

Understanding principles of encoding navigationally-relevant variables in entorhinal cortex

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To survive, animals must maintain an internal representation of position and movement at all times. Medial entorhinal cortex (MEC) likely supports this representation, as MEC neurons modulate their activity with the animal's position, head direction, and running speed. In particular, the superficial layers of MEC have attracted attention for containing strikingly regular cell types encoding a single spatial variable, namely position-encoding grid cells. Despite this attention, many (>50%) of cells in this region remain uncharacterized by conventional tuning curve-based methods, indicating that current heuristics for identifying cell types may only reveal the tip of the iceberg of MEC coding properties. Specifically, uncharacterized cells may irregularly encode single spatial variables, as well as encode conjunctions of multiple variables, contrasting with the classical view that superficial MEC neurons encode only single variables.

To investigate this possibility, we employ a statistical approach to identify single-cell encoding properties. We fit a nested series of generalized linear models (GLMs) containing various combinations of position, head direction, and speed information, and used principled hierarchical probabilistic model selection methods to detect which variables each cell encodes. We confirm that classical heuristics miss many important features of entorhinal coding. First, we detect more navigationally-relevant neurons: of 799 neurons recorded from mice during open field navigation, we find that 71% encode at least one variable, while classical metrics based on tuning curves detect only 45%. Second, we observe increased multiple-variable encoding: we find that 37% of cells encode multiple variables, while classical methods report 6%. Lastly, we find that the fraction of multiple-variable cells increases with running speed, consistent with previous information theoretic analyses suggesting that conjunctive cells are advantageous when sensory inputs vary rapidly (Finkelstein et al., 2015).

Overall, our principled methods successfully confront MEC heterogeneity and uncover remarkable, adaptive behavioral-state dependent changes in its spatial coding properties.