space and time in the brain – cogs260/cogs177 – Nitz – winter, 2013

week 4 – allocentric space, head-direction cells, border cells, grid cells, place cells, speed registration, context registration

“We're not lost…we're right here” – Arthur Schmidt (circa 1979)
place cells are neurons, found only in the hippocampus, whose action potential generation is restricted to the presence of the animal in a particular region of the environment.

frequently asked questions:

- does place-specific activity persist in the dark?
- what defines the space of an environment?
- is place field activity direction-dependent?
- how big are place fields?
- are place fields everywhere in an environment?
- are place cells (and/or their fields) topographically organized?

O'Keefe and Dostrovsky, Brain Research, 1971
Markus et al., Hippocampus, 1994
for the most part, place cell fields distribute evenly throughout an environment and reliably appear in the same places across different run sessions
neighboring place cells (recorded on the same wire) show no tendency to fire in similar places

Redish et al., J. Neuroscience, 2001
dorsal hippocampal neurons have rat-sized place fields (including the tail) while ventral hippocampus neurons may have 5 meter-long fields
multiple reference frames can co-exist in hippocampus...but only to a certain tolerance (Gothard et al., JNS, 1996)

above: an experiment wherein the start/end sites on one side of a track, itself open to the full recording room, is varied

some place fields (D) maintain their position relative to this varying start/end point despite its movement relative to the full room while others maintain fields in the room frame (E)

the variability in this property across the whole population depends on the degree of mismatch between the space of the room and the space relative to the moving start/end point
context in space matters greatly
(Battaglia et al., JNS, 2004; Leutgeb et al., Science, 2009)

direction of travel through a space often strongly modulates in-field firing rates, but only for track-running as opposed to free-foraging in a 2D environment

on a track with many tactile and odor cues, bi-directional fields are more common, but the fields for each direction are not completely overlapping such that space coding appears as 'approach to a position' as opposed to 'presence in a position'

for two very similar 2D box environments placed in the same spot of the larger room (visible from the box itself), one may observe place fields in analogous regions of the environment but with significantly different in-field firing rates (i.e., a secondary code analogous to parietal cortex 'gain fields')
the role of inhibitory interneurons in place field determination and adaptation to novelty
(Nitz and McNaughton, JNP, 2004; Wilent and Nitz, JNP, 2007)

despite having some activity in all areas of an environment, hippocampal interneurons do have place fields (in fact, both ON and OFF place fields) and these can be quantified using a variant of Shannon’s Information Theory.

adding on a novel space to well-known environment causes the hippocampal system, as evidenced by its place fields, to adapt such that map for the now-larger space is achieved.

this process involves a massive decrease inhibitory interneuron activity over the same time frame associated with stabilization of new firing patterns.
discovery #2 - head-direction cells – neurons whose firing is specific to particular head orientations of the animal (relative to the environment)

Taube et al., J. Neuroscience, 1990

head direction cells are found in many brain structures and seem to grow out of an integration of angular velocity which is registered in cells of the dorsal tegmental nucleus and lateral mammillary nucleus.
Figure 1. Representative HD cell and angular head velocity cell tuning curves. Data for these cells was recorded over 8 (HD cells) or 16 min (angular head velocity cells) sessions while the rat foraged for randomly placed food pellets about the floor of a cylindrical enclosure. (A–C) HD cell tuning curves for three different cells. Note that each cell has a different peak firing rate and preferred firing direction. The cell in C has a larger directional firing range compared to the other two cells. Cells were recorded in (A) postsubiculum, (B) anterior dorsal thalamus and (C) lateral mammillary nucleus. Ordinate for (A) and (C) are as noted in (A). (D–F) Different types of angular head velocity cells recorded in the dorsal tegmental nucleus. (D) Symmetric angular head velocity cell. Note that firing rate increases linearly as a function of angular speed for both clockwise (CW) and counter-clockwise (CCW) head turns. (F) Asymmetric angular head velocity cell. Note that except for very slow angular head velocities (<12°/s) firing rate is proportional to head turning speed for both CW and CCW directions, but that firing rate increases for faster head turns in only one direction (CCW) and decreases for faster head turns in the opposite direction (CW). Nonetheless, the gain in firing rate is similar for both turn directions. (F) Asymmetric angular head velocity cell. Note that the firing rate is proportional to head turning speed in only one direction (CW) and is not influenced by head turning speed in the opposite direction (CCW). This cell thus has unequal gains in firing rate. CW and CCW directions for (D) and (F) are as noted in (E).
a ‘dead-reckoning task wherein the rat forages in an arena in the dark and, upon finding a food pellet, makes a direct-line return to the journey’s starting point.

Examples of HD cells for which shifts in the preferred direction during the foraging phase of the task predict the ensuing directional error in the animal’s heading.
a potential network architecture supporting head-direction cell activity among a population of neurons: combining specific patterns of connection strengths with an angular motion signal (CW vs. CCW)

Figure 1 | One-dimensional attractor map model for head direction encoding based on neural integration of head angular velocity signals. a) Head direction cells are arranged symbolically in a circle in order of their relative head directional preferences. Each cell (coloured dots) connects with nearby cells with a synaptic strength (or connection probability) that declines as a function of distance (red and grey lines). The network is subject to global feedback inhibition (not illustrated) that limits the total neural activity. Activity in such a network has a most probable configuration in which the activity is focused at one point and declines with distance from that point (warm colours represent high activity, progressively cool colours represent progressively lower activity). Such a network would keep track of head direction if the hill or ‘bump’ of activity could be made to rotate around the ring in correspondence with changes in head direction. b) Rotation of the bump in the clockwise or anticlockwise directions can be achieved by an intermediate group of two types of conjunctive neuron that receive information about head angular velocity from the vestibular system (dashed arrows) and information about current head orientation from the cells immediately above them in the outer ring. The intermediate group of cells must be of two classes: cells receiving information about clockwise motion project to the right of the cells in the outer ring from which they receive input, whereas cells receiving anticlockwise vestibular signals project to the left. These hidden layer cells drive the activity bump in the corresponding direction around the ring. In the absence of motion, activation of all hidden layer cells is assumed to be below threshold. In this figure, only active connections are indicated, with the line thickness representing firing rate.
extending the idea – place cell activity in a network wherein connection strengths (in 2 dimensions) are combined with head-direction inputs

Figure 2 | Extension of the one-dimensional attractor map concept to two dimensions: a model for path integration. Neurons arranged in a plane (a) have interconnections that decline in strength (or probability) monotonically with distance (red arrows). Notice that a boundary problem exists for connections near the edge of the layer of neurons. A solution for this problem is illustrated in Fig. 3. Global feedback inhibition (not shown) keeps the net activity within a narrow range, leading to a focused spot or 'bump' of activity somewhere in the plane (b). The bump can be made to move in correspondence with a rat’s motion using an intermediate layer of cells that are conjunctive for position on the plane and head orientation, if the activity of these cells is positively modulated by running speed and the cells encoding a given head direction project asymmetrically to the corresponding side of the cells in the attractor layer from which they receive input. The thresholds are arranged so that these hidden layer cells are silent when there is no motion.

McNaughton et al., Nature Reviews Neuroscience, 2006

turns out that head-direction sensitive place cells do exist – in the parasubiculum

Cacucci et al., J. Neuroscience, 2004
dorsomedial entorhinal cortex neurons (making up a major input to the hippocampus) exhibit multiple firing fields in any given environment.

creation of a spatial autocorrelation from their firing ratemaps reveals the distinct geometric relationships between the positioning of the fields.

fields are arranged along the nodes of a group of tessellated triangles.
grids! – the nodes of grid cells recorded in dorsal regions of the dorsomedial entorhinal cortex are spaced more closely than those of grid cells recorded in ventral regions

the orientation of grids relative to the environment is shared by neighboring neurons
neighboring neurons have similar grid orientations (relative to the environment) and similar grid node spacings, but grid nodes are nevertheless offset (and in a random fashion) not shown is that offsets of grid node placements persist in different environments not shown is that increasing the size of an environment increases the number of nodes rather than increasing the size of the nodes (i.e., grid space is absolute) in this way, the grid cell network differs from the place cell network – grid nodes for different neurons always have the same spatial relationships (i.e., the map is generic to all environments or ‘universal’)

Figure 3 | Distributed spatial phase of co-localized grid cells. a, Grids of the three cells in Fig. 2d, each with a separate colour. Left, trajectory maps. Middle, peak locations. Right, peaks are offset to visualize similarity in spacing and orientation. b, Spatial cross-correlations for the same three cells. c, Distribution of phase differences between co-localized neuron pairs, expressed as distance from the origin to the nearest peak in their cross-correlogram. Each circle indicates one cell pair. Simultaneously recorded cell pairs are connected (only recordings with > 5 cell pairs). Blue, large cylinder, red, small square enclosure.

Hafting et al., Nature, 2005
grids! – dorsomedial entorhinal cortex also contains a population of ‘conjunctive’ cells whose grid-like activity is only observed for particular head-directions – notably, these cells are especially speed-sensitive

Sargolini et al., Science, 2006
border cells (discovery #4)

these neurons are also found in the dorsomedial entorhinal cortex – they maintain firing against borders (usually one) of an environment

expansion of the dimension of an environment corresponding to a border neuron expands its firing in that dimension – expansion in another dimension does not
a revised look at the origin of place-specific activity: place cells from grid cells

Figure 6: Combining multiple periodic grids at different spatial scales can result in non-periodic place fields. (a) The effects of slight variation in grid scale (5% in this case) on the periodicity of a mapping space defined by the superimposition of the output of two grid modules. In general, the summation of two periodic signals that differ in frequency gives rise to a signal with amplitude maxima that occur with a much lower frequency (the difference between the fundamental frequencies). (b) Multiple grid fields with different scales, as expressed by cells at different dorsoventral levels of the medial entorhinal cortex can be combined, for example, by linear summation, resulting in an activity field that has only one large maximum. The spatial frequency of the patterns increases systematically from left to right. A simple thresholding operation applied to the summed grid fields (here implemented by a sigmoidal function shown in red) yields a field that is restricted to a region of space. This is a potential mechanism for the generation of non-periodic place fields such as those observed in the hippocampus.

McNaughton et al., Nature Reviews Neuroscience, 2006
monkey grids can map the space of video screen!

dising that the universal map that is the grid cell network can conceivably map ANY allocentric spatial frame of reference

in this case, updating is according to eye movement direction and distance as opposed to vestibularly-signaled movement of the head