, whether and how the subthreshold intrinsic oscillatory properties of single neurons affect the generation and properties of network oscillations is not well understood.

In recent work (Stark et al., Neuron, 2013) we have addressed these issues in the context of the hippocampal area CA1. Using optogenetic manipulations, we have found that, in the intact brain of the freely-moving animal, PYR do not exhibit theta-band spiking resonance by direct activation, apparently at odds with the 'in vitro' results. Instead, each PYR spikes at a different input frequency. In contrast, when PYR were indirectly activated through direct activation of parvalbumin-positive interneurons (INT), PYR displayed theta-band resonance. Only input frequencies in the theta frequency band produced a spiking response. Blockade of the h-current (known to underlie subthreshold resonance in PYR) abolished inhibition-induced spiking resonance.

In this study we use mathematical modeling, numerical simulations and dynamical systems tools to investigate the underlying mechanisms. Specifically, we present a minimal biophysical (conductance-based) model of a CA1 hippocampal network that captures the above-mentioned experimental results. The basic model includes PYR, INT, AMPA synaptic excitation and GABA-A synaptic inhibition. The extended models include also OLM (orients-lacunosum moleculare) interneurons and synaptic depression (from INT to PYR). Both PYR and OLM include h-currents. The mechanisms of generation of subthreshold resonance in these cells involve the complex interaction between the voltage-dependent nonlinearities and the time scale separation between the voltage and the h-current gating variable (Rotstein & Nadim, J Comp Neuroscie, 20143; Rotstein, J Comp Neurosci, 2015).

The PYR subthreshold resonance fails to be communicated to the spiking regime by direct PYR activation because of the relatively strong effect of the oscillatory input amplitude that causes the spiking activity to spread over a broad range of input frequencies (for which the voltage response is above threshold). PYR theta-band resonance through direct INT activation results instead from a combination of rebound spiking and a timing mechanism. Rebound spiking is responsible for the "spiking low-pass filter" (generation of spikes for input frequencies that are low enough for the voltage responses of both PYR and INT to be above threshold), but it is not enough to generate spiking resonance. The timing mechanisms are responsible for either erasing spikes generated by input frequencies lower that theta or failing to produce spikes for these input frequencies. We identified three such mechanisms: (i) network-mediated inhibition from OLM, (ii) synaptic depression of INT synapses, and (iii) subthreshold gamma resonance in INT.

Overall, these results provide a mechanistic understanding of network resonance at theta frequencies and make several predictions. The principles identified in this study are applicable not only to CA1 networks, but also to other systems that exhibit theta resonance such as neocortical networks. Finally, the results and ideas that emerge from our study are seminal for the construction of a theoretical framework for the investigation of the preferred frequency responses of neuronal networks to oscillatory inputs at a variety of biophysically realistic frequency bands.

This project is in collaboration with Eran Stark (Tel Aviv University, eranstark@post.tau.ac.il) and György Buzsáki (New York University Medical School, Gyorgy.Buzsaki@nyumc.org).

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Fragility in the human decision making system: When emotion hijacks logic

Decision-making links cognition to behavior and is a key driver of human personality, fundamental for survival, and essential for our ability to learn and adapt. It has been well established that humans make logical decisions where they maximize an expected reward, but this rationality is influenced by their emotional state. Psychiatric patients who have dysfunctional cognitive and emotional circuitry frequently have severe alterations in decision-making where emotion hijacks logic. Unfortunately, the function of relevant neural circuits in humans is largely uncharted at fine temporal scales, severely limiting the understanding of changes underlying disruption associated with age or psychiatric diseases. In this study, we localize neural populations, circuits, and their temporal patterns on a millisecond scale that are critically involved in human decision-making.

Twelve human subjects, implanted with multiple depth electrodes for clinical purposes, performed a gambling task while we recorded local field potential neural activity from deep and peripheral brain structures. The gambling task consisted of a game of high card, where the subject bets high (20)orlow(5) on whether her card will be higher than the computers card. We posited that each subjects decision-making system consists of a feedforward model with the playing card as the input and betting behavior as the output (e.g. how she bets and how quickly she bets). The behavior and gambling outcome is a feedback control signal to the model, which updates the internal latent state of the feedforward model. For each subject, we estimated the latent state variable from binary bets (high versus low) using maximum likelihood methods. Specifically, we modeled the probability of betting high as a function of this internal state and the players card, and the state updates on each trial as a function of observed quantities such as the card value, expected reward, and variance of reward.

In particular, we constructed the state update model in such a manner that the state increases when the subject presumably will feel good (e.g., gets a high card, wins a risky

bet) and decreases when the subject presumably will feel bad (e.g., gets a low card, loses on a risky bet). The probability models suggest a spectrum of decision-makers that range from emotionally-dominant to logically-dominant, and analysis of the neural data suggest that oscillations in populations of neurons of key structures limbic and cognitive structures.

Further, neural correlates for the internal state trajectory and components that update the internal state are present in key limbic structures suggesting that the internal state is correlated to the subjects emotions. In particular, specific oscillations in brain structures, including amygdala, cingulate cortex, and the entorhinal complex are shown to influence betting behavior (what you bet and how quickly you make the bet) in a profound way. These findings provide new insight into how humans link their internal biases (e.g. emotions) to decisions.

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Overexpressed striatal ? FosB is associated with altered striatal activity and dyskinetic behavior in response to dopamine in parkinsonian monkeys

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Objective: To determine the effects of overexpressed striatal ? FosB in response to chronic dopamine treatment in striatal projection neurons (SPNs) activity and dyskinetic movements in the non-human primate (NHP) model of Parkinsons disease (PD).

Background: Levodopa is the most suitable symptomatic treatment of PD. However, over time, levodopa treatment leads to the emergence of abnormal involuntary movements, known as dyskinesias that are related to adaptive changes in striatal signaling pathways. The chronic transcription factor FosB, which is overexpressed in striatal neurons after chronic levodopa inputs, is supposed to mediate these adaptive alterations.

Methods: We infused rAAV (recombinant adeno associated virus) viral vectors that expressed either high levels of FosB or GFP (control virus) in the striatum of MPTP-treated NHPs nave of chronic drug administration. We recorded extracellular SPNs activity

changes during different levels of dopamine stimulation every week for 3 months in both groups of NHPs. Single SPN activity was recorded continuously during the parkinsonian state, its reversal during the "On condition, and during the dyskinetic state induced by levodopa input. Electrophysiological recordings were followed by behavioral assessment.

Results: Striatal overexpression of FosB induced abnormal motor behaviors including involuntary movements in response to acute levodopa tests. However, NHPs with control virus developed dyskinetic movements after 10 weeks. Increased SPN firing frequency was observed during "off medication in parkinsonian state. However, levodopa administration induced both increases and decreases in the firing rate of SPNs during on motor state. Furthermore, dyskinetic movements were associated with distinctive bidirectional activity of SPNs in response to the dopamine. Abnormal bidirectional SPNs activity related to the involuntary movements was present in most of the striatal cells (¿ 60%) in NHPs overexpressed with FosB.

Conclusions: These results demonstrate that the increased level of striatal ? FosB in the progression of chronically treated PD could underlie the mechanism of involuntary movements and the altered and disproportionate SPNs activity in response to the dopamine.

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A sequential monte carlo approach for parameter estimation for leaky Integrate-and-Fire models from spike times

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Estimating the parameters of dynamical models of neural systems using only observed spiking information is an important area of research that has direct application to computational neural modeling. Here we present a sequential monte carlo (SMC) approach to estimate from a leaky integrate-and-fire (LIF) model parameters related to the input drive, the leak time constant, and the process noise using only an observed set of spike times. Previously, multiple approaches have been proposed to address this question, including approaches based on the method of moments, Laplace transforms, the Integral Equation method, and the full likelihood of the data. However, these methods have a number of limitations such as requiring many observations, large computation times, or specific assumptions about the parameters to estimate. Recently, methods based on SMC methods, or particle filtering, have been proposed to address this problem. However, it is not clear how to sample efficiently in the SMC procedure to generate trajectories consistent with the observed spike times. Here, we construct a new iterative algorithm that allows us to estimate the (distribution of) parameters for a LIF model or more general dynamical spiking models by deriving a set of forward and backward iterative equations to simulate the trajectories of the process conditioned on the observed spike times. We implemented

this SMC algorithm on a small set of simulated data (20-50 spikes), and found that it could accurately and efficiently estimate (the distribution of) all identifiable parameters simultaneously. We also prove that our estimator is consistent and explore the convergence rate. Finally, we discuss how this approach can be generalized to a wide class of dynamic models of neural spiking systems.

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Deep brain stimulation (DBS) is a growing therapeutic strategy for various neuropsychiatric illnesses. DBS involves surgical implantation of depth electrodes into key regions of the brain thought to mediate pathological signaling in larger brain networks. Despite its growing use, a model of how DBS modulates signaling in pathological brain networks is lacking. Our lab has adopted an innovative approach to multimodal electrophysiology and dynamical modeling in order to study pathological signaling in human subjects implanted with DBS for treatment resistant depression (TRD) throughout the course of their treatment.

Direct stimulation of subcallosal cingulate (SCC) white matter tracts is thought to give rise to therapeutic benefit. In this abstract, I will show preliminary data demonstrating rapid changes in network oscillatory activity differentiating direct stimulation of SCC white matter vs SCC gray matter. Using a prototype DBS device (Activa PC+S) and dense-array EEG, I demonstrate unique cortical signatures reflecting stimulation target that can be critical in validating surgical implantation. I then present a kuramoto-style model of network oscillatory behavior that reflects empirical data and provides a way to interpret collected data in the context of oscillatory network activity, network connectivity, and intrinsic oscillatory modes. This model will be critical in testing hypothesized mechanisms of action for SCC DBS and provide a systematic framework to make clinical decisions about stimulation parameters.

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Measuring neural maturation in the developing human brain: characterization of network dynamics from longitudinal electrophysiological recordings

Postnatal neural maturation is a relatively long, highly dynamic and heterogeneous process that is particularly rapid during the first few years of life. During this time, the human brain's neural circuitry undergoes profound topological changes: redundant and/or weak neural connections are selectively eliminated and remaining connections are strengthened and reorganized into increasingly parsimonious networks that facilitate efficient neural information processing. Despite its critical role in cognitive function across the lifespan, the dynamics of neuronal network optimization in the first few years of life are poorly understood. Robust statistical characterization of this process in the developing human

brain is challenging. Longitudinal electrophysiological recordings from large cohorts of typically developing infants are critical for improving our understanding of how brain activity changes at the network level over a period of years. Using a graphical models, the dynamics, topologies and properties (stability, redundancy and efficiency) of functional brain networks were estimated longitudinally from a relatively large cohort of infants (n = 140) during the critical period of the first 3 years of life. Although several core networks that are essential to survival appeared to be connected as early as 6 months, their topologies and properties changed significantly during the first 3 years of life. Furthermore, extended networks associated with higher level functions appeared to develop and change topologically at distinct rates from core networks, suggesting hierarchical and differential neural maturation across the brain in response to increasingly complex cognitive demands.

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Introduction. Accurate detection of mild traumatic brain injury (mTBI) using quantitative tools remains elusive. The abnormalities are typically not apparent on conventional magnetic resonance imaging (MRI) or computer tomography (CT) scans. In turn, diagnosis is usually a clinical judgement based on self-report measures and behavioural assessments. However, despite the lack of apparent injury on routine clinical scans, the presence of lingering post-concussive syndromes in subset of patients indicates the presence of a subtle brain injury. Thus, there is a need to develop sensitive imaging tools to objectively quantify mTBI and to monitor brain recovery.

Methods. In the present study, we recorded 5 minutes of resting state magnetoencephalograms (MEG) from adults (all males) with mTBI (n=20, 21-44 years of age, mean=317), all within three months injury (32 18 days since injury). The patients had concussion syndromes while in emergency, with a clear cause of head injury, with Glasgow coma scale equal to or higher than 13, and had no abnormalities on CT scans. We also collected 5 minutes of resting state MEG from controls (n=20, all male adults, 20-39 years of age, mean=275). Neuromagnetic source activity was reconstructed with a vector beamformer at anatomically selected 90 seed locations, which represented the cortical and subcortical brain regions in the Automated Anatomical Labeling (AAL) atlas. Inter-regional phase synchrony was estimated between 1-75Hz. Three multivariate analyses were performed: (i) to explore frequency-specific group differences in functional connectivity; (ii) to explore correlations between the phase synchronization and the length of time elapsed between injury and scan; and (3) to classify mTBI from inter-regional phase synchronization using machine learning methods.

Results. We found that the group differences between mTBI and controls were characterized as the interplay between synchronizations and de-synchronizations in different frequency bands. Specifically, mTBI was associated with deccreases in network connectivity at the delta and gamma (¿30Hz) frequencies as well as increases in the slower alpha

band (8-12 Hz). A similar temporal pattern was found for correlations between network connectivity and the length of time between the injury and the MEG scan. Also, we were able to detect mTBI with 88% accuracy, with the alpha rhythms contributing the most to classification. Finally, classification confidence was found to be corrected with clinical symptom severity scores.

Conclusion. Our results provide the evidence that MEG network connectivity, in combination with machine learning tools, has the potential to detect the presence of mTBI, to quantify its severity, and to provide quantitative tools for monitoring the recovery of the brain from the injury.

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Neural connectivity among d neurons may be described by means of a graph, where each cell is represented by a node, and two nodes are linked by an edge if the two neurons are dependent conditionally on the activity of the remaining d-2 cells. A Gaussian graphical model is determined by the partial correlation matrix R. However, in the absence of extremely large numbers of trials, statistical inference about R becomes challenging when d is large, and estimates must be regularized to make them well-defined and to reduce their variability. A popular L1-penalized likelihood estimation approach is the Graphical Lasso (Glasso). The circumstances under which Glasso performs well are of questionable relevance to neural data and, furthermore, in its standard form Glasso does not take into account known neurophysiology, such as inter-neuron distance and tuning curve similarity. We have developed a Bayesian variant of the Glasso that, by incorporating neurophysiological auxiliary information, substantially outperforms Glasso. We apply this methodology to populations of neurons recorded with a multielectrode array implanted in macaque primary visual cortex.

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Dopamine neurons are known to calculate reward prediction error (RPE), or actual reward minus expected reward. How neural circuits actually compute RPE, however, remains unknown. Previous models have proposed that specific brain areas signal specific terms, such as actual and expected reward, and that dopamine neurons combine these signals to compute RPEs. To directly test this hypothesis, we established an awake electrophysiological recording system with transsynaptic, optogenetic-tagging and characterized the activity of neurons presynaptic to dopamine neurons in seven brain areas. We show that relatively few input neurons signal information in a pure fashion. Instead, many input neurons signal combinations of multiple types of information. We also found that RPE is partially computed before these inputs converge onto dopamine neurons. Our results demonstrate that the information required for RPEs is not localized to specific brain areas; rather, RPE computations are distributed across multiple nodes in a brain-wide network.

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We introduce a separable two-dimensional (2D) random field (RF) model of neural spike rasters for which the intensity function over time and trials depends on two latent Markovian state sequences that evolve separately but in parallel. The two state sequences are intended to capture the variability within and across trials respectively. The lack of a of total order on the 2D plane implies that the evolution of the joint state sequence cannot be written as a simple random walk in one dimension (e.g. time), and is therefore not amenable to classic methods for estimating a state-space model from point process data. We derive a Monte Carlo Expectation-Maximization algorithm to maximize the marginal likelihood of the data from this separable 2D RF. In the E-step, we leverage the Polya-Gamma latent representation of Bernoulli random variables to generate Gibbs samples from each of the state sequences. The sampler uses a highly efficient forward-filtering backward sampling algorithm for which the forward step can be implemented exactly and elegantly as Kalman filter, while the backward step uses Bayes rule to correct the filter samples. We demonstrate this new model on data collected from neurons in the anterior cingulate cortex (ACC) in an experiment designed to characterize the neural underpinnings on the observational learning of fear in mice. Our algorithm provides a more precise delineation of both the trial and time at which neurons in ACC learn a fear response.