

Spatial memory in individual and populations of neurons of the non-human primate hippocampus

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Introduction

Mixed selectivity has been reported to be more prevalent in the non-human primate (NHP) hippocampus than selectivity for single variables. We characterise the prevalence of NHP place, view, and head direction selectivity during a virtual goal-directed navigation task and dissociate the confounding influences of each spatial variable in mixed-selective cells. Additionally, we investigate selectivity to non-spatial variables in these same cells, on the single-cell and population levels.

Methods

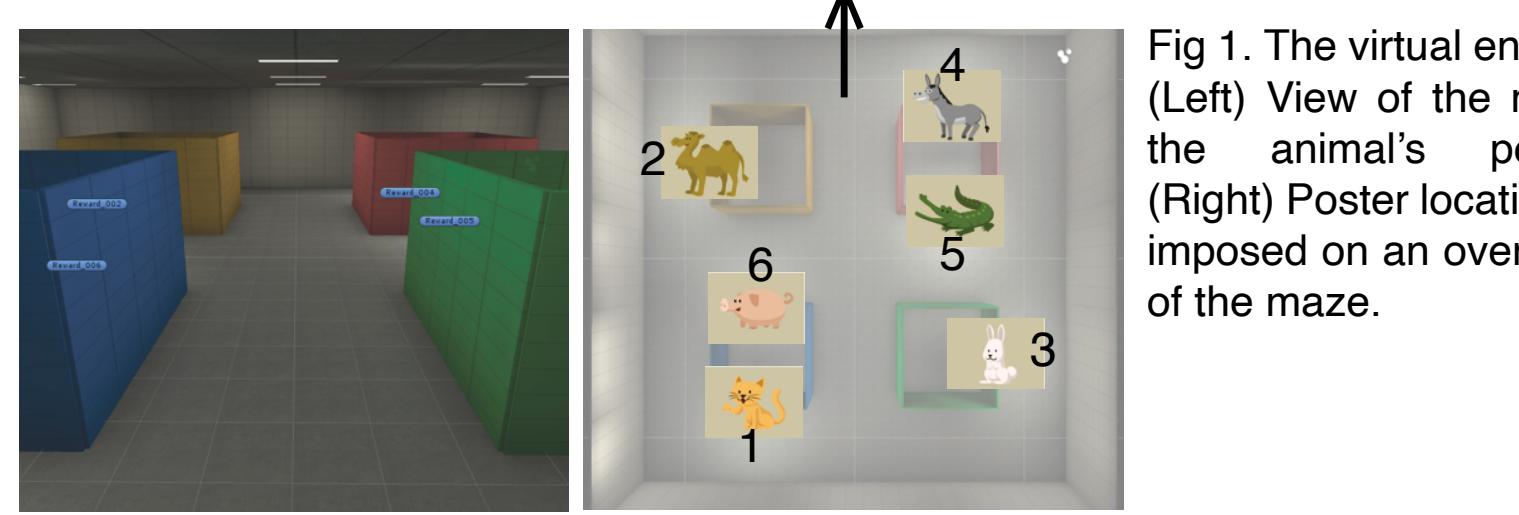


Fig 1. The virtual environment. (Left) View of the maze from the animal's perspective. (Right) Poster locations superimposed on an overhead view of the maze.

Animal and Implant: 1 male macaca fascicularis was chronically implanted in the left hippocampus with 124 independently movable electrodes (Gray Matter Research).

Data Acquisition: Neural activity was recorded at 30,000 samples/s (Ripple Neuro), eye gaze was tracked with an infrared camera (Eyelink 1000 Plus, SR Research) at 1,000 samples/s.

Behavioral Task: The animal performed 400 trials per session of a continuous match-to-sample navigation task set in virtual reality (Unity 3D). A randomly chosen target poster was shown at the start of each trial, with a 25 second time limit for navigation to the correct target location.

Spatial Cell Characterization: Cells with 1) spatial information (SI; place and view) or Rayleigh vector scores (RV, head direction) that exceeded the respective 95th percentile time-shift shuffled thresholds, 2) had peak firing rates > 0.7Hz qualified as selective. To quantify contributions of sampling biases and dissociate the independent contributions of each spatial variable, the distributive hypothesis (Muller et al., 1994) and maximum likelihood model (Burgess et al., 2005) were calculated.

Mixed Selectivity Characterization: Mixed selectivity was tested for non-linearity by comparing in-field vs out-field firing (two-sample t test) of rate maps conditioned on firing fields for each pair of spatial variables. Firing fields were delineated from at least 15 contiguous bins with activity greater than 1) 70% of peak firing rate and 2) 2 standard deviations from the mean.

Pseudopopulation Analysis: Cell responses across multiple sessions from each trial phase (cue phase, hint viewing instances, last second of navigation phase) were grouped by their {start poster, end poster} tuples and then concatenated together in chronological order (earlier trials first) to form a pseudopopulation.

Information Gain Characterization: Information gain with respect to goal identity was calculated for single-cells across non-overlapping 100 ms time windows throughout the cue phase, with non-overlapping 100 ms time windows across the entire session used as the unconditioned reference. Probability distributions for the cell responses were obtained empirically.

Cross-Temporal Decoding: A Linear Discriminant Analysis (LDA) classifier was trained and cross-validated on the pseudopopulation responses during each of the trial phases (cue phase, hint viewing instances, last second of navigation phase) to classify the goal of the trial, then tested on the other two trial phases. An additional 'None' class was added for cross-temporal predictions that did not meet a prediction probability threshold.

Pseudopopulation Trajectory Characterization: Pseudopopulation responses across non-overlapping 100 ms time windows throughout the cue phase were grouped by their {start poster, end poster} tuples, and the mean of each group across time was visualized in 3-dimensional PCA space.

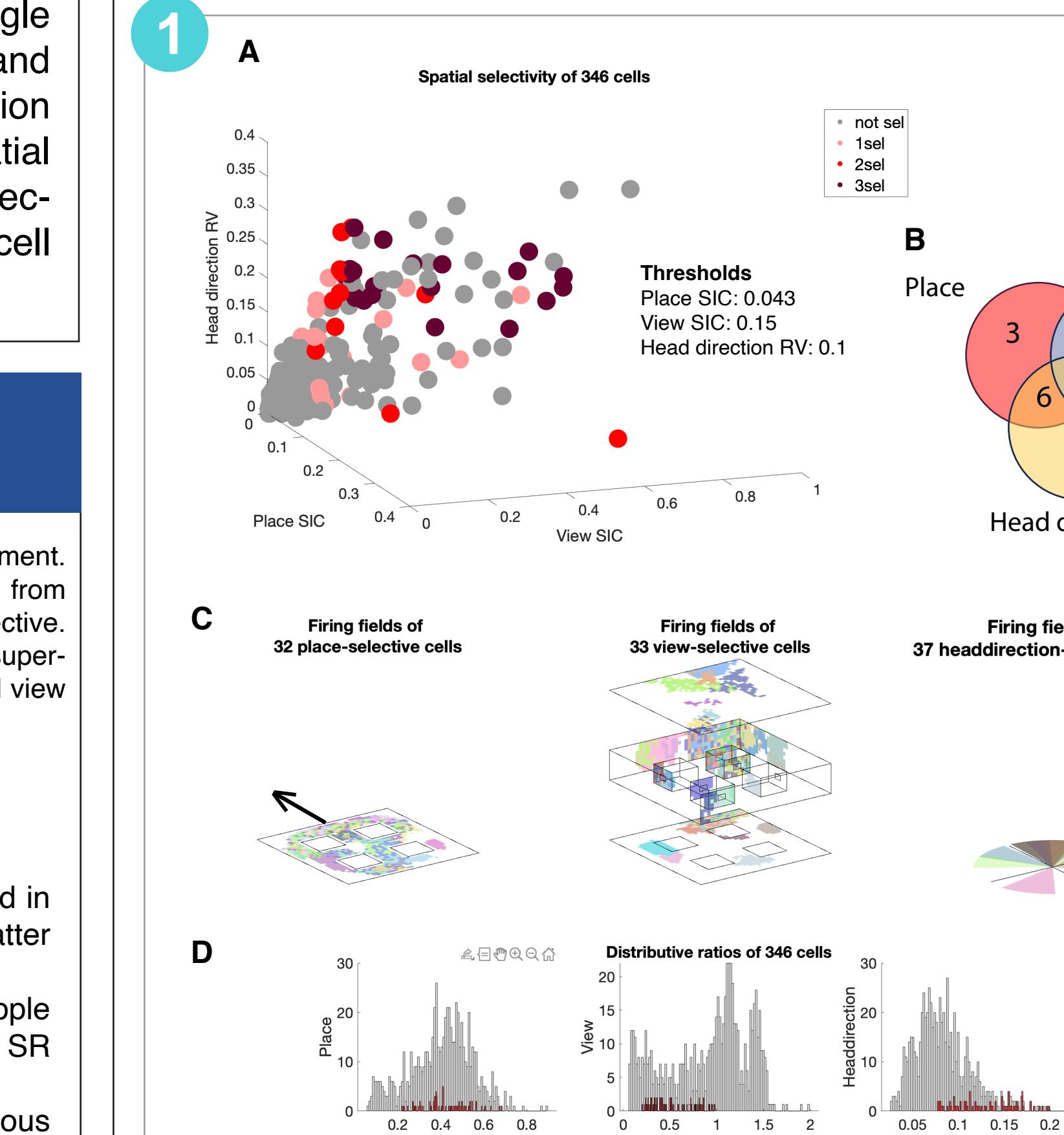
Summary

NHP hippocampal neurons are predominantly mixed-selective for place, view and head direction during goal-directed navigation in virtual reality. This mixed-selectivity is non-linear, with most mixed-selective cells conjunctively active to the spatial variables they represent. Additionally, these cells also often encode non-spatial information in a way that coincides with their spatial fields. Non-spatial information can be extracted from the population activity across navigation and planning phases of the task.

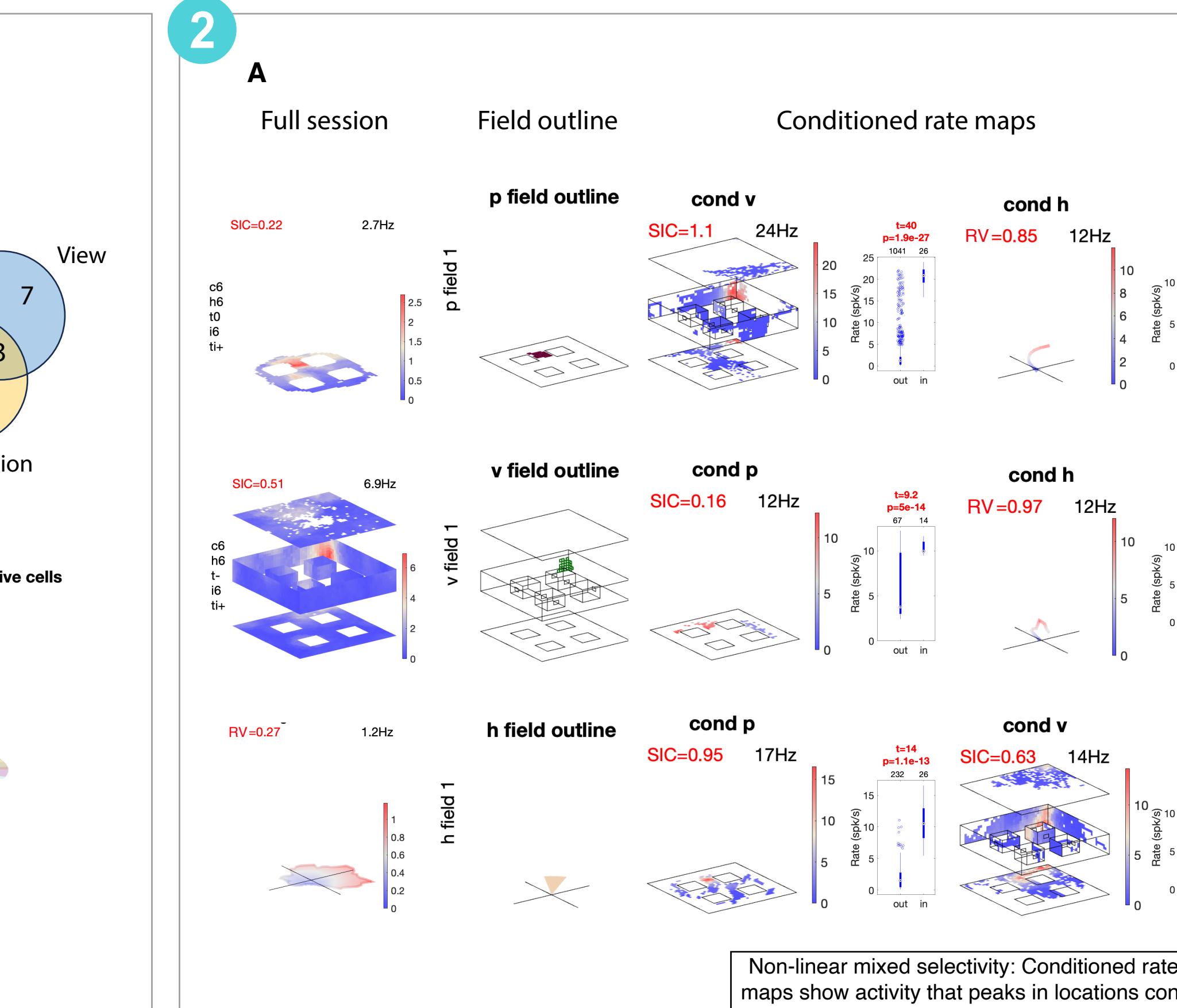
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Results

Hippocampal neurons are predominantly non-linear mixed-selective for spatial variables

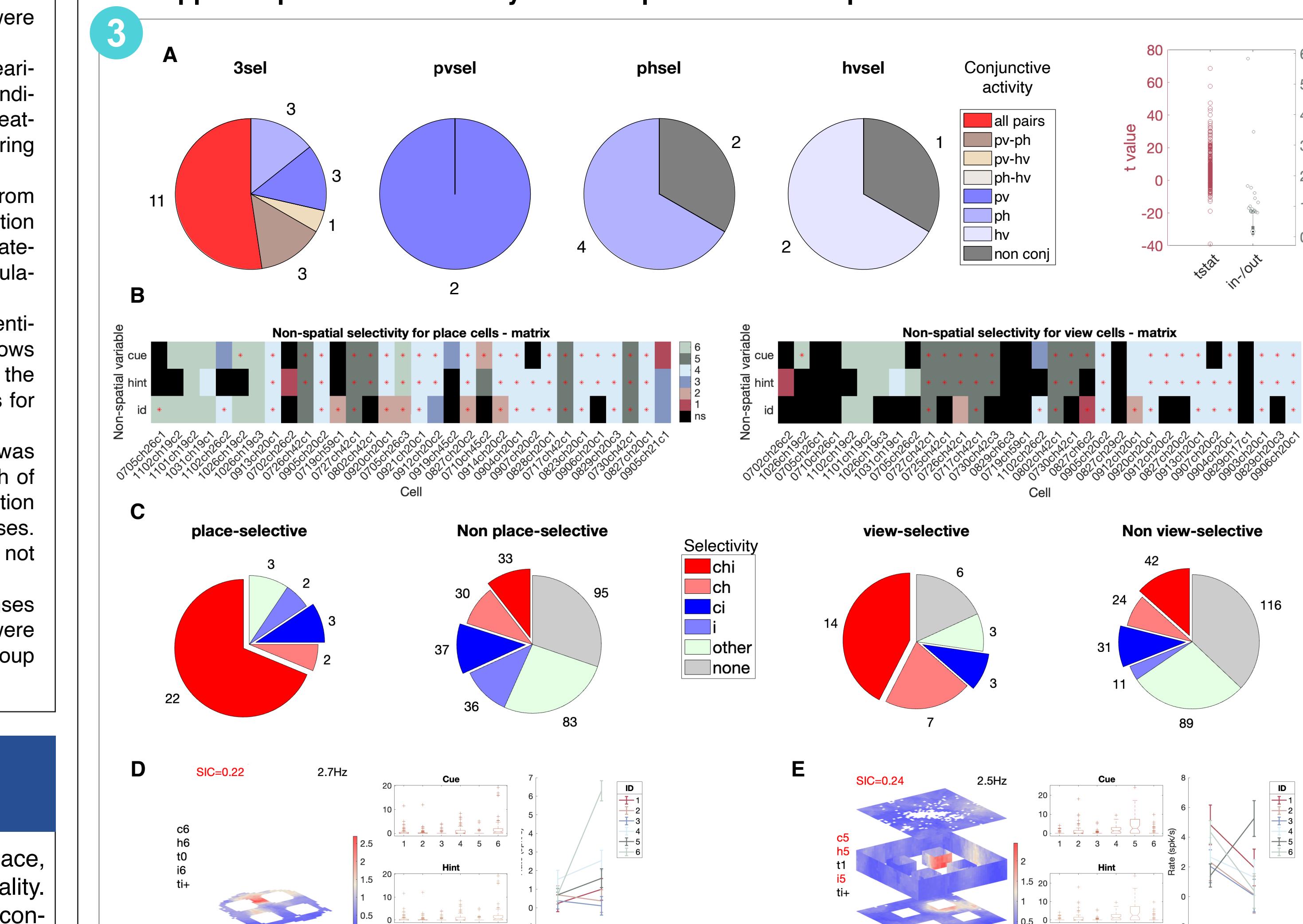


Hippocampal neurons are predominantly mixed-selective for spatial variables. (A) Scatter plot of SIC and RV values for cells mixed selective for place (p), view (v) and head direction (h). (B) Venn diagram showing overlap between Place, View, and Head direction. (C) Firing fields of 32 place-selective cells, 33 view-selective cells, and 37 headdirection-selective cells. (D) Distributive ratios of 346 cells.

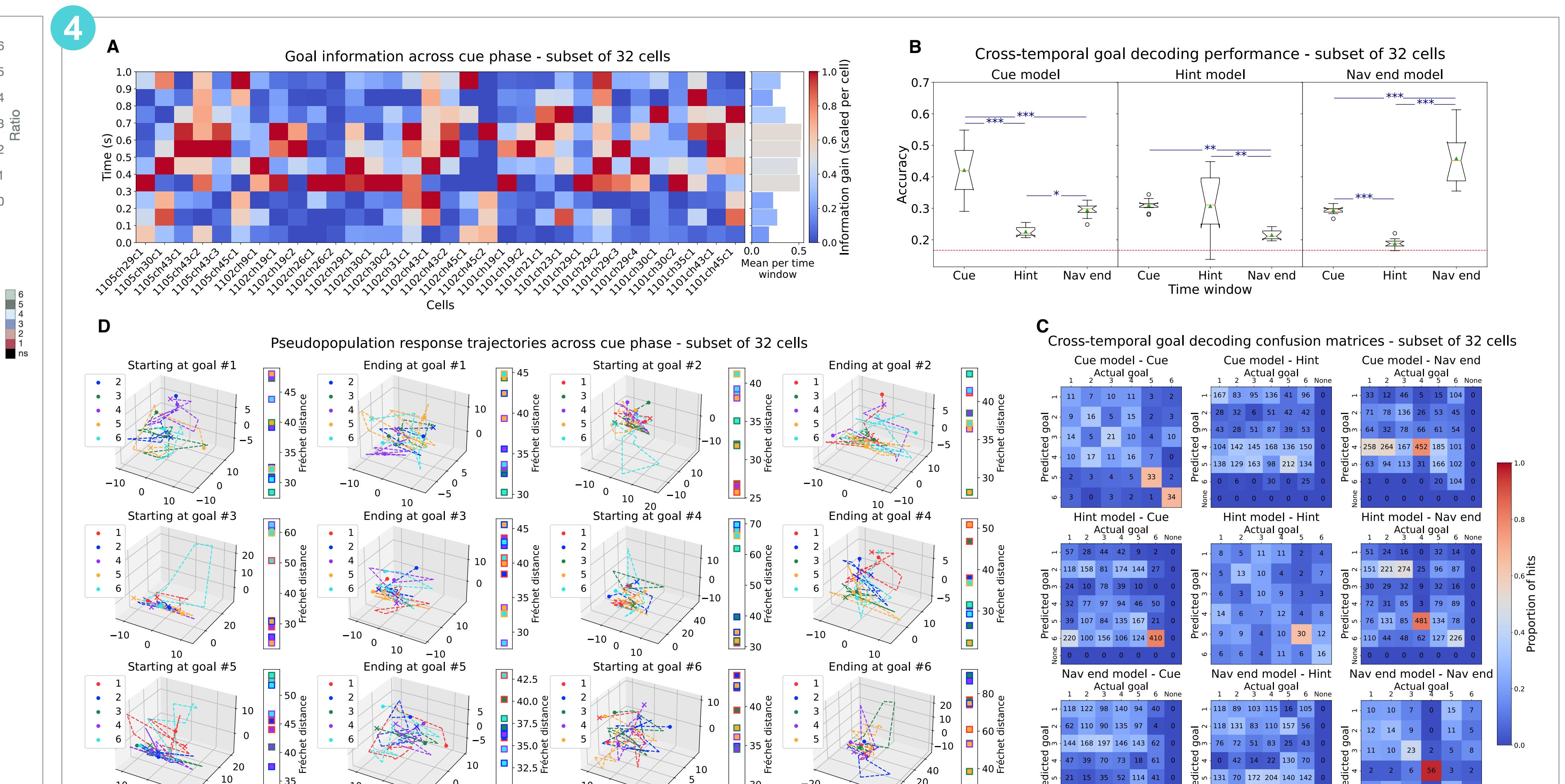


Mixed selectivity for space in the NHP hippocampus is predominantly non-linear. (A,B) Cell examples. Columns: 1. Full session firing rate maps 2. Firing fields 3. Rate maps conditioned on each of the other 2 variables with box plot insets of in-field vs out-field activity of conditioned map, with sample numbers for each category. 4. Full session rate map with conjunctive activity removed. 5. Distributions of activity in original rate maps and those with conjunctive activity removed, with the 99th percentile of activity in the original rate map indicated (red line). SIC/RV and peak rates are shown respectively in the top left and top right corners of each rate map. (A) Example of a cell non-linearly mixed selective for p, v, and h. Activity in each conditioned rate map is significantly higher in the cell's actual spatial field than outside (two-sample t tests, alpha 0.05). Removing the conjunctive activity resulted in a reduction of SIC. (B) Example of a cell with both non-linear and linear mixed selective fields.

Hippocampal neurons flexibly encode spatial with non-spatial information



Hippocampal neurons flexibly encode spatial with non-spatial information. (A) Pie charts of 3sel, pvsel, phsel, hvsel cells. (B) Non-spatial selectivity for place and view cells. (C) Non-place-selective cells. (D) SIC vs RV. (E) Single cell examples.



Population activity is informative of goal identity in the cue phase. (A) Information gain with respect to goal across the cue phase for 32 cells, with values min-max scaled within each cell for better resolution. (B) Cross-temporal goal decoding accuracy of pseudopopulation responses for each trial phase (differences in decoding performance tested with ANOVA & Tukey's HSD, alpha 0.05). Dotted red line indicates chance level of 1/6. (C) Cross-temporal goal decoding confusion matrices of pseudopopulation responses for each trial phase. (D) Pseudopopulation response trajectories across the cue phase. Dots denote responses in the first time window, and crosses denote responses in the last time window. Fréchet distances between each pair of (start goal, end goal) tuple quantity the distances between their mean response trajectories (each data point is marked with the colours of the two groups being compared).