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Behavioral Correlates of theta and delta oscillations in the hippocampal formation

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Certificate

This is to certify that this thesis entitled Behavioral Correlates of Theta and Delta Oscillations in the hippocampal formation submitted towards the partial fulfillment of the BS-MS dual degree program at the Indian Institute of Science Education and Research Pune represents original research carried out by "Vishnu K N at IISER Pune, under the supervision of Dr. Collins Assisi during the academic year 2015-2016.

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Declaration

I hereby declare that the matter embodied in the report entitled Behavioral Correlates of Theta and Delta Oscillations in the hippocampal formation" are the results of the investigations carried out by me at the Division of Biology, IISER Pune, under the supervision of Dr. Collins Assisi and the same has not been submitted elsewhere for any other degree.

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Abstract

The goal of this project is to characterize the relationships between the behavioral state of the animal and the frequency phase and the amplitude of theta and delta oscillations observed in the hippocampal formation. The behavioral state of the animal is characterized by its position in space, the velocity, direction and statistical properties of its movement over time. Theta amplitude, frequency and phase reflects movement properties and may act as carriers of information that bridges the gap between environmental and proprioceptive streams of information in the brain. Our analysis revealed that theta and delta oscillations are indeed important players in the dynamics of hippocampal network and are closely related to the locomotion of the animal. The causal role of movement in theta generation was evident as a general positive modulation of the oscillatory variables as a function of movement properties. It was also found that spatial cues have modulator power on theta even though we couldn't pin down the accurate nature of the relationship. Delta power was found to be modulated by the running direction with a six fold symmetry, which could possibly give rise to the symmetry of the network. The study found that these oscillatory bands and associated modulations are important in the dynamics of the network and is intricately associated with the behavioral properties of the animal. This provides a tool by which we can gain insights in to the working of neurons and networks from a behavioral perspective.

Contents

1 Introduction **6**

2 Materials and Methods **8**
2.1 Experimental Paradigm . . . 8
2.2 Data set description . . . 9
2.2.1 Linear Track . . . 9
2.2.2 Square Enclosure . . . 9
2.2.3 The Circular Track . . . 10
2.3 Data format and related software . . . 12
2.4 Data sorting . . . 12
2.4.1 Linear Track . . . 13
2.4.2 Circular Track . . . 13
2.5 Analysis . . . 13

3 Results and Discussion **14**
3.1 Position of the animal . . . 14
3.1.1 Random Walk . . . 15
3.1.2 Phase diffusion . . . 18
3.2 Velocity of the animal . . . 21
3.2.1 Frequency . . . 21
3.2.2 Amplitude . . . 24
3.3 Acceleration of the animal . . . 26
3.3.1 Frequency . . . 26
3.3.2 Amplitude . . . 28
3.4 Head Direction . . . 28

4 Appendix **35**

A Acceleration **35**
A.1 Amplitude . . . 35
A.2 Frequency . . . 38

B Velocity **41**
B.1 Amplitude . . . 41
B.2 Frequency . . . 44

List of Figures

1 Photograph of the CIrcular Texture Track 10
2 Method Description 11
3 Random Walk and Phase Reset 16
4 Phase Diffusion 20
5 Direction Modulation of Power 30

List of Tables

1 Circular Track :Correlation:Velocity- Frequency 22
2 Circular Track : Regression: Velocity- Frequency 22
3 Linear Track :Correlations: Velocity- Frequency 23
4 Linear Track :Regression: Velocity- Frequency 23
5 Square Enclosure: Correlation:Velocity - Frequency 23
6 Square Enclosure:Regression:Velocity - Frequency 24
7 Circular Track : Regression: Velocity- Amplitude 25
8 Circular Track : Correlations : Velocity - Amplitude 25
9 Linear Track :Correlations: Velocity- Amplitude 25
10 Linear Track :Regression: Velocity- Amplitude 25
11 Square enclosure :Correlation:Velocity- Amplitude 26
12 Square enclosure : Regression : Velocity- Amplitude 26
13 Circular Track :Correlation: Acceleration- Frequency 27
14 Linear Track :Correlation: Acceleration- Frequency 27
15 Square Enclosure: Correlation:Acceleration - Frequency 27
16 Circular Track :Correlation: Acceleration- Amplitude 28
17 Linear Track :Correlation: Acceleration- Amplitude 28
18 Square Enclosure : Correlations : Acceleration - Amplitude . . 28

1 Introduction

Navigation is a complex process that needs to integrate information about place, distance and direction in order to accurately determine one's position in the environment. The grid cell network in the entorhinal cortex provides a directionally oriented, topographically organized, tessellating neural metric representation which maps the entire environment available to the animal. The grid map has hexagonal symmetry and is scalable so as to cover environments of any size. Once the grid map has been established, it can persist even in darkness, i.e without any explicit allocentric cues [Hafting et al., 2005]. The network accurately computes, represents and updates self position information of the animal in concordance with the hippocampal place cell representation of the environment, a process that has been referred to as path integration. The persistence of the grid fields in the darkness and the recurrent connectivity to the hippocampus made grid cells the likely candidate to perform path integration[Terrazas et al., 2005][Samsonovich and McNaughton, 1997][Hartley et al., 2014][Moser et al., 2008]

The implications of such a map is far-reaching both in navigational and memory contexts. It has been hypothesized that grid cell network provide the hippocampus with a presumptive tool for de-correlation of individual spatial representation and this circuit may be the core mechanism for declarative memory formation. The dual role of the entorhinal-hippocampal system in navigation and spatial memory is theatrical but is evident and indisputable[Buzsáki and Moser, 2013] [Cutsuridis et al., 2010] [Moser et al., 2015][Burgess, 2006].This idea almost lays the groundwork for theories on mnemonic space navigation. These findings would have profound effects on the way we understand Alzheimer's disease or any form of dementia that is also associated with navigational impairments.

The remarkable periodicity of the grid network has inspired a legion of computational models and theories to explain the type of dynamics observed in the entorhinal-hippocampal circuits. The emphasis of these conceptualizations is that, the development and maintenance of grid map is closely related to the behavior so much so that each parameter that is used in the construction of the network is computed from the idiothetic information obtained from the locomotor behavior of the animal [Giocomo et al., 2011][McNaughton et al., 2006].

The theoretical models can be largely classified into two categories, the oscillatory interference models and the network attractor models. The former suggests that grid fields emerges from interference between an incoming theta rhythm and an intrinsic membrane oscillation[Burgess et al., 2007], while the latter explain the grid network dynamics by local connectivity and evolution of attractor dynamics to represent the position of the animal[Burak and Fiete, 2009]. Some models are based on both the mechanisms[Bush and Burgess, 2014], however a signal from the vestibular system, presumably velocity[Burgess, 2008], is essential for continuously updating the spatial position of the animal[Zilli and Hasselmo, 2010][Giocomo and Hasselmo, 2008]. This signal could as well be acceleration considering that vestibular system explicitly calculate instantaneous acceleration[Jacob et al., 2014][Hitier et al., 2014]

Interestingly, a study evaluating the behavioral correlates of theta and delta oscillation in the EC reported that the previously observed correlations between frequency and running speed could be a misattribution of effects of acceleration. This eventually lead to the discovery of a specific population of cells in the entorhinal cortex termed as speed cells, which exhibits a linear response to the speed of animal invariable of the context[Kropff et al., 2015]. This finding has showed a new perspective to the field, the accurate representation of speed signal inside the network excludes the need for speed signal to be computed outside and fed into the network.

A wide range of theories in different aspects of cognition suggests subthreshold oscillatory activities in different frequency bands to be acting as distinct information channels. The most important of the ideas that prevail in the theoretical framework of grid cells is the adoption of these information channels into the network computations of navigation. Theta and delta are the prominent brain rhythms observed in the entorhinal-hippocampal circuits. Evidently, they have been associated with many of the modulations seen in the network from a behavioral and computational perspective[Schu, 1999]. From the long list of all the overt and covert behaviors that has been attributed to theta, very few has been validated and established with experimental results[Buzsáki, 2005]. The prevalence of delta oscillation in the network has received attention much later than that of theta and consequently have not been studied extensively.

Locomotor behavior is causally related to the generation and maintenance of theta oscillation in the network and it has been widely accepted that the self motion signal such as velocity and position is carried through theta[Carmichael, 2012][Buzsáki, 2002]. Yet another variable that has to be fed into the network is the direction of movement. It has been hypothesized that direction information (vestibular and head direction cell input) and optic flow are carried through delta oscillation to be fed into the network[Terrazas et al., 2005][Watrous et al., 2011].

The multitude of models that has come up recently are able to duplicate several if not all of the dynamics observed in the network, but do not fully converge in to fit the observed characteristics of the system. For example, attractor dynamics models does not really address the role of theta oscillation in the network, but are still able to explain some of the grid dynamics. The main motivation to this project is to find the behavioral relevance of these oscillatory activities and their role in this network computation. This is done by statistical analysis of locomotory characteristics and the observed oscillatory activity obtained by evasive recordings from the entorhinal cortex and hippocampus. Also, to the possible extent, some of the axioms of the existing grid cell models has to be evaluated in the light of these results, with the hope of coming up with a better groundwork for theoretical models of grid cells.

2 Materials and Methods

2.1 Experimental Paradigm

The electrophysiology data that has been used for these analyses are obtained from different labs. The linear and the square enclosure track data are obtained from the Moser Lab and has been made available online through www.CRCNS.org. The plain and textured circular track has been provided by Dr. Yoganarasimha Doreswamy's Lab at NBRC,Manesar. Together these three data sets provide one with a contrasting behaviors of spatial exploration which is used in this analysis to understand the behavioral correlations of theta and delta oscillations.

2.2 Data set description

2.2.1 Linear Track

The linear track is a rectanglular enclosure with two platforms connected by a linear track on which the animal runs from one platform to the other. One of these platforms has a food reward and the other does not. The rat has been trained to run from one platform to the other to collect the reward and run back to where it started. In one session the rat runs back and forth 20-30 times. Forward run (to collect food) and Backward runs(Home Run) are treated differently as previous studies suggests that the rat codes these two trajectories differently A linear track is the most constrasting environment in which one can dissect the role of velocity in the oscillatory dynamics.Along a 'one dimension' track one can potentially consider only a single running direction thereby reducing the effects due to turning movements and components of velocity that are not along the fixed running direction This data set has been used by and is one of the pioneering experiments in the field which eventually lead to the discovery of grid cells

The length of track is 300 cms.

The micro-electrodes used for EEG recordings are placed at multiple locations in the entorhinal cortex and is obtained at a sampling rate of both 4096 Hz and 250 Hz. The position of the animal is recorded by a camera placed above and X and Y co-ordinates of the animal is obtained from this at a rate of 50 Hz.

2.2.2 Square Enclosure

The square enclosure is a square box in which the animal moved freely and explored without any definite behavioral training. This replicates the natural exploration paradigm and on this 2-D enclosure the firing of single neurons showed a characteristic hexagonal symmetry. This track also offers the kind of paradigm where the variation in the velocity is minimal and the instantaneous velocities achieved by the animal are realistic

This is an ideal environment to look at the effect of different variables in the oscillatory pattern that helps the construction and maintenance of grid network.This data set has been used by [Hafting et al., 2005]to demonstrate the existance of grid cells in the mEC

The length of side is 100 cm

The LFP of the rat is obtained through micro electrode implants in the Entorhinal Cortex of behaving rat. LFP is recorded from multiple anatomical locations in the same recording session at a sampling rate of 4096 or 250 Hz. The position of the animal is recorded by a camera placed above and X and Y co-ordinates of the animal is obtained from this at a rate of 50 Hz.

2.2.3 The Circular Track

The circular track has an inner radius of 150 cm and a width of 10 cm on which the animal runs several laps continuously. This leads to a continuous monotonic change in the direction of motion. It also offers a continuous force in terms of the torque acting on the animal. The rhythmic nature of the behavioral paradigm is also important to see how repetition/rhythmic of the behavior affects theta and delta oscillations. The obvious advantage being the continuous nature of the behavior unlike in the linear track. One can also argue that this type of running can be considered as running on an infinitely long linear track.

The experiment was analysed to test the hypothesis that spatial cues available to the animal has affects the reliability of theta oscillations. The animal has access to both proximal and distal cues in the environment. These cues are spatially localized for one trial and do not change their positions.There are two variants of the track design. The plain track has no spatial cues available to the animal.The texture track has tactile cues which are the texture on the track (Proximal cues) and visual cues which are symbols hanging in the room (Distal cues) in which the track is placed. The plain track (PT) serves as a control for the experiment.

Figure 1: Photograph of the CIrcular Texture Track

The LFP is recorded from multiple anatomical locations of mEC and hippocampus in the same run at a sampling rate of 4096 Hz. The position of the animal is recorded by a camera placed above and X and Y co-ordinates of the animal is obtained from this at a rate of 50 Hz.

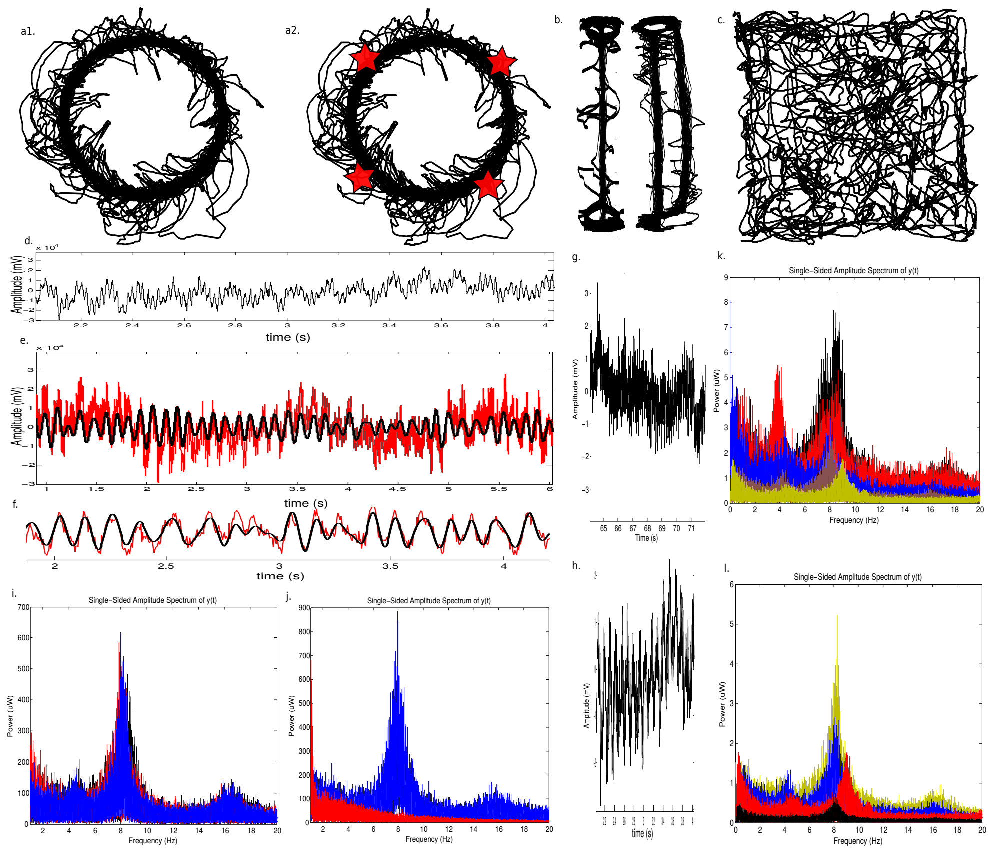

Figure 2: Method Description

Figure 2: a1, a2. The circular track has two variants. a1 represents the track without any cues (Plain Track) and a2 represent the track with cues. The stars on the track are representatives of the tactile cues on the track. b. The linear track. Two types of behavior are represented here.One the animal uses different paths for forward and backward running(on the right), two, the animal uses the same trajectory for forward and backward running(on the left). In either case the forward run and the backward run are

considered differently. c. The square enclosure d. EEG trace from the plain circular track. The eeg oscillations in theta frequency. Faster gamma oscillations can also be observed. The regular nature of these oscillation on the circular track is striking e. The red signal is the EEG trace from the textured track and black trace represents the filtered theta oscillation. The theta oscillation and the eeg seems to be riding on top on a slower oscillation in the delta range f. The filtered theta oscillation is overlaid on top of the EEG trace obtained from the linear track. g. The graph depicts a monotonous decrease in the average amplitude over a length of 5s. h.The graph depicts a monotonous increase in the average amplitude over a length of 10s. Although it is in the delta range, it seems to be different from the delta which is normally seen in the eeg spectrum which peaks at 2-4 Hz. i,j,k,l. Fourier spectrum of the EEG signal obtained from Textured circular track, Plain circular track, Linear track and the square enclosure respectively, depicting the peaks at theta and delta frequency range.

2.3 Data format and related software

The data from Moser lab is available in matlab binary format, the data from NBRC is available as .ncs file for the LFP and .ascii for position and direction. The data acquisition was done using Neuralynx software. I have converted the .ncs file to a .mat file using the file conversion facility that Neuralynx provide.

2.4 Data sorting

Each data sample consists of one LFP recording and corresponding position information of the animal. Depending on the track the locomotion is either continuous or discontinuous and based on this factor the data is split into laps. If it repetitive such as in the case of linear and circular track while for the square enclosure, due to the lack of rhythmic pattern in the behavior, trial division does not make sense. Position of the animal is sampled at a different sampling rate than that of EEG.The difference in the sampling rate decided whether to up sample or down sample the data set. If the difference was big such as in the case of circular track (30 Hz and 4096 Hz respectively) the data is down sampled. In the case of square enclosure and linear track, data is available on both 4096 and 250Hz. The low sampling rate data(250 Hz LFP) is analyzed with an up sampled position to match the instances of eeg sampling.

Data divided into trials based on the position of the animal on the track. Rhythmic behaviors in the environment is used to find out statistically significant trends in the data.

2.4.1 Linear Track

Forward run and Backward runs are treated separately. The pattern of spikes generated by single grid cells is known to vary in each direction. Each run is called a lap and each session is called one trial in the analysis.

2.4.2 Circular Track

One rotation around the circular track is considered as one lap and one recording session consist of such 20 laps. After each session the rat is taken in a box and the position of distal cues are changed but the proximal cues, that is, the textur on the track remains the same. The rat is then introduced back into the environment and the next session starts. The proximal cues remains the same but the animal is introduced back into the environment at random positions. Since there is changes in the cues, each session is treated a different trial.

2.5 Analysis

Velocity is calculated from the position values of the animal and so is acceleration. In the case of a circular track the motion direction obtained during the experiments is used for the analysis, while in other casesm where it is not available, head direction is explicitely calculated from the x and y co-ordinates of animal at any time.

Fourier analysis is used to obtain all the spectral properties of the signal.Theta and delta band oscillations in the LFP is filtered by a band-pass filter provided by EEGLAB [Delorme and Makeig, 2004] toolbox which uses Matlab environment. The Matlab environment has been used for all the analysis and data visualization.

3 Results and Discussion

3.1 Position of the animal

The accuracy and periodicity of grid cells are remarkable.How are they able to accurately represent position of animal is the most important of the questions that is in the air. Theoretical models have adapted theta oscillations to provide the framework on which these positional calculations can be done.

Theta oscillation in the hippocampal formation is generated by neuronal current oscillators which are maintained and modulated by inputs relevant to the functionality of the network. The inputs are assumed to be stimulus from the environment. The forces which are responsible for the generation of these oscillation are primarily thought to be locomotor in nature.Many experimental observations suggests that theta phase is associated with the position of the animal.[Colgin, 2013]Hence, we hypothesized that phase of the theta oscillations have a positional dependence and phase is reliable with respect to the positon of the animal.

We first sought to understand whether theta oscillation play a role in ensuring the reliability of spiking pattern. If spike timing reliability depended on theta then the attributes of theta namely, frequency, amplitude, or phase may persist at specific locations

To understand the effect of position on theta oscillation we postulated 3 potential scenarios and examined which of these or a combination of thereof might be manifested in the data providing us an insight into the mechanism of theta generation and environmental perturbation to theta.

The motivation for a random walk experiment was to understand the nature of the resetting phenomenon, as to know what to look for.The theta oscillation in the rat hippocampal formation is hypothesized to take specific cues possibly with a strong spatial component or the space itself as reset instances.At the event of reset phase and the variability in the system is transiently reduced or set to zero

3.1.1 Random Walk

Constant Frequency Oscillator

Theta oscillations are modeled as oscillators with constant frequency. This scenario depicts the reliable nature of the oscillation over many trials. Their phases at a particular position align with each other over many trials

Noisy Oscillator

Uniform noise is added to the oscillator for simulating random phase diffusion. When the phases are sampled for different oscillators at the same time, initially they lined up as they should but the noise drifted them apart. The variability of the phase was found to be saturating at 1.4. This observation was consistent across trials.(Figure 2) The amplitude of the noise determined the time to achieve the maximum variability. Irrespective of the noise amplitude, the phase variable spread uniformly to achieve a maximum variability.

Forced Resets

A cue is needed to reset the drifting phase and this is important for grid cells as the position needs to be represented accurately to sustain the grid network activity. The process of path integration is prone to noise and accumulates errors cumulatively.[Burak and Fiete, 2009]

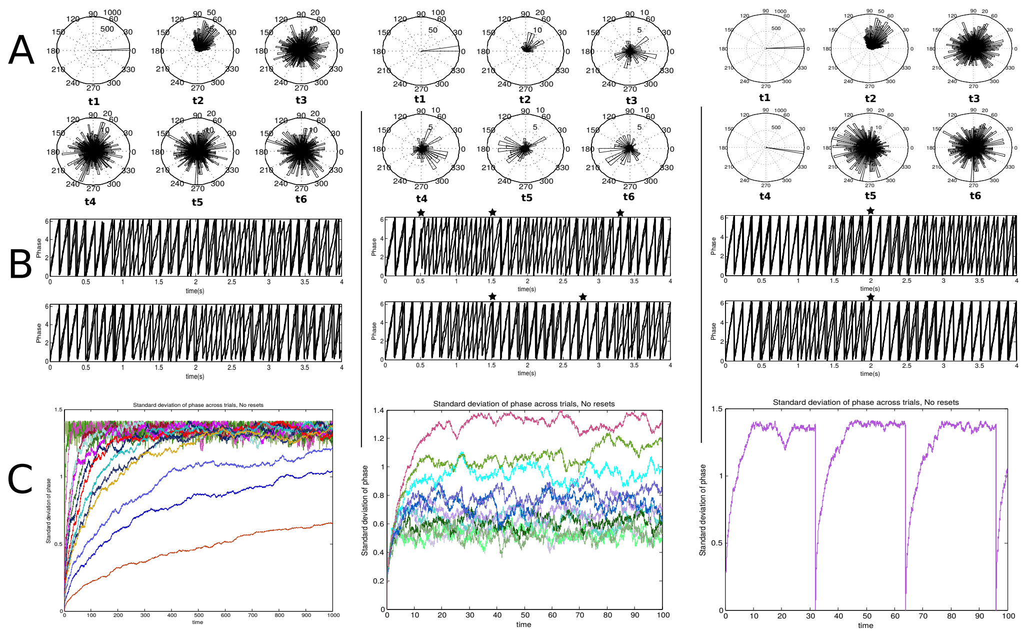

Figure 3: Random Walk and Phase Reset

Figure 3:Left Panel, Phase diffusion without any instances of reset to the drifting phase. First row, the angle histogram plot for different oscillators at a time point showing the variability in the phase at time = t. The phase starts to drift as time pass and finally attain a uniform distribution. Second row, the phase of a single oscillators is plotted against time. The noise keeps the oscillators from synchronizing their phases. Third row, The standard deviation of phases for different noise levels are plotted against time. The phase of the oscillators starts accumulating noise and they slowly drift away and attain a maximum variability.Middle Panel, Phase diffusion with random reset instances which reset the drifting phase at random points in space. First Row, The distribution of phase is not as uniform as random walk without reset but still has a considerable amount of variability in the phase. Second row, Reset instances reset the phase to match it with the underlying

signal. These resets points are random and do not have spatial distribution.Right Panel, Phase diffusion with specific instances of reset which reset the drifting phase at specific location space. First row, The distribution evolve from zero variability to uniform distribution and the reset instance is signified by the reduced variability depicted in the angle histogram. The phase again starts to drift till the next reset point. Second row, the phase of a single oscillators is plotted against time.Resets are located at definite points in space and all the oscillators are reset at the same point in space. The stars on the middle row represents the reset instance

The reset instances can be of two types, one is different oscillators reset themselves at different positions in space and time. These can be called non-specific cues since they are not spatially specific for each oscillators and neither for the system. The reset cue could be any sampling instance of the environment and need not be a spatial cue. The other is a common cue for all the oscillators and is localized in space. The spatial specificity is important as without it it could not be affecting all the oscillators simultaneously.

Random reset scenario is simulated as follows. The phase of the oscillator is randomly reset to zero, These resets are not matched in time or space for different oscillators. The no of resets determined the maximum achievable variability of the system. As the number of reset instances increased the maximum variability of the system decreased. This is unlike the real scenario because the variability in the system always saturates at 1.4 regardless of the experimental design and reset cues. Therefore we can assume that in the experiment, the noise added to the phase is significantly large that random resets (if any) do not prevent the variability across trials from being maximum

Specific reset scenario is simulated as follows. The reset instances are matched in space and time to simulate specific instances of reset of all the oscillators. The phase of the oscillators are reset at specific points in space which reduces the variability in the system. . The Maximum variability did not depend on the no of reset instances and always achieved a the maximum variability of 1.4. Thus we have three potential hypothses as to how the the phase reset phenomenon could manifest in the LFP. One is that, there is no reset phenomenon, second is that, the reset phenomenon are random meaning there is no spatial specificity for the reset cue and finally third is that the reset cues are spatially localized cues. Working hypothesis for the following experiment is that, the phase of the oscillation is pinned to the position of the animal and as it diffuses because of the accumulation of noise, reset cues reset the phase of the oscillation transiently reducing the noise in the system.

3.1.2 Phase diffusion

Circular Track

The phase diffusion curve of theta oscillation in a plain track did not show any instances of zero variability reset. The standard deviation of phase was saturated all along the positions on the circle. Since the track did not contain any explicit reset cue, this was the expected behavior.

Most of the trials in the textured track did not show any significant reduction in the standard deviation of phase besides random fluctuations. But three of these trials, were found to have significantly different phase diffusion characteristics. Out of these three, one shows prominent decrease in the standard deviation of theta phase over the positions. As the other two were also having decreased standard deviations in certain bins, but were only moderately different from others.

The distribution of variability of phases suggests that most of the points are near the saturation value, and it is a wider distribution than that of the textured track. This lack of points away from the saturation value and a wider distribution suggests that, there is no significant reset events in the theta oscillation on the plain track. This is was expected behavior of the plain track. on the other textured track, the distribution is narrower but have a wider tail and have lesser values of phase diffusion.

Delta oscillation shows similar characteristics to that of theta. Delta also shows a similar dip in the variability at a position near to the reset position of theta. The plain track also have a dip in variability at the same position. Therefore, most likely this dip is not because of any specific cue. Here, the trials which showed resets in the theta bands has less variability in the delta oscillatory phase as well. The amplitude of theta and delta oscillations is kept relatively constant amplitude over the plain track.

The overall distribution looks uniform, but individual trials have significant modulation in the amplitude with respect to position of the animal. Theta amplitude is more variable in the position axis when compared to the delta amplitude.

Theta and delta bands did not show any zero variability instances even though both of them showed reduced variability at certain points or even as a whole trial. These reset points did not look like they have any spatial pattern. Even the plain track showed reduced variability at certain points. Therefor, it is most likely that they are random fluctuations in the bands and not because of a specific spatial cue. However the distribution of variability was narrower in the texture track. This suggests that cues have an effect on theta and delta oscillation and the reduction in the variability is significant even though they are not relevant within the regimes of our hypothesis. The two sample F-test for variance suggested that the phase variability distributions corresponding to the plain track and cued track have significantly different variances with a 95% confidence. The cued track has a wider distribution of variances of phase while plain track has a narrow distribution. What this suggests is that, in cued track the variability in phase is low while on the plain track the variability in phase is high. Which means, the cues have a positive effect on the variability of phase. Which is to suggest that cues have an effect on the phase of theta oscillation

Linear Track

Some trials on the linear track shows significant reduction in the variability of phases along the track, Out of many runs, only some runs shows this reset in their variability, The backward run has more instances of reset than that of the forward run.

The delta phase diffusion curve is interesting than theta phase diffusion curve because the no of instances signifying the reduction in variability of phase were greater. The Histogram distribution suggests that there is a second peak in the variability which is lower than that of the maximum value, this outlying distribution could signify reset.

The positional dependence of these resets needs to be checked, the graphs suggests there might be a positional dependence of reset, but it is highly probable that they are random.

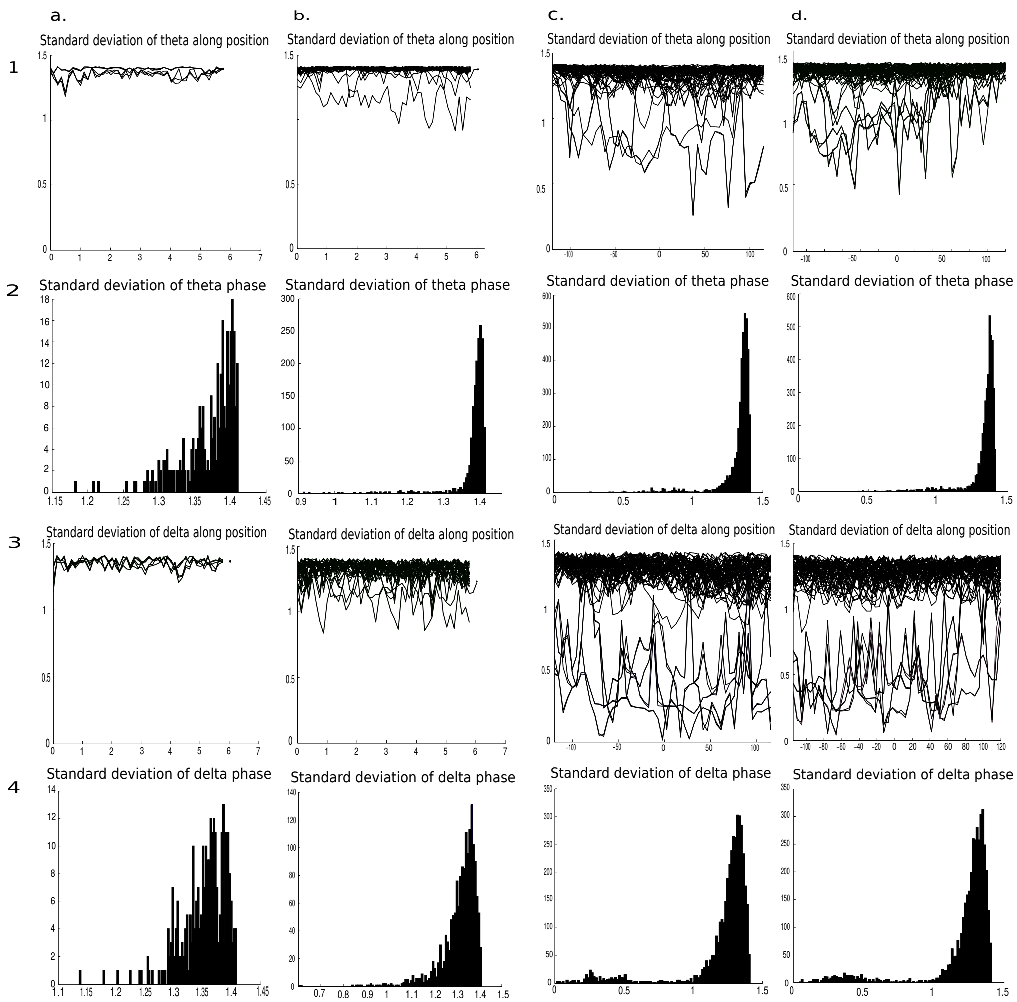

Figure 4: Phase Diffusion

Figure 4 : a,b. Plain and textured circular tracks respectively c,d. Forward and backward runs on the linear track respectively Row 1 : Standard deviation of theta phase plotted along the position of the animal on the track Row 2 : Histogram for the standard deviation of theta phase Row 3 : Standard deviation of delta phase plotted along the position of the animal on the track Row 4 : Histogram

for the standard deviation of theta phase

Some trials shows a position dependent gradient in delta amplitude. But theta amplitude more or less seem to be uniformly distributed along the position on the track.

Theta band did not show any instances of zero phase variability. But there were instances of reduced variability. The histogram of variability also suggests that the reduced variability instances were random fluctuations as the peak was at the maximum variability and the reduced variability instances were outliers to the distribution.

Interestingly, delta band showed a considerably different behavior. even though the phase diffusion diagram showed similarities to that of theta, the histogram revealed that there was a smaller peak at lower values of variability which is a different distribution. This might suggest that there was instances of reset associated with delta.The positional dependence of these resets were not in support for the hypothesis as they did not occur at any specific points in space.

3.2 Velocity of the animal

3.2.1 Frequency

If position is assumed to be coded in the phase of the oscillations then the derivative of phase that is the frequency of the oscillation should represent the velocity of the animal.Along this line of thought, many experiments have found that frequency is modulated by the running speed of the animal. There has been a prediction put forth and verified by [Jeewajee et al., 2008] that the frequency of theta is linearly dependent on the running speed of the animal in a square enclosure.The study was only concerned about the magnitude and not the direction of the velocity.

We checked the validity of this result in the three different scenarios that we have not only for theta but also for delta oscillations. These three paradigms offer a contrast to the results because of the differential modulation of velocity and running direction. The instantaneous frequency of the oscillation was calculated and corresponding instantaneous velocity was obtained for analysis of the linear dependence between the two variables

Circular Track

The track provides a continuous change in the direction of motion and thus we can assume that the modulating effect of direction be either uniform or minimal since the pattern is repetitive.

The regression analysis did not yield a significant linear dependence and the correlation was only marginal. The texture track and plain track were showed different characteristics in their response curve, but both of them yielded negative results for the hypothesis under consideration. The distribution was less variable in the texture track compared to that of the plain track.

Band	Plain Track	Texture Track
Theta	0.0494	0.0340
Delta	0.1397	-0.0226

Table 1: Circular Track :Correlation:Velocity- Frequency

Band	Plain Track	Texture Track
Theta	-0.0069x + 8.1414	0.0002x + 9.0506
Delta	-0.0006x + 4.2709	-0.0022x + 2.2793

Table 2: Circular Track : Regression: Velocity- Frequency

The analysis did not reveal any linear dependence between frequency and running speed. However, one cannot miss the positive nature of the frequency modulations brought about by the running speed of the animal. This notion is also consistent with the view that entorhinal and hippocampal network firing rates are affected by the velocity of the animal to keep up the firing in their respective firing fields.

Linear Track

The linear track lets one disentangle the direction and magnitude of velocity. This is essentially like a one dimensional motion.The linear regression and correlation analysis did not reveal any linear dependence. The correlation analysis yielded smaller positive values than that of the circular track which could be because of the reduced effect of movement direction. The delta oscillation also showed correlations with running speed but these trends cannot be considered as significant trends.

Band	Forward Run	Backward Run
Theta	0.008	0.0039
Delta	0.0876	0.1394

Table 3: Linear Track :Correlations: Velocity- Frequency

Band	Forward Run	Backward Run
Theta	1.1181x + 6.0412	0.5378x + 7.636
Delta	0.182x + 1.769	0.1139x + 2.136

Table 4: Linear Track :Regression: Velocity- Frequency

The coefficients have greater positve values, but their significance is highly doubted because the distribution og frequency and velocity do not look like they could support a linear regression. [Figures added in Appendix B.2]

Square Enclosure

The distribution look as if it could support a linear dependence. But the regression analysis suggested that there is no linear trend in the data and the correlations between frequency and velocity were only marginal.

Band	Correlation
Theta	0.1431
Delta	-0.14

Table 5: Square Enclosure: Correlation:Velocity - Frequency

The delta frequency modulations were uniform and is consistent with the previous analysis in this report.The track offers a less variable velocity regime to look for the trend but this advantage did not show up in the statistics. Jeewajee et al. [2008] found a clear linear trend between running speed and frequency of theta in a square enclosure. We could not replicate this result in our data, moreover the nature of the frequency response curve did not show a linear dependence between velocity and frequency.

Band	Linear Fit
Theta	0.0036x + 8.5713
Delta	-0.01197x + 2.7118

Table 6: Square Enclosure:Regression:Velocity - Frequency

The frequency of theta was dependent on both the magnitude and direction of velocity. The linear nature of this dependence was not evident in the analysis. Nevertheless, it was evident that theta is positively modulated by the navigation variables and that it is a general trend in the network.

Conclusions

The analysis yielded a negative result compared to the existing literature in terms of the nature of the relationship. But it was evident that the frequency is modulated by the running speed and the modulation is positive in nature. [Figures added in appendix B.2]

3.2.2 Amplitude

Theta is hypothesized to play a role in sensorimotor integration.The amplitude of theta oscillation is said to be dependent on the running speed of the animal so as to meet the increased needs of sensory processing. Although it is evident that this is not the only role of theta on the network the relationship could have implications to the causal role of movement in theta generation.

Circular Track

The velocity amplitude distribution has a slight positive slope. The general dependence of theta oscillation is reflected in the amplitude resposes. The analysis failed to produce a linear response curve with significance between velocity and amplitude. The correlation between these variables were also low.

Even though theta amplitude did not yield any statistically significant trends with the running speed of the animal, it was considerably different from the uniform distribution of delta oscillation. The textured track which offers sensory inputs to the system also failed to produce a linear amplitude response curve for velocity.

Band	Plain Track	Texture Track
Theta	0.0038x + 1.1668	-0.0001x + 1.4298
Delta	0.001x + 0.63049	0.0003x + 0.91262

Table 7: Circular Track : Regression: Velocity- Amplitude

Band	Plain Track	Texture Track
Theta	0.025	0.0069
Delta	-0.0146	-0.0168

Table 8: Circular Track : Correlations : Velocity - Amplitude

Linear Track

The correlation analysis and regression analysis did not yield any promising result even though the behavioral paradigm offers a velocity changes in a continuous fashion. The positive trend in the data was also evident in this case but failed to produce any statistically significant trend.

Band	Forward Run	Backward Run
Theta	0.0367	0.0371
Delta	0.036	0.037

Table 9: Linear Track :Correlations: Velocity- Amplitude

Band	Forward Run	Backward Run
Theta	10.7729x + 671.54	12.7269x + 495.3686
Delta	4.0379x + 261.1862	4.8995x + 188.619

Table 10: Linear Track :Regression: Velocity- Amplitude

Square Enclosure

As in the case of the linear and circular track the data shows clear positive trend even though the statistics suggests that there is no standing linear pattern in the data. The regression yielded only a small trend and the correlation coefficients were also small.

Band	Correlation
Theta	0.0864
Delta	-0.0062

Table 11: Square enclosure :Correlation:Velocity- Amplitude

Band	Fit
Theta	0.0184x + 9.277
Delta	-0.005x + 2.8627

Table 12: Square enclosure : Regression : Velocity- Amplitude

[Figures attached in appendix B.1]

3.3 Acceleration of the animal

3.3.1 Frequency

A recent study [Carmichael, 2012] suggested that the velocity frequency correlations could be a mis-attribution of effects due to acceleration. This argument seems viable since all vertebrates can sense acceleration explicitly and it is the most efficient way to sample space. Hence the hypothesis is that the frequency modulations are brought about by the acceleration of the animal. Acceleration is calculated instantaneously and the effects are assumed to be transient, that is a linear dependence is not attributed rather a correlation is expected

Circular Track

The correlation analysis suggests that the acceleration of the animal is better correlated with the frequency of the theta rather than velocity in the case of both theta and delta oscillation. Also it is worth noting that the textured track shows a higher correlations compared to that of plain track. This signifies the effect of cues in the properties of theta oscillation.

Band	Plain Track	Texture Track
Theta	-0.022	0.15035
Delta	0.001766	0.006341

Table 13: Circular Track :Correlation: Acceleration- Frequency

Linear Track

Band	Forward Run	Backward Run
Theta	0.008	0.004
Delta	0.0876	0.139

Table 14: Linear Track :Correlation: Acceleration- Frequency

Acceleration was found to have little effect on the frequency of theta and a marginal effect on the frequency of delta oscillation

Square Enclosure

The data suggested that there is no correlation between the frequency and acceleration of both theta and delta oscillations.

Band	Correlation
Theta	0.0263
Delta	0.0318

Table 15: Square Enclosure: Correlation:Acceleration - Frequency

[All the figures attached in appendix A.2]

3.3.2 Amplitude

Circular Track

Band	Plain Track	Texture Track
Theta	0.0093	0.0240
Delta	-0.01299	0.00089

Table 16: Circular Track :Correlation: Acceleration- Amplitude

Linear Track

Band	Forward Run	Backward Run
Theta	0.0047	0.004
Delta	0.0048	0.0041

Table 17: Linear Track :Correlation: Acceleration- Amplitude

Square Enclosure

The correlation analysis suggested that acceleration is not responsible for the modulation in the amplitude of theta and delta oscillations

Acceleration does not vary systematically with the amplitude of both theta and delta oscillations as the correlation analysis yielded very low coefficients

Band	Correlations
Theta	-0.0185
Delta	0.03007

Table 18: Square Enclosure : Correlations : Acceleration - Amplitude

[Figures attached in appendix A.1]

3.4 Head Direction

The firing fields of grid cells occupy a hexagonally symmetric lattice in space. Intracellular recordings of grid cells have revealed that as the animal traverses the grid field of a cell, the neuron receives a depolarizing input that tapers off as the animal nears the end of the grid field [Domnisoru et al., 2013]. Further, recent experiments have revealed that within specific regions of the mEC, grid cell firing fields share the same spatial frequency and orientation. The phase of the grid associated with different neurons can vary and tessellate the physical space that the animal covers. A consequence of a common grid orientation is that as the direction of travel changes, so does the distance between the grid fields that the animal encounters. This inter peak distance changes periodically over 360 degrees peaking six times to reflect the hexagonal symmetry of the grid.A study using fMRI to look at the grid cells have found that there is a six fold symmetry in the modulation of a BOLD signal while .[Doeller et al., 2010] subjects performed a virtual navigation task.

The overal modulation of the activity is consistent with the firing rate modulation of neurons in these areas. This observation lead us to hypothesize that the six fold symmetry in the grid architecture could be inherited from input to the mEC from other regions and may be reflected in the LFP. Depending on which channel it is inheriting the symmetry from, we can deduce the behavioral correlation of such a symmetry. If theta or delta were to show such a symmetry it is possible that the self motions cues are responsible for the grid symmetry, and if it is the gamma oscillation that is showing such a symmetry it can be attributed to the local computations within the network.

While theta is responsible for the movement related modulations in the LFP, the definite correlate of direction has not been found. The construction of a 2D grid map needs definite direction input which comes from the head direction cells. Directional of motion of the animal modulates delta oscillations that are thought to be containing vestibular inputs and direction of motion as well. Therefore, it is likely that the grid symmetry could be inherited from the path integration of motion direction and not just from the environmental cues.

We have found that delta oscillations show such a six fold symmetry in the running direction of the animal. The distribution of power along the running direction of the animal shows a six fold symmetry. We could observe 6 peaks with a relatively constant angular distance between them. Inter peak distance (IPD) is defined as the distance between consecutive peaks and the distribution of IPD peaks at 60 degree.[The cicular equivalent of binomial test is applied to obtain the significance of the result. The test was in agreement to the hypothesis that the mean IPD is 60 degree.]

The close relationship of theta and delta with the behavior and the construction of grid map lead us to think that the symmetry of grid network is inherited from the delta oscillation and delta oscillation inherit it from the direction of motion of the animal.

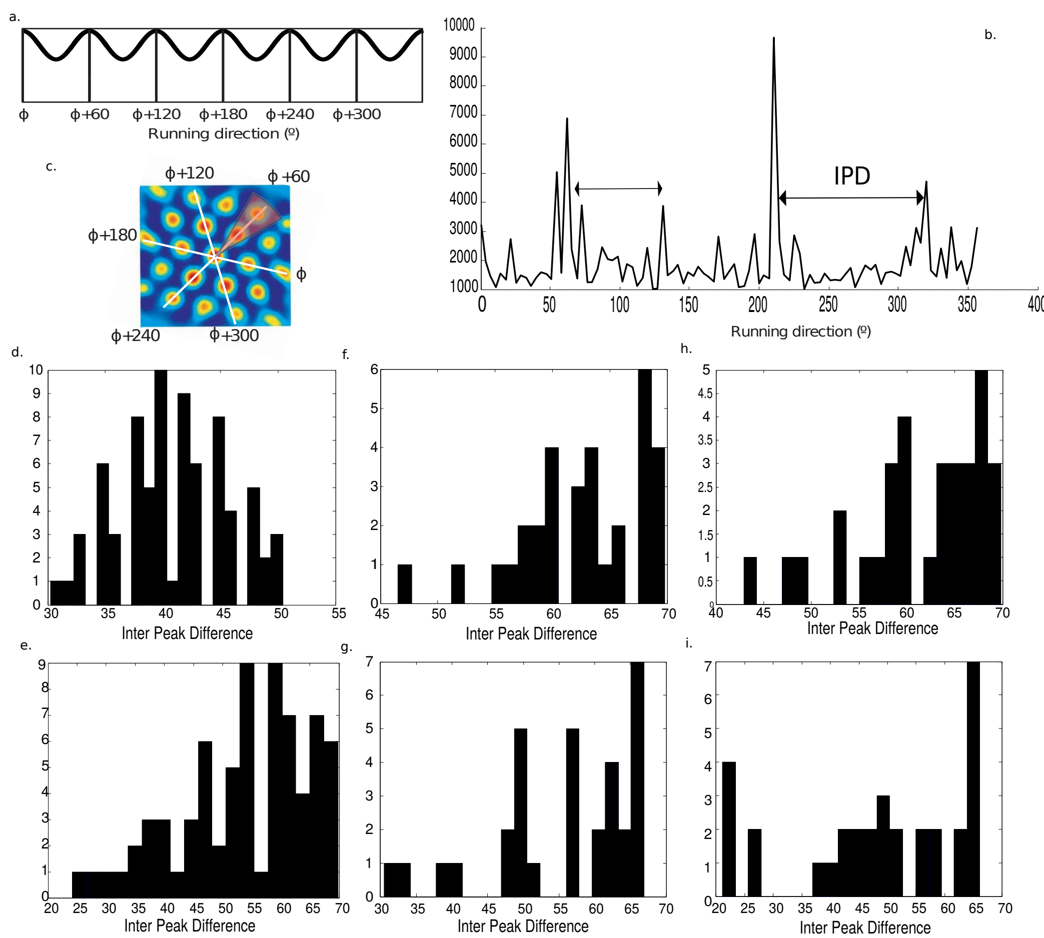

Figure 5: Direction Modulation of Power

a. fMRI signal modulation over the running running direction. (adapted from Doeller et al. 2010) b. Delta power modulation over the running direction for the square enclosure. IPD stands for inter peak difference and is the average distance between the highest peaks in the modulation spectrum. c. The spatial autocorrelogram of a single grid cell. The white lines shows the three main grid axes. The distance to the nearest grid field symmetrically changes with the running direction, with least values in the direction of the grid axes and highest in between the axes.d,e. Histogram for the IPD of theta and delta respectively in the square enclosure.[mean IPD=54.45;SD=31.5 degrees. CI =[45.7 - 63.1 degrees]; f,g. Histogram for the IPD of theta and delta respectively for the plain circular track. [mean IPD=46.3;] h,i. Histogram for the IPD of theta and delta respectively for the textured circular track.[mean IPD=46.4; SD=13.10

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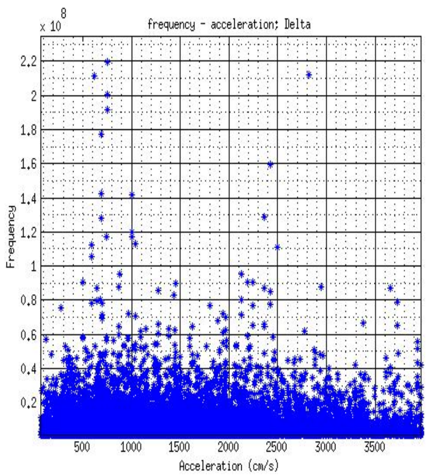
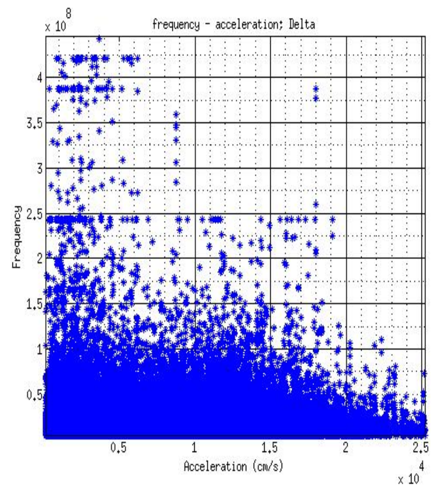
4 Appendix

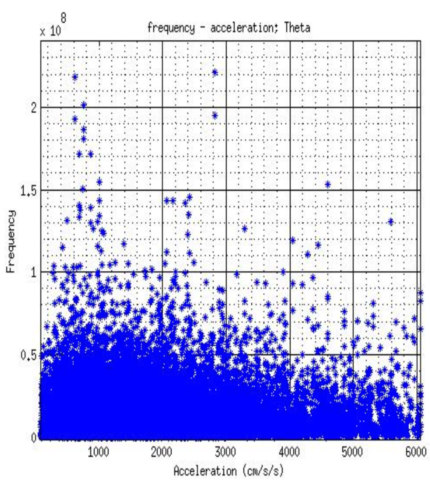
A Acceleration

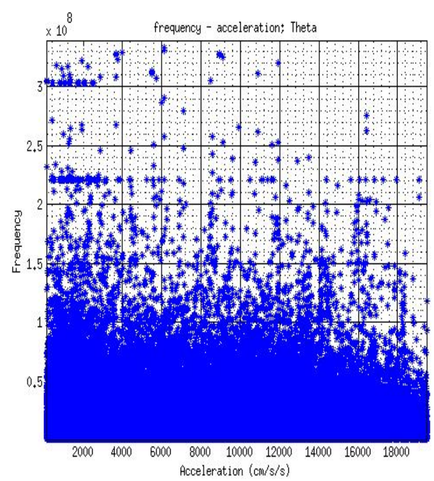
A.1 Amplitude

Circular Track

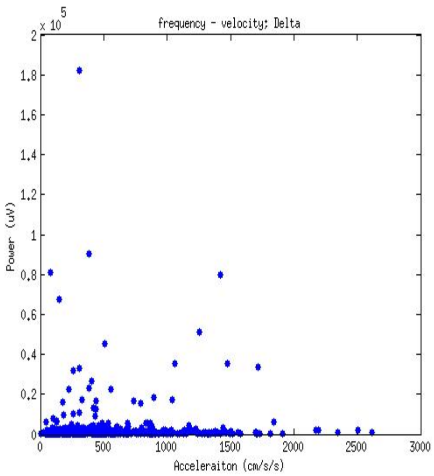


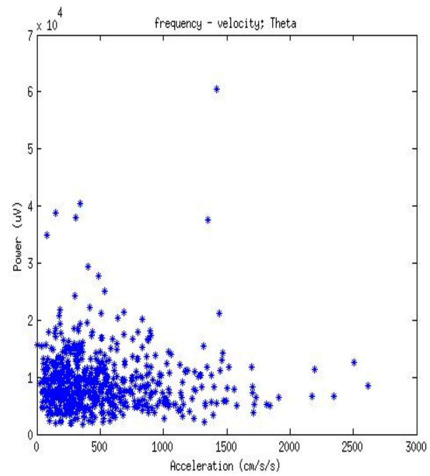




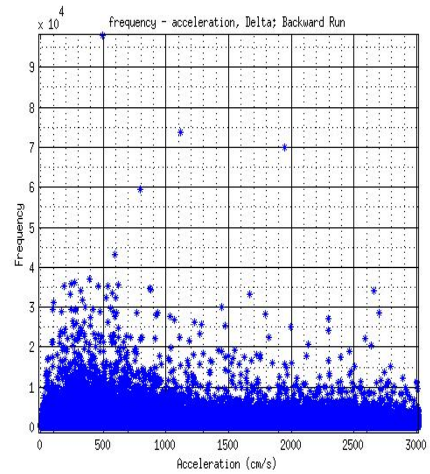


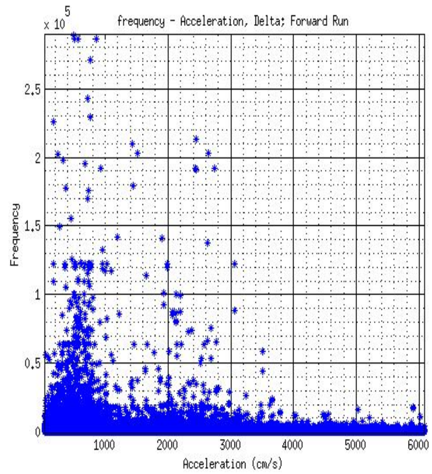
Square Enclosure

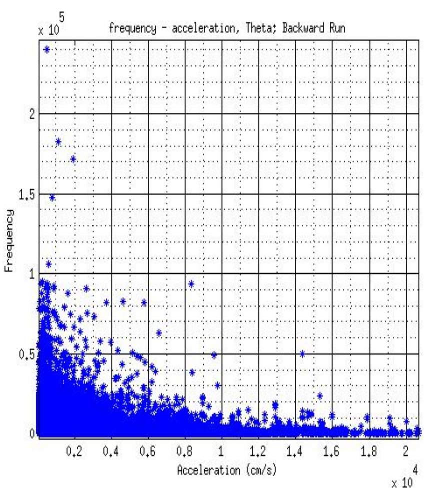


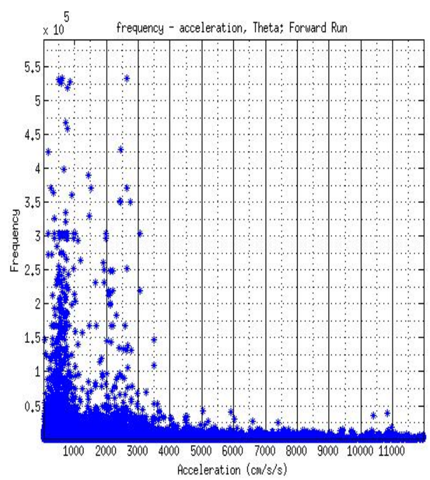


Linear Track



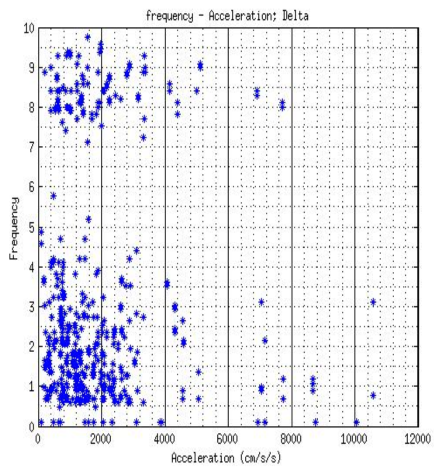


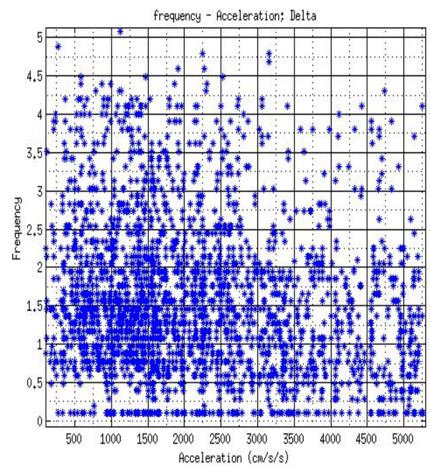


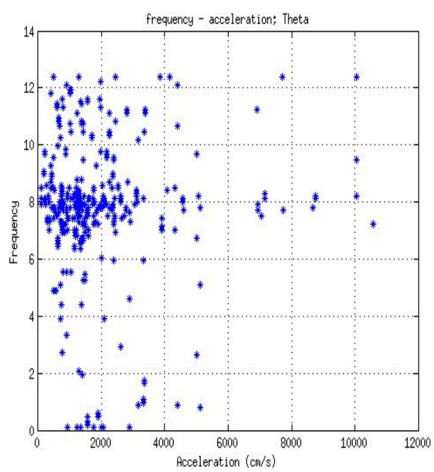


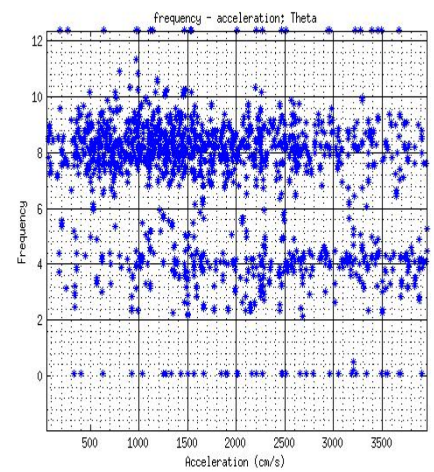
A.2 Frequency

Circular Track

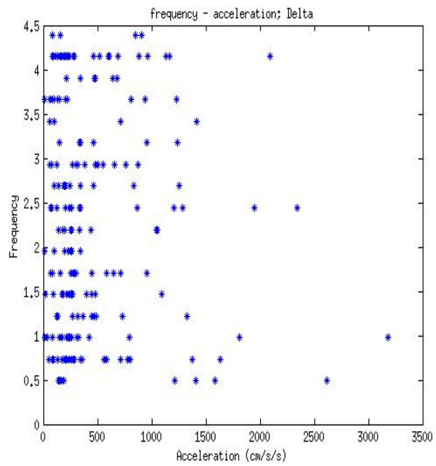


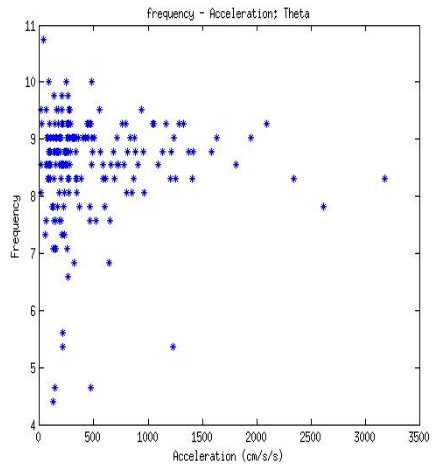




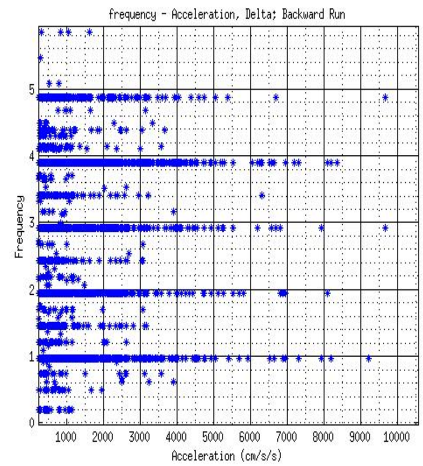


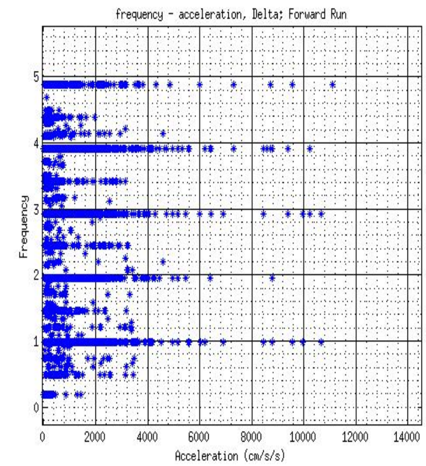
Square Enclosure

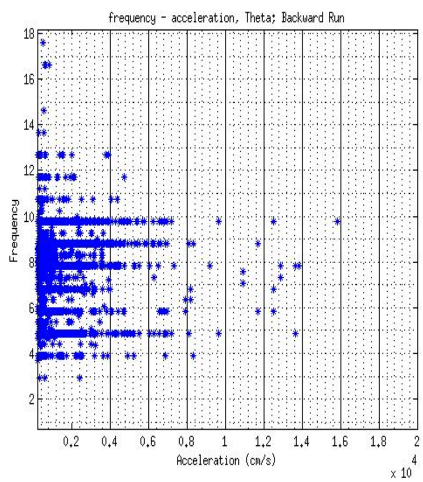


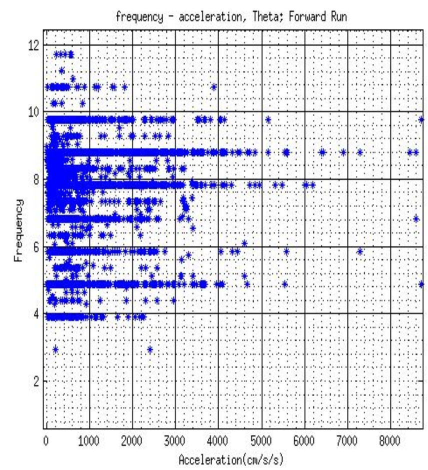


Linear Track





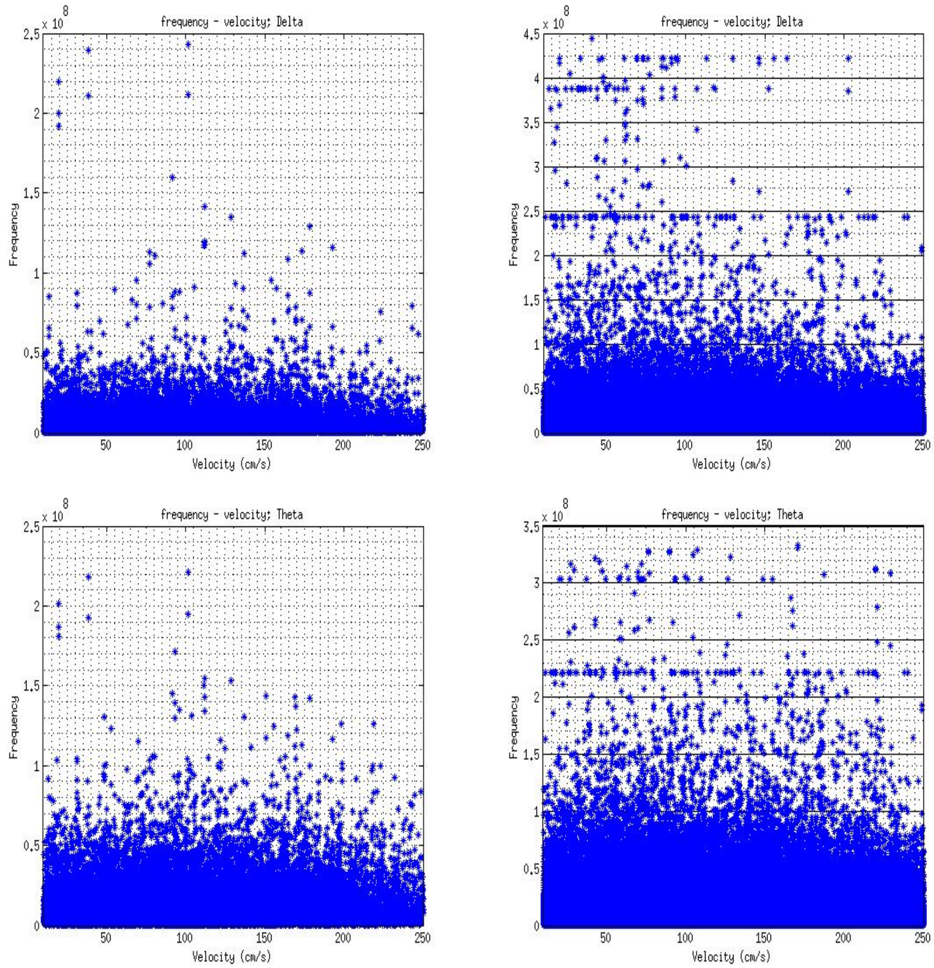




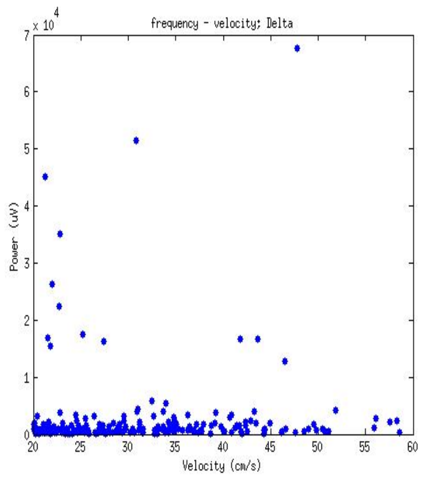
B Velocity

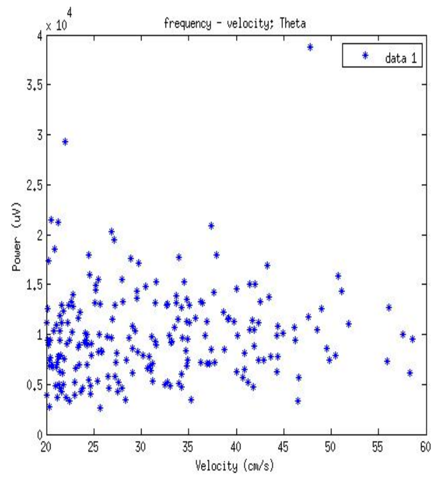
B.1 Amplitude

Circular Track

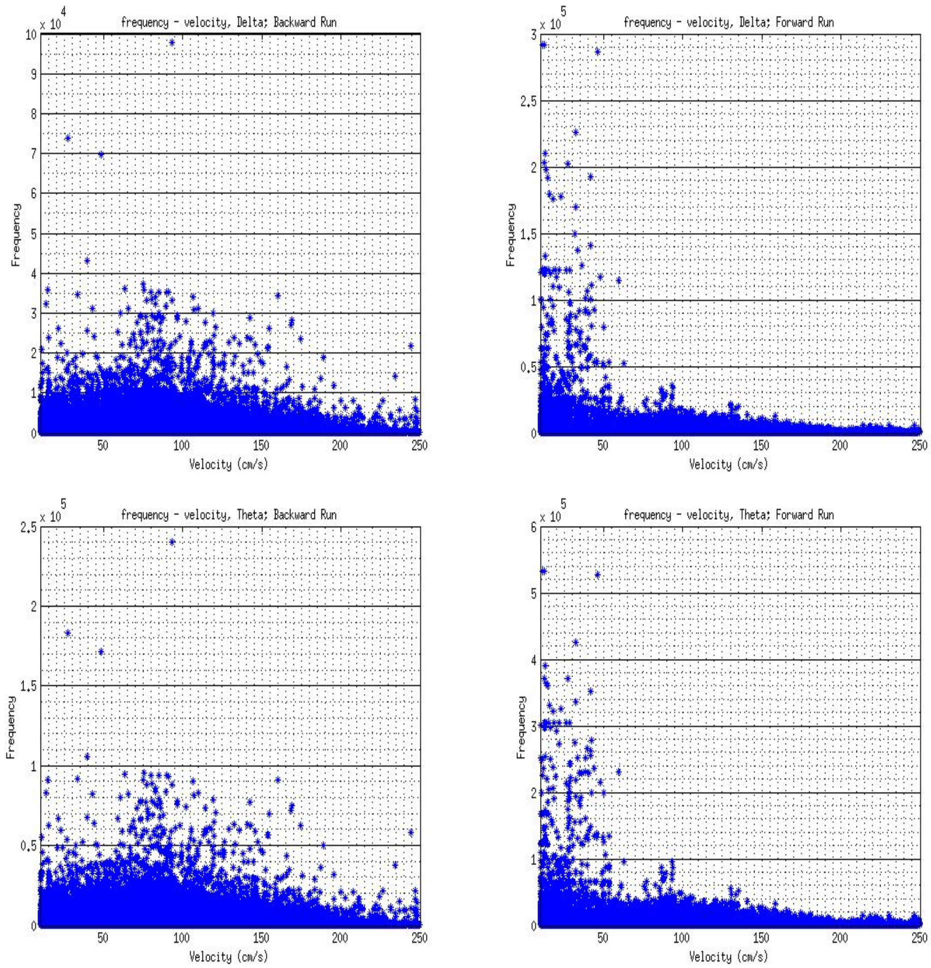


Square Track



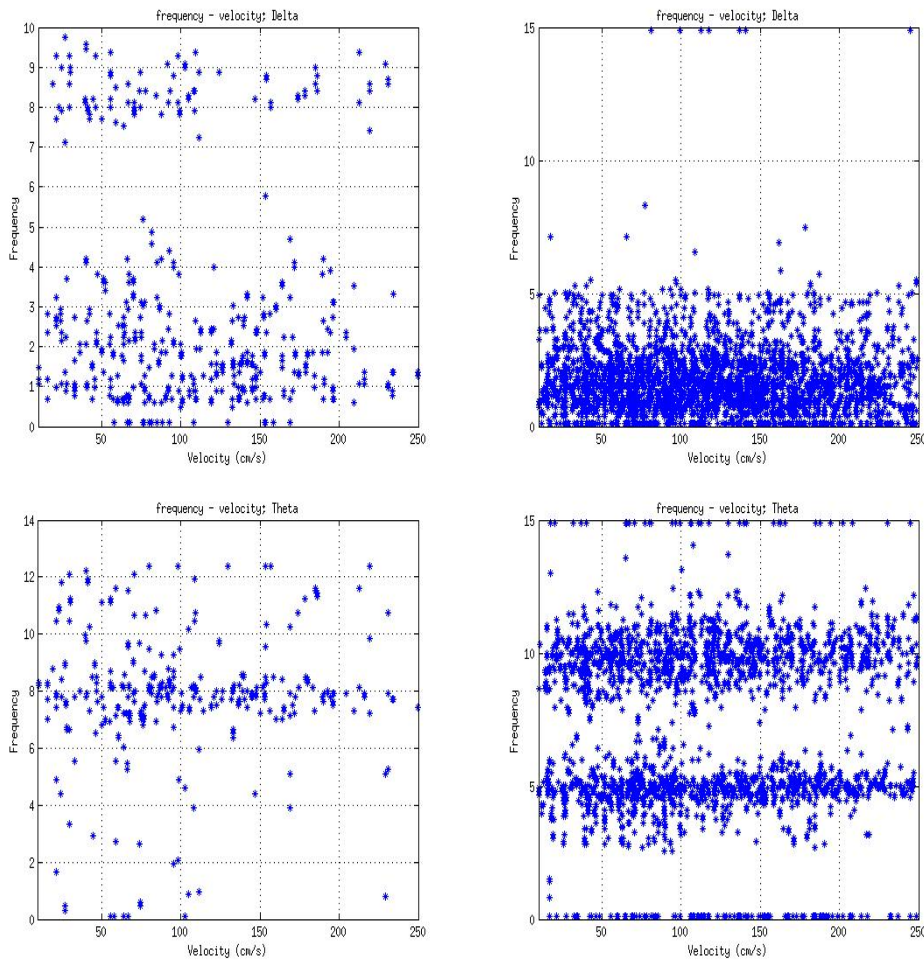


Linear Track

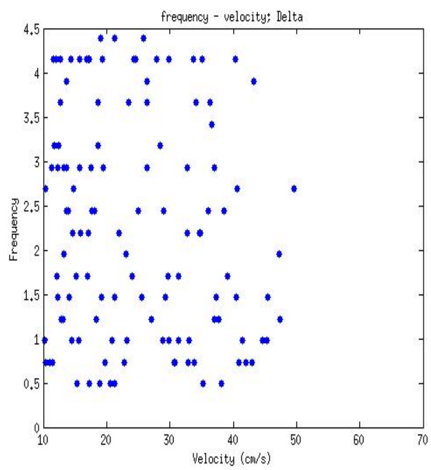


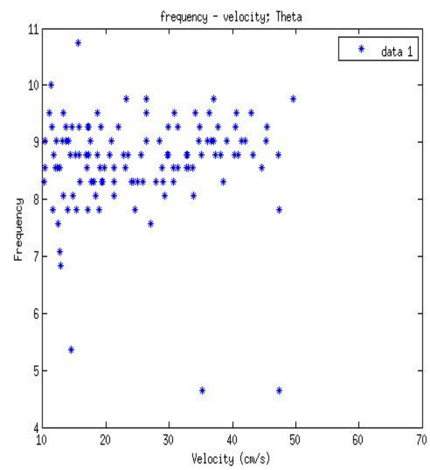
B.2 Frequency

Circular Track



Square Enclosure





Linear Track