What can MaxEnt reveal about high-density recordings and what can high-density recordings reveal about MaxEnt?

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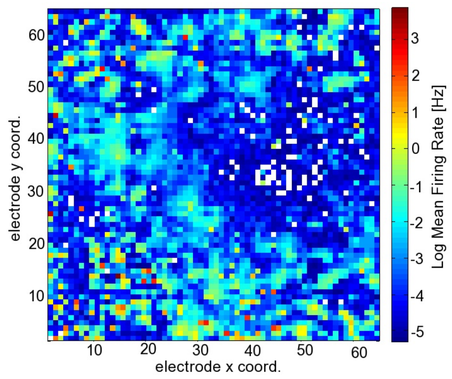
Introduction

APS - New generation Microelectrode Array (MEA)

New generation electrophysiology tools open exciting possibilities for understanding populations of neurons: APS (Active Pixel Sensor) MEA [1,2] allows for simultaneous recording from **4096 channels**. Its 64 by 64 grid of **21-micrometre electrodes** spaced 42 micrometres apart provides a **near-cellular resolution**.



MaxEnt - Maximum Entropy modelling

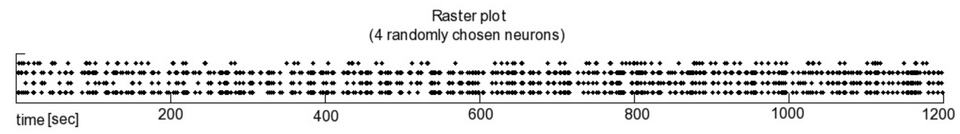
To analyse such volumes of parallel spiking data beyond simple measures (mean rates, correlations) we examine MaxEnt. It is a statistical model that explains a distribution of spiking patterns in terms of individual neuron **'local firing field' h_i** and **neuron-neuron interacions j_{ik}** (where s_i is the state of neuron i: spiking 1 or not spiking -1):

$$P(S)=\frac{1}{Z}\cdot\exp\left(-\sum h_i\cdot s_i-{}^1\!/_2\cdot\sum\sum j_{ik}\cdot s_i\cdot s_k\right) \qquad Z=\sum_S \exp\left(-\sum h_i\cdot s_i-1/2\cdot\sum\sum j_{ik}\cdot s_i\cdot s_k\right)$$

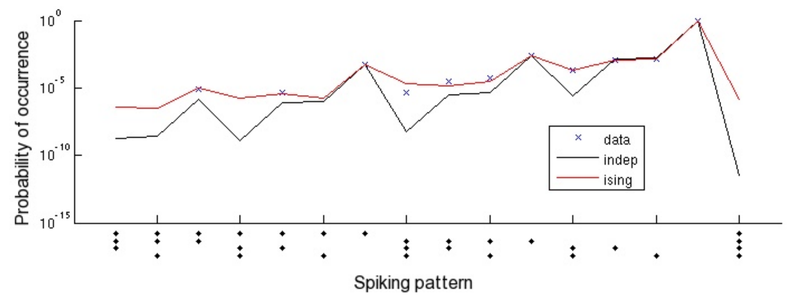
MaxEnt has been shown to characterize spiking patterns suprisingly robustly in many cases [3,4]. Arguably, this model is not without computational limits, and it has also been shown to fail for short-range in vivo recordings [5]. Here we try to assess the utility of fits - and failures - of MaxEnt.

Methods

Dissociated cortical cultures were recorded on the APS MEA for 10, 15 and 20 minutes. Only channels with rates of 0.1 - 10 Hz were considered for analysis. Spikes were binned into 5ms time bins.



A fixed number of channels (4 or 6) was repeatedly and randomly chosen (2000 and 400 sets, respectively). For each such subset, a MaxEnt model was fit to the distribution of spike patterns. In the case of 4 neurons fits, half of the subsets consisted of close-by neurons (within 8 electrodes), and half - of faraway neurons (more than 22 electrodes apart).



Quality of the fits was assessed in two ways: by Kullback-Lieber divergence between data and model probability distributions (equivalent to log likelihood ratio); and by fraction of multiinformation, i.e. portion of entropy difference between independent model and the data explained by the MaxEnt.

Results

FIGURE 1. **Dense culture of neurons**: comparison of statistics of MaxEnt fits between close-range subsets of neurons and far-range subsets of neurons.

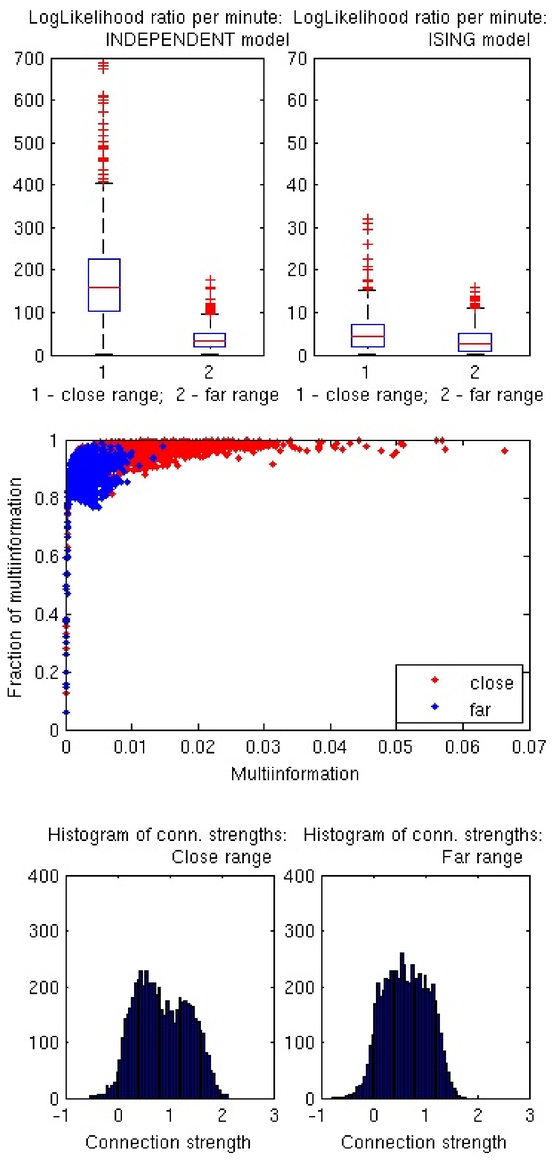


FIGURE 2. **Sparse culture of neurons**: comparison of statistics of MaxEnt fits between close-range subsets of neurons and far-range subsets of neurons.

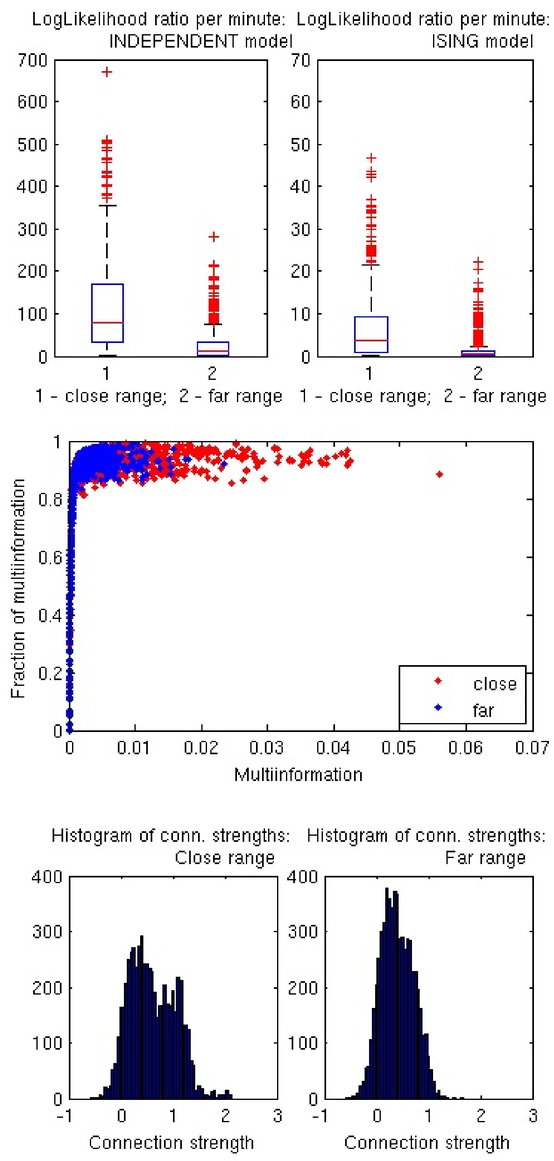


FIGURE 3. **Distance dependence in high-density culture data**: simple measure (pairwise interaction calculated from data) shows no correlation with distance (correlation coefficient -0.044) while model-inferred connection strengths change with distance (correlation coefficient -0.401). Same dataset as in Fig.1. Mean multiinformation captured: 89%. Mean LLR/min of independent model: 124. Mean LLR/min divergence of MaxEnt model: 12.

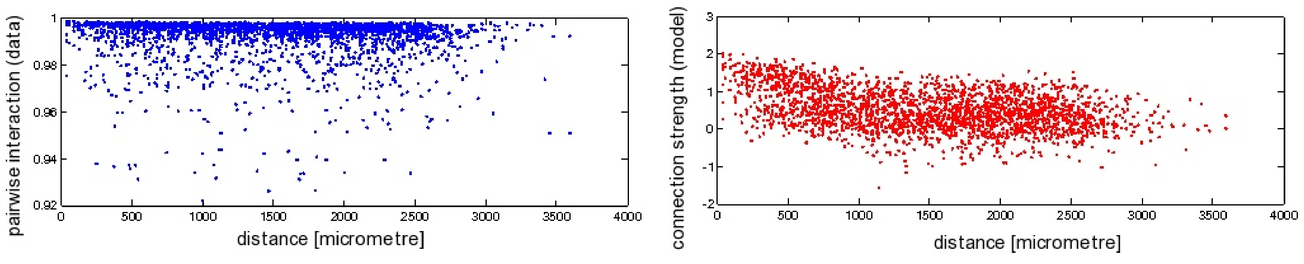
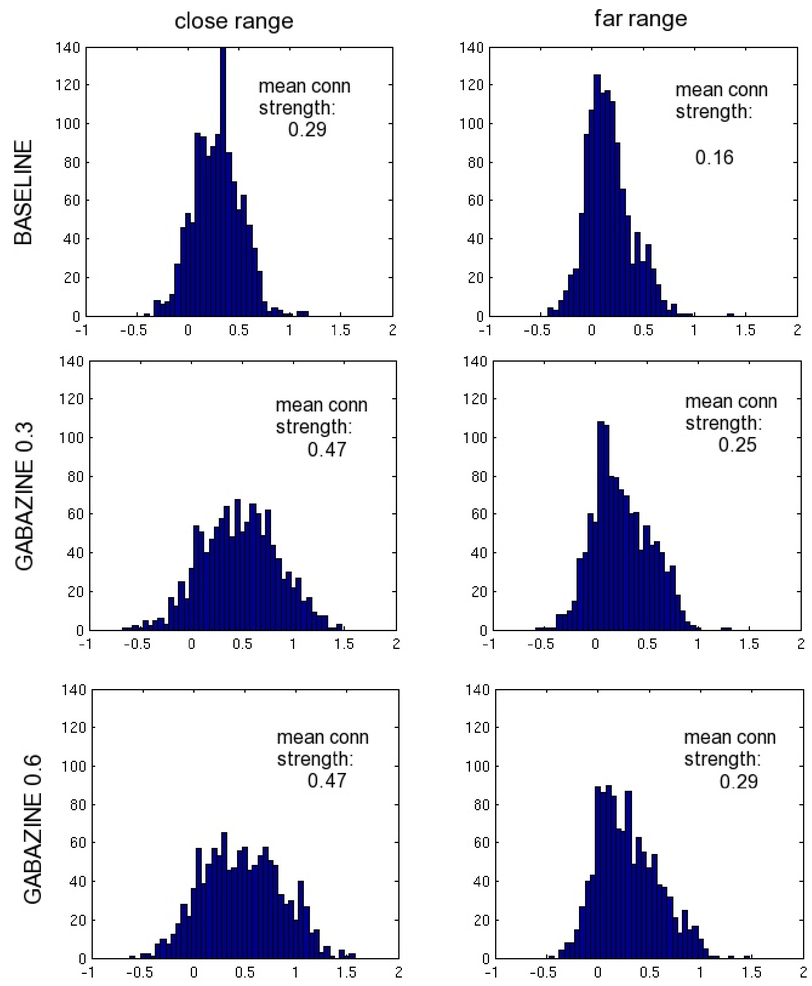


FIGURE 4. **Pharmacological intervention in low-density culture data**: comparison of connection strength distribution changes with the application of GABA blocker Gabazine; two spatial scales were considered separately.



Conclusions

It is computationally not feasible to compute a single MaxEnt model for a complete population of thousands of neurons. However, with high-density recordings it is possible to sample the population extensively. While such a method doesn't provide exact functional connectivity, it can still reveal interesting properties of the distribution of connections. Such as here, demonstrating that while correlations between neurons are low and distance-independent, the underlying connection strengths appear to be distance dependent. Such information could be used to constrain models of interacting populations of neurons.

Another interesting observation is the varying degree of MaxEnt model 'failures'. As reported in [5], fits with high KL divergence most likely indicate higher-order correlations. Here we can see that in sparse cultures the higher-order processing seems to be confined to close-by neurons (much like in vivo data from [5]) while dense cultures are more uniform in that respect.

References

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