Position Reconstruction of Awake Rodents by Evaluating Neural Spike Information from Place Cells in the Hippocampus

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Abstract — **Place cells are located in the hippocampus of the brain and play an important role for spatial navigation. In this study neural spike activity of freely moving rats along with the position of the rats was acquired. The study was performed to investigate if position reconstruction is possible if the rat is freely moving in open arenas of different sizes based on neural recordings from CA1 and subiculum regions.**

The neural spike activity was measured using tetrodes from 6 chronically implanted rats in CA1 and subiculum regions. The position of the rats was monitored using a video tracking system .In the encoding step spike activity features of the place cells and position information from the rats were used to train a computer system. In the decoding step, the position was estimated from the neural spiking activity. Different reconstruction methods were implemented: (i) Bayesian 1-step and (ii) Bayesian 2-step. The results show, that the reconstruction methods are able to determine the position of the rat in 2-dimensional open space from cell activity measured in the CA1 and subiculum regions. Better accuracies were achieved for CA1 regions because the firing fields show more localized spots. Higher accuracies are achieved with a higher number of place cells and higher firing rates.

Keywords — **place cells, hippocampus, online position reconstruction, Bayesian 2-step method**

I. Introduction

Cells with spatially modulated firing rates have been found in almost all areas of the hippocampus and in some surrounding areas. Such place cells (PC) encode an internal representation of an animal's position in its environment. The background firing rate of a PC is very low (0.1 Hz), but when an animal enters the receptive field of the neuron, its firing rate rapidly increases (up to ~ 5- 15 Hz) [1,2]. The location inducing the increased cell activity is called the firing field (FF) or place field (PF) of the particular neuron. However, also other sensory cues can influence place cell activity, but visual and motion-related cues are the most relevant [3].

Recently place cells were also used to reconstruct the foraging path of rats by investigating the firing field patterns [1, 5]. In an encoding stage the place cell spiking activity together with video tracking information is used to train a computer system on the data. In a decoding stage only the spike activity is used to reconstruct the path of the animal. In this study it was of interest to test if position reconstruction is also possible in open environments in contrast to the linear arenas used in previous studies [5]. The reconstruction was tested in square arenas with different side length (0,5m, 0,7m, 0,1m, 1m) and a square arena with a smaller square barrier inside (outer square: 1m x 1m, inner square: 0,6 x 0,6m). Two different algorithms based on Bayesian methods were implemented after a Template matching approach was ruled out for reconstruction.

II. Material and methods

A. Neural spike and video data acquisition

Action potential data were measured from 6 rats from CA1 or subiculum by the Instituto de Neurociencias de Alicante (Universidad Miguel Hernández-CSIC, UMH), Institute of Cognitive Neuroscience (University College London, UCL) and Center for Neural Systems, Memory and Aging (University of Arizona, UA). The rats were connected to the recording system via a head stage pre-amplifier. From 1 to 8 tetrodes were used for the recordings. Each data channel was amplified up to 40,000 times and a sampling frequency of 48,000 Hz was used. For tracking purpose small infrared light-emitting diodes were attached to the rat's head and a video camera system was mounted above the experimental arena. The number of recorded cells, the recording region and the arena sizes and shapes are shown in Table 1. The sampling frequency for the position-tracking signal was 50 Hz (*UMH, UA*) and 46.875 Hz (*UCL*).

Table 1: Recording information of the 6 rats.

Rat #	1	2	3	4	5	6
No. of cells	5	26	9	6	4	11
Hippocampal region	CA1	CA1	CA1	CA1	Subiculum	Subiculum
Test field side length [m]	0,7	0,8	0,5	1	1	1
Test field shape						

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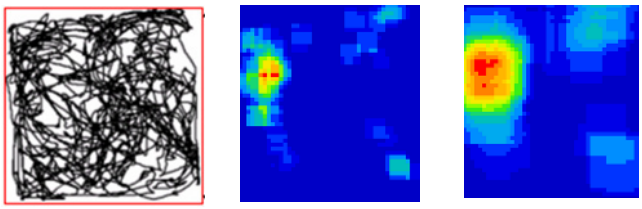
B. Dwell Time and Firing Rate

In the first step the recorded spike activity was used as input for the cluster cutting. The cluster cutting was performed manually to separate neuronal activity picked up by the electrodes into single cell activity. In a second step firing rate maps were created. Therefore the arena was divided into small subsets of space and class labels were assigned to these subsets (pixels). Then the firing rate for each pixel was calculated by counting the number of spikes in each class. The test fields were divided into 64x64 classes, leading to an edge length for each class of 1.09 cm (rat 1), 1.25 cm (rat 2), 0.78 cm (rat 3) and 1.56 cm (rats 4, 5, 6). Figure 1A shows the movement trajectory of a rat obtained from the video tracking system for one full experiment with one rat.



A B C

Figure 1: A: arena divided into 64 fields, the cells are firing with a specific rate at each position. B: movement trajectories of the rat recorded with the video tracking system seen from top. C, D: firing maps of 1 neuron with different smoothing factors (5x5 and 10x10 Kernel).

The average firing rate of a cell *i* for each position $\boldsymbol{x}$ is described by the firing rate distribution, i.e. a vector of firing rates per cell *i*: $f(x) = (f_1(x), f_2(x), ..., f_N(x))$. In the training step, the firing rate maps *f(x)* are calculated for the whole population of *N* recorded cells and for every single position $\boldsymbol{x}$. The average firing rates are calculated from the total number of spikes collected for a cell while the rat was at position *S(x),* divided by the total amount of time the rat spent there *V(x).*

$$f(x) = \frac{S(x)}{V(x) \cdot \Delta t} \tag{1}$$

Δt is the time interval of the position tracking system.

The firing rate distribution is independent of how often the rat populates a certain position, it rather describes the tendency of a cell to fire at a given position $\boldsymbol{x}$ as shown in Figure 1B for one neuron.

C. Position reconstruction algorithms

First firing rates of all cells within a sliding time window are compared with the firing rate vectors of each class that were setup in the training phase. Depending on the algorithm, a matching class number is returned which identifies the reconstructed position. To calculate the reconstruction error, the reconstructed position can be compared to the position known from the position tracking data. Then the time window is moved to the next reconstruction position.

For position reconstruction the two algorithms were implemented that were already tested in linear arenas: (i) Bayesian 1-step and (ii) Bayesian 2-step with continuity constraint. For the analysis all datasets were divided into three equally long parts. Training was performed on two thirds of the recordings; the other third was used for the testing and reconstruction.

Bayesian method (1-step)

When the rat moves to specific positions then certain spike trains are produced as response to the sensory stimuli The probability of observing a number of spikes $n = (n_1, n_2, ..., n_N)$ given the stimulus $\boldsymbol{x}$ is $P(n \mid x)$. The probability of a stimulus (rat at position $\boldsymbol{x}$) to occur is defined as $P(x)$. The joint distribution

$$P(n, x) = P(n \mid x) \cdot P(x) \tag{2}$$

measures the likelihood of observing both a stimulus $\boldsymbol{x}$ and a spike train n.

For the reconstruction, the observation of a number of spikes n found in the measured data occur with a probability of $P(n)$. The likelihood of observing both stimulus and spikes is finally given by [5]

$$P(x \mid n) = C(\tau, n) \cdot P(x) \cdot \left(\prod_{i=1}^{N} f_i(x)^{n_i} \right) \cdot \exp\left(-\tau \cdot \sum_{i=1}^{N} f_i(x) \right) \tag{3}$$

Were $C(\tau, n)$ is a normalization factor and τ is the length of the time window. In this study the normalization factor $C(\tau, n)$ was set to 1.

The most probable position will be regarded as the animal's position:

$$\hat{x}_{Bayes,1-step} = \arg\max_{x} P(x \mid n) \tag{4}$$

Bayesian method with continuity constraint (2-step)

A continuity constraint can improve the accuracy of reconstruction. Sudden jumps in the reconstruction are observed by the low instantaneous firing rates of the recorded place cells. If not enough cells are firing then there is a lack of information. However the firing information is needed for the position reconstruction. The continuity constraint incorporates the reconstructed position from the preceding

time step as well as the current speed information. Based on the 1-step Bayesian method the reconstructed position at the preceding time step $t-1$ is also used to calculate the reconstructed position at time *t:*

$$P(x_t \mid n_t, x_{t-1}) = k \cdot P(x_t \mid n_t) \cdot P(x_{t-1} \mid x_t) \quad (5)$$

For more on this approach and details see [5].

III. Results

Figure 2 shows the reconstruction results computed with the Bayesian 2-Step algorithm of rat 3. Data from seconds 160 to 480 were used to train the algorithm and the interval 0 to 160 was used to test the method. The figure shows that the reconstructed path follows the real path very well in many data points of the recording. The mean reconstruction error of rat 3 was 9.5 cm. Figure 2 shows clearly erratic jumps of the reconstructed path in both x- and y-coordinates. If the reconstruction is only performed for time intervals where a minimum number of spikes (4 spikes in reconstruction window) are present the accuracy is increased as shown by the grey thin line in Figure 2B. In this case the mean error is 8 cm. Interesting is the erratic jump around second 51 were the running speed (Figure 2C) was almost 0.

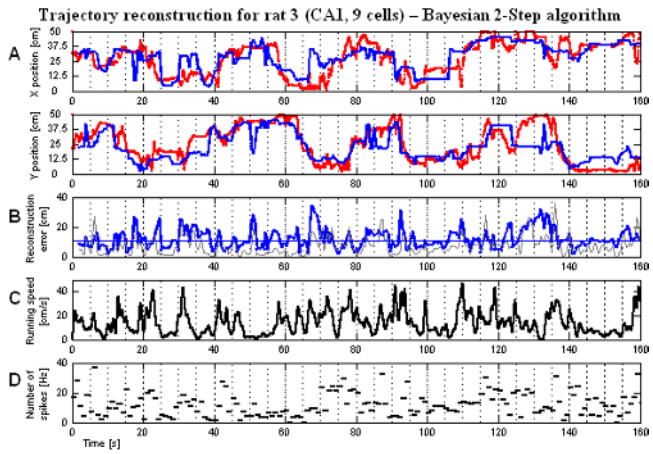


Figure 2: Reconstruction results for rat 3. A: Real (red) and reconstructed x- and y-positions. B: Reconstruction error (thick line), reconstruction error weighted by the instant place cell firing rate (thin line) and median error of the whole recording (horizontal line). C: Running speed. D: Firing rate of all neurons.

The two reconstruction algorithms were tested on all 6 rats by using a 3 x 3 fold cross-validation technique. Additionally, the Bayesian 2-step algorithm was trained and tested on 100 % of the data to test the theoretically achievable accuracy. In Figure 3 one example of CA1 cells and one example for subiculum cells are shown. Rat 3 reached a minimum error of 9.4 cm for a reconstruction window of 4 seconds using CA1 neurons. Rat 6 reached 26 cm with subicular units. For all rats the Bayesian 2-step (100 % training) version performed obviously best.

The horizontal dotted line at 5cm in each graph displays the intrinsic tracking error, which is defined as the average uncertainty in position tracking, due to the size of the diode (LED) arrays, the distance of the diodes above the rat's head and variations in posture [6].

IV. Discussion

The reconstruction algorithms for neural spike trains were implemented and applied to hippocampal place cell activity. The goal was to reconstruct the position of the rats just by investigating the spike activity as accurate as possible and therefore to minimize the reconstruction error. The best performance was found for the Bayesian 2-Step algorithm. The reason is that the algorithm considers also the previous position of the rat and does not allow large jumps from one reconstruction point to the next one. The Bayesian 1-Step algorithm performed less accurate but it is very interesting to see the results because it is only based on the current reconstruction window.

Despite subicular units tend to be more stable than CA1 cells, the results show that position reconstruction is more accurate with CA1 units. However, it is also interesting that subicular units contain enough information for the reconstruction. This can also be seen from the place field density plots, where the place fields of subicular units are much more blurred than place fields of CA1 units. Distinct place fields in combination with a high number of cells guarantee good reconstruction results. But it must be noted that only 2 data-sets from the subiculum and 4 data-sets from CA1 regions were investigated. The investigation of more data-sets is necessary to proof that.

Theoretically the reconstruction error is inversely proportional to the square root of the number of cells. This has been confirmed by the data analysis of all 6 rats as well as in other publications [5,7]. Interesting is that for 3 rats (1, 2, 3) the reconstruction error was below 20 cm with less than 10 place cells. Wilson [7] reported an error of 33 cm with 10 cells and Zhang [5] of 25 or 11 cm for 10 cells. This shows that with even a few cells the reconstruction can already be performed. But important is to consider the different arena sizes.

Erratic jumps occur also when the animal stops running. This has two reasons: (i) the firing rate is modulated by speed and therefore lower and (ii) the animal received food