Results:

As a first step, I wanted to closely examine the patterns of neuronal activity that emerge when the mice get reward, during a simple task that combines (?) the use in place cells., as a marker for spatial memory. For this I used previously published data (Rubin & Geva et al., 2015) and some unpublished data that was collected by Nitzan Geva from the lab, which imaged, using previously described calcium imaging routine (Rubin et al., 2015; Ziv et al., 2013), hippocampal CA1 pyramidal cells in freely behaving mice that repeatedly explored one or two familiar environments. Each session consisted of five to eight 3-min trials in one environment, and one 3-min bucket trial before and after the session. To maximize the perceived differences between the environments, Geva et al constructed linear tracks (environments A and B) that differed in shape, floor texture, surrounding proximal and distal visual cues, odor, and flavor of the water reward at the edges of the track. The bucket trials didn’t contain any reward. The unpublished data has the same structure per session, but contains only environment A. the imaging data was processed using commercial software (Mosaic, version 1.1.1b, Inscopix) and custom MATLAB routines [should I say more?]In order to find a possible pattern of neuronal activation, to be used as a feedback for the memory based BMI, we looked at the neuronal activity at rest epochs, where the mice get a reward. First we wanted to see, to what extent the activity at the edges represents the activity during the run epochs. To do so, we divided each trial to segments of run and edge epochs, and coupled them as rest before run or rest after run. Then we calculated for each neuron the conditional probability to be active at the rest epoch given the activity in the run epoch (active\not active) per session. To test the difference between the two conditional probabilities, we conducted a matched T-test for each session, and calculated the effect size of the difference between them. As seen in fig. 1A, for most of the sessions that conducted on a linear track (n=X out of Y sessions from 9 mice), the activity during run epoch didn’t affect the activity during rest epoch before\after the run significantly. Also, the effect size is small for both cases (fig 1B). For the L-shape track we see that many sessions (n=X out of Y sessions from 4 mice) show significantly higher probability to be active at edge given lack of activity during run epoch (fig 1C, D). This means that the activity at the edge is mainly unique to those bins, and may be relate to the reward itself.

Another analysis that supports this result examine the activity of synchronous calcium events (SCE), as described in two photon experiments (Malvache et al., 2016). At each rest epoch we count the number of events in a sliding time window at a length of 200 ms. Time windows that had number of events above chance level (that was calculated by shuffled activity for each session separately) were labeled as SCE. We then looked for the shared neurons that were active both in SCE and the following run (fig 2 D-E as positive example), and found that each SCE had only few to none of these (Fig 2c). This further suggests that the majority of activity seen at the edges don’t carry information about the run epochs, and may be informative about the reward. (Should we say a word about the lack of lick meter in those experiments? And how?)

Next we wanted to examine the activity patterns off-context, to see if we still get a representation of the edges. For this we used a memory-less maximum likelihood decoder for the bins from both environments and tested it on the bucket trials. First, the activity of place cells from the linear and L-shaped session was used as a training data for the decoder. The test was done on the bucket trials from both sessions, and gave estimation for each frame – what are the most likely bin and environment the activity vector of that frame represents.