Inferring interactions between neurons, stimuli, and behavior

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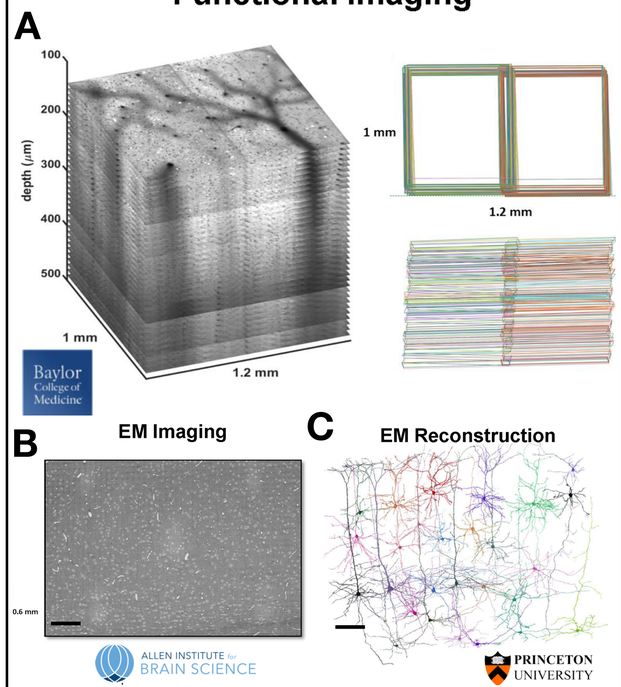
1. Abstract

We are developing mathematical methods to interpret new recordings of large-scale neural populations. Methods include:
- inference of time-dependent interactions
- combining models from non-simultaneous neural recordings
- flexible, context-dependent interactions between neurons driven by stimuli, and different latent states.
- inference of joint statistical relationships between neural activity, external stimuli, and animal behavior.

We validate methods against measured synaptic connectivity in real neural tissue, and against known connections in rich artificial neural networks, including both biologically constrained networks and networks trained to perform machine learning tasks. The team also includes an experimental group developing techniques that is recording from tens of thousands of cells simultaneously in the visual cortex of awake, behaving mice.

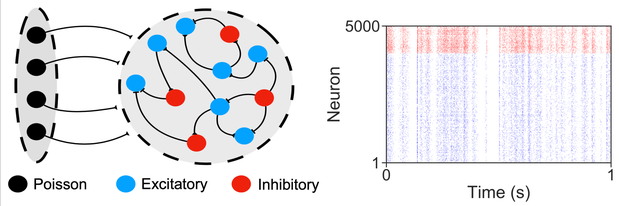
Large scale multi-photon imaging Functional Imaging



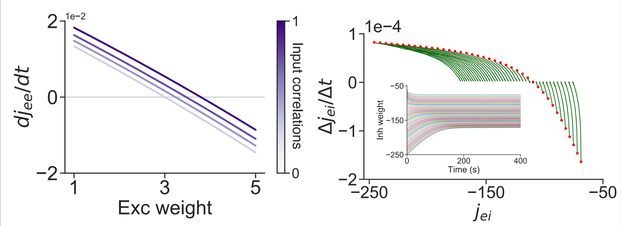
(A) Functional imaging: BCM; **(B)** EM imaging: AIBS; **(C)** Selected neurons from EM reconstruction (all neurons are segmented): Princeton University (scale bars = 100 μm)

Massive scale data generated from the MICrONS project (funded by IARPA, see other poster) records both functional responses to natural movies, and the nanoscale wiring diagram for the same 100,000 neurons. We are developing methods to examine the interactions between neurons based on coactivation, and comparing these graphs to the ground truth anatomical connectivity. We also aim to describe the connectivity motifs in terms of simpler principles of connectivity, using the Exponential Random Graph Model. Preliminary findings show that neurons are connected reciprocally more than expected by chance.

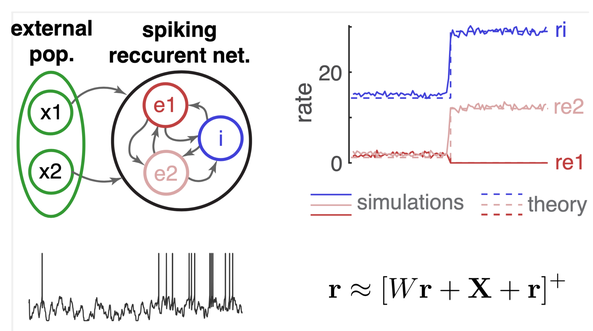
Theory of spike-timing-dependent plasticity in balanced networks



We developed a theory to describe mean-field dynamics of neural networks undergoing a range of plasticity rules (Hebbian, iSTDP, Kohonen, Oja, etc.). Mean field results show that weight changes are driven mostly by firing rates, with corrections for correlations. In general balance is preserved, but under inhibitory plasticity (iSTDP) the theory fails due to correlated weights and rates, and extended theory to account for this.



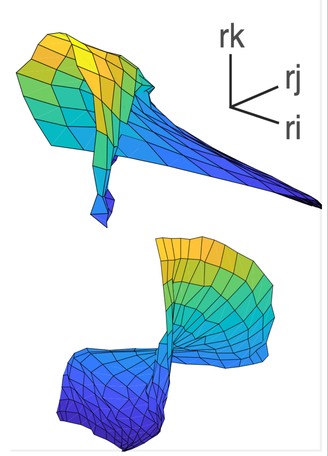
Nonlinear stimulus representations in neural circuit models with excitatory-inhibitory balance



$$\mathbf{r} \approx [W\mathbf{r} + \mathbf{X} + \mathbf{r}]^+$$

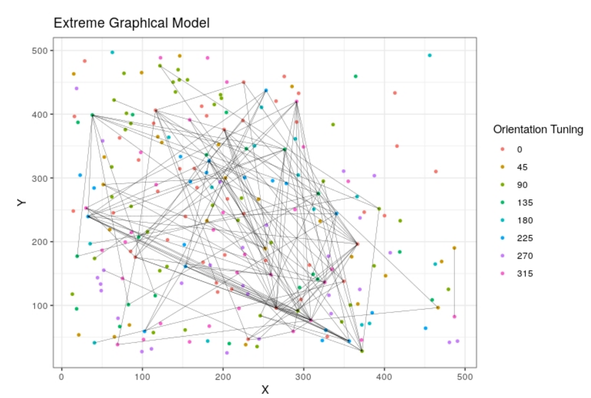
- We generalized the mathematical theory of excitatory-inhibitory balance in recurrent neuronal networks. The resulting theory extends the applicability of the theory to more general classes of networks, provides an accurate approximation to stimulus-dependent firing rates, and shows that balanced networks can perform nonlinear computations.

Neural manifolds



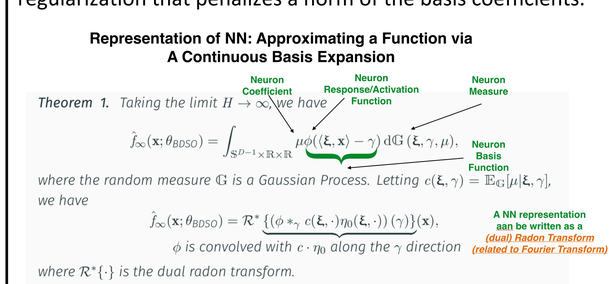
Extreme Graphical Models

How are neuronal circuits organized with respect to functional connectivity, defined as the statistical relationships between the spiking activity of neurons in the brain? Graphical models are a commonly used tool for analyzing full conditional dependency structures in high-dimensional settings, such as functional neuronal connectivity patterns in the brain. However, raw neuronal activity recording data presents several challenges: the data are highly non-Gaussian and the important information lies in the extreme values or neuronal spikes rather than the average ones. Instead of using multi-step data pre-processing methods common in the current neuroscience literature that either estimate neural spikes or convert the empirical data distribution to be Gaussian, our goal is to develop a graphical model method which can properly analyze functional neuronal connectivity using only raw neuron activity data. We establish a new class of graphical model distributions, called the extreme graphical model, which is based upon a subclass of the Subbotin distribution. We apply our method on recordings of neuronal activity from various calcium imaging experiments in order to conduct analyses of functional neuronal connectivity and gain insight into the network structure of the brain.



Inductive Bias of Neuronal Nets

What is the inductive bias (IB) of the Brain? This question lies at the heart of the Brain's ability to learn quickly and perform early in life. Recent theoretical advances have elucidated the representation and IB of artificial neural nets (ANNs). Here we extend this work to NNs with arbitrary monotonic activation functions and higher dimensional inputs. Our theory makes manifest that shallow feedforward neural circuits are overcomplete basis expansions (see Theorem 1 below), closely related to wavelets, and that the form of the IB is a regularization that penalizes a norm of the basis coefficients.



Novel generative model for ubiquitous computational feature

- Statistical transistor: Generative model component for three-way multiplicative interactions (Figure 1)
- Examples: Color constancy, shape constancy, gating
- Inference with statistical transistor gives canonical computation of flexible divisive normalization
- Reproduces context-dependent neural tuning (Figure 2, compare to Mixture of Gaussian Scale Mixtures (MGSM) in [1])

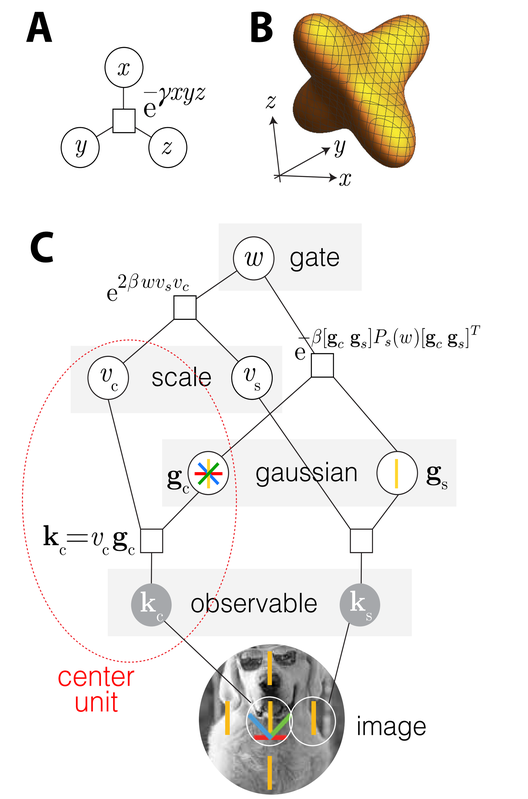


Figure 1: Third order interactions. A: Third-order motif as graphical model. B: One variable modulates the interaction between the other two. C: Graphical model between the center Receptive Field (RF) and one surrounding RF in third-order version of an MGSM model.

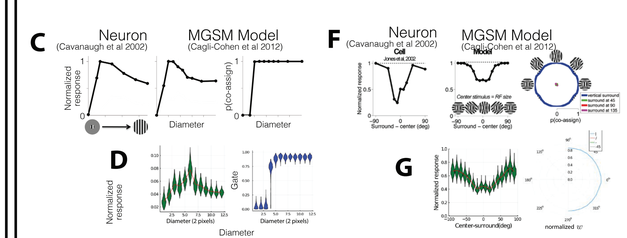


Figure 2: Neural tuning derived from third-order motifs. A: Neuron with vertical tuning in center RF responds with the same vertical patterns when presented with round vertical stimuli with increasing diameter. The divisive normalization effect is predicted by the MGSM model. B: Similar predictions from our model. C: For a stimulus with a center grating covering the whole center RF and partially covering the surround RF, the normalization degree depends on the angle between center and surround stimuli. D: Similar predictions from our model.

[1] R. Coen-Cagli, P. Dayan, O. Schwartz, PLoS Comput Biol 8, e1002405 (2012).