

contribution to synapsis initiation as meiosis progresses.

Another function for centromere coupling might be the distributive disjunction system, which ensures the segregation of chromosomes that failed to cross over. Centromere regions in female flies have been shown to be important for distributive disjunction (16). In yeast, nonexchange chromosomes associate at their centromeres before segregation, and interfering with this association increases the rate of nondisjunction (17).

Centromeres appear to contribute to homolog alignment and segregation in other species as well, although the underlying mechanisms may be somewhat different. Nonhomologous centromere coupling is observed before homolog pairing during meiosis in wheat, but it is also observed in premeiotic tissues, arguing that centromere coupling does not depend on an SC protein (18, 19). In fission yeast, only centromeric regions are able to pair independently of meiotic recombination (20). The contributions of centromeres and SC proteins to homolog pairing in higher eukaryotes remain to be elucidated.

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Materials and Methods

Fig. S1

References

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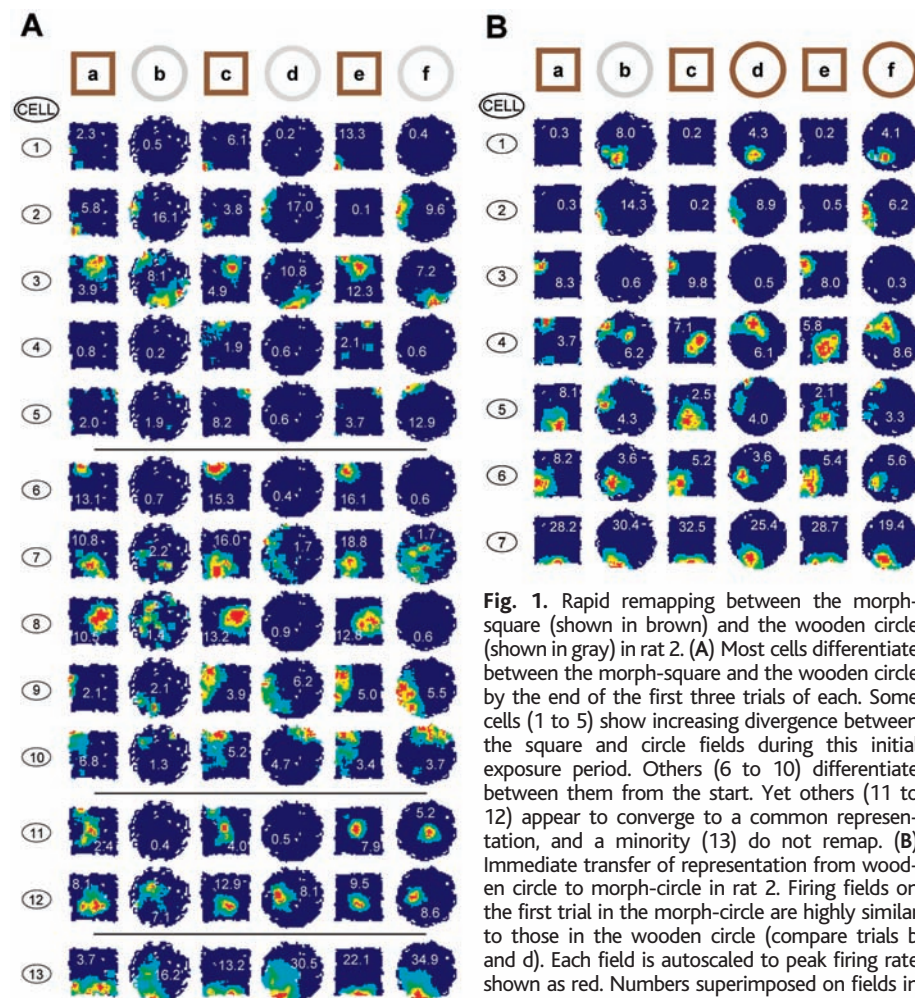
# Attractor Dynamics in the Hippocampal Representation of the Local Environment

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Memories are thought to be attractor states of neuronal representations, with the hippocampus a likely substrate for context-dependent episodic memories. However, such states have not been directly observed. For example, the hippocampal place cell representation of location was previously found to respond continuously to changes in environmental shape alone. We report that exposure to novel square and circular environments made of different materials creates attractor representations for both shapes: Place cells abruptly and simultaneously switch between representations as environmental shape changes incrementally. This enables study of attractor dynamics in a cognitive representation and may correspond to the formation of distinct contexts in context-dependent memory.

For more than 30 years, autoassociative or attractor dynamics based on Hebbian synaptic modification have been central to neuronal models of memory, with particular focus

on the dense recurrent collaterals of the hippocampus and its crucial role in context-dependent episodic memory (1–14). We investigated whether attractors were present in



**Fig. 1.** Rapid remapping between the morph-square (shown in brown) and the wooden circle (shown in gray) in rat 2. (A) Most cells differentiate between the morph-square and the wooden circle by the end of the first three trials of each. Some cells (1 to 5) show increasing divergence between the square and circle fields during this initial exposure period. Others (6 to 10) differentiate between them from the start. Yet others (11 to 12) appear to converge to a common representation, and a minority (13) do not remap. (B) Immediate transfer of representation from wooden circle to morph-circle in rat 2. Firing fields on the first trial in the morph-circle are highly similar to those in the wooden circle (compare trials b and d). Each field is autocorrelated to peak firing rate shown as red. Numbers superimposed on fields in this and subsequent figures show peak firing rates in Hz, to one decimal place.



the hippocampal representations of different environments.

Place cells in the mammalian hippocampus signal the location of the animal within its environment by firing whenever it visits a specific region [the “place field” (10, 15)]. This representation can be specific to the environment, with different cells being active in different environments or the same cell being active at different locations in different environments (16). The change in representation between environments is known as “remapping.” After foraging in square and circular boxes which differed only in their shapes (not texture or color), CA1 hippocampal place cells took considerable time (many days or weeks) to differentiate between the two boxes, with simultaneously recorded cells remapping at different times (17). Individual cells appeared to represent a location in one or both environments independently of other cells.

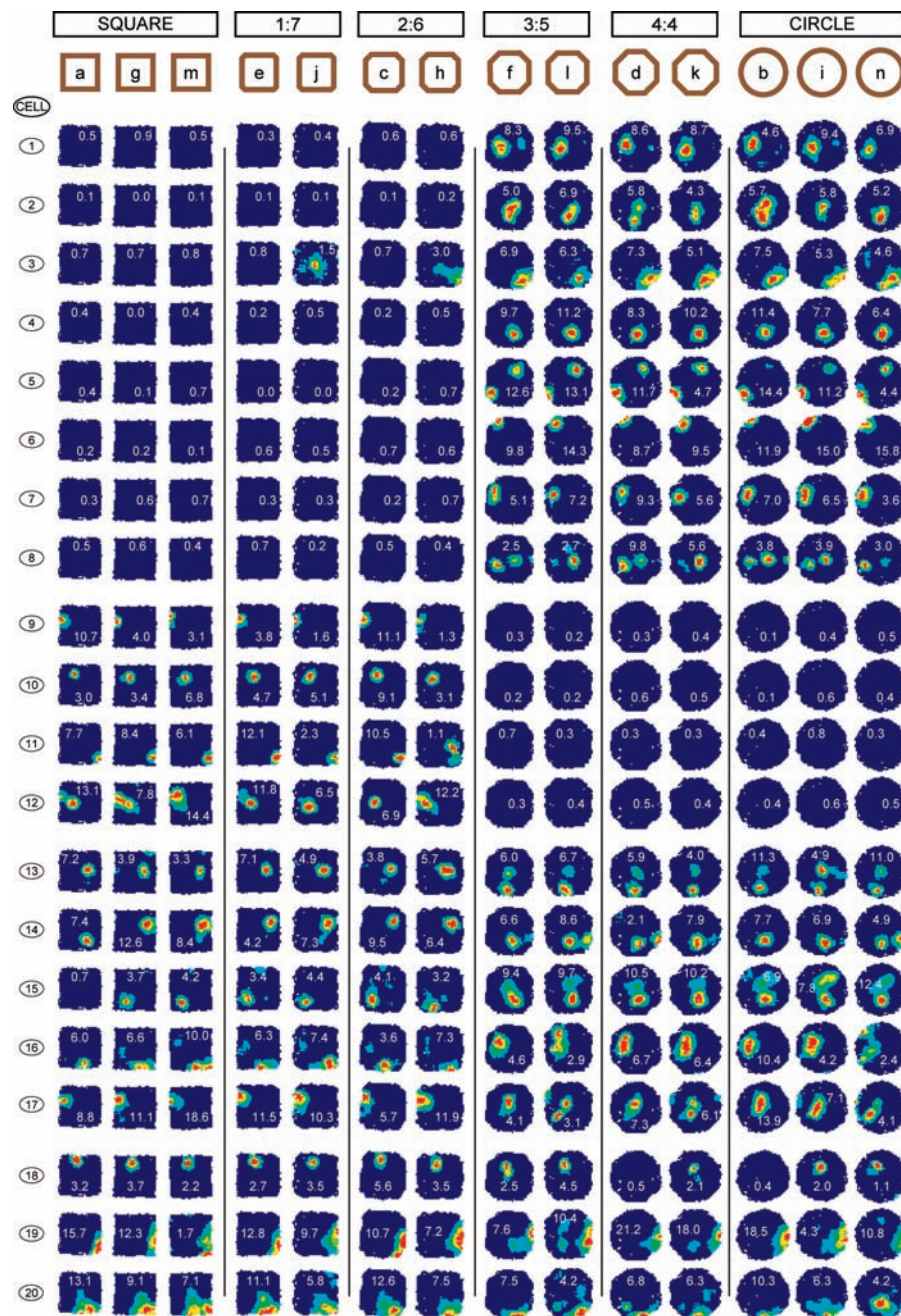
We recorded from CA1 place cells in a paradigm designed to produce more rapid remapping (18). Animals were initially exposed to a square and a circle that differed in color, texture, and shape. The square was a morph-box (17) (which can be configured in various shapes, see fig. S1, A and B); the circle was made of painted wood. This led to rapid remapping with the majority of cells (92%, that is, 48 out of 52) differentiating between the environments at the end of the first day’s six trials (three in each box, see Fig. 1A). After 3 days of this training, the animals were trained in the morph-box configured as a square and a circle on alternate trials for an additional 3 days (fig. S1C). The place fields of the majority of remapped cells (40 out of 46) transferred successfully to the morph-circle and showed the same pattern as in the wooden circle (see Fig. 1B). Different place fields in two configurations of the morph-box can only be cued by environmental shape, as other attributes such as texture and color do not vary. Of the six animals, one failed to show rapid remapping in the morph-square and wooden circle, and one did not show wooden circle to morph-circle pattern transfer. In these cases, the experiment was terminated. This paper describes results from the remaining four animals.

Are the different hippocampal representations of the morph-square and morph-circle after remapping due to the formation of separate attractors for each shape? If so, each representation would lie at the bottom of a “basin of attraction” within which other representations inevitably evolve into the

attractor representation under the system’s dynamics: Representations of intermediate shapes would revert to either the square or the circle representation (3, 6) (fig. S3, A to C). If not, representations of intermediate shapes would remain intermediate to those of the circle and square.

We recorded from groups of neurons during a series of probe trials in a set of octagonal morph-boxes (18) that varied from squarelike

(adjacent side ratio 1:7) to circlelike (adjacent side ratio 4:4) through more ambiguous intermediates (see Fig. 2 top row; fig. S1D). Almost all simultaneously recorded cells (28 out of 33) showed an abrupt switch from the squarelike pattern to the circlelike one across the octagonal series. The firing fields of 20 simultaneously recorded place cells in the series are shown in Fig. 2. Trials are presented in order of most squarelike on the left to most



**Fig. 2.** Abrupt and coherent expression of squarelike or circlelike representation during probe trials in intermediate octagonal environments in rat 4. The 17 of 20 place cells simultaneously recorded from rat 4 with different (remapped) firing patterns in the square and the circle almost all switch from the squarelike to circlelike pattern between the 2:6 and 3:5 octagons. Eight cells had fields in the circle but not the square (cells 1 to 8); four in the square but not the circle (9 to 12); five fired in both but in different places (13 to 17); and three did not reach our criterion for remapping (18 to 20) (18).

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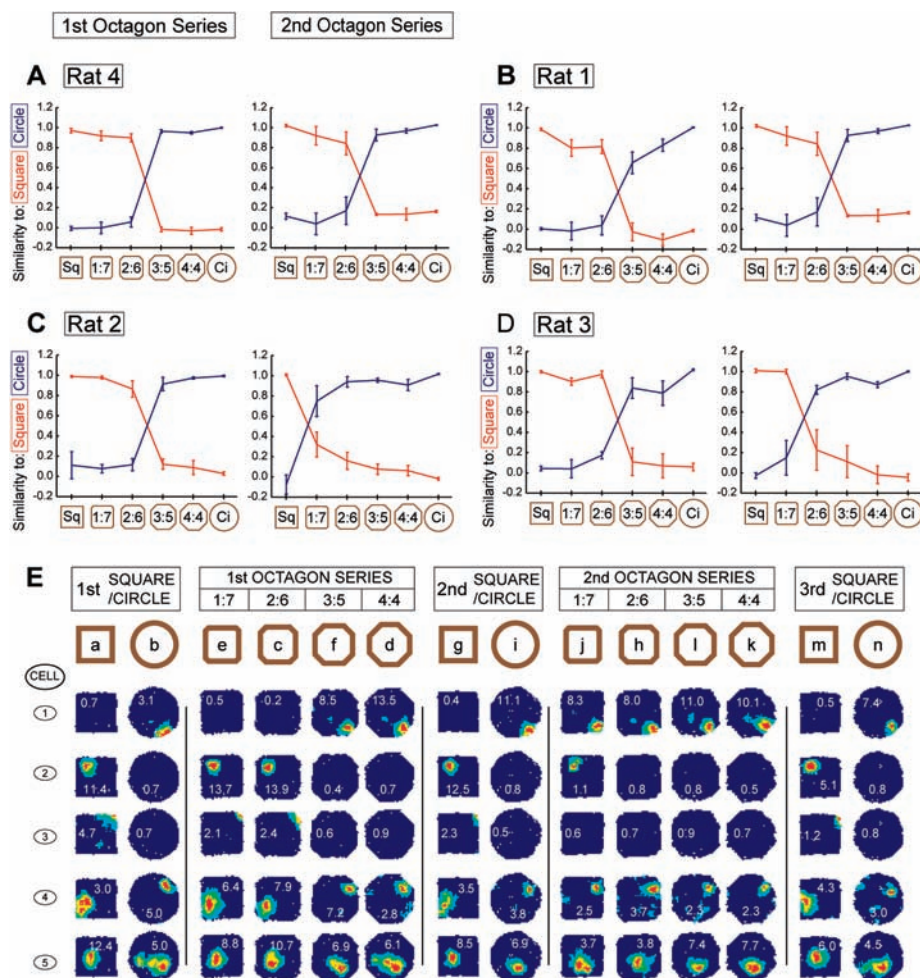
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circlelike on the right but were run in two series of interleaved and balanced order (fig. S1E). Seventeen of the 20 cells clearly remapped between the square and the circle: 12 remapped by changing rate (only firing in one or other shape), and 5 remapped their field position (firing in different places in the two shapes). The remaining three cells did not reach our criterion for remapping (18). Almost all of the cells abruptly switched from the squarelike to the circlelike pattern at the same transition point. This effect is quantified in Fig. 3A by comparing the similarity of each cell's firing in the octagons to that in the square and circle (18). A similar pattern was seen in the other three animals (Fig. 3, B to D left side).

The abrupt and coherent remapping of the place cell ensemble seems to require coordinated action, as in an autoassociative network, rather than to reflect cells independently

responding to the same subtle environmental changes. For example, if each cell independently remapped at any of the five shape transitions, the probability of  $N$  cells remapping at the same point would be  $0.2^{N-1}$  ( $P < 10^{-11}$  for the 17 cells from rat 4 in Fig. 2;  $P < 10^{-4}$  for rat 1 in fig. S2A;  $P < 0.05$  for rat 2 and rat 3, Fig. 3E and fig. S2B, respectively). This impression is strengthened by the remapping pattern in two of the four animals. In one animal (rat 2), the cells remapped between the 2:6 and 3:5 octagons during the first series of probe trials, but remapped between the square and 1:7 octagons during the second series (Fig. 3, C and E). Significantly, all cells again switched at the same point. Another animal (rat 3) showed a similar pattern, remapping at the 1:7 to 2:6 transition in the second series (Fig. 3D), whereas the remaining two animals remapped at the same point in both series (Fig. 3, A and B).

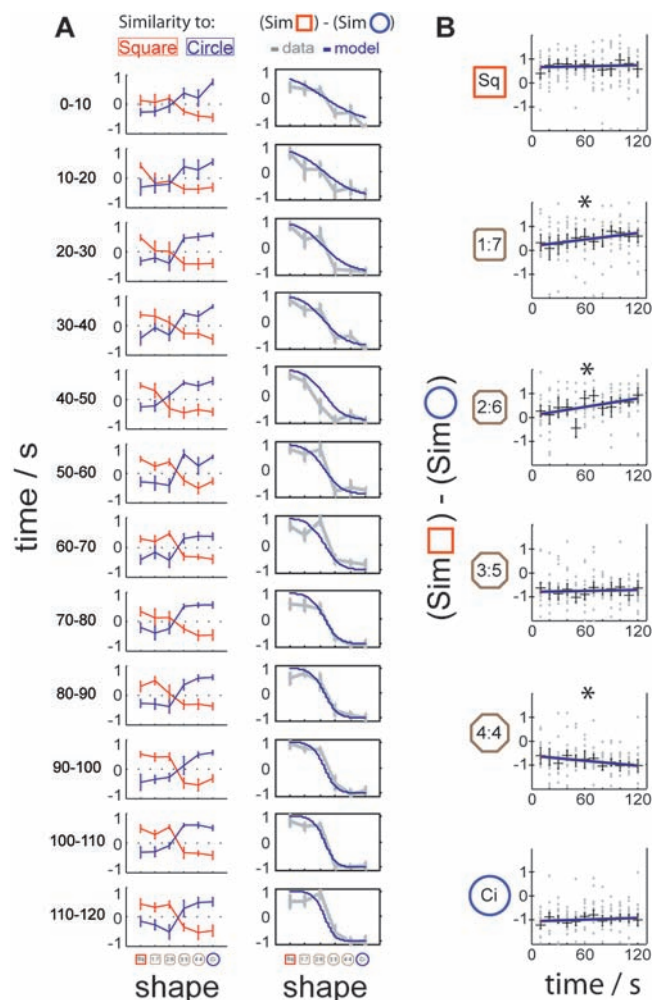


**Fig. 3.** Coordinated shift in square-to-circle switch point between the first and second octagon series. (A to D) Plots show the similarity of place cells' firing patterns in probe trials of varying shape to their firing patterns in square (red) or circle (blue) baseline trials [mean and SEM across cells (18)]. In the first series of octagons, all animals show abrupt remapping between the 2:6 and 3:5 octagons (A to D, left side); in the second series (right side), rats 4 (A) and 1 (B) again remap at this point, whereas rat 2 (C) remaps between the square and 1:7 octagon, and rat 3 (D) remaps between the 1:7 and 2:6 octagons. (E) Firing rate maps for all remapped cells for the two octagon series for rat 2.

Are attractor dynamics observable at the start of a trial? The firing patterns in intermediate shapes might take time to reach the circle or square representation, when starting from more intermediate representations (see fig. S3, A and B). The firing patterns in successive 10-s intervals from the start of each trial were examined (18) in our largest dataset (17 remapped cells, see Fig. 4, A and B). Several results should be noted. First, the similarity of the firing patterns in square and circle probe trials to square and circle baselines is stable across intervals (with the possible exception of the very first interval in the square). Second, the firing in the squarelike octagons (1:7 and 2:6) is already more squarelike than circlelike in the first 10-s interval, but slowly becomes more squarelike over the following 2 min. A similar pattern is seen in one of the two more circlelike octagons (4:4). This result indicates a surprisingly slow component to attractor dynamics that should be studied further with larger samples of cells (a similar trend that did not reach significance was seen for our next-largest dataset, the eight remapped cells in fig. S2A).

Previous experiments, including our own, did not find the integrated cooperative behavior among pyramidal cells shown here (19–22). For example, the place cell representation initially adjusts continuously to changes in environmental shape alone, consistent with purely feed-forward processing (22, 23), and individual place cells slowly and independently learn to differentiate between square and circular environments made of the same material (17). One possibility is that synaptic modification in the CA3 recurrent collaterals is triggered by multimodal changes (e.g., of environmental shape, color, and texture) but not by unimodal changes, consistent with a hippocampal role in forming cross-modal associations between stimuli represented in disparate neocortical areas (7, 24). Greater remapping was also seen when both proximal and distal cues were changed than when either set was changed alone (25).

The results suggest the operation of both pattern separation, which creates radically different representations from highly similar environmental inputs, and coordination of large numbers of place cells to create a global maplike representation of each environment (2, 4, 5, 7, 10, 26). These functions are likely to originate in the hippocampus. Remapping has not been observed in its main cortical input, the entorhinal cortex (27, 28), and we expect cells there would respond incrementally to the gradual changes in the octagon series. Although our recordings were made in CA1, following previous authors (2, 4, 5, 7–9, 14), we hypothesize that pattern separation takes place in the dentate gyrus, whereas autoassociative integration takes place in the CA3 recurrent collaterals (see fig. S3C). Four



**Fig. 4.** Attractor dynamics of environmental representations. **(A)** Evolution of the firing pattern in successive 10-s intervals of trials in the different shaped environments. (Left column) The similarity of firing to that in square and circle baseline trials (mean and SEM for the 17 remapped cells in Fig. 2). (Right column) The difference in similarity of the firing pattern to square and circle baseline patterns. Gray line shows mean and SEM over cells of the difference between the red and blue curves shown in the left column. This becomes steadily more pronounced over time, and can be fitted by a sigmoid whose slope increases linearly with time (blue line:  $y = 2/(1 + \exp(-(a_0 t + a_1)(s - s_0))) - 1$ , where  $t$  is time in seconds,  $s = 1$  to 6 corresponds to the series of shapes from square to circle, and  $a_0 = 0.019$ ,  $a_1 = 0.674$ ,  $s_0 = 3.29$  were chosen to fit the data). **(B)** Firing patterns in intermediate 1:7 and 2:6 octagons become more squarelike over time, the patterns in 4:4 octagons become more circlelike, while the patterns in the square and circle remain unchanged (\* $P < 0.05$  one-tailed, linear regression) (18).

examples are consistent with CA3's acting as an autoassociative network: the inability of mutant mice with disabled CA3 *N*-methyl-D-aspartate receptors to compensate for the removal of subsets of cues in the Morris water maze (14), the high sparsity of the CA3 representation (20, 25), signs of hysteresis within it (29), and the coherent response of CA3 place cells to inconsistent rotation of two sets of cues. CA3 place cells mainly followed proximal cues, whereas CA1 cells followed combinations of proximal and distal cues (21).

Our finding of coherent activity of place cells specific to each environment has several potential functional consequences. Such representations or "charts" (26) could serve to reduce interference between environments by providing orthogonal representations for each. They would also allow the firing of

large numbers of cells to be combined to provide an improved estimate of location (30). The capability for integrating information at distant locations with the representation of the current location may allow for short-cut and detour behavior (10, 31). More generally, attractor dynamics are thought to underlie context-dependent recollection [as opposed to, for example, familiarity-based recognition (32)]. Thus, understanding the creation of new attractors, and their dynamics, may directly inform the nature and function of "context" in context-dependent episodic memory and its failure in amnesia. Finally, the ability to study this mechanism at the single unit level allows for electrophysiological, pharmacological, and genetic investigation of the mnemonic function of the hippocampus in health and disease.

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