

Position Reconstruction From an Ensemble of Hippocampal Place Cells: Contribution of Theta Phase Coding

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Jensen, Ole and John E. Lisman. Position reconstruction from an ensemble of hippocampal place cells: contribution of theta phase coding. *J. Neurophysiol.* 83: 2602–2609, 2000. Previous analysis of the firing of individual rat hippocampal place cells has shown that their firing rate increases when they enter a place field and that their phase of firing relative to the ongoing theta oscillation (7–12 Hz) varies systematically as the rat traverses the place field, a phenomenon termed the theta phase precession. To study the relative contribution of phased-coded and rate-coded information, we reconstructed the animal's position on a linear track using spikes recorded simultaneously from 38 hippocampal neurons. Two previous studies of this kind found no evidence that phase information substantially improves reconstruction accuracy. We have found that reconstruction is improved provided epochs with large, systematic errors are first excluded. With this condition, use of both phase and rate information improves the reconstruction accuracy by >43% as compared with the use of rate information alone. Furthermore, it becomes possible to predict the rat's position on a 204-cm track with very high accuracy (error of <3 cm). The best reconstructions were obtained with more than three phase divisions per theta cycle. These results strengthen the hypothesis that information in rat hippocampal place cells is encoded by the phase of theta at which cells fire.

INTRODUCTION

Particular types of sensory input can cause a cell to fire, but it remains unclear which aspects of the firing pattern are important. Many aspects of spike trains could potentially carry information, including the average firing rate, the occurrence of specific interspike intervals, the occurrence of a burst, or the degree to which different cells fire in coincidence (Eggermont 1998; Engel et al. 1992; Lisman 1997; Rieke et al. 1997). The spike properties that contribute usable information define the "neural code." In networks governed by an oscillation, the phase at which a cell fires relative to the oscillation could also carry information (Hopfield 1995; Perkel and Bullock 1968). The possibility of such phase-coded information is suggested by observations on rat hippocampal place cells. Each place cell fires when the animal is in a particular position in an environment and the cells collectively map the entire space (O'Keefe and Dostrovsky 1971; Olton et al. 1978). The firing of place cells is linked to a theta frequency (7–12 Hz) network oscillation in a complex way. There is little firing when the animal is outside the "place field" of a cell. As the animal moves into the place field, firing occurs during each theta

cycle until the animal leaves the place field. Thus firing rate is greatly increased when the rat is in the cell's place field. The importance of the phase of firing relative to the theta oscillation was discovered by O'Keefe and Recce (1993; see also Skaggs et al. 1996). They found that as the animal moves through the place field, the phase of firing becomes progressively earlier on each successive theta cycle, a phenomenon known as the "theta phase precession" or "theta phase advance."

The findings of O'Keefe and Recce suggest that the neural code in the hippocampus involves both phase-coded and rate-coded information. If pure phase coding were present, a cell would fire on each theta cycle (i.e., at constant rate), and information would be encoded only by changes in its phase of firing. Because place cells change their rate of firing, the code may be some hybrid of rate and phase information. It would clearly be desirable to have a quantitative way of evaluating whether phase-coded information is significant compared with that provided by rate alone. A general strategy for evaluating such coding issues is to reconstruct the environmental factors that triggered spikes from the spike trains (Rieke et al. 1997). If including a given property of these trains improves the accuracy of reconstruction, this property can contribute to the neural code.

The hippocampus is a particularly favorable region for using this approach because it is possible to record simultaneously from an ensemble of hippocampal neurons and to map their place fields. Several groups (Brown et al. 1998; Fenton and Muller 1998; Wilson and McNaughton 1993; Zhang et al. 1998) analyzed ensemble data of this kind to reconstruct the animal's position in its environment using sophisticated algorithms for reconstruction (e.g., Bayesian and Template; see METHODS). Surprisingly, these studies suggested that phase might not contribute substantially. Specifically, Zhang et al. (1998) suggested that it was unlikely that phase carried useable information because their optimal time window for reconstruction was much longer than the period of a theta cycle. Furthermore, Brown et al. (1998) showed that reconstruction was not improved by considering the theta amplitude modulation of the firing rate of the place cells. This work, although not ruling out the importance of phase information, has nevertheless raised serious doubts about whether the contribution of phase-coded information is quantitatively significant compared with rate-coded information. Because the basis of neural coding has such important implications for hippocampal function (Lisman 1999), we have reexamined this issue.

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METHODS

Recordings

The data we have analyzed were generated as part of the study reported by Skaggs et al. (1996). Before surgery the rat was trained to run for food rewards placed on the middle of the arms in a triangular maze (204 cm long, 8 cm wide). Single-cell recordings were made from 10 tetrodes placed in the hippocampus. The theta population activity of the field potential was recorded from the hippocampal fissure. A threshold level was adjusted by eye that detected most theta peaks in the raw signal. This threshold was then applied to band-pass filtered data (6–10 Hz) to automatically detect peaks and assign them a time stamp. If the interval between two adjacent peaks was too short (<100 ms) or too long (>167 ms) to be considered a theta period, it was eliminated from further analysis. If the interval was within this range, spikes within this theta cycle were assigned a phase and entered into the data set analyzed for coding questions. This procedure minimizes the contribution of activity during non-theta “large irregular activity” periods.

The rat’s position was determined by monitoring light-emitting diodes (LEDs) placed on the rat’s head stage. The position of the LEDs was established using a video-tracking device (256 × 256 pixels, 2.3 pixels per cm). Some uncertainty in the animal’s position is nevertheless present because the LEDs are actually above the animal’s head and their position can be influenced by head angle (Skaggs et al. 1996). The position of the rat recorded in x - y coordinates was projected onto a straight line representing each arm of the maze.

Reconstruction algorithms

The triangular maze was linearized to one stretch of 204 cm and divided into 150 bins (defining the variable, x). The actual position of the rat was calculated from the tracking device and projected onto the linear maze. The place fields for each of the 38 cells were constructed using the first 500 s of data (~9 runs in the maze). The place fields were represented by the vector $\mathbf{f}(x) = [f_1(x), f_2(x), \dots, f_{38}(x)]$ where x is one of the 150 bins. $f_i(x)$ represents the firing rate of cell i as a function of space, x (the total number of spikes in collected bin x divided by the total time the rat was in bin x). After the place fields were constructed, they were smoothed with Gaussian kernels (width = 2.7 cm). Using the subsequent 500 s of data, the reconstruction algorithms were applied using a sliding time window of width Δt . At each time window, spikes from the place cells were collected: $\mathbf{n} = (n_1, n_2, \dots, n_{38})$. n_i represents the number of spikes from cell i . For each time step, the position was reconstructed on the basis of collected spikes (\mathbf{n}) and the place fields [$\mathbf{f}(x)$]. The reconstructed position was compared with the position measured by the tracking device. The mean absolute error (m.a.e.) was used as a measure of the reconstruction

$$\text{mean absolute error} = \frac{1}{N} \sum_i |x_{\text{predicted}}^i - x_{\text{measured}}^i| \quad (1)$$

Mehta et al. (1997) have shown that place fields are not stable, but tend to expand asymmetrically during the 1st 15–20 laps a rat traverses a maze. Obviously, if one could find a method to incorporate this effect into the reconstruction algorithm, the error of reconstruction would be reduced. However, we expect that the conclusions regarding the phase precession would remain the same.

Template matching method

A template, $\mathbf{f}(x)$, is defined as a vector of firing rates from the 38 cells at bin x . The best match of the collected spikes (\mathbf{n}) to 1 of the 150 templates defines the reconstructed position (Wilson and McNaughton 1993; Zhang et al. 1998)

$$x_{\text{reconstructed}} = \arg \max_x \sum_i n_i f_i(x) \quad (2)$$

BAYESIAN METHOD. Bayes’ rule was used to calculate the probability of the animal to be at position x , given the number of spikes (\mathbf{n}) collected in t

$$P(x|\mathbf{n}) = \frac{P(\mathbf{n}|x)P(x)}{P(\mathbf{n})} \quad (3)$$

The probability distribution of positions $P(x)$ was calculated during the first 500 s (when constructing the place fields). $P(\mathbf{n})$ does not have to be calculated because it is given by the normalization of $P(x|\mathbf{n})$. The term $P(\mathbf{n}|x)$ is derived using the firing rates $\mathbf{f}(x)$ from the place fields assuming that 1) the firing of place cells are statistically independent and 2) place cells fire according to a Poisson distribution (Zhang et al. 1998)

$$P(\mathbf{n}|x) = \prod_i P(n_i|x) = \prod_i \frac{\Delta t f_i(x)^{n_i}}{n_i!} \exp[-\Delta t f_i(x)] \quad (4)$$

Inserting these expressions into Bayes’ rule (Eq. 3), the probability distribution $P(x|\mathbf{n})$ for all x is calculated. The maximum of this distribution defines the most probable position

$$x_{\text{reconstructed}} = \arg \max_x P(x|\mathbf{n}) \quad (5)$$

Theta phase precession

The phase precession was applied by dividing each theta period into N subperiods. A place field was then divided according to which subperiod the individual spikes belonged (e.g., Fig. 4A). This resulted in the vector $\mathbf{f}(x) = [f_1(x), f_2(x), \dots, f_{N*38}(x)]$, where the elements 1 to N are the subdivisions of the first place field, elements $N+1$ to $2*N$ the next subfield, and so forth. The vectors of spikes $\mathbf{n} = (n_1, n_2, \dots, n_{N*38})$ are constructed similarly. After the division, the reconstruction was performed as before, using the template and Bayesian methods. When using the Bayesian method, it was useful to apply the method under conditions where phase information was absent. This was done by a shuffling procedure in which each spike in a theta cycle was reassigned a random phase.

Correction excluding tracking error

If the variance is $\sigma_{\text{reconstruction}}^2$ for the reconstruction algorithm and $\sigma_{\text{tracking}}^2$ for the tracking system, then the measured variance is

$$\sigma_{\text{measured}}^2 = \sigma_{\text{reconstruction}}^2 + \sigma_{\text{tracking}}^2 \quad (6)$$

Because the mean absolute error (m.a.e.) of a Gaussian distribution with variance σ^2 is $\sigma(2/\pi)^{1/2}$, the reconstruction error corrected for the tracking error is

$$\text{m.a.e.}_{\text{reconstruction}} = \sqrt{\frac{2}{\pi} (\sigma_{\text{measured}}^2 - \sigma_{\text{tracking}}^2)} = \sqrt{\text{m.a.e.}_{\text{measured}}^2 - \frac{2}{\pi} \sigma_{\text{tracking}}^2} \quad (7)$$

RESULTS

The data utilized in this study were obtained from an investigation of place cells in a behaving rat by W. Skaggs, C. Barnes, and B. McNaughton, who kindly supplied the data to us. Recordings were made from 10 tetrodes placed in the hippocampus. Individual cells were identified by a standard cluster technique (Skaggs et al. 1996). Out of a total of 75 cells identified, 38 cells showed spatially localized firing. Of these, 34 were in the CA1 region and 4 were in the dentate gyrus. All 38 cells are considered together in our analysis. Note that these

TABLE 1. *Effect of using phase information of mean reconstruction error**

	All Spikes	>9 Spikes/t	>9 Spikes/t, No Food-Stand Data
Template			
No phase information, cm	12.6	7.8	7.6
Seven phase bins, cm	12.2	6.4	5.3
%Improvement†	3	22	43
Bayesian			
No phase information, cm	15.4‡	6.0‡	4.3‡
Six phase bins, cm	14.4	4.8	3.0
%Improvement†	7	25	43
Number of time windows	3,332	848	498

On average, 4.2 ± 2.0 of the 38 cells being recorded contributed to the firing during the 150-ms time window. Collectively all cells that fired during a time window produced an average total of 9.8 ± 4.1 spikes. * Mean absolute error (see METHODS). † (Decrease in reconstruction error)(error with phase information) \times 100%. ‡ Phase was used after random phase shuffling.

place cells were not preselected according to whether they showed phase precession. Data were collected as the rat ran counterclockwise on a triangular maze (arm length = 68 cm; total track = 204 cm). The rat was motivated to traverse the track by food placed at food stands at the middle of each arm. The animal went around the track 20 times, and the rat's actual position was continuously determined by a video tracking system.

In the initial step of position reconstruction, the properties of individual place cells were characterized by correlating cell firing with actual position during the 1st 10 passages of the

track. Then, using the 2nd 10 passages, the rat's current position was reconstructed from the spikes that occurred in a time window (Δt), using the previously established properties of individual place cells and either of two reconstruction algorithms described by Zhang et al. (1998). These algorithms are termed the "1-step Bayesian method" and the "template matching" method (also termed the "direct basis method"). The template matching method is relatively straightforward: during the 1st 10 passages, one establishes for each position (x) on the track a reference template that relates firing rate to cell number (*cell 1* $f_1(x)$ spikes/s; *cell 2* $f_2(x)$ spikes/s, etc.). For each Δt during the 2nd 10 passages, one finds the reference template that best matches the profile generated by the spikes that occur in that period (Eq. 2). The Bayesian method is more complex and depends primarily on two functions (Eq. 3). The first is the probability that the observed profile of spikes could arise from the reference template for a given position. The second is the probability of being at a given position, $P(x)$, based on past history (this is highest at the food stands where the animal often lingers). From these two sources of information and the assumption of Poisson firing, the most likely current position can be computed. Comparing these methods, both Zhang et al. (1998) and Brown et al. (1998) found the Bayesian method to be the more accurate.

In our first series of reconstructions, only rate information was used. The mean reconstructed error was in the range of 14–16 cm (Table 1) with both template and Bayesian methods. The individual reconstructions using the Bayesian method are shown in Fig. 1A. In this figure, the reconstructed position is plotted as a function of the measured position. If the recon-

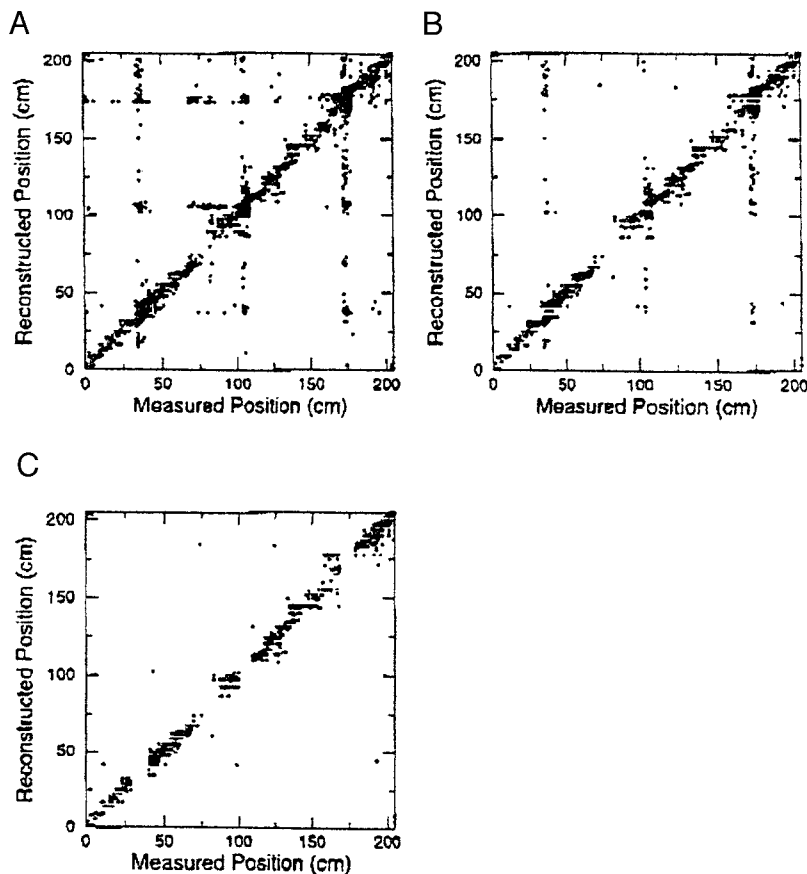


FIG. 1. Reconstructed position (estimated by the Bayesian method) is plotted vs. measured position. These reconstructions do not take phase information into account. Each dot represents a reconstruction. *A*: reconstruction for a 150-ms time window. Note that there are a significant number of large errors that lead to erratic jumps in the reconstructed position. These errors tended to cluster around the reconstructed positions at 39, 102, and 170 cm; the locations of the food stands. *B*: reconstructions for time windows in which there was >4 total spikes collected from the 38 place cells within a time window. Note that the number of large errors is reduced. *C*: reconstructions when there were >4 spikes per time window and when the animal was not at a food stand.

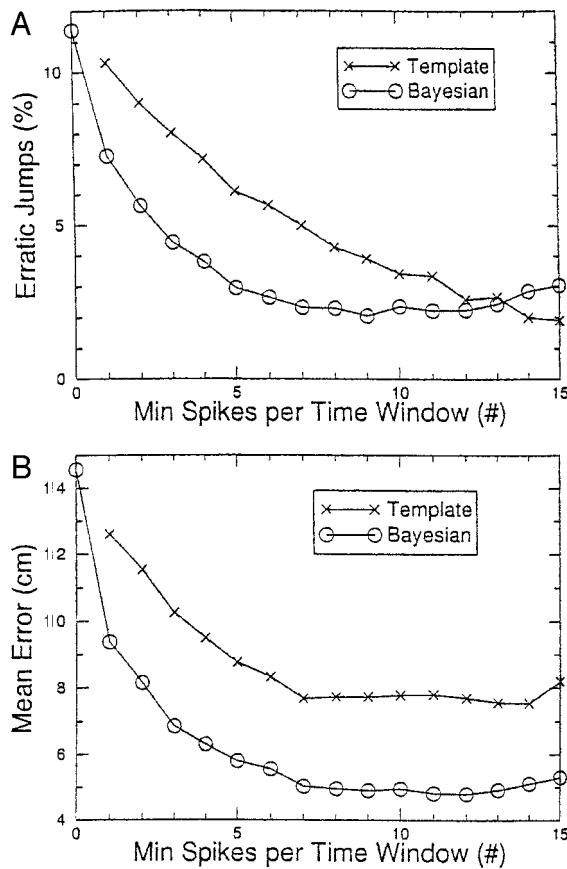


FIG. 2. If an estimate is made only if a minimum number of spikes occur during a time window, reconstruction errors are reduced. *A*: effect on the percentage of analyzed windows that have erratic jumps. An erratic jump is defined as occurring when the prediction error is >10 cm. *B*: effect on mean absolute error in analyzed windows.

reconstructions were perfect, all the points would fall along a diagonal line with a width of several centimeters reflecting the measurement error of the rat's actual position (see *Recording's* in METHODS). It can be seen that most points fall along the diagonal, but that there are also many points that fall far from the diagonal. These large errors (defined as errors >10 cm) are termed "erratic jumps." Figure 1A shows that there is a systematic source of these large errors because they tend to fall along vertical and horizontal lines.

It was clearly of importance to identify the sources of these systematic errors. It can be seen that a large number of them fall along horizontal lines at the reconstructed positions of ~ 34 , 102, and 170 cm. These are the positions of the food stands. Such errors are expected if the time window that serves as the basis of the computation contains little information (few or zero spikes) because when this occurs, the Bayesian method picks a reconstructed position based on the peaks in the position probability distribution, $P(x)$ (see Eq. 3). The peaks of $P(x)$ are where the animal spends the most time, which turns out to be at the food stands.

To determine whether most erratic jumps indeed arise when the number of spikes in Δt is low, reconstructions were made only when the total number of spikes was >4 . This procedure greatly reduced the number of erratic jumps (Fig. 1B), especially those in which the predicted position is a food stand (these formed the horizontal bands in Fig. 1A). Figure 2 shows

how the number of erratic jumps and the mean reconstruction error falls as the threshold for the minimum number of spikes per time window is raised (if only time windows with >4 spikes were considered, this excluded 11% of the spikes and 33% of the time windows; if the threshold was >9 , this excluded 45% of the spikes and 70% of the time windows). It is important to recall that, although many place cells (38) were monitored, these were still only a very small subset of the total ($\sim 10^5$). Given this limited sampling, it is to be expected that there will be time windows when little of the information present is collected. We conclude from this analysis that when evaluating the details of position coding, time windows having a small number of spikes produce a large systemic error that could dominate the mean reconstruction error.

The presence of systematic errors is serious because it could obscure the effect of factors, such as phase, that might potentially affect the quality of reconstruction. Zhang et al. (1998) argued that phase information was unlikely to be of use because consideration of phase requires Δt corresponding to a theta period (~ 150 ms), but when they reduced Δt to such values, reconstruction accuracy deteriorated. This result is replicated in Fig. 3 (all spikes; both Bayesian and Template matching methods). However, as noted above, this conclusion may be affected by the large systematic reconstruction errors that occur when little information is available in a time window. To test this possibility, we repeated the

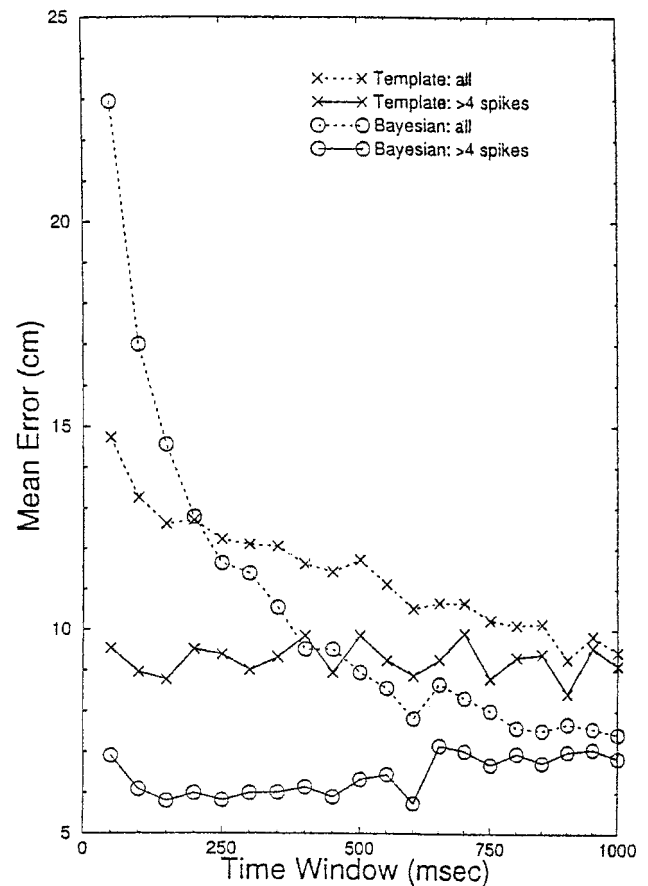
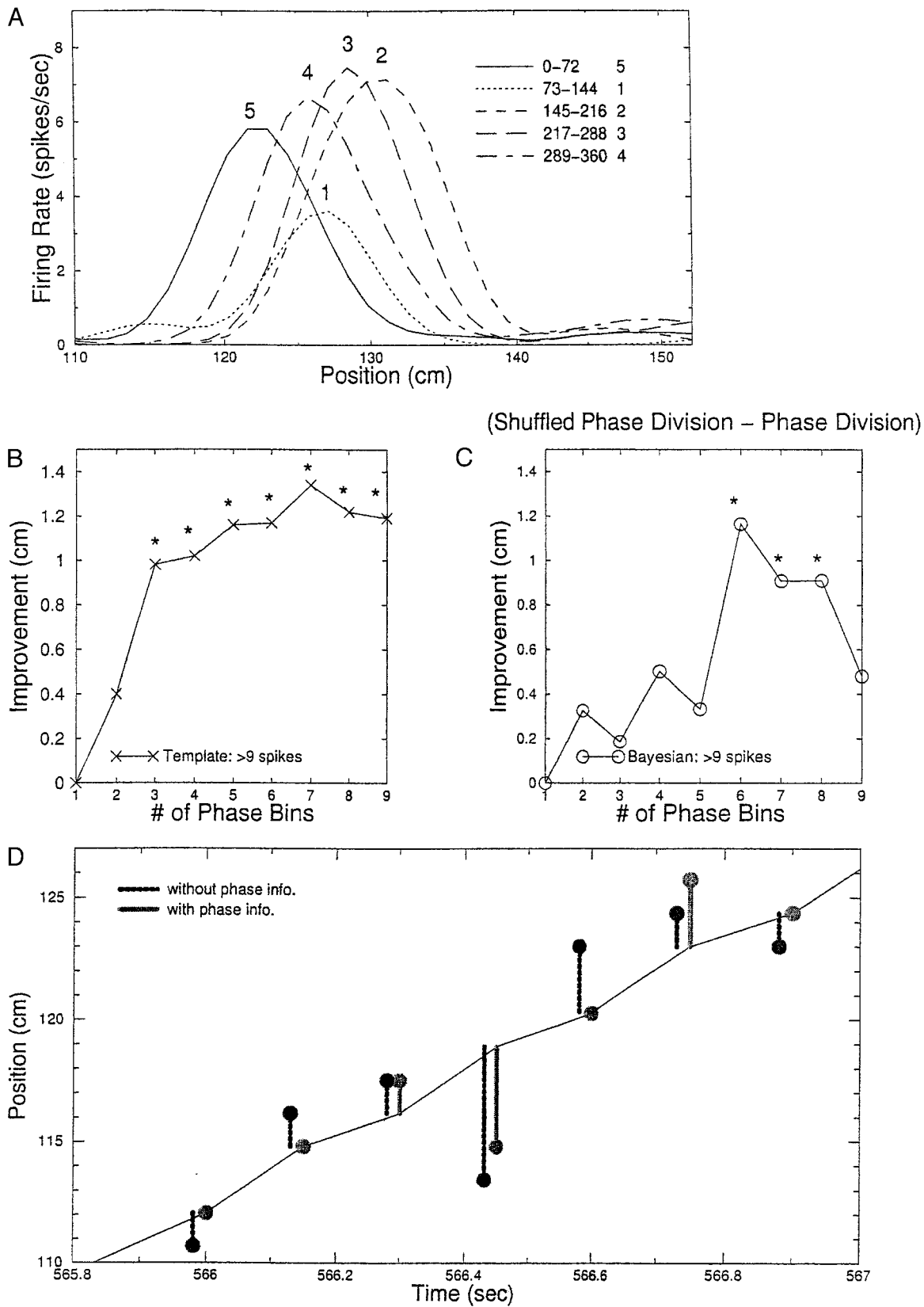


FIG. 3. Good reconstructions of position can be made even using short time windows if only time windows with >4 spikes are considered. \cdots , reconstruction error for the Bayesian and template matching method using all time windows. --- , reconstruction error with a threshold >4 spikes per time window for both reconstruction methods.



analysis after excluding all periods with <4 spikes. When this was done, it was found that reconstruction was as good for short time windows (~ 100 ms) as for long ones (Fig. 3). This has important implications because it now becomes reasonable to use the theta period (150 ms) as the time window and to study the effect of spike phase within that window.

Before proceeding with studying the effect of phase on reconstruction accuracy, we first tested whether we could observe the dependence of position on phase that was previously reported (Skaggs et al. 1996). Figure 4A shows the spatial distribution of firing for different phases of a representative place cell. There is an ordered progression of the spatial profile as a function of phase, with one exception (the phase with lowest firing rate). Because these results are similar to what has been previously reported, we proceeded to study how reconstruction was affected by taking phase into consideration.

Our general strategy for studying the effect of phase and rate information on reconstruction accuracy was to subdivide each theta cycle (see METHODS) into a discrete number of phase bins. In separate analyses, the number of bins was varied from 1 to 9. If there was only one phase bin, then there was no phase information and the reconstruction depended only on rate information. Alternatively, phase information was analyzed for a given number of bins and compared with the reconstruction for the same number of bins when spikes were shuffled between bins (see BAYESIAN METHOD in METHODS). If phase information was shuffled, the reconstruction depended only on rate information.

Figure 4, B and C, shows how the reconstruction accuracy improved as we increased the number of phase bins into which a theta cycle was divided, for both the Template and Bayesian methods. For the Template method, the reconstruction accuracy improved progressively as the number of phase bins was increased to seven (Fig. 4B): the absolute error was reduced by 1.4 cm (22%) by using phase. Figure 4C shows that when the Bayesian method was used, the error was reduced by 1.2 cm (25%) when six phase bins were used. When the number of phase bins was nine, the improvement was no longer significant, suggesting that there is an optimal number of phase bins between five and nine. An example showing the benefit of using phase information on individual reconstructions in a small (15 cm) region of the track between food stands is shown in Fig. 4D. Based on the results of Fig. 4, we conclude that phase information improves the reconstruction of position by 20–25% (Table 1).

The percentage reduction in reconstruction error is a measure of the importance of phase information relative to rate information alone. However, this percentage will be reduced if there are large systematic sources of error that affect both types of reconstructions. It was therefore desirable to eliminate as

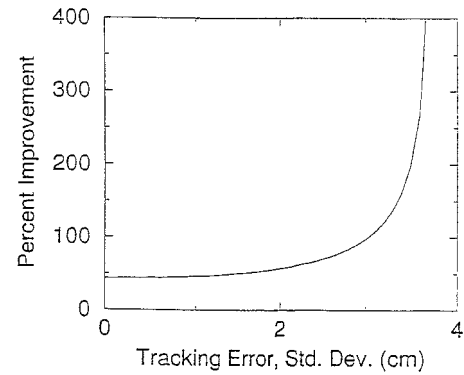


FIG. 5. Percent improvement in position reconstruction produced by taking phase into consideration depends on the SD of the tracking error. The Bayesian method is used here. The tracking error has been estimated to be as large as 5 cm. If the error were actually this large, the % improvement in reconstruction error would be unreasonably high, suggesting that the mean tracking error may be smaller.

many sources of systematic error as possible. The reconstruction shown in Fig. 1B is only for time windows where there are substantial number of spikes (>4), a condition that reduced the erratic jumps (compare to Fig. 1A). There are nevertheless some remaining large systematic errors that tend to fall along vertical lines. We found that raising the number of spikes required did not greatly reduce these errors. It can be seen that these errors occurred primarily when the animal was at food stands. It is known that when an animal is eating, large-amplitude irregular activity (LIA) occurs that can be difficult to distinguish from theta (Vanderwolf 1969). Given this possibility, it was of interest to examine the effect of phase information when these large errors at food stands were not a factor. We therefore redid the analysis of phase information considering only the positions *between* food stands (Fig. 1C). Table 1 shows that under these conditions, taking phase information into account produced a 43% improvement in reconstruction accuracy compared with what could be achieved using rate information alone.

An additional factor that could influence the percent improvement produced by phase information is the error in the measurement of the actual animal's position. The animal's position was measured by monitoring the position of LEDs mounted above the rat's head. It has been estimated that changes in head angle and other factors could lead to a "tracking" error of as much as 5 cm (Skaggs et al. 1996; Wilson and McNaughton 1993). Unfortunately, a quantitative determination of this error is not available. We have therefore made calculations for a range of values of the tracking error. It can be seen in Fig. 5 that if there is no correction for tracking error, phase information produces a 43% improvement in reconstruction

FIG. 4. When phase information is used, reconstruction accuracy is improved. A: illustrative example of how the firing of a cell at a given phase depends on position. *Insert*: the phase windows relative to the peaks of field theta. Note that the large peaks are in order (as indicated by the number at their peak). The phase with lowest firing rates is out of sequence. B: the reconstruction is improved by increasing the number of phase bins when the template matching method is used. Significant improvement ($P = 0.05$) in reconstruction compared with the case where phase information was not used is indicated by asterisks. C: improvement also occurs when the Bayesian method is used. Significant improvement ($P = 0.05$) compared with the case where the phase bins were shuffled is indicated by asterisks. D: illustration of individual reconstructions and their errors, with and without the use of phase information. Thin black line is the measured position as a function of time during a 1.2-s period. Vertical solid and dashed lines connect the reconstructed position to the measured position and illustrate the magnitude of the errors, with and without phase information. Note that some of the reconstructed positions appear to be absolutely exact, but that this exactness results from the fact that position was discretized by 1.36 cm. For all reconstructions in this figure, only time windows in which there were >9 spikes in a time window were considered.

tion error. On the other hand, if the tracking error was actually 5 cm, virtually the whole reconstruction error is accounted for by the tracking error and the percent improvement in reconstruction produced by phase becomes $>400\%$. We think it is unlikely that the tracking error is actually as large as 5 cm and taking an intermediate value of the tracking error (3 cm) seems more plausible. In this case the actual reconstruction error is 1.8 cm and the percent improvement produced by taking phase into consideration is $\sim 100\%$.

These results raise the possibility that the estimate of position based on brain recordings is more accurate than that based on actual measurement. This is not unreasonable because the reconstruction algorithms use functions derived from *multiple* measurements of position, which can lead to an averaging out of measurement error. More generally, these results indicate that reconstructions have become so accurate, that the tracking errors are problematic. It would therefore be very desirable to reduce these if possible in future experiments. On the basis of the available information, we conclude that phase produces a minimum improvement in reconstruction error of 43% and that the improvement is probably much larger (Fig. 5).

DISCUSSION

The phase precession of individual hippocampal place cells (O'Keefe and Recce 1993; Skaggs et al. 1996) is a striking phenomenon, and the fact that it occurs suggests that the hippocampus uses a neural code that depends on phase-coded information in addition to rate-coded information. We have more rigorously tested this possibility using the ensemble activity of 38 place cells to reconstruct the rat's position as it moves around a triangular track. This form of analysis makes it possible to quantitatively estimate the effect of taking phase information into account. Our results clearly show that when phase-coded information is used, the accuracy of position reconstruction is greatly improved. This demonstrates that the phase-coded information is quantitatively significant and that the neural code in the hippocampus uses a combination of a rate code and a theta-phase code.

To reveal the utility of phase-coded information, we first had to remove systematic sources of error not related to positional coding. These sources of error (Fig. 1) occurred during periods when there were an insufficient number of spikes available to make a good estimate or when the animal was at a food stand. When these periods of systematic error were eliminated, the remaining data were used for reconstruction, with or without phase information. Because this comparison was made on the *same* data, there is no bias toward any particular result. By making this comparison, we found that phase-coded information is of great utility in reconstructing position (Figs. 4 and 5; Table 1). We estimate that an animal's position can be predicted with an error of <3 cm, much smaller than the actual size of the rat, and that the improvement produced by taking phase information into account is $>43\%$ (Table 1; Fig. 5). Importantly, predictions of this accuracy can be made on the basis of a relatively small number of spikes (10–20) obtained from a relatively small number of cells (~ 5) that fire during the brief time window of single theta cycles (150 ms; Table 1).

The observation that some reconstructions lead to large erratic jumps in positions has been previously noted by both Zhang et al. (1998) and Brown et al. (1998). As a mean of

dealing with these errors, they implemented a continuity constraint in the Bayesian reconstruction algorithms. The continuity constraint ensures that a reconstructed position is close to the previous reconstructed position (Zhang et al. 1998: the Bayesian 2-step method). In this way erratic jumps were prevented. This constraint requires that the previous reconstructed position be stored temporarily and used to interpret the meaning of current spiking. In contrast, we find that very good estimates of position can be made using current spike activity alone, provided that time windows with zero or few spikes are ignored.

Number of phase bins

Figure 4, *B* and *C*, indicates that reconstruction accuracy is improved by increasing the number of phase bins within a theta cycle, at least up to six bins. There is some hint that there might be an optimum at about six to seven, but the data are not sufficiently reliable to be certain about this. We have examined the statistical significance of this dependency. Using a Wilcoxon rank test on the template-method results (Fig. 4*B*), we find that seven phase bins is better than one, two, or three ($P < 0.03$) for data excluding food stands. For the Bayesian method (Fig. 4*C*), we find that six phase bins is better than one, two, or three and also better than nine ($P < 0.03$). Taken together, these results indicate that the number of meaningful phase divisions is more than three. This conclusion is consistent with the previous suggestion that place cells have approximately seven discrete phases of firing within a theta cycle (Jensen and Lisman 1996, 1997; Lisman and Idiart 1995). This proposal was based on the observation from *in vivo* recordings during movement showing that ~ 7 – 10 high-frequency (40–100 Hz) gamma cycles are nested within each theta cycle (Bragin et al. 1995; Csicsvari et al. 1999; Soltesz and Deschenes 1993). During each gamma cycle, the network of hippocampal interneurons produces a short-lasting hyperpolarizing input to the pyramidal neurons that transiently suppresses spike activity. This inhibitory activity would be expected to divide a theta cycle into a series of discrete phase bins.

Function of phase coding

Although our results show that the ensemble of place cells contains phase-encoded information, little is known about how this information is used. One idea is that the brain could use an algorithm not unlike the Bayesian algorithm to combine information from *different* phase bins and to thereby produce a prediction of current position (Zhang et al. 1998). Alternatively, information in *individual* phase bins may be detected by downstream neurons that are phase-sensitive detectors (Jensen 1999). Such detectors would not only have to receive the phase-specific hippocampal activity, but a theta reference signal by which to decode it. It is known that theta activity is found in brain regions that receive input from the hippocampus, including the entorhinal and cingulate cortexes (reviewed in Bland and Oddie 1998). It is implicit in some models of the phase precession (Burgess et al. 1994; Jensen and Lisman 1996; Lisman 1999; Skaggs et al. 1996; Tsodyks et al. 1996) that cells representing sequential upcoming positions fire sequentially within a theta cycle, i.e., with increasing phase delay. Thus detectors with sensitivity to specific phases could

determine whether a given position is nearby (if firing occurs with early phase) or remote (if firing occurs with late phase).

Conclusion

Our results provide the strongest evidence to date that phase-coded information is expressed by ensembles of hippocampal neurons and that cells express this information in a form that allows substantial improvements in position estimation compared with what can be achieved using rate information alone. Our findings relate only to the rat hippocampus, but theta oscillations have been found in other brain areas in rodents and in humans (Gevins et al. 1997; Kahana et al. 1999; Klimesch et al. 1997; Macrides et al. 1982; Nicolelis et al. 1995; Tesche 1997). It will be important to determine whether phase-coded information is also present in these areas.

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