

# A statistical physics approach to infer cortical neuronal networks structure

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Understanding how cortical neuronal network structure from neuronal activity data remains a fundamental open question, with deep implications for how networks evolve spontaneously or under stimulation, and how plasticity and learning emerge. Addressing it requires principled tools to infer the effective structure and composition of a network directly from observed activity.

We present a probabilistic inference framework by employing tools from statistical physics, Bayesian inference and principled machine learning, devised to reveal the effective architecture of biological neuronal networks from spiking data [1]. Activity is mapped onto the kinetic Ising model [2,3], which shares key features with neuronal systems: (1) binary states, (2) non-equilibrium asymmetric interactions, and (3) multi-neuron couplings. Building on earlier work on asymmetric kinetic Ising inference [4,5], we extend the formalism with latent variables identifying (i) the excitatory/inhibitory type of each neuron and (ii) the existence of effective links, together with biologically motivated priors encoding distance-dependent connectivity and log-normal coupling distributions.

Inference follows a generalized maximum-likelihood (GML) procedure implemented via a two-layered variational expectation–maximization scheme. In particular, a macro EM estimates couplings and local fields, while a nested micro EM infers latent variables and hyperparameters. This jointly recovers, from single spontaneous recordings and without invasive manipulation, the effective synaptic strengths, neuronal type, and link existence, which is a combination unattainable by existing methods.

We validate the approach on three complementary datasets: synthetic data from the kinetic Ising model; *in silico* activity from an Izhikevich-based spiking emulator [6] of cultures on topographically patterned substrates; and *in vitro* calcium imaging of rat and mouse cortical cultures on patterned and homogeneous substrates. The method accurately recovers modular organization, classifies neuronal types with high precision, and returns excitatory and inhibitory strengths consistent with ground truth. Benchmarking against generalized transfer entropy [7] and mean-field approaches [4] shows clear improvements in true- and false-positive rates of link identification, and superior reproduction of equal- and delayed-time covariances via Monte Carlo simulation of the inferred model.

Beyond the methodological advance, the framework opens concrete routes to study plasticity, design stimulation protocols for neuron-based computing devices, and probe the interplay of structure and function in living neuronal networks.

## References:

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