Exploring extracellular electrophysiology data

The goal is to analyze extracellular electrophysiology data acquired in a delayed-response task. This set of exercises is for Matlab and modified from what was prepared by Ziqiang Wei, Hidehiko Inagaki, and Karel Svoboda for the JHU coding bootcamp.

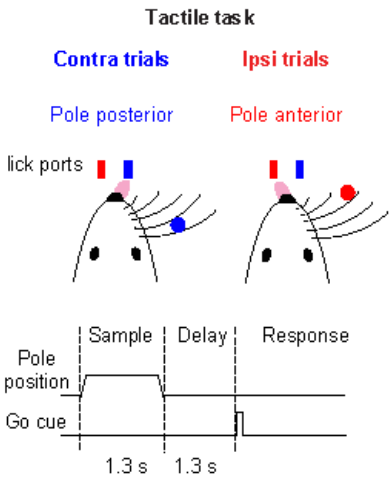
- See "Dataset description" for the structure of the data, including behavior and electrophysiology.
- See "Tutorial" about the analyses to be performed.
- Access: https://github.com/hidehikoinagaki/IMPRS_ephys_course2022/ for files.

Dataset Description

Task description

The data set was acquired in mice performing a "tactile delayed response task". Recordings were made in the premotor cortex using 64ch silicon probes (for more information, see ref: Guo, Z, Li, N et al. 2014 Neuron; Li, N, Daie, K et al. 2016 Nature).

- An object was presented to the whiskers during a "sample epoch". The object location instructs the direction to move (lick left or right). Because recordings were made in the left hemisphere, left and right are referred to as ipsi and contra directions.
- The sample epoch was followed by a "delay epoch", during which the mouse had to maintain a memory of future licking direction.
- At the end of the delay epoch, and the beginning of a "response epoch", a brief "go cue" (100ms) instructs the animal to move.
- When the animal licks in the correct direction, it receives a water reward (correct trials). Licking in the wrong direction results in reward omission (error trials).
- Neurons in the premotor cortex show preparatory activity during the delay epoch. Preparatory activity is the neural correlate of motor planning. Preparatory activity correlates with movements, sometimes long before the movements occur. Let's analyze preparatory activity both at the single neuron and population level.



Task structure

- Pre-sample : -3.1 to -2.6 sec.
- * Sample : -2.6 to -1.3 sec.
- * Delay : -1.3 to 0.0 sec.
- * Response : 0.0 to 2.0 sec.

Data structure

The data is from 3 recording sessions. Each session contains hundreds of behavioral trials with different trial types. Multiple units (neurons) were recorded simultaneously. We did not provide the raw extracellular waveforms, but only 'sorted' spikes. The process (some would say dark art) of 'spike sorting' is beyond the scope of this tutorial.

- Spikes are stored in a structure array named **ephysDataset**. The data set has 125 units, each with its own structure.
- sessionIndex: index of the session in which each neuron was recorded. For example, the first 26 units all derive from session 1.
- nUnit: index of the neuron(unit) in each recording session. nUnit for the first 26 units runs from 1-26, and then resets to 1 for the first unity of session 2, etc.
- depth_in_um: recording depth of the unit in um. We don't use this info here.
- cell_type : putative pyramidal cells -- 1; fast-spiking interneurons: 0.
- st_right: time of each spike in correct right-lick trials (sec).
- st_left: time of each spike in correct left-lick trials (sec).

- st_right_error: time of each spike in error right-lick trials (unit in sec).
- st_left_error: time of each spike in error left-lick trials (unit in sec).

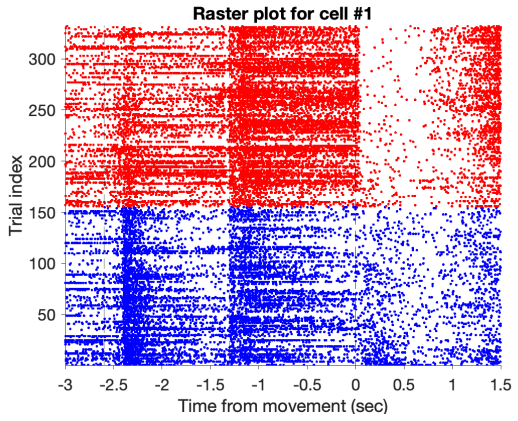
Tutorial

Load data file

```
load('ephysDataset.mat')
```

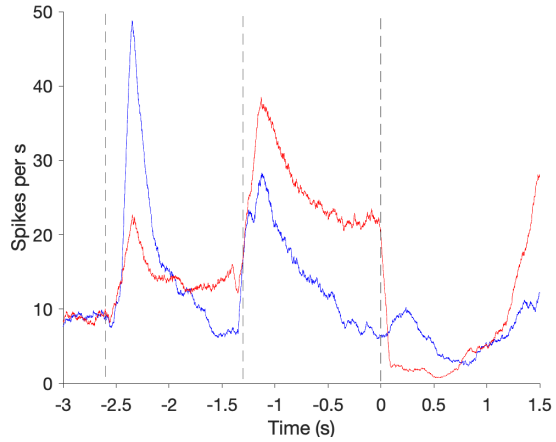
Single cell analysis

1) Access the data and plot raster plots
   - Plot spikes in all correct right and left trials. Trials are arrayed in the vertical dimension, time in the horizontal dimension
   - See example code (plot_raster.m). It shows how to access the data.

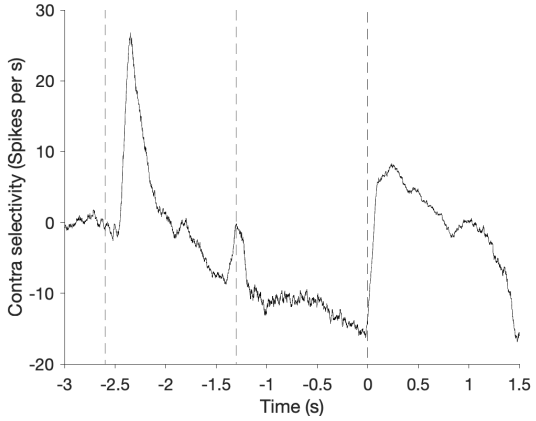


2) Plot mean spike rate for different trial types

- Spiking is a point process: need to average many trials to infer “spike rate” (spikes per sec)
- Plot mean peri-stimulus histogram (PSTH): estimate average spike rates for different trial types; plot correct lick right trial in blue and correct lick left trial in red
- Tips: use 1ms bin between -3.5s to 2s (tAxis = -3.5:0.001:2). And calculate mean spike rate per bin. Hist function in Matlab is useful for this.



3) Compute and plot selectivity
   - Selectivity is a difference in neural activity between behavioral conditions such as sensory stimuli, trial types, or movement, i.e., how a neuron encodes information.
   - Here, selectivity is defined as the spike rate difference between correct lick right and left trial types



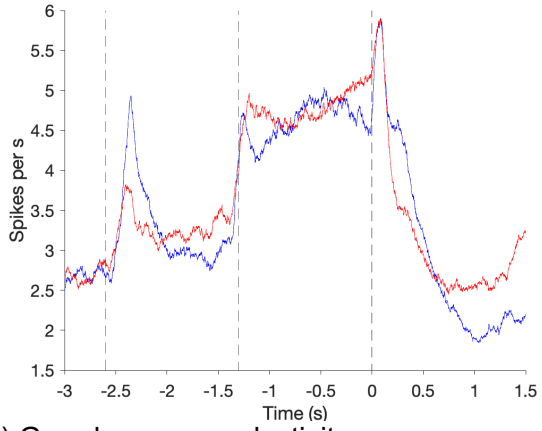
4) Error trial analysis — is an activity similar to or different from correct trials? What does it mean?
   - Run analyses above using error trials.

<u>Population analysis (based on data from the same session)</u>

- Only analyze the regular spiking cells (putative pyramidal cells; SpikeWidth > 0.5ms) within the session as fast spiking cells (putative GABAergic neurons) show different properties.

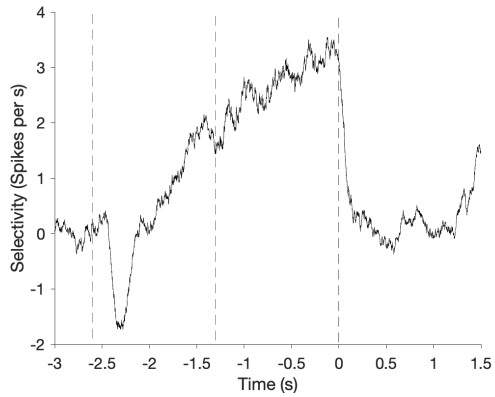
5) Plot grand average PSTH
   - Tips: Use the “for” loop to compute the mean spike rate for correct trials in lick-right and left conditions for each cell

- Tips: average across cells in each condition



6) Grand average selectivity

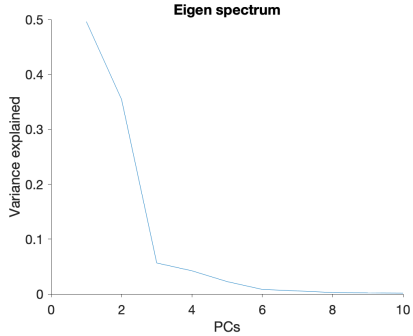
- Tips: Some cells are contra selective, and others are ipsi selective. If you simply average them, they will cancel out. Flip selectivity if it is negative during the delay epoch.



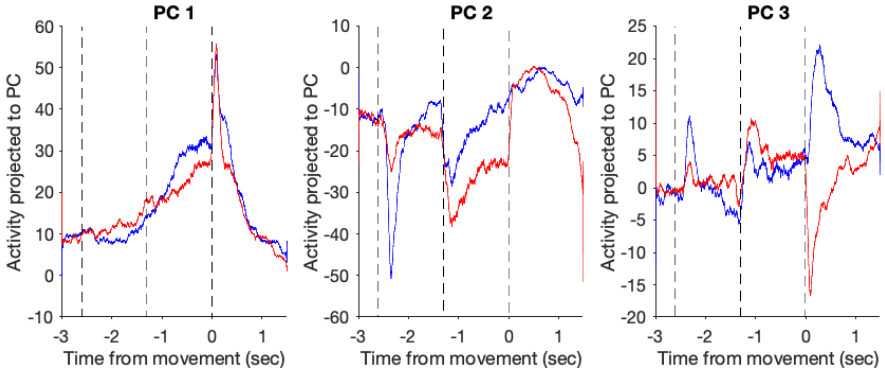
Dimensionality reduction

7) Perform PCA

- See “PCA_tutorial.m” to learn how to perform PCA for time series data
- Then analyze the data in **ephysDataset**
- Average Lick-right and -left trials to perform PCA (i.e., PCA of average activity)
- Plot the eigen spectrum



- Explore neural activity projected to the first 3 PCs
- Tips: to cross validate & avoid overfitting, randomly select half of the trials to estimate modes and use the rest to project data onto these modes, respectively



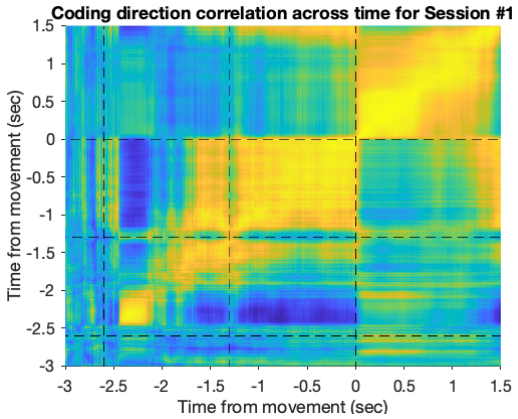
8) Analyze the Coding direction (CD)

- CD is the direction in activity space where trial types can best be discriminated
- We will use the simplest definition:

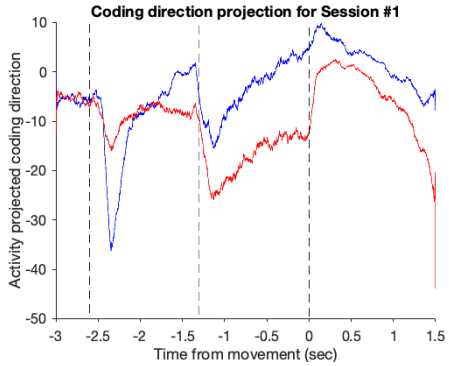
  sr_R(i)-sr_L(i)

  where sr_R is the spike rate in lick-right trials, sr_L is the spike rate in lick-left trials, and i is the cell index.

- Calculate this vector for each time point, then normalize (divide by norm) to produce a unit vector.
- Explore correlation of coding direction across time



- Explore neural activity projected to the coding direction
- To project population activity to CD, calculate inner dot: sr_R * CD.



- Plot what fraction of selectivity is explained by CD (“square of selectivity along CD” divided by “squared sum of selectivity of all units”)