Intrinsic current generated, omnidirectional phase precession and grid field scaling in toroidal attractor model of medial entorhinal path integration

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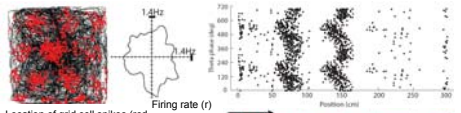
INTRODUCTION

Grid cells

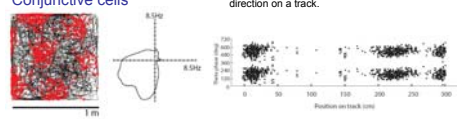


Location of grid cell spikes (red dots), as a rat runs through square environment.

Firing rate (r) versus heading direction (θ).

Theta phase of spikes as the rat runs in one direction on a track.

Conjunctive cells



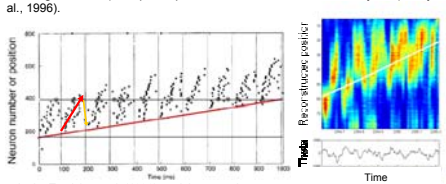
►Cells in the superficial layers of the medial entorhinal cortex (MEC) fire in specific locations in an environment, forming a rhomboidal grid (Hafting et al., 2005).

►"Grid cells" fire independently of which direction the rat is moving, while "conjunctive cells" include information about both heading direction and grid location (Sargolini et al., 2006).

►Grid cells fire at earlier and earlier phases of the theta rhythm as the rat passes through a grid field, while conjunctive cells consistently fire at the same phase (Hafting et al., 2008).

►Grid cells located in ventral regions of the MEC have larger grid fields than more dorsal cells, forming a gradient of grid field sizes.

►To model these characteristics of grid cells, we have combined and built on previous attractor models of spatial tuning by path integration (Samsonovich and McNaughton, 1997) and phase precession in relation to the theta rhythm (Tsodyks et al., 1996).



►In the Tsodyks et. al. (1996) model, precession was caused by "look-ahead" of the place cell network every theta cycle, driven by asymmetry in the connections among place cells. Network activity was "reset" to the actual position of the rat at the beginning of each theta cycle, by a spatially tuned input.

Such a look-ahead is observed in hippocampal place cells, when a population vector of place cell activity is used to reconstruct position of the rat on a short time scale (A.P. Maurer, unpublished data).

MODEL DESIGN

Network architecture

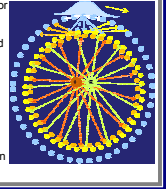
►We created a one dimensional version of the toroidal attractor model. The architecture resembles the Skaggs et al., 1996 model for head direction cells.

►"Grid cells" symbolically arranged on a circle were connected with weights decreasing as a Gaussian with distance.

►Inhibitory connections modulated the total activity of grid cells, allowing an activity bump to form.

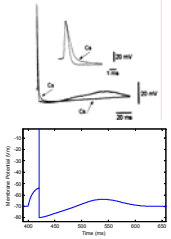
►A second layer of "conjunctive cells" connected to the grid cells with an offset allowed the bump to move, with a speed proportional to the firing rate of the conjunctive cells.

►"Head direction cells" (center of image) determine which group of conjunctive cells will be active, and are modulated in amplitude to simulate an increase in running velocity, so that an increased velocity increases the firing rate of the conjunctive cells.



After-depolarizing current

►Following an action potential, stellate cells in layer II of the MEC show an after-hyperpolarization (mAHP), followed by a depolarization (ADP). Both are blocked by the K^+ channel blocker Cs+ (Klink and Alonso, 1993).



►The ADP phenomenon has been found in hippocampal and cortical neurons (Andrade 1991; Caeser et al. 1993; Storm 1989; Libri et al. 1994) and has been modeled as a mechanism for short-term memory maintenance over the time period of one theta cycle (Lisman and Idiart, 1995).

►We hypothesized that this phenomenon could cause a "reset" or "jump-back" of the grid cell activity bump at the start of each theta cycle, because it would reactivate neurons active in the last theta cycle.

►We modeled the ADP and mAHP as conductance changes following each action potential with time constants which caused the peak of the after depolarization to occur at ~110 ms.

►The H-current has been modeled to be responsible for the intrinsic oscillation and the mAHP of stellate cells (Fransen et al., 2004) and may also contribute to the ADP. The time constant of the H current decreases with depolarization of the cell, and also in cells along the dorso-ventral axis of the MEC (Giocomo and Hasselmo, 2008).

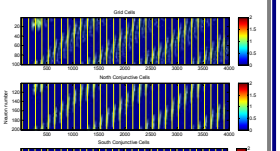
MODEL RESULTS

Network simulation

►When theta modulated "head-direction" input activated one set of conjunctive cells, this bump moved in one direction during the peak of theta. This caused the grid cell network to "look-ahead" to grid cells representing positions ahead of the 'actual' position for the remainder of the theta cycle.

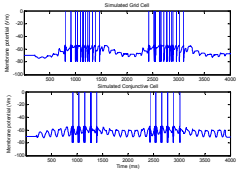
►At the trough of theta, a lack of inputs and inhibition caused the bump to collapse.

►The ADP current helped the bump to reform at the group of cells active ~110 ms ago.



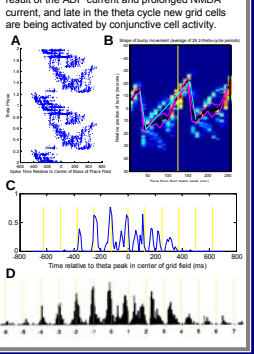
Theta phase precession

►Because of the look-ahead and jump-back of the bump of activity during one theta cycle, each grid cell fired at earlier and earlier phases of this cycle during progression trough the field.



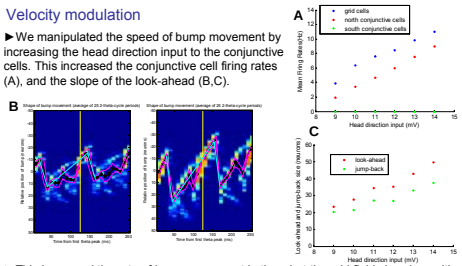
►The two causes of grid cell spiking are also seen in plots of place fields aligned to theta peaks (Skaggs et al., 1996; plot of CA1 place field, D, compare to spike timing of model grid cells, C). In the middle of the field, two peaks occur in one theta cycle, as the cell may be activated by both ADP currents and conjunctive cell activity. Peaks at the end of the field, due to activation by ADP currents, are broader than peaks at the beginning of the field. Because the activation of grid cells by conjunctive cells is more precisely timed than the reactivation of grid cells by ADP currents, the spike timing is more precise for early parts of the grid field.

►The shape of theta phase precession (A) depended on the shape of the look-ahead of the bump (B), in particular by the fact that early in the theta cycle, grid cells are reinitiating spiking as a result of the ADP current and prolonged NMDA current, and late in the theta cycle new grid cells are being activated by conjunctive cell activity.

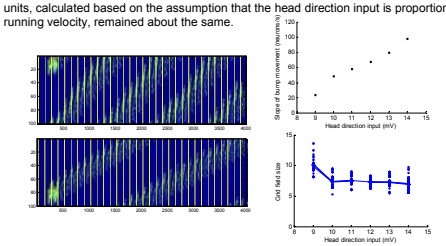


Velocity modulation

►We manipulated the speed of bump movement by increasing the head direction input to the conjunctive cells. This increased the conjunctive cell firing rates (A), and the slope of the look-ahead (B,C).



►This increased the rate of bump movement in time, but the grid field sizes in position units, calculated based on the assumption that the head direction input is proportional to running velocity, remained about the same.

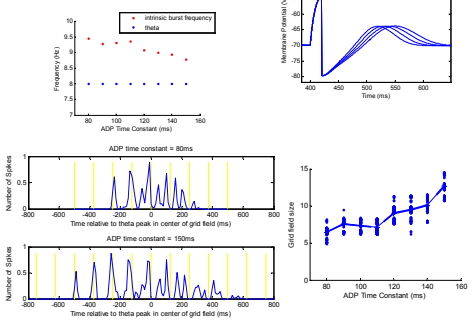


Time constant modulation

►The time constant of the H-current in stellate cells varies along the dorso-ventral axis of the MEC (Giocomo and Hasselmo, 2008) as does the scale of grid fields (right).

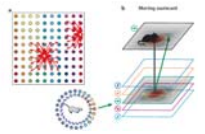
►Increasing the time constant of the ADP should increase the jump-back size, which would increase the grid field size.

►We modulated the ADP time constant (right) to control the burst frequency of the grid cells (below), and thus the size of grid fields (bottom).



DISCUSSION

►We show that an attractor network of grid cells and conjunctive cells connected as described previously (McNaughton et al., 2006) with an intrinsic current reset mechanism can account for the reoccurrence of grid fields, and for omni-directional grid cell phase precession.



►Varying the amplitude of the input from head direction cells linearly varies the speed of movement through network states, and thus perceived running velocity. Given the correct relationship between input amplitude (depolarization of cell) and time constants of intrinsic currents, this accounts for how grid field size stays constant at different running velocities.

►Varying the time constants of intrinsic currents changes the intrinsic burst frequency of simulated grid cells and the number of theta cycles they stay active for. This may account for the varying scale of grid fields along the dorso-ventral axis of the MEC.

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