Grid to Place Cell Connectivity in Eleven Different Rooms

Abstract.
To understand the grid to place cell connectivity, we took place cell firing data from Moser lab. In MATLAB, we created grid cell firing patterns. Connection weights between the two were learned with backpropagation algorithm. The smaller place fields could be learned from grid cells with single spatial firing frequency. But bigger, multiple and irregular place fields could only be learned from grid cells with multiple spatial firing frequencies. Weights learned were normally distributed with a wider spread and multimodal distribution for rooms with uneven, larger or multiple firing fields. We conclude that each place cell is connected to single modules of grid cells with similar spatial firing frequency. Place cells connected to multi-frequency grid cells are fewer. Our results also show that grid cells resolve the space into spatial distance, orientation, and phase offset. Unique firing patterns of the place cells codify each room with this information.

Introduction. With their unique firing patterns, the hippocampal place cells are thought to encode for place in the environment in allocentric coordinates. Ever since their discovery [7], scientists have been trying to understand the origin of their firing patterns. In this pursuit, grid cells were discovered [8]. These are thought to be the primary input to the place cells. Grid cells have varying spatial firing frequencies, orientations and phases. Initially, researchers thought that the place cell firing patterns can be realized by combining the grid cell firing patterns of various spatial firing frequencies [9, 10, 11]. However, anatomically this does not seem to be feasible as different spatial firing frequencies of grid cells are seen at different positions along the dorso-ventral axis of the entorhinal cortex. And grid to place cell connectivity is between corresponding cells at a location along this axis [5, 6]. In [12], we proposed a computational model of place cell firing based on connection to grid cells of single spatial firing frequency. The model was purely computational with simulations using Hodgkin Huxley and integrate and fire neurons. We wanted to test our model with real data. Therefore, in the current paper, we took 342 place cell recordings from 8 animals in eleven different rooms from the Moser lab [1] and tried to decipher their connectivity to 4500 different grid cells (25 different phases, 3 different frequencies and 60 different directions). We created grid cell firing patterns in matlab using the model described in [2]. Then we trained the grid to place connectivity patterns using the recorded place cell firing patterns in the eleven rooms using the backpropagation learning algorithm.

Methods: To decipher the grid cell to place cell connectivity, we took lab data [1] for 342 place cells from 8 animals in 11 different rooms. With an activity threshold of 0.1Hz, around 240 of the cells were active. Of these, around 210 cells were active in at least one room, 103 were active in only 1 room, 44 were active in 2 rooms, 21 were active in 6 or more rooms, 10 were active in 8 or more rooms. Only 2 of the cells in the distal most CA3 fired in all 11 rooms. Since different place cells were firing in different rooms – some in more than others, we took three of these place cells for further analysis. The first place cell that we considered, fired in all the 11 rooms, the second one in 6 rooms and the third one in only 1 room.

Since we did not have simultaneously recorded grid cell data, we created grid cell firing patterns with three different spatial firing frequencies (28, 39 and 50 cm), 60 different orientations (0-60 degrees) and 25 different phases (5 in the x and 5 in the y-direction) based on the model described in [2]. At the beginning of the analysis, connectivity between the grid and the place cells was randomly assigned between 0 and 1. Thereafter, the place cell firing patterns recorded from each of the eleven rooms were learned using the backpropagation algorithm. 100 trials with 10000 iterations (one million iterations) each were used to learn the weights for all the rooms for each experiment.

In the first experiment, grid cells of single (28cm) frequency, 25 phases and all 60 directions (1500 grid cells in total) were connected to the place cell firing in all the eleven rooms. In this experiment, some of the place cell firing patterns were learned properly but not others. Therefore, in the second experiment, grid cells with 3 frequencies (28cm, 39cm and 50cm), 25 phases and 60 directions (4500 grid cells in total) were connected to the place cell firing in all the eleven rooms. These were

successfully learnt. Next, we wanted to explore how the connectivity between grid and place cells varies for place cell firing in fewer rooms. So, in the third experiment, all the 4500 grid cells (as in second experiment) were connected to the place cell that fired in six rooms. And then, in the fourth experiment, all the 4500 grid cells were connected to the place cell that fired in a single room.

The four sets of weights so obtained were analyzed to understand the connectivity. For this, the histogram of weights was created for each of the eleven rooms for each experiment. The magnitude of weights was also analyzed for each direction, phase and frequency of the grid cell that is connected to the place cell.

Results.

Experiment 1.

In the first experiment, one of the place cells firing in all the rooms (Fig. 1(a)) was connected to 1500 grid cells with single (28cm) spatial firing frequency, 25 phases and 60 directions. 100 trials of the backpropagation learning algorithm with 10000 epochs each were used to learn the connectivity between the cells. While learning, the single, small place cell firing fields could be learned but not the multiple or larger ones. The results are shown in Fig. 1 (b). In Figs 1(a) and (b), the room numbers go from left to right in each row (1→ 4) and then in the next row (5→ 8 and 9→11) in increasing order. It is seen that the smaller place fields (rooms 1, 2, 3, 9, 10 and 11) can be learnt with a single spatial firing frequency of grid cells and multiple phases. But the larger (rooms 4 and 8), multiple (room 5 and 6) or irregular place fields (room 7) are not learnt properly. The weights were analyzed next. Histograms of weight distribution can be seen in Fig. 1 (c). It shows a normal distribution of the weights for all rooms. For each room, the weight distribution is different than that for other rooms. Analyzing the magnitude of weights for different directions and phases in each room, there is sinusoidal pattern (Fig. 1(d)). It is seen in all the rooms though every room has a different phase of the sinusoid. Here, the phases are marked along the x-axis, in between phases are the directions from 0-60 degrees.

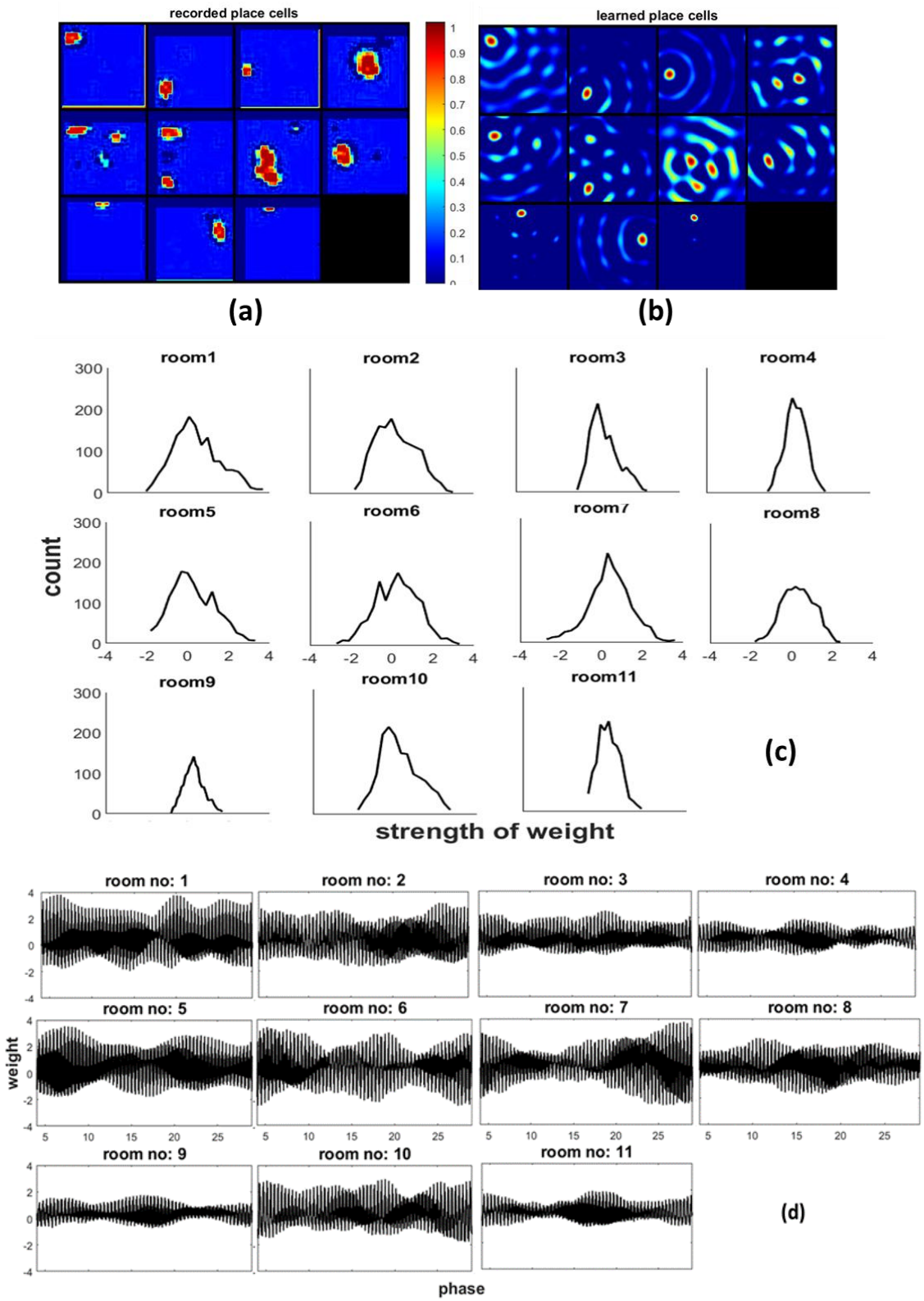

Fig. 1 For (a) and (b), room numbers are labelled from 1 to 4 horizontally in the first row in that order, 5-8 in the second row and 9-11 in the third row. (a) recorded place cell firings in eleven different rooms. (b) learned place cell firing patterns in the eleven rooms using backpropagation learning algorithm, 1500 grid cells with 25 phases, 60 directions and single firing frequency. It is seen that the smaller place cell firing patterns are learnt but not the multiple, bigger or irregular ones. (c) all weights over the 100 trials with 10,000 iterations each have a gaussian distribution. The weights for rooms with smaller firing patterns have a narrower distribution than the ones with a larger firing pattern. The peak of the distribution is centered around 0. (d) phase label on the x-axis indicates phase of firing of the grid cell. In between the phase values are the different directions (from 0 to 60) of orientation of the grid cells. The strength of the weights varies with the phase and direction of the grid cell. The overall pattern of weight distribution is sinusoidal. The pattern varies with the room.

Experiment 2.

In the second experiment, the place cell firing in all 11 rooms was connected to 4500 grid cells with 3 different spatial firing frequencies, 60 directions and 25 phases. The firing patterns in all the 11 rooms could be learned successfully. Results from learning are shown in Fig. 2 (b) below and compared with the recorded place cell firings in Fig 2(a). In these two figures, the room numbers go from left to right in each row (1→ 4) and then in the next row (5→ 8 and 9→11) in increasing order. Next, we analyzed the weights from 100 trials with 10,000 iterations (1million iterations) each. Firstly, we plotted histograms of mean weights for each room (Fig. 2 (c)). Weights learned were normally distributed. The spread of weights is wider for rooms with uneven, larger or multiple firing fields. While for the rooms with smaller firing fields, the weight distribution is narrower, and for those with medium sized fields, weight distribution has a medium spread. For small and medium firing fields, the weights have unimodal distribution. Larger and multiple firing fields are associated with multimodal distribution of weights. Weights did not differ a lot across the 100 learning trials. But weights learned for each room have a different pattern. To look at how much each grid cell with a given phase, direction and spatial frequency contributes to a place cell firing, we plotted mean weights for each frequency versus phase and direction. The results are shown in figure 2(d) below. Here, the phases are marked along the x-axis, in between phases are the directions from 0-60 degrees. The weights vary sinusoidally with the phase and direction for a frequency. Rooms with small single place firing patterns (rooms 1, 3, 9 and 11) are associated with similar and smaller contributions from each grid cell with different spatial frequency. Rooms with relatively bigger but regular single place fields (rooms 2, 4, 8 and 10) have higher contribution from grid cells with higher spatial firing frequencies (39 and 50cm) rather than grid cells with smaller spatial firing frequency (28cm). In room number 7, the place field is big and irregular. If we examine the weight distribution in this room, it has higher contribution from the 50cm spatial frequency. The weights associated with this frequency have multiple waves of overlapping sinusoids.

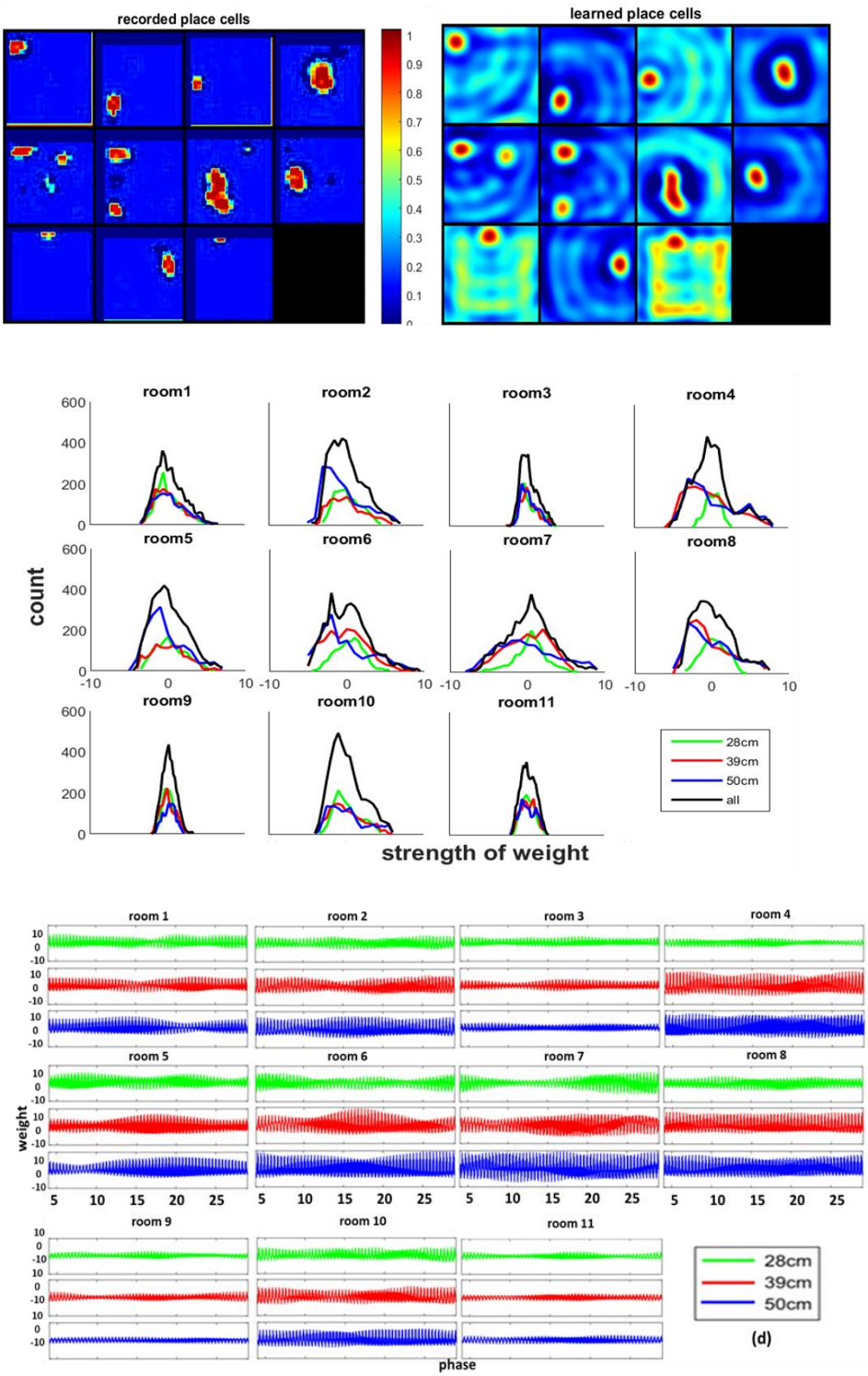

Fig. 2 For (a) and (b), room numbers are labelled from 1 to 4 horizontally in the first row in that order, 5-8 in the second row and 9-11 in the third row. (a) recorded place cell firings in 11 different rooms. (b) learned place cell firing patterns from 4500 grid cells with three different spatial firing frequencies (28, 39 and 50cm), 60 directions (0-60 degrees) and 25 phases (1-25). The results indicate that the unique firing patterns of the place cell could be learnt for each room separately with inputs from all 4500 grid cells. (c) Histograms of mean weights over 100 trials indicate that the weights have normal distribution. Rooms with smaller place fields (rooms 1, 3, 9 and 11) have narrower and those with bigger fields have wider distributions. Rooms with multiple or irregular place fields (rooms 5, 6 and 7) have multimodal distribution of weights while those with single place fields have unimodal distribution. (d) shows sinusoidal variation in magnitude of weights with phase and direction. X-axis indicates phases from 1-25 and between two phases are the 60 directions for each phase. Rooms with bigger fields have higher contribution from the grid cells with higher spatial frequencies. All the plots show a sinusoidal pattern. Rooms with small single place firing patterns (rooms 1, 3, 9 and 11) are associated with similar and smaller contributions from each grid cell with different spatial frequency. Rooms with relatively bigger but regular single place fields (rooms 2, 4, 8 and 10) have higher contribution from grid cells with higher spatial firing frequencies (39 and 50cm) rather than grid cells with smaller spatial firing

frequency (28cm). In room number 7, the place field is big and irregular. If we examine the weight distribution in this room, it has higher contribution from the 50cm spatial frequency. The weights associated with this frequency have multiple waves of overlapping sinusoids.

Experiment 3.

The above two experiments on the place cell firing data from single place cell firing in all the eleven rooms helped understand the grid cell to place cell connectivity somewhat. However, we also wanted to study the connectivity patten for a place cell that fires in some environments but not in others. For this we studied a place cell which fired in 6 different rooms (Fig. 3(a)). We connected the 4500 grid cells (3 frequencies, 25 phases and 60 directions) to this place cell. The firing patterns were successfully learnt in all the rooms (Fig. 3(b)). In Fig. 3 (a) and (b), the room numbers increase from left to right along a row (from 1→ 4 in first row, 5→ 8 in second row and 9→ 11 in third row). Next, we created histograms of the mean weights over the 100 trials (Fig. 3(c)). Similar normal distribution of weights was observed as for the cell firing in all 11 rooms except for a narrower distribution. The mean was centered around 0. The spread of the distribution was more for the rooms with firing (rooms 1, 2, 3, 6, 8, 9) than with no firing. The spread was also more for rooms with bigger and irregular (room 1, 2, 6, 8, 9) spatial place fields than those with smaller fields (room3). No multimodal distribution is seen for any room. Even though distributions are similar for rooms with no firing, they are different from each other in rooms where the place cell fires (rooms 1, 2, 3, 6, 8, 9). Next, distribution of weight magnitudes for different phase and direction of grid cells was plotted (Fig. 3(d) – note x-axis has phase labels, in between each phase are the 60 directions). The distribution has sinusoidal variation as seen in Fig. 2 but the magnitude is lower. For the rooms with no place cell firing (rooms 4, 5, 7, 10 and 11), the contribution from all the grid cells was similar irrespective of frequency. For rooms with increasing size of place fields (rooms 3, 2, 8, 9 and 1 in that order), the magnitude of weights for various grid cell frequencies increases. For room with irregular place cell firing pattern (room 6), the maximum contribution is from the grid cells with 50cm spatial firing frequency.

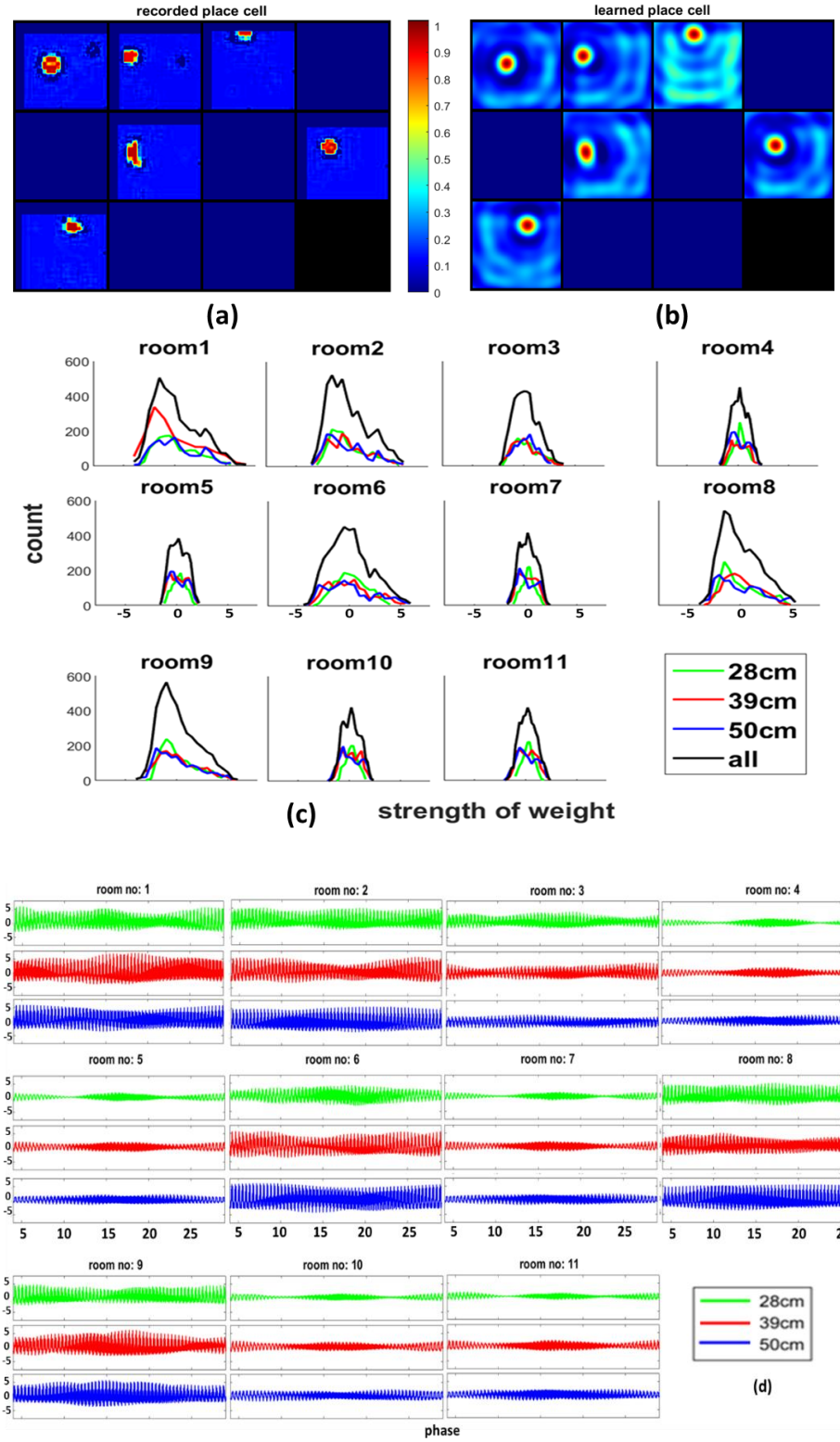

Fig. 3 For (a) and (b), room numbers are labelled from 1 to 4 horizontally in the first row in that order, 5-8 in the second row and 9-11 in the third row. (a) Recorded place cells in eleven different enclosures. (b) Successfully learned place cell firing patterns in the eleven rooms with 4500 grid cell inputs and weights between the grid and place cells using backpropagation algorithm. (c) Histogram of mean weights learned over 100 trials shows the normal distribution of weights with narrower distribution as compared to those in Fig. 2. The weights corresponding to rooms with bigger firing patterns have a wider distribution than those corresponding to smaller or no place fields (rooms 3, 4, 5, 7, 10, 11). No multimodal distribution is seen for any room. Even though distributions are similar for rooms with no firing, they are different from each other in rooms where the place cell fires (rooms 1, 2, 3, 6, 8, 9). (d) (x-axis labels indicate grid cell phases from 1 to 25. In between each phase are 0-60 directions corresponding to each phase) Magnitude of weights varies sinusoidally with phase and direction of grid cells. For rooms with smaller or no place fields (rooms 3, 4, 5, 7, 10, 11), there is small equal contribution from grid cells with all frequencies. For rooms with bigger firing patterns, the contribution from grid cells with all spatial frequencies increases with maximum contribution from higher frequencies.

Experiment 4.

Lastly, we wanted to explore the grid cells to place cell connectivity for the 103 place cells that fired in a single room. We learned the connection weights of all these cells (taken one at a time) using 4500 (3 different frequencies, 25 different phases and 60 different directions) grid cells. Here, we present results from one of the representative cells. The recorded and learned place cells are shown in Fig.4(a) and (b) respectively (room numbers are labelled from 1 to 4 horizontally in the first row in that order, 5-8 in the second row and 9-11 in the third row). Corresponding weights learned are shown in Fig. 4(c) and (d). From Fig. 4(c), we can see that all the weights are normally distributed. The weights in the room where the place cell is firing are more widespread while those in the rooms where the place cell is not firing are more narrowly distributed. This is like what has been observed in previous experiments except for lower magnitude. In fig. 4(d) weight distribution with phase and direction for a frequency shows sinusoidal distribution of the weights for all rooms with similar magnitude of weights for all rooms except for room 5 where the place cell is firing. This increase in magnitude in room 5 is more pronounced for 28cm frequency than others. (x-axis labels indicate grid cell phases from 1 to 25. In between each phase are 0-60 directions corresponding to each phase)

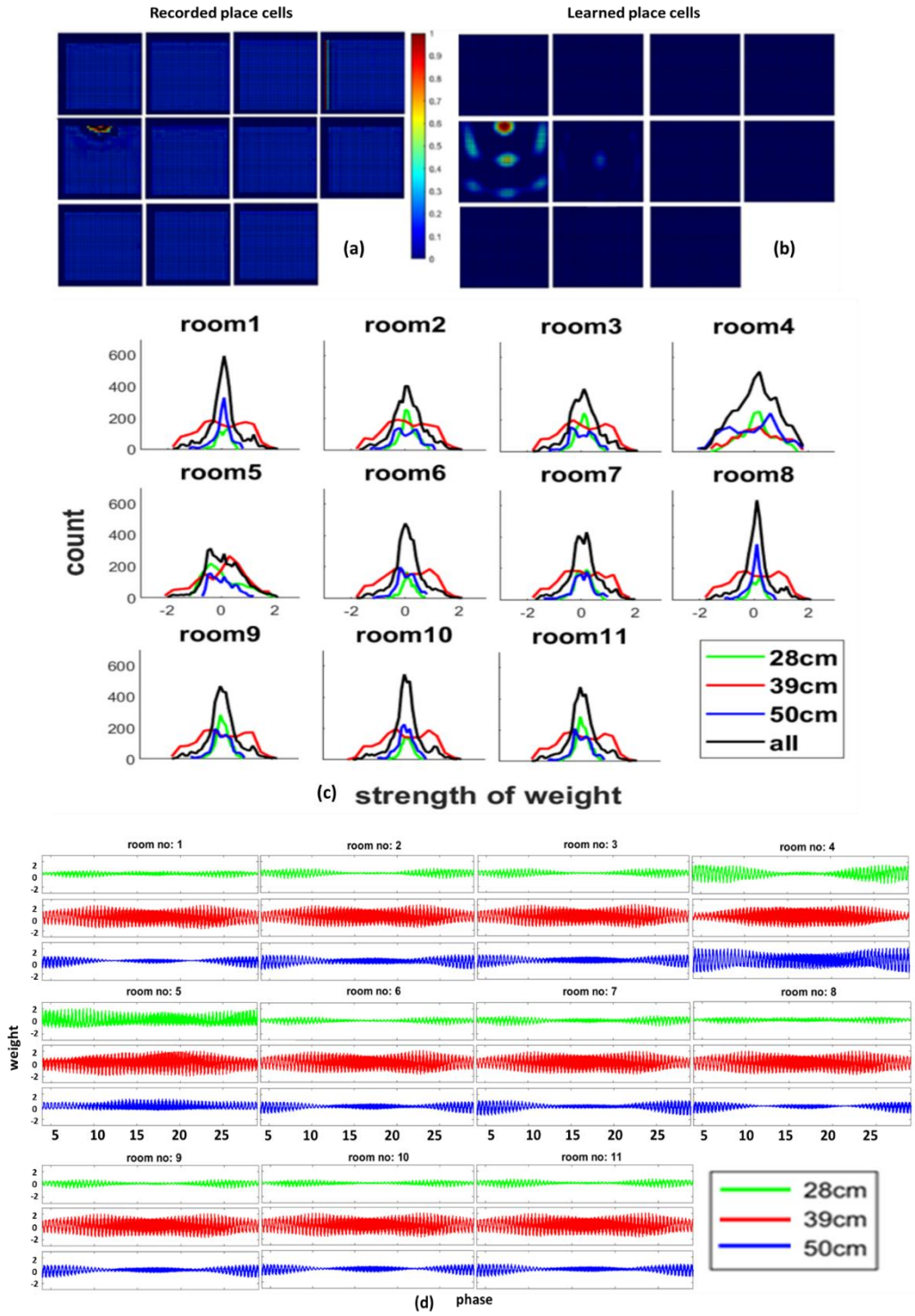

Fig. 4 For (a) and (b), room numbers are labelled from 1 to 4 horizontally in the first row in that order, 5-8 in the second row and 9-11 in the third row. (a) place cell recording from eleven rooms shows the place cell firing in room 5. This was successfully replicated by learning weights using the backpropagation learning algorithm, as shown in (b). (c) Histograms of weights from 100 trials are similar to those seen in Figs. 1-3 but much lower in magnitude. Most of the rooms have narrow weight distribution, peaking around zero. Only in room 5, there is a wider distribution of weights which is off-centered from 0. Weights from different frequencies have different peaks. (d) (x-axis labels indicate grid cell phases from 1 to 25. In between each phase are 0-60 directions corresponding to each phase) On plotting the magnitude of weights against direction and phase of grid cells, for all three freqeuncies of grid cells separately, it is evident that the pattern is sinusoidal as seen in prior experiments though of a smaller magnitude, contributions from 39 and 50cm spatial frequencies is similar for all rooms but that for 28cm frequency increases in room 5 where the place cell is firing.

We also did similar experiments with only 28cm spatial firing frequency and all 60 directions and all 25 phases of grid cells (total of 1500 grid cells). In case of grid cells firing in one room, the spatial firing patterns could be learnt unlike what was observed in the first experiment.

Discussion.

To summarize the work presented in this paper, the goal was to uncover the connectivity between grid and place cells. In addition, we wanted to find out how the remapping can be explained for the same place cell when the animal is placed in different environments. Finally, we wanted to understand the difference in connectivity patterns between a cell firing in a single room versus the one firing in multiple rooms. For this, using the backpropagation learning algorithm, we learnt the observed firing patterns of place cells in eleven different rooms from grid cell firing patterns. In all the experiments, the place cell firing patterns were successfully learnt when using 4500 grid cells (3 frequencies, 25 phases and 60 directions). Mean weights over 100 trials each for the eleven rooms were found to have normal distribution. The rooms where place fields were bigger had a wider distribution of weights while those with smaller place fields had a narrower distribution. The contribution of grid cells with higher spatial firing frequencies was more to the bigger place firing fields while those of smaller spatial frequency was less. Similarly, smaller place fields got higher or at least as much contribution from the grid cells with smaller spatial frequency. The strength of weights was more in rooms with bigger and more irregular place fields than in those with smaller place fields. The rooms with multiple place firing fields have multi-modal distribution of weights. For the irregular place fields, the peak of normal distribution of different spatial frequencies do not align. The place cells which fire in only one room also have smaller firing fields. When weights were plotted against the degrees and phases of grid cells to which they were connected, they had a sinusoidal distribution. The rooms without place cell firing showed a random distribution of weights with mean around 0 and very small magnitude as compared to those in rooms with place cell firing. Another observation, not reported here, was that the place cell firing pattern in a single room could also be realized with single frequency, 60 directions and 25phases (1500 total) of grid cells.

The wider distribution of weights in rooms where the place cell is firing as compared to where it is not indicates that they have a higher variance. And higher strength weights for place cells firing in more rooms than in fewer rooms indicates that these cells are more active than others. Higher contribution of grid cells with higher spatial frequency to rooms with multiple, irregular and bigger firing patterns indicates that the grid fields with higher spatial firing frequency are required to attain the bigger place firing fields. Similarly, higher or equal contribution of grid cells of smaller frequencies to rooms with smaller and single firing patterns indicates one to one correspondence of spatial frequencies of grid and place cells. Having unimodal distribution of weights for single place fields and multimodal distribution for multiple, bigger or irregular firing fields indicates that the small, single place fields can be realized with single grid cell spatial frequency whereas multiple, bigger or irregular place fields require multiple grid cell frequencies. The sinusoidal distribution of weights along the phase and direction of grid cells is expected given the periodic firing patterns of grid cells. This also indicates that there is direct mapping from grid to place cells, there is no requirement for intermediate transformation.

As we know, the connectivity between the grid cells and a place cell will not change across the eleven rooms within the short interval in which recordings were done. So, what do the results presented here indicate? We thought that the change in connectivity patterns between the grid and the same place cell across rooms as seen in the results above, indicates that some of the grid cells are not active in some rooms but are active in other rooms. This seems to be the case based on discussions with Professor Edward I Moser at the Society for Neuroscience conference (SFN) in Chicago, 2024 and the poster presented at the conference [4], from which it seems that there is the change in orientation of the grid cells as the animal is moved to another environment. This reorientation of grid cells in different rooms can explain how the same connectivity between the grid cells and the place cell can change the contribution of grid cells to place cells and cause the re-mapping of place cell in different rooms. This implies that the grid cells are re-mapping rather than the place cell when animal is placed in different rooms.

In this project, we used the grid cells with different spatial firing frequencies to connect to a place cell Given the anatomical distribution of grid cells of varying spatial frequencies along the dorsoventral axis of the entorhinal cortex and the connectivity of these grid cells to corresponding place cells [5, 6], it seemed unlikely that the grid cells of varying spatial frequencies could be connected to a single place cell. This could also be a reason why most of the cells were active in single room (only 2 out of 342 cells recorded were firing in all eleven environments, 21 were active in six or more rooms, and 103 were active in only one room [1]). Based on the anatomy [5, 6] and our results, we thought that the place cells with different sizes of place fields could be realized at the corresponding places in the hippocampus where there is transition boundary between grid cells with varying spatial firing frequencies in the entorhinal cortex. So that grid cells of different frequencies could be connected to single place cell. Combining this with findings in [3], we think that there could be single grid cell modules that have multiple frequencies within the same module. These cells have been recorded at the boundaries of transition between different grid cell frequencies. So, these cells could be connected to the place cells which fire with large and irregular fields. Since such grid cells are limited in number, the place cells firing in multiple environments are also limited in number.

All the results indicate that each place cell is connected to a grid cell module with single firing frequency. The results also indicate that the place cell remapping is due to the grid cell remapping – that is change in grid cell orientation and/or phase based on which enclosure an animal is placed. Thus, each place in the environment can be represented by a unique combination of inputs from the grid cells. This combination of grid cell inputs happens at the place cell, which combines information from several grid cells and provides a sort of code for animal place in the environment. This information is stored in episodic memories as the place of the animal during the episode.

Conclusion & future work. We conclude that each place cell is connected to single modules of grid cells with similar spatial firing frequency. Those with smaller fields could be connected to grid cells with smaller frequencies alone but those with bigger firing fields must be connected to grid cell modules with multiple spatial frequencies. Place cells connected to multi-frequency grid cells are fewer than those connected to grid cells with single spatial frequency. Most of the place cells are connected to grid cells with a single spatial firing frequency. Our results also show that grid cells (and not place cells) resolve the space into spatial distance, orientation, and phase offset. Unique firing patterns of the place cells codify each room with this information. Currently, we are working on the place cells firing in single room. Initial results indicate that the grid cell modules with single spatial firing frequency are enough to successfully replicate the firing patterns of these place cells. Next, we are trying to identify if the place fields can also be learnt with fewer grid cells of various directions and phases and if so, what are the least number of grid cells within a module required to correctly replicate the place cell firing patterns.

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