University of Tübingen

Master Thesis

Thesis Title

Author:
Shrisha Rao

Supervisor:
Dr. Anton Sirota

A thesis submitted in fulfilment of the requirements
for the degree of Master of

in the

Research Group Name
Centre For Integrative Neurosciecne

June 2013

Declaration of Authorship

I, Shrisha Rao, declare that this thesis titled, 'Thesis Title' and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed: _____

Date: _____

"Thanks to my solid academic training, today I can write hundreds of words on virtually any topic without possessing a shred of information, which is how I got a good job in journalism."

Dave Barry

UNIVERSITY OF TÜBINGEN

Abstract

Faculty Name
Centre For Integrative Neurosciecne

Master of

Thesis Title

by Shrisha Rao

The Thesis Abstract is written here (and usually kept to just this page). The page is kept centered vertically so can expand into the blank space above the title too...

Acknowledgements

The acknowledgements and the people to thank go here, don't forget to include your project advisor...

Contents

List of Figures

List of Tables

Abbreviations

LAH **L**ist **A**bbreviations **H**ere

Symbols

a	distance	m
P	power	W (Js^{-1})
ω	angular frequency	$rads^{-1}$

For/Dedicated to/To my...

Chapter 1

Internal representation of space

Spatial representation in animals is essential for their survival since they to search for food and mates, which demands considerable spatial processing to succeed. Representation of space requires that the geometric relationship between objects in the environment are encoded using a convenient metric. The relevant objects and landmarks in the environment can thus be organized in a spatial framework, although the structure of space is independent of the sensory input through which the former is extracted. Spatial information provides the context for adaptive behaviors. Storing spatial relationships over time could be a plausible framework for encoding episodic memory.
Egocentric or allocentric representations can be used to encode and store spatial information. Egocentric space corresponds to the representation relative to the viewer's current location. If the viewer moves, the egocentric representation also changes correspondingly. In allocentric representation, the spatial relationships of landmarks and objects in the environment are encoded relative to each other, independent of the viewer. Unless the objects move, the allocentric representation is stable even when the viewer moves.

1.1 Spatial navigation in the the rat

1.1.1 Place cells

Place cells were first discovered by O'Keefe and Dostrovsky [1]. Following this discovery, O'Keefe and Nadel [2] conceived of a functional role of hippocampus, they proposed that the hippocampus is the substrate for a cognitive map which is formed while the rat explores its environment. This is known as the *cognitive map theory*. They suggested that the primary function of the hippocampus was to encompass mechanisms

that would allow for the existence of the map in the hippcampal network. The cognitive map represents spatial information in allocentric space. So the relative spatial metrics of the landmarks in the incoming stimuli have to be computed. This map can then be utilized for for solving navigational tasks while the various structures of the hippocampus provide the spatial information related to place, head direction, and current view. They also suggested that the map is stored in the hippocampus and it is used in conjunction with information stored in other areas. By extending their theory to humans they postulated that episodic memory derives its basis from similar mechanisms that enable spatial processing in animals. Leison studies corroborate their claims. The fornix fibres are one of the predominant fibre tracts into the hippocampus . Lesions in the track lead to partial deficit in spatial learning in rats, but cue learning is preserved.

Place cells are the pyramidal cells in the rat and mice hippocampus. Place cells derive their name form the fact that their discharge is strongly correlated with the position of the animal in the environment. In a given unchanging environment, each cell has a preferred location called the place field where the cell fires maximally. The cells that are active in one environment may not participate in another. The total number of cells active in a given environment is proposed to be 25-30 % providing a sparse representation which increases storage capacity and reduces interference between representations[3**?**]. Recent Ca^{2+} imaging of CA1 pyramidal cells are consistent with this account [4]. Place cells are found in the CA1 and CA3 regions of the dorsal hippocampus. They have also been found in the ventral hippocampus. Place cell activity in response to environmental manipulations have been intensively studied. The trajectories traversed by the rat determine the directionality of the place cell [5]. If the place cell is indeed coding for a specific location, then its firing must be independent of head direction. The angular firing distribution is found to pass this test in the open field and the modulation of firing by head direction in a maze can be explained as a result of non-uniform sampling of head directions at every location [6]. It is possible that in the open field the place cells achieve omni-directionality by associative binding of local views [7]. Hence, omnidirectional might develop through andom exploration rather than directed exploration in a maze.

- place fields can be also associated with non-visual cues Muller-Kubie 1987 and O'Keefe, Speakman 1987 -
- Place fields continued to persist after the visual land marks were removed [8]
- removing some cues did not disrupt the place fields but removing all cues did Pivo 1985 - Quirk, Muller and Kubie 1990 - place fields persisted in the dark when the

animals are placed with light and the light turned off.
O'keefe, Recce 1993 and Skaags 1996 - spike fired precesses with theta phase as the animal traverses the place field, also occurs in 2D
Mehta, Barenes and Mc Naughton1997 - pfs shift backwards after repeated traversals along the same trajectory Place cell firing is also correlated with speed, direction, and turning angle and stage of the task
Markus 1995 - pfs are task sensitive, pfs rapidly changed when the task changed to random foraging and search for food at the corners of a diamond
Skaags McNaughton 1996 - found significant correlated temporal bias during SWRs in the SWS after exploration on a linear track.
extra hippocampal cells have also been reported, but show different characteristics the hippocampal place cells
Wilson MccNaughton 1993 - place cells recorded with tetrode shower fewer subfields

- Huxter, Csicsvari 2008, Nat.Neur; Theta phase-specific codes for two-dimensional position, trajectory and head- ing in the hippocampus.

phase precession

1.2 Head Direction cells

Often when someone is given a map and asked to find his way to a certain goal location, one starts by orienting oneself with the help of a compass or cues such as the sun or the starts. Thus for successful spatial navigation and route planning with the cognitive map, there must be a neural system which provides a stable reference direction in an environment. A subset of cells in the postsubiculum are found to be sensitive to head direction [9]. [head direction tracking achieved through angular integration]...The head direction system is perhaps wired to implement a continuous ring attractor which receives vestibular and visual inputs. These inputs are integrated to generate a stable activity distribution along the perceived head direction. If there is considerable mismatch between the inputs will result in the reference direction being reset along the orientation implied by the stronger input. [lab meeting paper][10]

1.3 Grid Cells

[11]

1.4 Path integration

Path integration, also referred to as dead reckoning is one of the strategies that can be used for spatial navigation. It keeps track of the the current location with respect to a reference point in the current reference frame. The ability to path integrate is vital for the survival of animals, it provides a means of computing the home location after the animal has traveled away from home location in search of food. Self motion information (speed and acceleration) and heading direction are essential information that need to be available for path integration. If the speed and heading direction is known at an arbitrary location, then the future location can be readily computed. Unless the ideothetic information is noisy, a perfect path integration system is capable of maintaining location information with respect to a reference point. Any noise that enters the measurements of speed and direction will lead to accumulative error in the predicted location. This increasing error can be corrected if the system has access to location information with respect to external landmarks. In animals this is the sensory input that is constantly available. Both self motion cues and sensory information when used together provide a better estimation of the current location. Interesting experiments can be designed in virtual reality by introducing appreciable conflict between sensory input and ideothetic information.

1.4.1 Multichart architechture

One of theories proposes that the synaptic connections of the CA3 pyramidal cells are pre-configured to represent a large number of two-dimensional surfaces [12]. These two dimensional surfaces are continuous attractors with localized activity patterns as their stable states. A simple way to understand how the weights are assigned is to imagine a plane, then placing a randomly chosen subset of cells on this plane. Then the synaptic strength between any proximally located pair of cells is given by a two dimensional gaussian function of the distance between them. The cells further away receive inhibitory connections. This synaptic connectivity scheme produces 2 dimensional quasi-continuous attractors. The imaginary arrangement of a population of place cells on an abstract plane such that each cell is fixed at a location where it shows maximum firing activity is termed to as a chart. When this chart is bound to an environment, then each cell shows peak firing at the appropriate location in the physical location to which it has been mapped. Their model proposes that multiple charts are available which could be potentially used to represent several environments or the same environment in differing contexts. These charts exhibit no significant correlations. A chart is referred to as the active chart if the activity of cells in that chart appears to be localized at a specific location thus forming

a place field. The distribution of activity can remain localized even in the absence if external stimuli since it is a stable state of the network. The active chart would then be the current reference frame used for spatial processing. Other charts would would display rand activity as dictated by the synaptic connections.
In their model place cells connect to a PI(path integration system) which sends back asymmetric projections to cells along the direction of motion of the animal. Thus the localized activity pattern in the active chart follows the actual movement of the animal.

1.5 remapping

When certain features of the environment are varied by small amounts the place cell firing characteristics are altered [8]. The firing rates are observed to show drastic changes. Some place cells change their place fields to new locations while others completely vanish and new fields emerge. This is often referred to as *remapping*, resulting from the changes in the spatial information of the environment. Thus distinct representations are formed for differing environments and even similar environment with apparently minor modifications.
Storage of memory requires that the each unique memory engram produces decorrelated patterns of activity. If the memories share some common features, it will lead activation of very similar activity patterns and the distinction might be lost. This is often referred to as interference and is a possible mechanism of forgetting. To keep memories distinct a decorrelation operation of the overlapping memories must be performed to so as to produce orthogonal representations before storage. Remapping might belie the underlying decorrelation of overlapping inputs that occurs when memories are encoded.
Two types of remapping can be identified. Rate remapping occurs when the location of the place fields remain essential the same while the firing rate changes. Global remapping occurs when the cells arbitrarily change their firing rates and develop new place fields. These categories of remapping signal different kinds of environmental manipulations. Rate remapping was observed when the location was unchanging while the color and shape of enclosures were changed. Global remapping was induced in identical enclosures at different location [13]. Changing cue configurations also produce global remapping [13]. Rate remapping probably occurs when only the relevant non-spatial features change while the spatial structure is preserved. Thus the spatial information content in the population is identical for rate remapped representations since it is only the non-spatial component of the stimuli is varying. In the Ca^{2+} imaging study [4], $15-25\%$ of CA1 cells were found to consistently encoding for space over weeks. Rate remapping could then also be the short time scale characteristic of the ensemble encoding scheme. This would enable the encoding of other non-spatial information as episodes in

an unchanging spatial setting. The only overlapping patterns the ensemble code would be coding for the same environments.

Global remapping is almost always induced when the location is changed. The magnitude of dissimilarity between the relevant environmental features dictates the likelihood of global and rate remapping.

The earlier experiments made discrete changes in the environment. The naturally occurring stimuli are usually continuous. The hippocampal network then has to generate dynamically varying patterns to encode the continuously changing stimuli. In a study by Leutgeb [14],the flexible enclosures were slowly morphed from square to circle with several intermediate stages. The animals were initially familiarized with both square and circular enclosures so as to allow for stable representations of each to be learnt. Rate remapping was observed for the gradual changes from square to circle. [transitions in the representation]

In another study [15], the square and circular enclosures were designed to induce global remapping. There was abrupt transition to a learnt representations based on the similarity of the current environment to the previously acquired one.

The CA3 pyramidal cells are observed to produce significantly distinct patterns in response to apparently minor changes in the environment. Since the CA3 network is also thought to function as an auto-associative memory, this would be an advantageous feature increasing the network capacity. The encoding scheme has to produce non-redundant codes for effective performance of the auto-associative network. The Dentage Gyrus input seems to be critical for pattern separation in the CA3. The Dentate Gyrus granulae cells are hypothesized to perform the computational operation of orthogonalization of the input patterns before feeding them to the CA3 network. The sparse yet effective connectivity between the granulae cells and the CA3 pyramidal cells could provide the critical architecture.

The grid cells in the Medial entorhinal cortex(MEC) show little change in the grid parameters whenever the environmental change produces rate remapping in CA3. But when global remapping occurs in CA3, the grid cells show coherent shift and rotation of their fields. The time course of grid realignment and remapping seem to be closely follow each other [16]. Perhaps the grid realignment in the MEC contributes to global remapping in the CA3. Since the CA3 also back projects to the MEC, it is also not known whether the realignment of the grids occurs first in the MEC and then leads to CA3 remapping or vice versa.

Remapping the is less pronounced in CA1 in comparison to CA3 [13, 17]. It also possible that the CA1 representation changes over a longer time scale. The interneuron network assists the formation of new cell assemblies and supression of old ones [18]

1.6 Replay

... Marr [3] proposed that long term storage and classification of information as the functional role of neocortex. He also proposed that the neocortex would be required to be trained during sleep to classify overlapping pieces of information. The hippocampus is thought to be a temporary storage for memory [19, 20]. Then the hippocampus has to meet the computational demands of rapid encoding and later recapitulation of salient memory traces for transfer to long term storage. Marr also suggested that the anatomically the short term storage structure must have the means to communicate with every other part of the brain. The Ento-rhinal cortex has reciprocal connections to [.....]

Chapter 2

Dynamical systems framework

This chapter will review some concepts from dynamical systems and how these are being used to understand hippocampal population activity. Dynamical systems theory deals with time varying systems. It dwells on questions of how the behavior of systems evolve over time. Non-linear dynamics is a powerful analytic tool for studying complex systems. A network of neurons can be formalized as a system of differential equations, lending them to be studied in the same framework. There is the long standing idea that interesting abstract properties emerge in a population of interacting objects obeying certain local rules. This framework might prove to be useful in developing further insights into the mechanisms that give rise to emergent cognitive faculties.
The electrophysiology of the hippocampus has revealed several internally self generated patterns. Some of which are thought to be essential for memory consolidation. Although this is not restricted only to the hippocampus. The brain in general exhibits internally self generated activity even in the absence of external stimulus. The usual examples include the recordings form humans and animals during sleep. Although during sleep the sensory input is at a minimum, these recordings show a lot of interesting phenomena.

2.1 Basic ideas

2.1.1 Differential equations

Differential equations provide a convenient and straight forward technique to formalize and study dynamical systems. The variables in these are called state variables. Solving these equations given initial conditions we can predict the future states of the system. [.....] Higher order differential equations can be converted to a system if first order differential equations. The system of differential quations can be imagined as a

vector field in the state space where a vector is assigned to every point in the state space. The vector points in the direction of change of the state variables.

2.1.2 Fixed points

Fixed points are the states where there is no change or where the flow is zero ~~this figure shows a one dimensional system whose vector field is defined by some arbitrary function $f(x)$~~ When $f(x)$ is possitive the system moves towards $+\inf$ when $f(x) = 0$, there is no change. These states are called the fixed points of the system. ~~A fixed point is stable if a small perturbation causes the system to be pulled back to the fixed point..... An unstable fixed point A mechanical equvivalent is atn inverted pendulum~~

fig- show a two dimensional system where different types of fixed points result when the parameter a is varied. These are the stable nodes star node , line of fixed points , saddle node.

A usual procedure used to analyze and visualize dynamical process is to compute the energy function for the system, if it exists. The standard picture is to imagine a ball rolling down the hill towards the valley. The energy landscapes can be complex in biological systems. Some systems are highly sensitive to initial conditions. fig - the ball can go either way depending on where it starts.
The stable fixed points of the systems are interesting since it they exist, The transients die out and the system will eventually settle to one of the stable states. These sable states are called attractors of the system. The topology of the attracctors can be very interesting and helpful in predicting the behaiour of the system in different states.
point. line attractor If end points of the line attractor are joined, a ring attractor is obtained which is proposed a model of the head direction system.
limit cycle attractor gives rise to periodic behaviour of the system, Limit cycles cannot occur in linear systems. Biological pattern generators can be understood in terms of limit cycles. Here is an exaple of modified HH model... x axis is tteh membrane voltage , y is teh potassium activation variable, Initially th model neuron is at rest correspondingf to a stable point. If a stronf pulse of current is injected in the membrane , it will take the neuron to the basin of attraction of the limit cycle and the neuron will produce rhythmic spikes.

2.1.3 Stability analysis

The stability of fixed points can be analyzed by linearizing the system at the fixed point and tehen applying linear stability analysis techniques. This gives correct predictions of stability ..... It can be shown that the ....hyperbolic fixed point....the stability is is correctely predicted by linearization.....
when linear fails Layapnov stability analysis approach is usually adopted. Lyapnov funcion provides a generalized energy landscape and conservative estimate of domains of attraction . Here is an example of bistable system which has been used for modelling working memory. one of the states is the resting state, other is with persistant activity which could function as working memory.

2.1.4 Bifurcations

Bifurcations occur when the system changes its qualitative behavior . Like when a solid changes to liquid state. Bifurcations reflect the dependence on parameteres. When a parameter is varied at a critical value the dynamics of the system might drasticlly change. In neural networks, the same network could beswitched betweendifferent regimes to implement different computations. Bifurcations are classified as local and global. Global if the bifurcation effects a large portion of the state space.

Saddle node bifurcation occurs when a stable and an unstaable node collide and disappear. ...fig as the parameters r is varied the fixed points get closer and closer, then collide and the fixed points vanish. This can be dipicted as a bifurcation diagram. The parameter is teh independent variable and the fixed points are plotted as the dependent variable. The dotted lines indicate the unstable nodes and the stable mode.

pitchfork bifurcation occurs in symmetric systems as the parameter r is varied it loses stability and two new fixed points are created, The bifurcation diagrams are show fig....
eg - a beam with load

Hopf bifurcation occurs when a stable spiral loses its stability and a limit cycle is created. .fig— model neuron the injected current as the aprameter , when ramu current is applied at a critical value the spiking.....

2.2 Attractor networks

attractor networks have stable patterns as their attractors and depending on the initial conditions the network will settle down to one of the stable patterns. Depending on the type if attractor different kinds patterns can be achieved. It has been proposed the recurrent network in the CA3 might function as an auto-associative network..... The characteristics of the attractor determines which patterns are stable. This type of continuous attractor dynamics has been proposed as a mechanism for path integration (sec. 1.4, p. 4). Localized activity patterns are achieved by local excitation and long range inhibition. In networks with shift invariant structures it is possible to stabilize activity pattern on each node. Thus if we have a line of attractors in the limit of infinite nodes a continuous manifold of point attractors can be generated.

2.2.1 Auto-associative network

fig - auto associative network which has learnt a few patterns and when presented woth noisy patterns... Each pattern can be thought of as a minima in the energy landscape. Pattern completion occurs because of the recurrent synaptic architecture. When a few neurons of a certain pattern are active, then they activate others because of strong synaptic connectivity strength. The

2.2.2 Models of place selectivity

The basic requirement to get place cell is localized firing patterns, so that the this pattern might then be utilized to encode distinct locations in the physical space. Second requirement is to have a mechanism by which this localized activity can be conveniently updated as the animal traverses in the environment.
The firing of the place cells show theta phase precession in one dimensional tracks [21] as well as in unconstrained open field [22] [one more ref]. When the rate enters its the place field of a cell, the cell fires at late phase of theta and as the rate traverses through the place field it fires at earlier phases of successive theta cycles. The cell fires maximally at the trough of theta when the rat is at location corresponding to the peak of the place field tuning curve. Thus the theta phase of the spike times is correlated with the distance the animal has traveled inside the place field. This is often referred to as temporal coding [23]. When several cells are recorded, the cells with overlapping place fields fire at different phases of theta, which is suggested as an encoding strategy for compressing sequences in time. This has the advantage that these sequences are arranged in the time scale of LTP to influence the synaptic connectivity between the

cells participating in the sequence.
Contrary to the view that there is an explicit temporal code, it has been suggested that the correlation between position and phase of theta could be explained as a consequence of sequential computation occurring within a theta cycle. Across the population of place cells, different phases the theta cycle encode positions offset into either future or past along the rat's trajectory . The past and future locations robustly predict the CA1 place cell activity at different phases. This indicates that the information content in the cell activity at different phases of theta is actually correlated with the past and future locations of the animal. It was also show that this phenomena is not a direct consequence of phase precession, rather might actually be a causing the observed phase precession [24].

2.2.3 Itskov 2008, theta-mediated dynamics of spatial information in hippocampus

- the correlation between position and phase of theta could be a byproduct of theta-dependent dynamics of spatial information flow (??); .
- the alternative view postulates that the organization of spike times is a signature of ongoing computation happening through the sequential activity of hippocampus cell assemblies within a theta cycle
- this view is supported by the fact that the spike times show greater coordination than expected from independent temporal coding of location
- in this study the authors tested the hypothesis that across the population of place cells, different phases within the theta cycle encode positions offset into either future or past along the rat's trajectory in a 2-D environ.
- models predicting the activity of the place cells were fit to the CA1 place cell data.
- it was found that spikes on different phases of theta were best predicted by the rat's immediate future or past locations
- theta phases corresponding to 'future' and 'past' locations are consistent across the CA1 population
- this phenomenon might contributing to phase precession , but it can be shown that it is not a consequence of phase precession; because randomized data where phase precession of individual cells were preserved did not show this behavior

~~Ifig – model~~ This is the rate model where this is the excitatory input and the firing rate is a sigmoidal function of voltage. The simulation of the model produces stable

activity around the peak of the external input even though the input is noisy [basin of attraction]... The activity tracks the input peak location as it moves. ... when extended to spiking neural network .... The connection is in the same with one addition that is is asymmetric in the direction of motion. The pyramidal cells receive information about the location of the rat simulating the entorihnal input..... The inhibitory interneurons receive theta input which is the simulated input from medial septum to the GABAergic interneurons . The simulation of the network shows thea t as teh rat moves along the track the external excitation drifts through a group of neurons. The network tends to build a peak of activity at the location of peak of the input. Due to the asymmetry in the synaptic connections the activity spontaneously propagates forward in every theta cycle. The phase precession of the cell marked by a circle. fig

2.2.4 Internal sequences in the rat hippocampus

In the study by Pastalkova [25], multi-unit recordings were obtained form the rat hippocampus in non-sleep state. They report observation of internally self sustained cell assembly sequences. The animals were trained to run in a wheel during the delay period in an alternation task. The CA1 pyramidal neurons were recorded during the delay period. Some of these neuron assemblies were sequentially activated. These sequences were predictive of the time the rat spent in the wheel upto 20 seconds [26]. The sequences were unique for different behavioral choices including the ones which were incorrect choices. Since the location of the rat was stationary, one would expect to see only place cells for that location to be active.
time/distance cells

It has been proposed that this could be a means by which the networks keeps track of time elapsed. A model was proposed suggesting a possible mechanism for the generation of cell sequences in a network with no strong inputs. The two critical ingredients of the model are adaptive thresholds and Mexican hat synaptic connectivity. In the model, every spike fired by the neuron will result in the increase of its spiking threshold. This threshold then exponentially decays to it default value with a time constant in the order of seconds. Thus a neuron gets increasingly discouraged to fire as its firing rate increases, which will eventually silence the neuron.The Mexican hat type connectivity ensures that the activity remains localize to a small number of neighboring neurons. The symmetry in the connectivity is broken by introducing uncorrelated noise in the connectivity matrix. In fact, to ensure that the dynamics displayed by the model is not just a result of the perfect synaptic tuning; the strength of the correlated Mexican hat connectivity was chosen to be weaker as compared to that of the heterogeneous component. This model generates a continuum of bump attractors, for the network, this

implies that if the bump were to be moved laterally by some means, it would stabilize in the new position. The introduction of threshold adaptation will result in the increase of the thresholds of neurons participating in the localized activity. Gradually, on the time scale of seconds (i.e. the time scale of threshold relaxation), this bump will lose its stability as the neurons become quite due high values of threshold. Assuming the input noise levels are low, the heterogeneity in the network connectivity will dictate the next position of the stable bump, which will remain so until it is destabilized again by the same mechanism. The bump in essence is moving away from the neurons with recently updated thresholds. In this setting, activity bump shifts its peak constantly without ever stabilizing at a particular location. Thus the model exhibits self generated sequential activation of cells, captured by the bump constantly moving along continuous trajectories in the state space. The model produces reliable trajectories even with weakly noisy input, provided that it starts with the same initial conditions. Hence, the similar heterogeneity and threshold levels across trials provide identical contexts which results in reproducible behavior. It was also shown that these sequences can be inherited by succeeding layer of neurons without recurrent connections receiving sparse feed-forward input from the layer with recurrent connectivity.Since the CA1 region does not have recurrent connectivity and the sequences were observed in CA1, it is possible that they are inherited form sequences are generated elsewhere.

Further as The idea of continuous attractors are used to model these cell sequences. ....

2.2.5 Itskov 2008, theta-mediated dynamics of spatial information in hippocampus

- the correlation between position and phase of theta could be a byproduct of theta-dependent dynamics of spatial information flow (??); contrary to the view that there is an explicit temporal code.
- the alternative view postulates that the organization of spike times is a signature of ongoing computation happening through the sequential activity of hippocampus cell assemblies within a theta cycle
- this view is supported by the fact that the spike times show greater coordination than expected from independent temporal coding of location
- in this study the authors tested the hypothesis that across the population of place cells, different phases within the theta cycle encode positions offset into either future or past along the rat's trajectory in a 2-D environ.
- models predicting the activity of the place cells were fit to the CA1 place cell data.

- it was found that spikes on different phases of theta were best predicted by the rat's immediate future or past locations
- theta phases corresponding to 'future' and 'past' locations are consistent across the CA1 population
- this phenomenon might contributing to phase precession , but it can be shown that it is not a consequence of phase precession; because randomized data where phase precession of individual cells were preserved did not show this behavior

Appendix A

Appendix Title Here

Write your Appendix content here.

Bibliography

[1] J. O'Keefe and J. Dostrovsky. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, 34(1):171–175, November 1971. ISSN 00068993. doi: 10.1016/0006-8993(71)90358-1. URL http://dx.doi.org/10.1016/0006-8993(71)90358-1.

[2] L. Nadel J. O'Keefe. *The Hippocampus as a cognitive map*. 1971. ISBN 0198572069.

[3] D Marr, Philosophical Transactions, Royal Society, Biological Sciences, and No Jul. Simple Memory : A Theory for Archicortex. 262(841):23–81, 1971.

[4] Yaniv Ziv, Laurie D Burns, Eric D Cocker, Elizabeth O Hamel, Kunal K Ghosh, Lacey J Kitch, Abbas El Gamal, and Mark J Schnitzer. Long-term dynamics of CA1 hippocampal place codes. *Nature neuroscience*, 16(3):264–6, March 2013. ISSN 1546-1726. doi: 10.1038/nn.3329. URL http://www.ncbi.nlm.nih.gov/pubmed/23396101.

[5] E Save, a Cressant, C Thinus-Blanc, and B Poucet. Spatial firing of hippocampal place cells in blind rats. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 18(5):1818–26, March 1998. ISSN 0270-6474. URL http://www.ncbi.nlm.nih.gov/pubmed/9465006.

[6] U Muller, S Taube, and Cell Biology. On the Directional of Hippocampal. 14 (December), 1994.

[7] Patricia E. Sharp. Computer simulation of hippocampal place cells. *Psychobiology*, June 1991. ISSN 0889-6313 (Print). URL http://psycnet.apa.org/index.cfm?fa=search.displayrecord&uid=1991-32443-001.

[8] John L Kubie. The Effects of Changes in the Environment Hippocampal Cells on the Spatial Firing of. 7(July), 1987.

[9] J S Taube, R U Muller, and J B Ranck. Head-direction cells recorded from the postsubiculum in freely moving rats. I. Description and quantitative analysis. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 10(2):

420–35, February 1990. ISSN 0270-6474. URL http://www.ncbi.nlm.nih.gov/pubmed/2303851.

[10] Stephane Valerio and Jeffrey S Taube. Path integration: how the head direction signal maintains and corrects spatial orientation. *Nature neuroscience*, 15(10):1445–53, October 2012. ISSN 1546-1726. doi: 10.1038/nn.3215. URL http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3458173&tool=pmcentrez&rendertype=abstract.

[11] Torkel Hafting, Marianne Fyhn, Sturla Molden, May-Britt Moser, and Edvard I Moser. Microstructure of a spatial map in the entorhinal cortex. *Nature*, 436 (7052):801–6, August 2005. ISSN 1476-4687. doi: 10.1038/nature03721. URL http://dx.doi.org/10.1038/nature03721.

[12] A Samsonovich and B L McNaughton. Path integration and cognitive mapping in a continuous attractor neural network model. *J Neurosci*, 17(15):5900–5920, August 1997.

[13] Stefan Leutgeb, Jill K Leutgeb, Carol a Barnes, Edvard I Moser, Bruce L McNaughton, and May-Britt Moser. Independent codes for spatial and episodic memory in hippocampal neuronal ensembles. *Science (New York, N.Y.)*, 309 (5734):619–23, July 2005. ISSN 1095-9203. doi: 10.1126/science.1114037. URL http://www.ncbi.nlm.nih.gov/pubmed/16040709.

[14] Jill K Leutgeb, Stefan Leutgeb, Alessandro Treves, Retsina Meyer, Carol a Barnes, Bruce L McNaughton, May-Britt Moser, and Edvard I Moser. Progressive transformation of hippocampal neuronal representations in "morphed" environments. *Neuron*, 48(2):345–58, October 2005. ISSN 0896-6273. doi: 10.1016/j.neuron.2005.09.007. URL http://www.ncbi.nlm.nih.gov/pubmed/16242413.

[15] Tom J Wills, Colin Lever, Francesca Cacucci, Neil Burgess, and John O'Keefe. Attractor dynamics in the hippocampal representation of the local environment. *Science*, 308(5723):873–876, May 2005. ISSN 1095-9203. doi: 10.1126/science.1108905. URL http://dx.doi.org/10.1126/science.1108905http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2680068&tool=pmcentrez&rendertype=abstract.

[16] Marianne Fyhn, Torkel Hafting, Alessandro Treves, May-Britt Moser, and Edvard I Moser. Hippocampal remapping and grid realignment in entorhinal cortex. *Nature*, 446(7132):190–4, March 2007. ISSN 1476-4687. doi: 10.1038/nature05601. URL http://www.ncbi.nlm.nih.gov/pubmed/17322902.

[17] Stefan Leutgeb, Jill K Leutgeb, Alessandro Treves, May-Britt Moser, and Edvard I Moser. Distinct ensemble codes in hippocampal areas CA3 and CA1. *Science (New York, N.Y.)*, 305(5688):1295–8, August 2004. ISSN 1095-9203. doi: 10.1126/science.1100265. URL http://www.ncbi.nlm.nih.gov/pubmed/15272123.

[18] David Dupret, Joseph ONeill, and Jozsef Csicsvari. Dynamic Reconfiguration of Hippocampal Interneuron Circuits during Spatial Learning. *Neuron*, 78(1):166–180, March 2013. ISSN 08966273. doi: 10.1016/j.neuron.2013.01.033. URL http://www.cell.com/neuron/fulltext/S0896-6273(13)00099-8.

[19] G. Buzsáki, Great Britain, and Pergamon Press. Two-stage model of memory trace formation: A role for noisy brain states. *Neuroscience*, 31(3):551–570, January 1989. ISSN 03064522. doi: 10.1016/0306-4522(89)90423-5. URL http://dx.doi.org/10.1016/0306-4522(89)90423-5.

[20] Francesco P Battaglia, Karim Benchenane, Anton Sirota, Cyriel M A Pennartz, and Sidney I Wiener. The hippocampus: hub of brain network communication for memory. *Trends Cogn Sci*, 15(7):310–318, July 2011. doi: 10.1016/j.tics.2011.05.008. URL http://dx.doi.org/10.1016/j.tics.2011.05.008.

[21] J O'Keefe and M L Recce. Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus*, 3(3):317–30, July 1993. ISSN 1050-9631. doi: 10.1002/hipo.450030307. URL http://www.ncbi.nlm.nih.gov/pubmed/8353611.

[22] W E Skaggs, B L McNaughton, M A Wilson, and C A Barnes. Theta phase precession in hippocampal neuronal populations and the compression of temporal sequences. *Hippocampus*, 6(2):149–72, January 1996. ISSN 1050-9631. doi: 10.1002/(SICI)1098-1063(1996)6:2\<149::AID-HIPO6\>3.0.CO;2-K. URL http://europepmc.org/abstract/MED/8797016/reload=0.

[23] John Huxter, Neil Burgess, and John O'Keefe. Independent rate and temporal coding in hippocampal pyramidal cells. *Nature*, 425(6960):828–32, October 2003. ISSN 1476-4687. doi: 10.1038/nature02058. URL http://dx.doi.org/10.1038/nature02058.

[24] Vladimir Itskov, Eva Pastalkova, Kenji Mizuseki, Gyorgy Buzsaki, and Kenneth D Harris. Theta-mediated dynamics of spatial information in hippocampus. *J Neurosci*, 28(23):5959–5964, June 2008. doi: 10.1523/JNEUROSCI.5262-07.2008. URL http://dx.doi.org/10.1523/JNEUROSCI.5262-07.2008.

[25] Eva Pastalkova, Vladimir Itskov, Asohan Amarasingham, and György Buzsáki. Internally generated cell assembly sequences in the rat hippocampus. *Science (New York, N.Y.)*, 321(5894):1322–7, September 2008. ISSN 1095-9203. doi: 10.1126/science.1159775. URL http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2570043&tool=pmcentrez&rendertype=abstracthttp://dx.doi.org/10.1126/science.1159775.

[26] Vladimir Itskov, Carina Curto, Eva Pastalkova, and György Buzsáki. Cell assembly sequences arising from spike threshold adaptation keep track of time in the hippocampus. *J Neurosci*, 31(8):2828–2834, February 2011. doi: 10.1523/JNEUROSCI.3773-10.2011. URL http://dx.doi.org/10.1523/JNEUROSCI.3773-10.2011.