We thank the reviewers for their analysis, appreciative words, and suggestions. We reply to major points only. The manuscript can be easily amended to address the points we don't discuss here.

Reviewer 1

1. It would be interesting to use the frequency distribution of the sample activity, measured in the recording, as a constraint, equivalent to n moment constraints. In fact, using it at the population level is less questionable than using at the sample level (activities with zero frequencies lead to zeroes in the maximum-entropy distribution, and these are unreasonable because the sample size is much smaller than the state-space size. This indicates that maximum-entropy is used beyond its range of validity). Its use, however, addresses a different question than the one discussed in our introduction, namely to define and measure 'cooperativity' by comparing maximum-entropy distributions constructed from different numbers of moments.

2. It's true, we forgot to discuss how the population-level application solves the sample-size-dependence of maximum-entropy results pointed out in previous literature. This should be addressed in an amended version of the paper.

Reviewer 2

1. We agree that the comparison with other approaches is important. But we believe that it's also important to carefully examine (1) the question we're asking, and (2) which first principles can be used to translate it into a mathematical problem. Some literature develops very refined – though often ad hoc – mathematical techniques, but then leaves us unsatisfied, with the lingering question 'why were we doing this?'. This is the reason for our long introductory discussion about the problem and about the first principles that can be used to address it. See also our reply to Reviewer 3 below.

2. The firing rate likely affects the results and the quantification of 'cooperativity'. The question is: Is this an issue? is our idea of 'cooperativity' invariant with respect to the firing rate, or not? Requirements of this kind constrain the translation of cooperativity into a mathematical quantity. This again shows the importance of defining the question we're asking first.

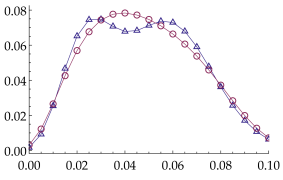
3. Regarding correlations: the method quantifies cooperativity using the measured correlations; see the 'protocol' 1–3 in the Introduction. Thus, correlations determine the result rather than affecting it.

4. We agree that there are many approaches in the literature. In the literature we have explored we've seen very little use of the basic sampling formulae presented in our paper. Honestly this surprised us, because they're surely essential even in a very basic analysis of the data.

Reviewer 3

1. We agree with the Reviewer that the main formulae of the paper, (17) and (19), probably have little *experimental* use today. But the formulae and the analysis behind them are important exactly for the points raised by the Reviewer:

   - The Reviewer says 'the differences between the sample level and population level distribution seem minor': this could be true, but we could not have known this, if we hadn't faced the whole problem and derived a formula showing that the difference is minor.
   - Application of the method with higher-order constrains can show more interesting differences between sample- and population-level distributions. See e.g. the plot on the right, obtained with fourth-moment constraints: the bimodal distribution is the marginalized, population-level one.



   - Calculations show that the population-level distribution can be less or more entropic than the sample-level one. But a more entropic distribution is not necessarily more correct (we could just use a uniform distribution then). The question is how the constraints are appropriately applied in the method.

   As this Reviewer and Reviewer 2 remark, the points and findings above deserve more discussion. Unfortunately there are space constraints, and we preferred to give more room to a careful analysis of the principles behind the method, to see whether the method is correctly applied. Our main wish is that our readers will give more thoughts to these matters. We could hurry up and produce a lot of mathematical results; but, whether positive or negative, any results are meaningless if the method isn't meaningfully applied. And it isn't always the case that a meaningful application of a method can be judged by its results alone.