Neural Response Analysis for Brain-Machine Interfaces

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***Abstract*—Neurological disorders such as Alzheimers and Parkinsons diseases are associated with malfunctioning neurons, and neuronal signaling and communication pathways. Restoring the neuronal function is considered one of the important areas of research to understand the brain and to develop treatment methods. Neurons that fire above their baseline levels when the head points in a specific direction are called head direction (HD) cells. Knowledge about the connection between the motor function and the HD cells can lead to a potentially efficient method of controlling neurons with brain-machine interfaces. In this study, we explore the possibility of using an existing neuronal model to describe the stimuli and responses of HD cells by comparing outputs of the computational model with recordings available through a dataset. For this, we use the computationally simple Izhikevich neuron model. The method used is flexible and can easily be adapted to other models as well as other types of spike metrics. The obtained results yield inconclusive inferences but do not exclude the possibility of other computational neuronal models being able to describe the behavior of the neurons with the proposed method. Further research is needed if the proposed method with some modifications can be applied using a complete waveform for the Izhikevich model.**

***Index Terms*—Head direction cells, Neurons, Computational models, Brain-machine interfaces.**

I. Introduction

Theoretical analysis and computational modeling are tools used to get a better understanding of the nervous system an understanding which hopefully shortens the path to helping people with disabilities and various problems. The knowledge of how different cells function and communicate could very well ease the process of finding treatments, cures, and ways to prevent the same problems from happening in the future.

Loss of normal nerve function can be a result of multiple traumatic injuries, and the prognosis after such injuries can be quite poor [1]. Neural Prostheses (NPs) [2] are external or implanted devices with the goal of restoring functions such as bladder control [3], limb movement [4], and memory [5]. A primary objective in developing NPs is to replace neurons in the brain that no longer function appropriately. NPs thus require artificial reconstruction of neural synaptic connections. Brain-Machine Interfaces (BMIs) are also external or implanted devices with the goal of delivering physical stimuli to the sensory organs [6], muscles [7], or disparate cortical areas in the nervous system [8]. The success of the BMIs depends on understanding the principles of neural signal processing, wiring, and communication.

The aim of this study is to understand and explain how neural cells function and communicate by exploring the possibilities of identifying a computational model describing their discharging. In particular, we select Head Direction (HD) cells that assist with spatial orientation due to the availability of real datasets [9]. The ideal feasible solution is a model capable of describing all HD cells from the dataset, taking the individual properties of each HD cell into consideration. The unknown and innumerable possible uses for such a model makes this highly motivating work.

The ultimate idea presented in this paper is to exploit new knowledge about HD cells. HD cells can be found in several areas of the brain, including the postsubiculum [10], which plays an integral part in several neurological diseases such as Alzheimer's disease and epilepsy [11]; diseases that pose a substantial burden of disease worldwide [12]. Hence, a better understanding of how HD cells in these areas function give insight on how to cure associated diseases. Moreover, the knowledge of how HD cells function may provide general insight on how to replicate the approach presented and control functions of other cortical cells, which in turn may be used for applications in BMIs.

II. Theory

A. Head Direction Cells

HD cells are neurons in the brain that discharge, or fire, with a rate dependent on the direction of the individual's head in the horizontal plane. They have been identified in mice [10], rats [13] and monkeys [14], but are thought to be present in all mammals [10].

There are three main properties of HD cells: the peak firing rate, the preferred firing direction (PFD), and the directional firing range [15]. A cell's peak firing rate is the maximum firing rate of the cell, which occurs when the head is in the PFD of the cell. The directional firing range is the angular range where the firing rate is above the baseline firing rate. In terms of the PFDs, all directions are represented equally in the total population of HD cells [10]. Fig. 1 is an example of a tuning curve of an HD cell. Here, the direction of the head is represented by the x-axis, while the y-axis represents the firing rate in spikes per time unit. The firing rate of the cell is zero, or almost zero for angles far away from the PFD, but increases quickly when the head direction is turning towards the cell's PFD. The directional firing range varies from cell

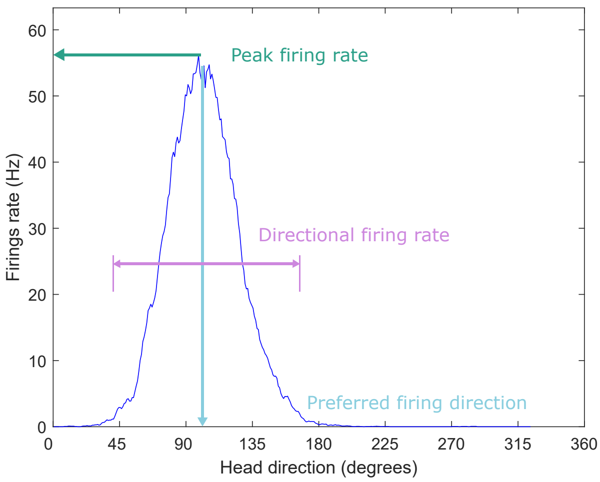

Fig. 1: Tuning curve of HD cell.

to cell, from around 60° to 150°, but with an average around 90°. The peak firing rate also varies from cell to cell, usually from 5 to >120 spikes per second. [10].

The response of the HD cells is constant even when the head is not moving, which indicates that HD cells are independent of motion input [15]. The firings of HD cells depend on landmarks and self-motion cues like the vestibular system and motor/proprioceptive information [10]. The HD cells are therefore considered a part of the allocentric system together with grid cells and place cells [16], which help with spatial orientation [10].

B. Dataset

The dataset used consists of neural recordings of mice searching for feed for 35-40 minutes in a closed environment, both preceded and followed by two hours of sleep. The complete dataset consists of 1077 neurons of different types, obtained through 42 recordings. The dataset includes times and waveforms of detected action potentials/spikes and the result of spike sorting. The head coordinates and directions are also included in the dataset, which are extracted from video files. Detailed description is provided in [9].

III. Methods

A. MATLAB Code Detecting HD Cells

The identification of HD cells is done with a MATLAB code smoothing the data with a Gaussian kernel and fitting with von Mises distribution, before calculating a concentration parameter and the peak firing rate. The inclusion criteria for HD cells are given as follows:

- Concentration parameter >1,
- Peak firing rate >1,
- Probability of non-uniform distribution <0.001.

B. Dividing Firings Into Sessions

Since the neurons' responses are dependent on the direction of the head, the recordings are divided into different "sessions" in order to compare the responses considering the continuous head movement. Each such session includes the firings of a specific HD cell when the mouse held its head inside a specific angle bin. If the mouse moved its head in a direction outside this angle bin, before moving it back again, these two instances are defined as two separate sessions.

C. Comparing Sessions

By comparing the different sessions for one HD cell, it is possible to see if the sessions follow the same pattern. A pattern emerging from this comparison enables identification of the coding used. Intuitively, it should be possible to extract a characteristic pattern from the sessions if the neuron follows the firings of a "typical" HD cell since the firings are mostly dependent on the direction of the head.

Sessions within an angle bin and between angle bins are compared to see if there are any correlations. This is done by using the Victor-Purpura metric with different values of the cost, q. The Victor-Purpura distance is a cost-based metric used to quantify the similarities, or dissimilarities between two spike-trains [17; 18]. When using this metric, the sessions should be of approximately the same length.

D. Model

Being able to describe the behavior of HD cells with one or several models, makes it possible to reproduce the responses of the HD cells for different stimuli, or find the stimulus applied to get a specific response. This might then lead to efficient artificial control of HD cells.

The three main properties of the HD cells must be taken into consideration when establishing a model describing the firings of HD cells: the PFD, the directional firing range, and the peak firing rate. Due to the variations of these variables between cells, it is not possible to create a generic model describing the firings of all the cells. It should also be tested whether or not these variables are independent. For example, if HD cells with large peak firing rates also have large directional firing ranges, these types of relations should be included in the model.

Finding a Model: The Izhikevich model for modeling large-scale networks is used [19]. The MATLAB script is modified to return the spiking times and take the duration of the simulation as an input parameter. The duration of the simulation is set to the duration of the session which it is going to be compared.

The model includes several elements of randomness to mimic that the different cells in the network have different dynamics, that the different synaptic connections between the neurons have different weights, and that the input varies. The first two factors are not relevant when it comes to the modeling of one neuron. The randomness of the input is removed to see if it is possible to find a model with a predefined input.

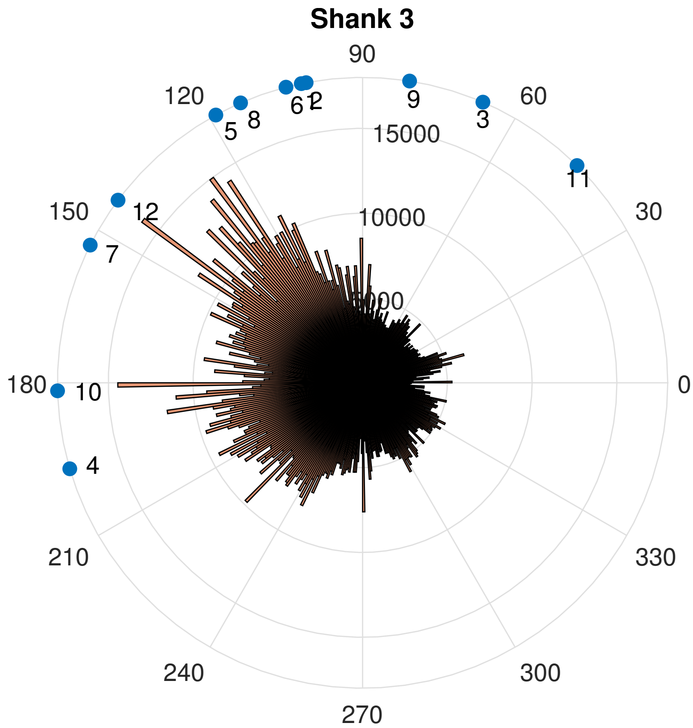

Fig. 2: The length of the bars represent time [ms] spent with head in direction, while the PFDs of the HD cells are represented by.

Some possible values of the model parameters, making the model exhibit the same properties as known cortical neurons, are provided [19]. Different combinations of parameter values are looped through, and the Victor-Purpura distance is found for each combination. The parameter values that yield the lowest distance are kept. Since different cost values yield different models, different values are tested since there are some uncertainties about the optimal value of this cost.

IV. Results

A. Delimitations

For practical reasons, the recordings from Mouse12-120806 are selected, and from this dataset, shank 3 is preferred due to the large number of HD cells. Out of 13 cells found, 12 are identified as HD cells. HD cell 8 is chosen for further inspection.

B. Initial Analysis

Head Directions Represented: The PFDs are provided from the MATLAB code. In Fig. 2, these values are plotted together with the head directions of the mouse during the wake period with an angle bin width of one degree. The figure indicates that the mouse held its head more in the directions between 100° and 240°. This, however, does not describe the continuous duration of the head in a particular direction. As Fig. 2 also shows, the PFDs do not always correspond to the time spent with the head in each direction. This means that the amount of data well suited for analysis is sub-optimal.

TABLE I: Directional firing range and peak firing rate found by visual inspection.

HD cell	Directional firing range	Peak firing rate [spikes/sec]
1	90°	3
2	100°	3.5
3	90°	55
4	120°	25
5	120°	35
6	100°	45
7	150°	15
8	110°	60
9	100°	16
10	100°	14
11	90°	5
12	90°	9

TABLE II: Number of extracted sessions.

Angle bin width	#spikes/session	#sessions
5°	10	168
5°	15	23
5°	20	3
10°	10	1016
10°	15	263
10°	20	74

Visual Inspection: Both the peak firing rate and directional firing range of the twelve HD cells are found by visual inspection, and the results are given in Table I. The peak firing rates varies between 3 and 60 spikes/second, and the directional firing range ranges between 90° and 150°.

C. Dividing Firings Into Sessions

The results from the extraction of sessions can be seen in Table II. Here, the number of sessions found are given for an angle bin width of 5° or 10°, and the minimum amount of spikes is set to 10, 15 or 20. From these alternatives, the 5° angle bin and 10 spikes is chosen for further inspection. This ensures a narrow angle bin and several sessions for data retrieval.

D. Comparing Sessions

Visual Inspection: After shifting the sessions, so they all start at time $t = 0$, it is possible to plot them on top of each other in the same graph to get an indication on whether or not they are similar. An example is shown in Fig. 3.

Mean Firing Rate: The mean firing rate is found per session. The averages over these sessions are then calculated. The results are given in Table III together with the standard deviations (SDs).

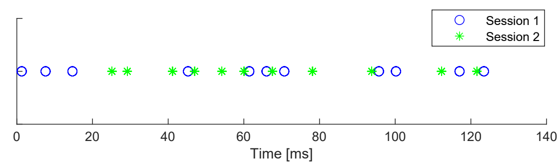

Fig. 3: Comparison of two same-length sessions from angle bin 115°-119°.

TABLE III: Mean firing rate and SD for angle bins of 5° and 10 spikes or more.

Angle bin	#sessions	Mean	SD
85°-89°	2	48.88	11.80
90°-94°	5	59.88	17.72
95°-99°	5	72.31	16.78
100°-104°	7	55.35	10.61
105°-109°	4	94.49	34.71
110°-114°	4	93.69	25.02
115°-119°	11	75.71	27.03
120°-124°	7	67.00	18.76
125°-129°	6	89.14	39.31
130°-134°	3	64.18	12.48
135°-139°	6	69.53	24.86
140°-144°	2	82.24	21.45

TABLE IV: Comparion of sessions.

Same/different	q = 0.07	q = 0.136	q = 1
Same	2.28	**9.60**	20.25
Different	1.66	10.44	20
Different	**1.58**	11.24	**18.05**
Different	1.75	11.05	20.25
Same	1.54	**8.16**	20.50
Same	0.84	10.23	20.45
Different	2.47	10.26	19.45
Different	**0.62**	8.86	**18.10**
Same	2.62	10.22	**18.84**
Different	2.46	**9.84**	21.45
Different	2.84	12.39	20.65
Different	**0.89**	10.92	19.45

Victor-Purpura Distance: Some of the results are given in Table IV. The compared sessions have a maximum differentiation of 5 ms in length. Three sets of session lengths have been chosen, separated by the horizontal lines. The first column depicts if the compared sessions are from within the same angle bin, and the rest are the Victor-Purpura distances for the given costs. The boldface results contain the shortest Victor-Purpura distance for the given cost q.

E. Finding a Model

Table V shows the optimal parameter values for the first three sessions $S1$, $S2$ and $S3$ for three different values of q. The value 0.136 is the average distance between spikes, while the values q = 0.07 and q = 1 are used for comparison. Table VI shows the Victor-Purpura distances for the three sessions in Table V when using the optimal values for q = 0.136 given in the same table. The bold-faced numbers are the distances for the sessions which optimized values are used. When plotting the session and the model with parameter values found as optimal for the given session, visual inspections reveal that even with a low distance, the session and model do not correspond well.

TABLE V: Optimal model parameter values.

	a	b	c	d	I	Distance
q = 0.07						
$S1$	0.08	0.24	-60	0.95	14	0.77
$S2$	0.07	0.21	-65	0.20	12	1.53
$S3$	0.06	0.20	-50	4.00	12	1.51
q = 0.136						
$S1$	0.08	0.24	-60	0.95	14	1.50
$S2$	0.05	0.25	-60	1.45	13	2.86
$S3$	0.06	0.20	-50	4.00	12	2.93
q = 1						
$S1$	0.09	0.25	-65	1.25	7	5.55
$S2$	0.10	0.21	-65	2.30	5	8.60
$S3$	0.04	0.20	-50	5.40	6	7.45

TABLE VI: Victor-Purpura distance for different optimal model parameter values for q = 0.136.

Session	Distance[a]	Distance[b]	Distance[c]
$S1$	**1.50**	3.18	5.33
$S2$	7.22	**2.86**	8.48
$S3$	8.85	7.60	**2.93**

[a] $\boldsymbol{a}$ = 0.08, $\boldsymbol{b}$ = 0.24, $\boldsymbol{c}$ = -60, $\boldsymbol{d}$ = 0.95, $\boldsymbol{I}$ = 14.
[b] $\boldsymbol{a}$ = 0.05, $\boldsymbol{b}$ = 0.25, $\boldsymbol{c}$ = -60, $\boldsymbol{d}$ = 1.45, $\boldsymbol{I}$ = 13.
[c] $\boldsymbol{a}$ = 0.06, $\boldsymbol{b}$ = 0.20, $\boldsymbol{c}$ = -50, $\boldsymbol{d}$ = 4.00, $\boldsymbol{I}$ = 12.

V. Discussion

A. Directional Firing Range and Peak Firing Rate

The directional firing range and the peak firing rate of the HD cells found in Table I are consistent with the literature. The directional firing range is similar to the published literature discussed in Section II-A, while the peak firing rate is a bit lower for two of the HD cells, with a firing rate below 5.

The exact values given in the results should, however, be interpreted with caution. The directional firing range and peak firing rate are only estimated from a visual inspection of the tuning curves. This is determined to be accurate enough for the simple initial analysis conducted. For a more thorough analysis, more accurate values should be used. One method for finding these values could be to estimate a fitted curve and then calculate the directional firing range and peak firing rate from this.

B. Dividing Firings Into Sessions

As described in Section III-B and IV-C, sessions within angle bins of 5° are extracted, and the sessions with less than 10 consecutive spikes are omitted.

With a lower number of minimum spikes per session, fewer sessions are omitted, but a certain number of spikes is also needed in order to compare the sessions accurately and be able to find patterns. A high number of minimum spikes per session makes it harder to analyze all of the HD cells the same way, since some of the HD cells have a low peak firing rate, and with narrow angle bins, the length of the sessions may be too short for a comparable amount of spikes to occur. The HD cells that suffer the most from this filtering are the ones with the lowest firing rates. This is because HD cells with low peak firing rates require the mouse to hold its head inside the same angle bin for a more extended amount of time to obtain a sufficient number of spikes for analysis.

While wide angle bins yield a more significant number of sessions, there are several downsides by choosing wide angle bins. The firing frequency changes with each angle, and by using a wide angle bin, the firings included fire with different rates. A possible pattern found will thus originate from several different angles with different average firing rate. Another problem is that it is not known how the head movements are inside the bin. With a narrow angle bin, the main problem is the lack of data.

C. Comparing Sessions

Visual Inspection: This method can give some indication of whether or not two sessions are similar, but it is not feasible for comparing larger sessions.

Mean Firing Rate: As can be seen from the SDs in Table III, there are large variations in the firing frequency for some of the sessions. Large angle bins yield larger values for the SDs. While narrowing the angle bins would decrease the SD, it would also give fewer spikes in each session. Increasing the angle bin also increases variations in the firing rate. The chosen part of the dataset does not provide enough data for testing with smaller angle bins as the number of firings per angle bin is too low. Large SDs, especially with smaller angle bins, are a good indication that HD cells communicate with a different coding scheme than only rate coding.

Victor-Purpura Distance: As shown in Table IV, it is not possible to say whether or not two sessions are from the same or different angle bins based on the Victor-Purpura distance alone.

One reason for the lack of similarity could be the size of the angle bins. Furthermore, the neural code used may differ too much for the different directions inside the angle bin. The sessions found to consist of an unknown number of codes with different features, in an unknown order. If these features differ too much, the task of finding a model is more complicated especially when generalizing the model for one HD cell, not only one session or angle bin.

D. Finding a Model

As shown in Table V and VI, the model parameter values that yield the shortest distance for one session are not the same as for another session from within the same angle bin, and the model parameter values that yield the shortest distance for one session give larger distances for other sessions in the same angle bin. The optimal choice of parameter values for one session are not the most optimal ones for the rest of the sessions.

Either, the lowest possible Victor-Purpura distance does not give the most optimal model, or, the Izhikevich model is not a suitable model to use for these types of spike sequences.

VI. Conclusion and Future Work

In order to develop a functioning NP that replaces the function of a neuron, a model able to reproduce response from given stimuli is needed. The results yield no definitive conclusion but do not exclude the possibility of other methods or metrics being able to describe the behavior of the neurons with such a model. Alternatively, other models can be tried with the same method to see if they yield any better results. The main issue was achieving valid comparisons of the spike-trains. A more extensive dataset along with other metrics should be tested to see if they yield more definite results.

For future work, a natural place to start is looking at the other days of recordings in the dataset. This will be to see if some of them include a larger set of usable data for the method explored. If the same approach is taken, sessions are extracted before a comparison of each HD cell to find a possible common pattern. However, a different comparison metric should be used to take advantage of the differences in session size, rather than being limited by it.

If no pattern is found when comparing sessions, other approaches should be considered. This can be done by disregarding sessions, or by using other ways than spike-trains for describing the sessions. The complete dataset from [9] includes spike waveforms, which may be used.

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