

1 We thank all reviewers for their careful reviews and many positive comments. Here, we address major questions and concerns that were
2 raised by the reviewers. We feel that the typos and minor issues are easily addressable and will be corrected.

3 **R1: Statistics for the prevalence of multiple representations and its effect on decoding.** In addition to Fig. 2 that illustrates the
4 existence of multiple representations of the same environment for a few sample neurons, we performed hypothesis tests for multiple
5 representations for all neurons (Appendix 3 first part) and summarized the results in L209-211 of our paper. We will add further
6 discussion of these results to the main body of the paper. Following the suggestion of R1, we added new analyses to show the effect of
7 incorporating multiple representations on decoding as follows. We fit two models, one with multiple representations ($K_j = 2$) and one
8 without ($K_j = 1$), and then compare the decoding results for trials within original environments (where we know the ground truth). For
9 each trial, the average probability (over time) that the correct environment has been decoded is computed. Fig. 5A (below) shows the
10 results for cells 13 and 56 (two cells that clearly have multiple representations based on Fig. 2) which clearly indicate that incorporating
11 multiple representations improves decoding significantly. Further, for each cell, the average probability of the correct environment (over
12 trials) is computed for the two models and the difference is depicted in Fig. 5C (curve indicated by "Approach (1)"). This shows that the
13 state space model improves decoding accuracy for 87% of cells. We will incorporate this analysis into a revision of the paper.

14 **R1: The existence of fluctuations between representations and its apparent conflict with the work of Sheintuch et. al. These
15 fluctuations seem to vanish for the full population.** We thank R1 for bringing this highly related work to our attention. We will
16 certainly add a discussion of the relation of this work to the paper. We believe that our results are not in conflict with those of this paper,
17 but rather compliment them. That work focuses on environments for which mice have previously developed spatial maps. In that case,
18 they find that a single spatial map is activated over any trial. Similarly, our model explicitly assumes that the representations over the
19 trained environments (morph 0 and 1) are fixed over each trial (L172-174). However, we propose that for "ambiguous" environments,
20 where mice have not yet developed a consistent spatial map, there may be rapid fluctuations between the original environments being
21 represented. Some previous studies have pointed out this phenomenon ([21, 27, 29, 30, 31, 32, 49]) and in addition, we performed
22 hypothesis tests for this (Appendix 3 second part). Furthermore, our analysis shows that these rapid fluctuations can happen at the
23 population level as well. This is hard to see in Figure 4, so we will add a panel (Fig 5b below) that illustrates these population-level
24 transitions over individual trials. **R1: Other values of K tested? All cells place cells?** Yes, we will mention these in our revision.

25 **R2, R3: Lack of comparison with other algorithms and methods.** As mentioned by R1 and R3, to the best of our knowledge, there
26 is no existing algorithm that explicitly models multiple spatial maps, models the dynamics of transitions between those maps, and uses
27 real data to decode the moment-by-moment representations. To justify the advantage of this model structure, we will add a comparative
28 analysis to the paper, where our current approach is compared with 2 naive approaches: (1) one using only a single spatial map (setting
29 $K_j = 1$) for all cells, and (2) one based directly on the likelihood of each map, without the state-space model. The results of approach
30 (1) are summarized in L7-13 of this response. By using approach (2), we observed that the decoded probabilities for each cell become
31 noisier, with means hovering around .5, and a large standard deviation of about 0.35. This low SNR results in increased uncertainty
32 about the represented environment, and could not be alleviated with simple approaches such as kernel methods. At the population level,
33 this noisiness drops significantly, but is still substantial, with an average standard deviation around 0.22. The average probability of
34 decoding the correct environment during the original, unambiguous environments for approaches (1) and (2) were computed and the
35 difference between these values and the same values when our state-space modeling approach is used is shown in Fig. 5C. This suggests
36 that the state space model improves decoding accuracy in 87% of cells. We observed these naive methods cannot yield similar results
37 shown in Fig. 4. A thorough comparison between these approaches and our state-space modeling approach will be added to our paper.

38 **R3: This paper has incremental technical contributions and the algorithm is a straightforward extension of previous state-
39 space models (HMMs).** While the model structure we used for the data analysis does fit into the general category of HMMs, the
40 algorithms for filtering, smoothing, covariance, and parameter estimation are not trivial and we believe that these derivations provide an
41 important contribution. The specification of this particular model structure also allowed us to uncover transitions in representations
42 that were previously undetected in this data. Finally, the general model structure we present (section 2.1) does not require the Markov
43 assumption (though we did assume this property in the specific analysis example here). For all these reasons, we believe that this work
44 provides an important contribution to the literature. We will add additional discussion of the generality of these methods to the revision.

45 **R3: The Gamma model in Eq. 6 is likely a poor model** Although in many cases simple Gamma models may perform poorly for
46 deconvolved Calcium response, our analyses suggest that this model fits very well to our data. This is demonstrated for two sample cells
47 in Fig. 5D. In addition, we performed a goodness-of-fit deviance analysis and found that the Gamma model was rejected for none of our
48 cells. Our revision will include a brief analysis of goodness-of-fit for this model to demonstrate this.

49 **R3, R4: The applicability of the proposed method and its potential applications in finding other qualitative theories.** While the
50 data example here focuses on estimating the cognitive representation of ambiguous environments, we believe that these methods are
51 broadly applicable to any situation where multiple representations of a stimulus or biological signal are present in a neural population.
52 Such multiple representations may reflect other factors, not controlled by the experiment, or may reflect alternate computational
53 principles within the brain. We believe that these methods provide statistical tools that will enable analyses of a wide range of
54 complex experiments involving multiple neural representations. For instance, one potential application is to detect sub-populations that
55 cooperatively represent an environment and study how these sub-populations change in response to alternation in the input stimuli.

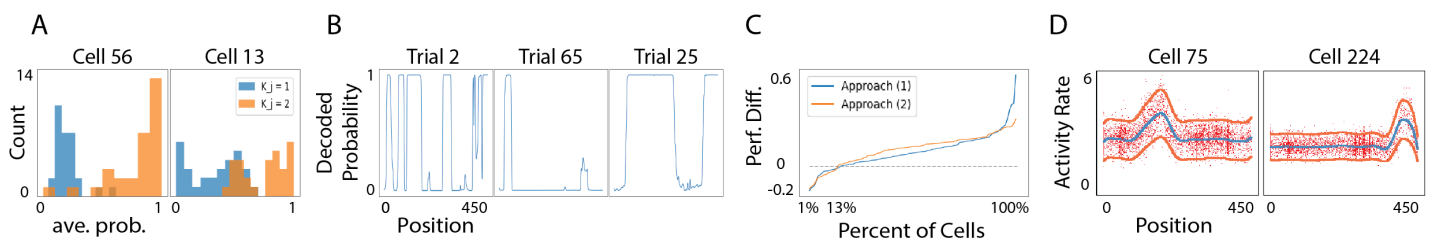


Figure 5: Extra plots that summarize our new analyses.