

Expansion and Shift of Hippocampal Place Fields: Evidence for Synaptic Potentiation During Behavior*

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Abstract

Rat hippocampal neurons fire in a spatially selective fashion [1]. We show that place fields enlarge (by 75%) and shift (by 1.4cm) in a direction opposite to the direction of movement of the rat, within a few traverses of a route, even if the environment has been experienced extensively on previous days. The expansion is not a result of locomotion or neural activity per se because it reoccurs when the rat runs on a different track immediately after running on the first one. This provides an evidence for systematic changes in neuronal firing properties due to and during experience. The results are consistent with the predictions of models [2, 3] of learning of sequences via Hebbian [4] synaptic potentiation. Thus, these data provide an evidence for Hebbian synaptic enhancement during behavior, and show that such learning occurs even when a rat enters a highly familiar environment after a day's absence.

Although it is a common belief that learning occurs via Hebbian long term potentiation (LTP) of the synapses, there is little evidence to suggest that such changes indeed occur during behavior. With the present technology, it is not possible to measure the strength of individual synapses during behavior. Most of the experiments on LTP involve artificial stimulation of brain tissue. These experiments show that the NMDA receptor mediated LTP is associative [5] and temporally asymmetric [6] –i.e. it occurs only if the postsynaptic neuron is depolarized within a short duration ($\sim 100\text{ms}$) *after* the spiking of the presynaptic neuron. It is not obvious that the anatomical connections between the neurons and the pattern of neuronal firing during behavior is indeed such that

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the pre and the post synaptic neurons have the required order of activation so as to strengthen the synapse. Thus it is important to investigate whether Hebbian LTP occurs during behavior. Given the present technological constraints, one has to devise indirect measures which would allow us to detect the consequences of changes in synaptic strengths. We have therefore looked for systematic changes in neuronal firing properties during behavior, which could arise due to Hebbian LTP.

The majority of experiments on LTP have been carried out on neurons of the Hippocampus. When a rat explores an environment, the neurons in the CA1 and CA3 regions of the hippocampus are known to fire in a spatially selective fashion [1] and are often called place cells. The region of space where a neuron fires selectively is called its place field. A large number of neurons were recorded simultaneously [7] from two rats as they ran repeatedly in a counterclockwise direction on the perimeter of an elevated, rectangular track.

The closed linear track was mapped onto a straight line for the purpose of analyses, with the rats running in the direction of increasing distance. Fig. 1 shows the location of each spike, from two different cells, as a function of the lap number. As can be seen, the amount of firing increased with experience and the location of the center of mass of the lap specific place field moved in a direction opposite to the direction of movement of the rat.

However, these data are noisy. Few spikes (~ 10) were emitted by each cell during each lap. In order to do a statistically meaningful analysis of changes in place field properties, the ‘ensemble averaged place field profile’ of a population of cells was computed for each lap, as follows. For each place field, the location of the place field center (averaged over all the laps) was subtracted from the location of each spike, thereby obtaining the relative location of each spike. The firing rate as a function of the distance from the center, averaged across all the cells, gives the average place field profile of a population of cells. This profile was computed separately for each lap. Such an analysis corresponds to evaluating the ensemble average over all the place fields for each lap as opposed to the usual, time average over all the laps for each cell. The area under the ‘ensemble averaged place field’ curve is called the size of the place field for the given lap and the center of mass of the profile is called the location of the place field for that lap.

Figure 2 shows the average size of the ensemble averaged place field as a function of the lap number (i.e. time). The size of the place field increases by about 75% in a saturating way with experience. Further, the firing rate distribution shifts to the left (Fig. 3) such that the place field center in the last lap is shifted by $1.4cm$ with respect to that in the first lap in a direction opposite to the direction of motion of the rat.

These changes could not arise due to changes in rat’s behavior because when some rats were run on a second maze immediately after running the first maze, the size of the place fields again increased and their locations again shifted backwards [8].

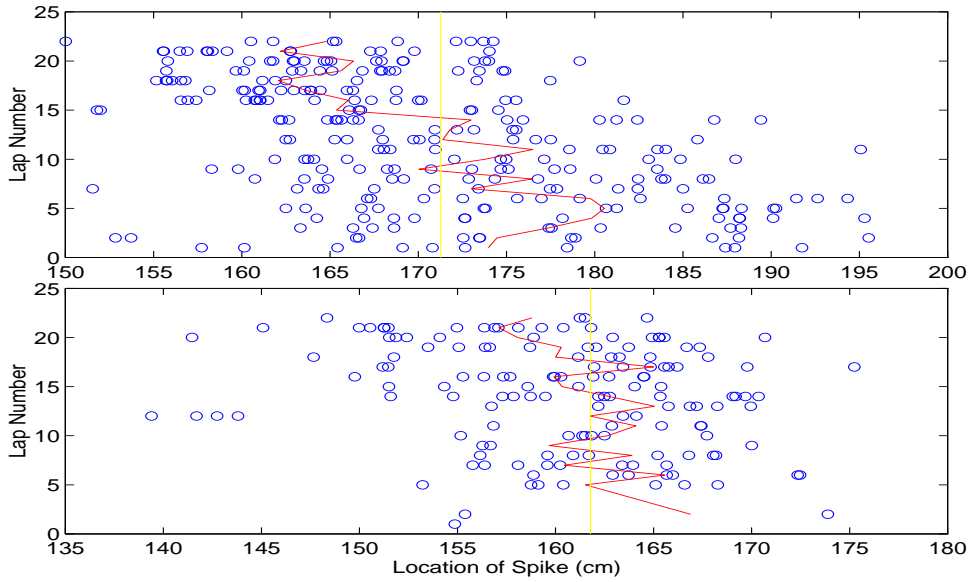


Figure 1: The location of the rat when two isolated cells (top and bottom panels) fired a spike is indicated by open circles, as a function of the lap number. The mean value of the locations of all the spikes fired by a cell during a lap corresponds to the location of the place field at that time. The place field locations during successive laps are joined by a solid line. The average value of all the spikes across *all the laps* corresponds to the place field center and is indicated by a light vertical line. The amount of firing per lap increased with time. In fact the cell in the bottom panel did not fire at all during some of the early laps. Further, the lap specific place field center shifted backwards.

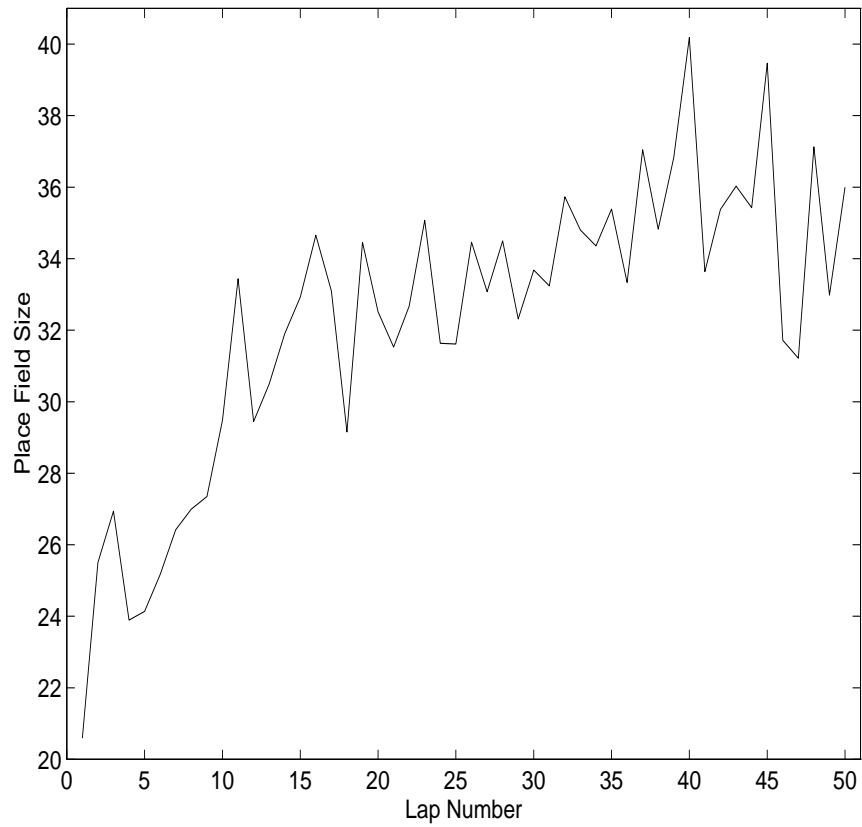


Figure 2: The size of the place field, averaged across 43 place fields is shown as a function of the lap number. The size increases by about 75% in fifty laps in a saturating way, with that most of the increase occurring within the first ten laps.

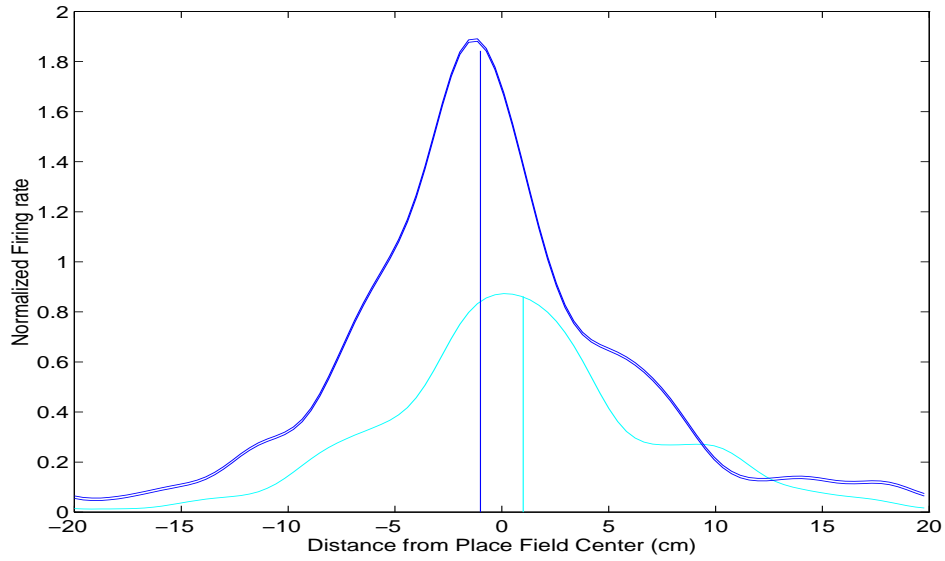


Figure 3: The ensemble averaged place field profile for the first(lower, light curve) and the last (upper, bold curve) laps are shown. The area under the curve is larger for the last lap than for the first lap and the firing rate distribution is shifted to the left in the last lap compared to that in the first lap. The center of mass of the two firing rate distributions (vertical lines) are 1.4cm apart.

These data were recorded from the hippocampi of rats which were highly familiar with the maze. Therefore these changes must occur every time the rat enters a familiar environment after a day's absence.

Place cells are activated in the same temporal sequence, every time the rat follows the same route. Artificially induced, NMDA mediated LTP is temporally asymmetric, occurring only if the postsynaptic neuron is depolarized after and within a short duration of depolarization of the presynaptic neuron. Thus synapses between place cells will be strengthened asymmetrically, i.e. the synapses from the cells which fire earlier on the maze, onto those that fire later on the maze, would become stronger; however the reciprocal connections would be relatively unaffected. Such an asymmetric strengthening would cause the post-synaptic neurons to fire earlier, and more vigorously, thereby expanding the place fields and shifting their locations backwards [2].

Hippocampal neurons fire in a noisy fashion in a small region of the environment, thus providing a sparse spatial code. For such a network, expanded place fields would result in an improved signal to noise ratio and hence the accuracy of the hippocampal population code would increase, as was observed by by Wilson and McNaughton [9] in data from rats exploring novel environments. However, we observe place field expansion in the familiar environments too.

The backward shift in the neuronal firing means that the cell commences firing before the animal reaches the location that was originally coded for by that neuron. This could enable the animal to learn to navigate in an environment [2].

To conclude, we have shown that place fields are rapidly modified by experience, even when a rat enters a familiar environment after a day's absence. This supports the hypothesis that the hippocampus is involved in short term memory. Further, the present results provide an indirect evidence for asymmetric Hebbian synaptic strengthening, which may underlie learning of sequences during behavior.

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