2019-08-14-pfeiffer-1d-non-oriented-vs-oriented-axonal-trees

August 22, 2019

```
In [1]: # %load imports.py
        %load_ext autoreload
        %autoreload 2
```

1 A 1d analog of polar interneurons

The analogue of a spherical axon in 1dim is a connectivity within a certain radius r of the interneuron somata. Correspondingly, the analogue of an ellipsoid, that is of an orientation, is a connectivity that has an asymmetry with respect to the somata, that is one branch has length $(1-\lambda)r$ and the other one $(1+\lambda)r$.

The advantage of going to 1d is that from the Rosenbaum 2014 paper (Balanced networks of spiking neurons with spatially dependent recurrent connections), we know that spatial patterns should delevelop in such a network and can then study how this patterns change, when the interneuron axonal morphology changes.

Another advantage is that in 1d, there are clear and simple difference between the two morphologies in terms of connectivity. Namely, the profile of the number of common neighbors between two interneurons versus distance changes when making the axons more oriented. Circular (non-oriented) axons have the highest number of common neighbors and this drops up to zero at $2r$. Oriented axons have a lower number of common neighbors at small distances, but can then share neighbors even distances exceeding $2r$. Moreover, the orientation might induce a directional bias, although the length of this bias will decay very fast when orientations are random.

Steps - connectivity matrix - activity - spatial analysis

1.1 Connectivity matrix

Neurons will be placed on a regular grid on a line from 0 to 1. Possibility of perturbing these positions with some noise of spatial width χ. Then the width of the axonal branch σ has to be chosen and each interneuron gets an ellipsoid index $e \in [-1, 1]$. For the start, we will assume that e is the same for each interneuron, only changes sign in a random fashion. This gives the inhibtory to excitatory connectivity. In the following, we assume **periodic boundary** conditions.

```
In [2]: import numpy as np
```

```
In [3]: def connect_interneurons_to_excitatory_neurons(in_positions, ex_positions, ellipsoid_i
            N_e = ex_positions.shape[0]

            sigmas_repeated = np.repeat(np.expand_dims(sigmas, axis=1),N_e, axis=1)
```

```
        ellipsoid_indices_repeated = np.repeat(np.expand_dims(ellipsoid_indices, axis=1),N_
        distance_to_right_end = (1+ellipsoid_indices_repeated)*sigmas_repeated
        distance_to_left_end = (1-ellipsoid_indices_repeated)*sigmas_repeated

        rel_position = np.repeat(np.expand_dims(in_positions, axis=1), N_e, axis=1) - np.re

        connected_via_right_branch = np.logical_or(np.logical_and(rel_position > -distance_
        connected_via_left_branch = np.logical_or(np.logical_and(rel_position < distance_to

        return np.logical_or(connected_via_right_branch, connected_via_left_branch)
```

In [4]:
```
N_e = 1000
N_i = 200
chi_e = 0.0/N_e
chi_i = 0.0/N_i
sigma = 0.1
e = 0.25
```

In [5]:
```
ex_positions = np.linspace(0,1, num=N_e, endpoint=False)+np.random.normal(loc=0, scale=
in_positions = np.linspace(0,1, num=N_i, endpoint=False)+np.random.normal(loc=0, scale=
```

In [6]:
```
ellipsoid_indices = e*np.random.choice([-1,1],N_i) #random
#ellipsoid_indices = e*np.ones((N_i,)) #one-sided

ellipsoid_indices_circ = np.zeros((N_i,))
```

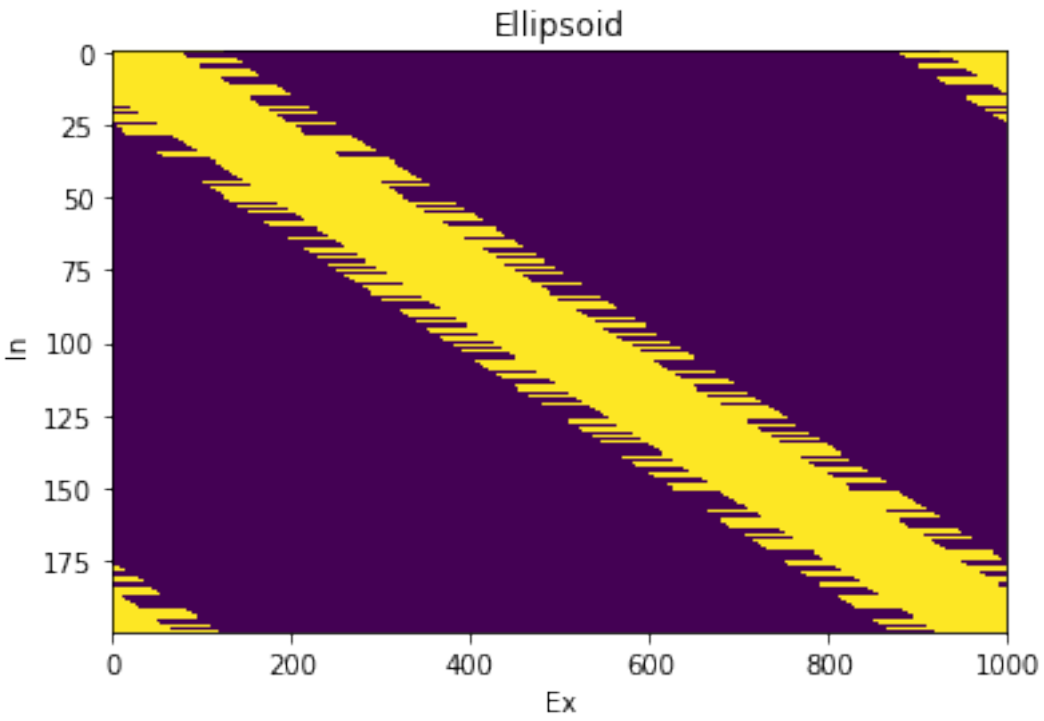
In [7]:
```
sigmas = sigma*np.ones((N_i,))
```

In [8]:
```
in_ex_connectivity_ell = connect_interneurons_to_excitatory_neurons(in_positions, ex_po
in_ex_connectivity_circ = connect_interneurons_to_excitatory_neurons(in_positions, ex_p
```

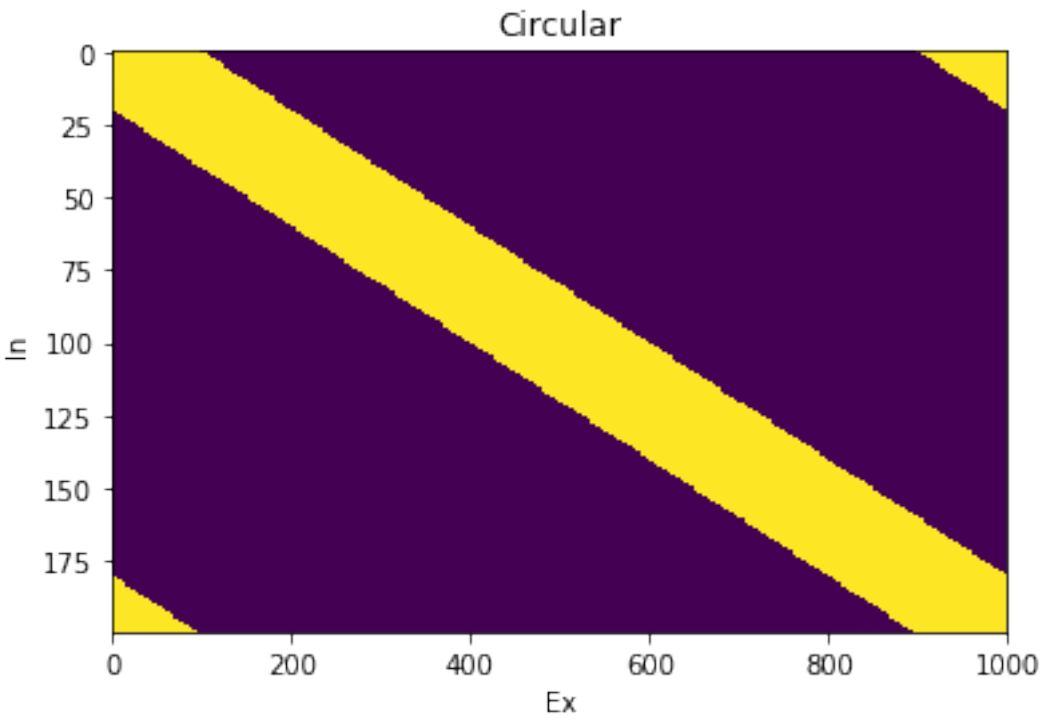
In [9]:
```
import matplotlib.pyplot as plt
```

In [10]:
```
plt.imshow(in_ex_connectivity_ell, aspect='auto')
plt.title('Ellipsoid')
plt.xlabel('Ex')
plt.ylabel('In')
```

Out[10]:
```
Text(0, 0.5, 'In')
```




```
In [11]: plt.imshow(in_ex_connectivity_circ,aspect='auto')
         plt.title('Circular')
         plt.xlabel('Ex')
         plt.ylabel('In')

Out[11]: Text(0, 0.5, 'In')
```



1.2 Network activity

```
In [12]: from brian2.units import *
```

Create the network

```
In [13]: dynamics_dict = {
             "excitatory": {
                "model": "placeholder",
                 "threshold": "v>v_threshold",
                 "reset": "v=v_reset",
                 "refractory": "tau_refractory"

             },
             "ex-in": {
                 "model": "w: volt",
                 "on_pre": "v+=w"
             }
         }

         model_string = """
             dv/dt = 1.0/tau* (-v + u_ext) :volt (unless refractory)
             tau :second
             u_ext : volt
```

```
        v_threshold: volt
        v_reset: volt
        tau_refractory: second
    """

    dynamics_dict["excitatory"]["model"] =model_string
    dynamics_dict.update({"inhibitory":dynamics_dict["excitatory"]})

    dynamics_dict.update({"in-ex": dynamics_dict["ex-in"]})
```

In [14]:
```
experiment_dict = {
  "duration": 10000*ms,
  "excitatory": {
    "tau": 10*ms,
    "v_threshold": -40*mV,
    "v_reset": -75*mV,
    "tau_refractory": 0.0*ms,
    "u_ext": -0*mV
  },
  "inhibitory": {
    "tau": 5*ms,
    "v_threshold": -40*mV,
    "v_reset": -75*mV,
    "tau_refractory": 0.0*ms,
    "u_ext": -35*mV

  },
  "ex-in": {
    "w": 0.4*mV
  },
  "in-ex": {
    "w": -1*mV
  },
  "initial_condition":{
    "excitatory": {
       "v": '-75*mV+35*mV*rand()'
    },
    "inhibitory": {
       "v": '-75*mV+35*mV*rand()'
    }
  }
}
```

In [15]:
```
from interneuron_polarity.actions.simulate_network_activity import create_neuronal_po
import brian2 as br

def run_1d_network(in_ex_connectivity, dynamics_dict, experiment_dict):
    ex_neurons, in_neurons, ie_syn, ei_syn = create_neuronal_populations_and_synapses
```

```
    ex_neurons.v = experiment_dict["initial_condition"]["excitatory"]["v"]
    in_neurons.v = experiment_dict["initial_condition"]["inhibitory"]["v"]

    ex_spike_recorder = br.SpikeMonitor(source=ex_neurons)
    in_spike_recorder = br.SpikeMonitor(source=in_neurons)

    run_experiment(experiment_dict, ex_neurons, in_neurons, ei_syn, ie_syn, [ex_spike

    excitatory_spikes = ex_spike_recorder.spike_trains()
    inhibitory_spikes = in_spike_recorder.spike_trains()

    return excitatory_spikes, inhibitory_spikes
```

```
In [16]: circ_ex, circ_in = run_1d_network(in_ex_connectivity_circ, dynamics_dict, experiment_c

INFO       No numerical integration method specified for group 'neurongroup_1', using method 'e
INFO       No numerical integration method specified for group 'neurongroup', using method 'exa


Starting simulation at t=0. s for a duration of 10. s
9.8141 (98%) simulated in 10s, estimated < 1s remaining.
10.0 (100%) simulated in 10s
```

```
In [17]: ell_ex, ell_in = run_1d_network(in_ex_connectivity_ell, dynamics_dict, experiment_dict

INFO       No numerical integration method specified for group 'neurongroup_2', using method 'e
INFO       No numerical integration method specified for group 'neurongroup_3', using method 'e


Starting simulation at t=0. s for a duration of 10. s
9.6926 (96%) simulated in 10s, estimated < 1s remaining.
10.0 (100%) simulated in 10s
```

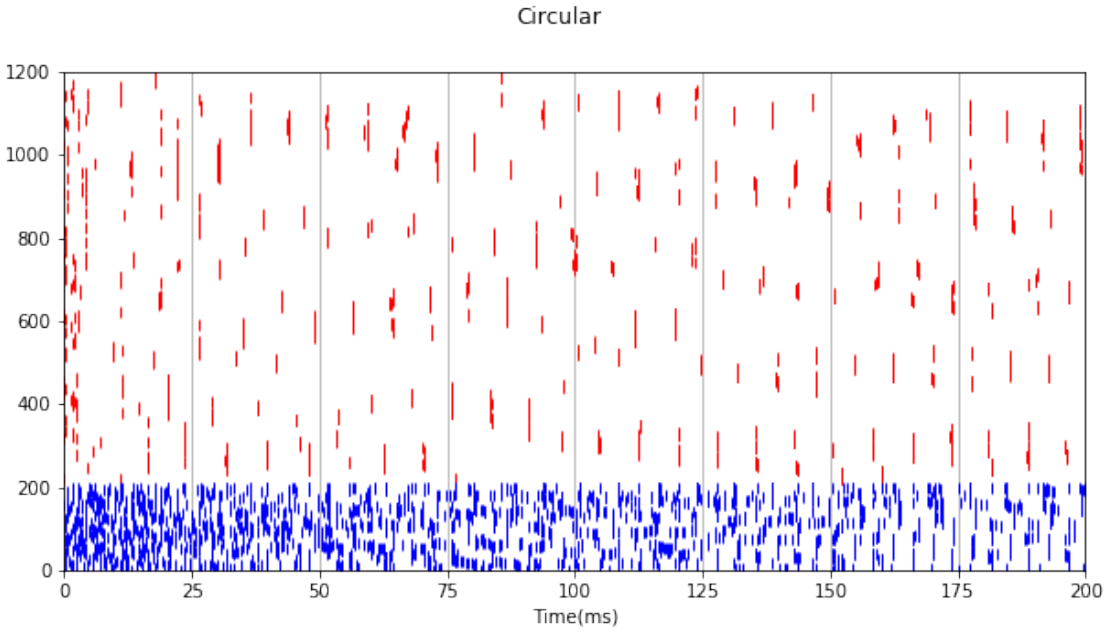
1.3 Analyze activity

1.3.1 Raster plots

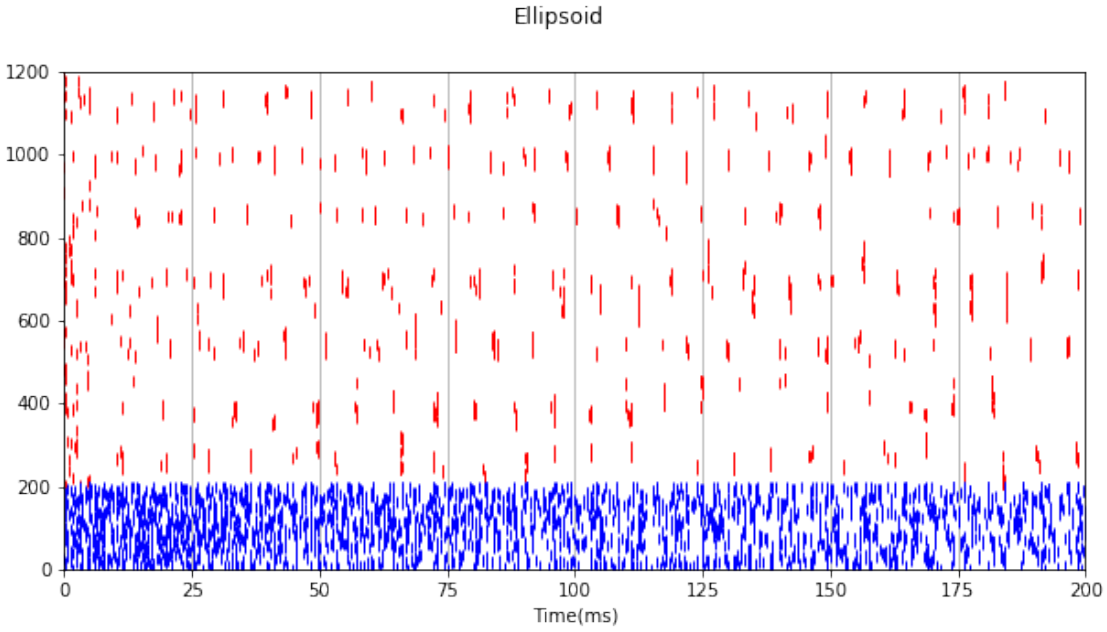
```
In [18]: from interneuron_polarity.actions.plot_network_activity import plot_spiking
```

Early

```
In [19]: fig=plot_spiking(N_e, N_i, circ_ex, circ_in, t_start=0, t_end=200)
         _=fig.suptitle('Circular')
```

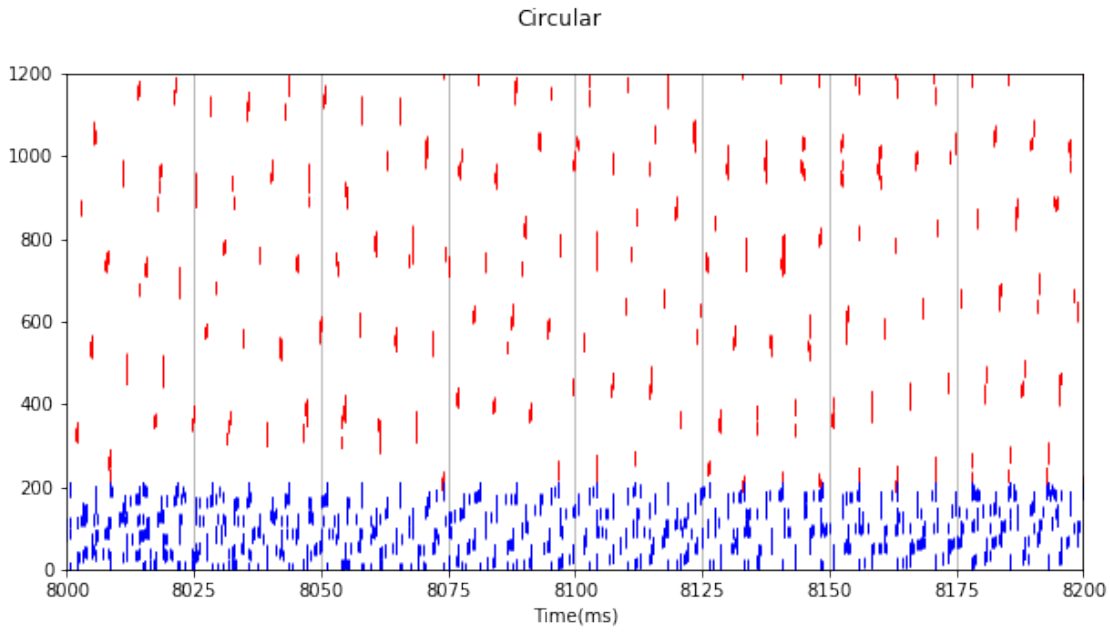


In [20]:
```
fig=plot_spiking(N_e, N_i, ell_ex, ell_in, t_start=0, t_end=200)
_=fig.suptitle('Ellipsoid')
```

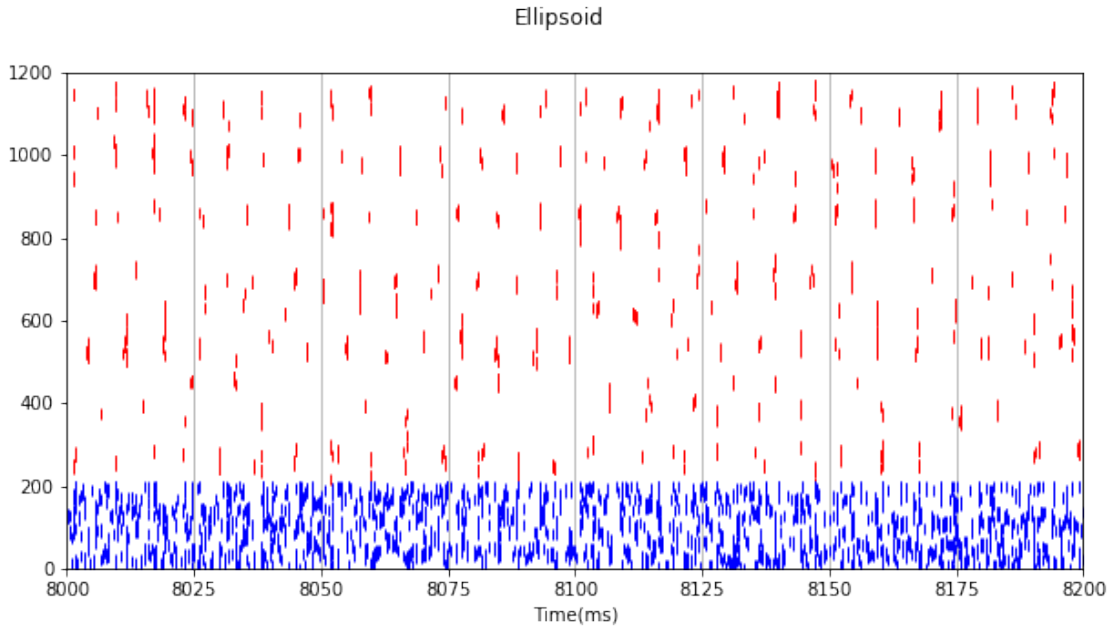


Late

In [21]:
```
fig=plot_spiking(N_e, N_i, circ_ex, circ_in, t_start=8000, t_end=8200)
_=fig.suptitle('Circular')
```



In [22]:
```
fig=plot_spiking(N_e, N_i, ell_ex, ell_in, t_start=8000, t_end=8200)
_=fig.suptitle('Ellipsoid')
```



1.3.2 Rate distribution in space

```
In [23]: from matplotlib.gridspec import GridSpec
```

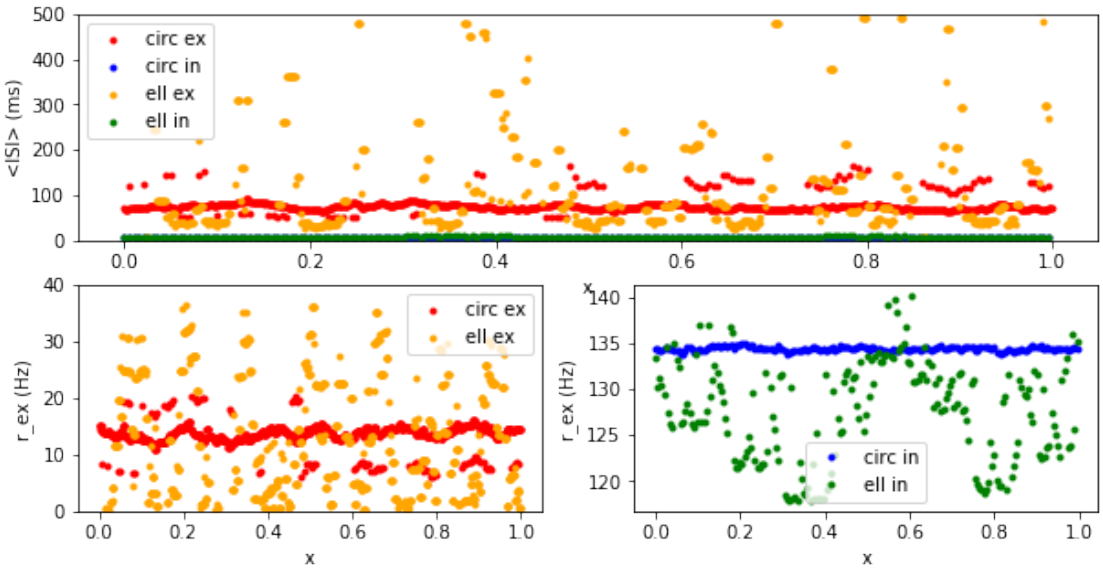
```
In [24]: def isi_to_rate(isi):
             rate = 1.0/isi
             rate[np.where(isi==0)] = 0*hertz
             return rate
```

```
In [25]: fig = plt.figure(figsize=(10,5))

         grid = GridSpec(2,2)
         ax = fig.add_subplot(grid[0,:])
         ax_ex = fig.add_subplot(grid[1,0])
         ax_in = fig.add_subplot(grid[1,1])

         spike_times = circ_ex
         positions = ex_positions
         label='circ ex'
         color='red'


         isis =  [np.ediff1d(spike_times[neuron_idx]) for neuron_idx in sorted(spike_times.keys
         mean_isi =[np.mean(isi) for isi in isis]
         ax.plot(positions, mean_isi/ms, '.', color=color, label=label)
         ax_ex.plot(positions, isi_to_rate(np.array(mean_isi))/hertz,'.', color=color, label=la

         spike_times = circ_in
         positions = in_positions
         label='circ in'
         color='blue'

         isis =  [np.ediff1d(spike_times[neuron_idx]) for neuron_idx in sorted(spike_times.keys
         mean_isi =[np.mean(isi) for isi in isis]
         ax.plot(positions, mean_isi/ms, '.', color=color, label=label)
         ax_in.plot(positions, isi_to_rate(np.array(mean_isi))/hertz,'.', color=color, label=la


         spike_times = ell_ex
         positions = ex_positions
         label='ell ex'
         color='orange'

         isis =  [np.ediff1d(spike_times[neuron_idx]) for neuron_idx in sorted(spike_times.keys
         mean_isi =[np.mean(isi) for isi in isis]
         ax.plot(positions, mean_isi/ms, '.', color=color, label=label)
         ax_ex.plot(positions, isi_to_rate(np.array(mean_isi))/hertz,'.', color=color, label=la
```

```
        spike_times = ell_in
        positions = in_positions
        label='ell in'
        color='green'

        isis =  [np.ediff1d(spike_times[neuron_idx]) for neuron_idx in sorted(spike_times.keys
        mean_isi =[np.mean(isi) for isi in isis]
        ax.plot(positions, mean_isi/ms, '.', color=color, label=label)
        ax_in.plot(positions, isi_to_rate(np.array(mean_isi))/hertz,'.', color=color, label=la


        ax_ex.set_xlabel('x')
        ax_ex.set_ylabel('r_ex (Hz)')
        ax_ex.legend()
        ax_ex.set_ylim(0,40)
        ax_in.set_xlabel('x')
        ax_in.set_ylabel('r_ex (Hz)')
        ax_in.legend()


        ax.legend()
        ax.set_xlabel('x')
        ax.set_ylabel('<ISI> (ms)')

        ax.set_ylim(0,500)
```

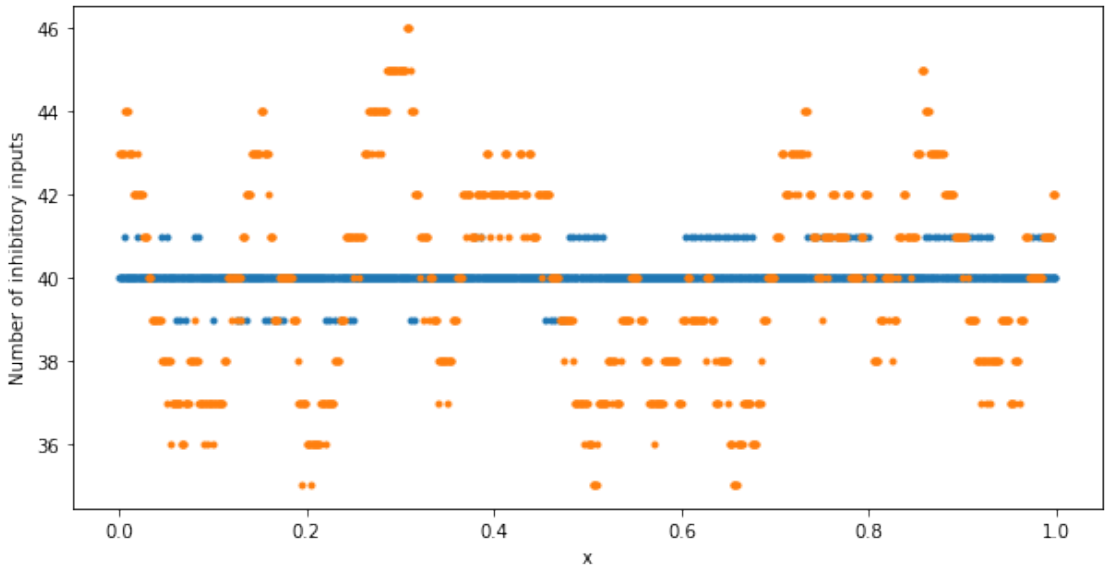
```
WARNING    /home/pfeiffer/Applications/miniconda2/envs/head_direction/lib/python3.7/site-packag
  return Quantity(func(np.array(x, copy=False), *args, **kwds), dim=x.dim)
 [py.warnings]
WARNING    /home/pfeiffer/Applications/miniconda2/envs/head_direction/lib/python3.7/site-packag
  ret = ret.dtype.type(ret / rcount)
 [py.warnings]
```

```
Out[25]: (0, 500)
```



Distribution of inhibitory input in space The ellipsoid axons generate a spatially heterogeneous input, that produce the ups and downs of the excitatory firing rates. The inhibitory axons mimic this, but depending on their orientation, they are a right shifted, respectively left shifted version of the excitatory profile.

```
In [26]: fig = plt.figure(figsize=(10,5))

         ax= fig.add_subplot(111)

         ax.plot(ex_positions, np.sum(in_ex_connectivity_circ, axis=0), '.')
         ax.plot(ex_positions, np.sum(in_ex_connectivity_ell, axis=0), '.')
         ax.set_xlabel("x")
         ax.set_ylabel("Number of inhibitory inputs")

Out[26]: Text(0, 0.5, 'Number of inhibitory inputs')
```



1.4 Spike counts

```
In [27]: from interneuron_polarity.analysis.spike_trains import spikecounts
```

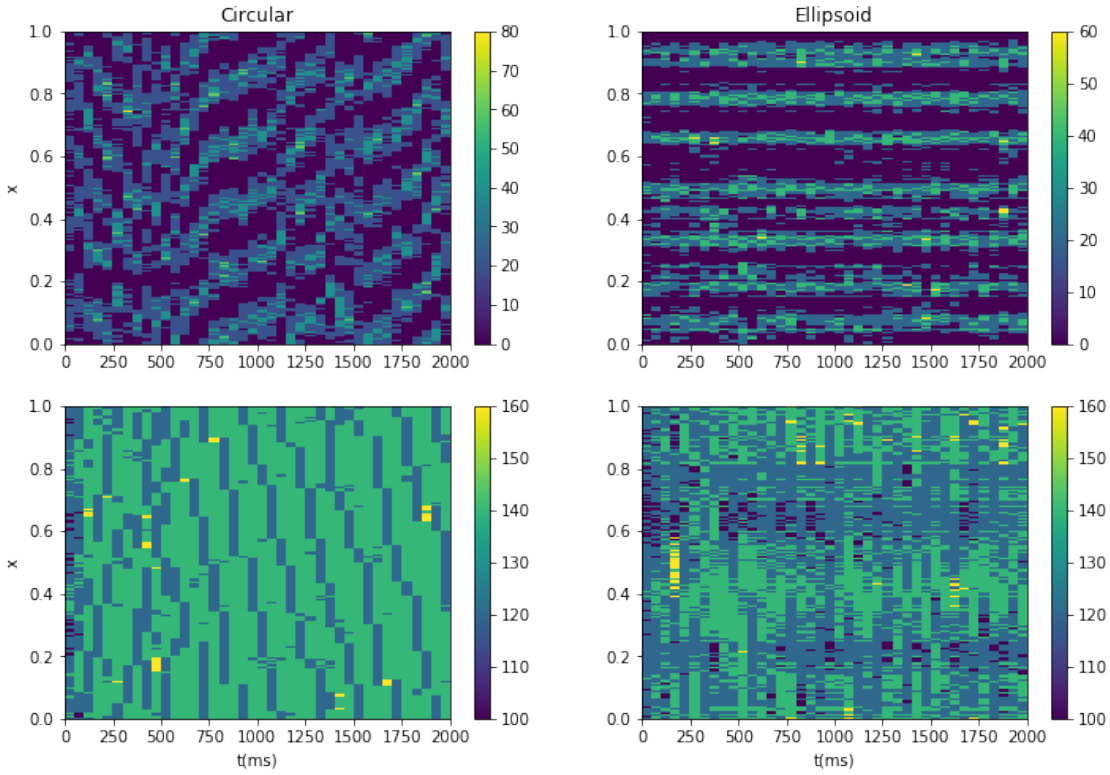
```
In [28]: dt = 50*ms
         t_start = 0*ms
         t_end = 10000*ms
         times = np.arange(t_start, t_end+dt, dt)*second -t_start


         circ_ex_counts = spikecounts(circ_ex, dt, t_start, t_end)
         circ_in_counts = spikecounts(circ_in, dt, t_start, t_end)

         ell_ex_counts = spikecounts(ell_ex, dt, t_start, t_end)
         ell_in_counts = spikecounts(ell_in, dt, t_start, t_end)
```

1.4.1 Rates in space and time

```
In [29]: fig = plt.figure(figsize=(12,8))

         grid = GridSpec(2,2)

         ax_circ_ex = fig.add_subplot(grid[0,0])
         ax_circ_in = fig.add_subplot(grid[1,0])

         ax_ell_ex = fig.add_subplot(grid[0,1])
         ax_ell_in = fig.add_subplot(grid[1,1])
```

```
min_idx = 0
max_idx = 40
im = ax_circ_ex.imshow(circ_ex_counts[:, min_idx:max_idx]/dt/hertz, aspect='auto', ext
fig.colorbar(im, ax=ax_circ_ex)

im = ax_circ_in.imshow(circ_in_counts[:, min_idx:max_idx]/dt/hertz, aspect='auto', ext
fig.colorbar(im, ax=ax_circ_in)

im = ax_ell_ex.imshow(ell_ex_counts[:, min_idx:max_idx]/dt/hertz, aspect='auto', exter
fig.colorbar(im, ax=ax_ell_ex)

im = ax_ell_in.imshow(ell_in_counts[:, min_idx:max_idx]/dt/hertz, aspect='auto', exter
fig.colorbar(im, ax=ax_ell_in)
```

```
ax_circ_ex.set_ylabel("x")
ax_circ_in.set_ylabel("x")

ax_circ_in.set_xlabel("t(ms)")
ax_ell_in.set_xlabel("t(ms)")

ax_circ_ex.title.set_text('Circular')
ax_ell_ex.title.set_text('Ellipsoid')
```



1.4.2 Spatial frequencies

Spectral analysis with unequally sampled data https://joseph-long.com/writing/recovering-signals-from-unevenly-sampled-data/

Here is how to get the phase as well https://stackoverflow.com/questions/49859075/lomb-scargle-phase

A better lomb scargle from astropy https://docs.astropy.org/en/stable/timeseries/lombscargle.html

```
In [30]: import scipy.signal as scs
```

```
In [31]: def get_spatial_periodogram(positions, spikecounts, spatial_frequencies):
             powers = [scs.lombscargle(positions, count, 2*np.pi*spatial_frequencies, precente
             return np.vstack(powers).T
```

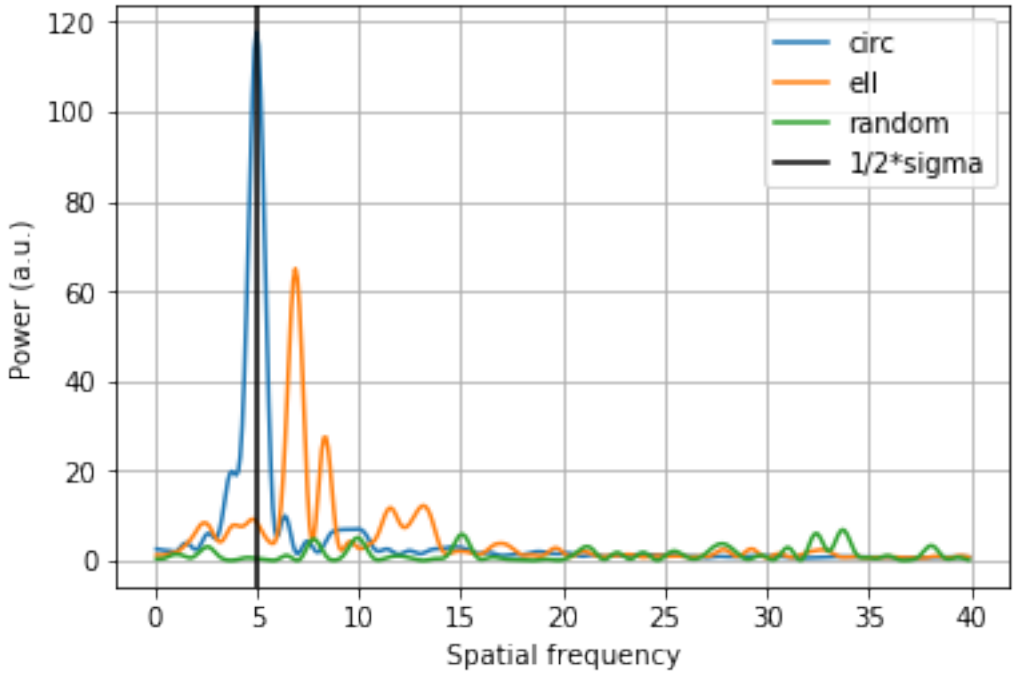
```
In [32]: spatial_frequencies = np.arange(0.1,40,0.1)
```

```
In [33]: circ_ex_spatial_powers = get_spatial_periodogram(ex_positions, circ_ex_counts, spatia
         ell_ex_spatial_powers = get_spatial_periodogram(ex_positions, ell_ex_counts, spatial_
```

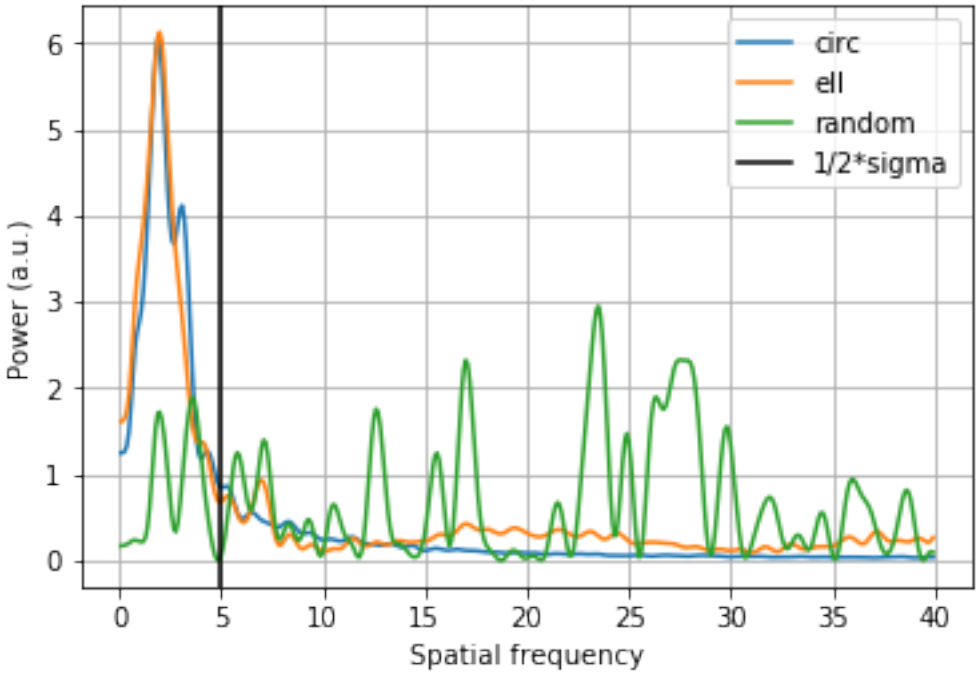
```
In [34]: random_power = scs.lombscargle(ex_positions, np.random.randint(np.min(circ_ex_counts)
```

```
In [35]: plt.plot(spatial_frequencies, np.mean(circ_ex_spatial_powers, axis=1), label='circ')
         plt.plot(spatial_frequencies, np.mean(ell_ex_spatial_powers, axis=1), label='ell')

         plt.plot(spatial_frequencies, random_power, label='random')
         plt.axvline(1.0/(2*sigma), color='k', label="1/2*sigma")
         plt.legend()
         plt.grid()

         plt.xlabel("Spatial frequency")
         plt.ylabel("Power (a.u.)")
```

```
Out[35]: Text(0, 0.5, 'Power (a.u.)')
```




```
In [36]: circ_in_spatial_powers = get_spatial_periodogram(in_positions, circ_in_counts, spatial
         ell_in_spatial_powers = get_spatial_periodogram(in_positions, ell_in_counts, spatial_

In [37]: random_power = scs.lombscargle(ex_positions, np.random.randint(np.min(circ_in_counts)

In [38]: plt.plot(spatial_frequencies, np.mean(circ_in_spatial_powers, axis=1), label='circ')
         plt.plot(spatial_frequencies, np.mean(ell_in_spatial_powers, axis=1), label='ell')

         plt.plot(spatial_frequencies, random_power, label='random')
         plt.axvline(1.0/(2*sigma), color='k', label="1/2*sigma")
         plt.legend()
         plt.grid()

         plt.xlabel("Spatial frequency")
         plt.ylabel("Power (a.u.)")

Out[38]: Text(0, 0.5, 'Power (a.u.)')
```



1.5 Intermediate summary

- Rosenbaum shows that in a spatial network with no recurrent connectivity there is no dynamic balance possible
- their results indicate that instead certain fourier modes stabilize so that the system has a spatial output profile
- although they have a more complicated connectivity rule, I tried to reproduce the periodicty in the spiking output
- my idea was to contrast this periodicity with spatial profiles in the case of ellipsoid axons
- my spatial analysis indicates spatial periodicity in the circular case (double check), however it is not stable and moves across the tissue
- with the 1d analogue of the ellipsoids this spatial profile dissolves and new spatial heterogeneity emerges, because inhibition is distributed in a non-uniform way
- I think the spatial periodicity only comes in when inhibition is strong enough to bring the excitatory neurons below threshold, it requires the non-linearity of the excitatory neurons
- in the same way that asymmeric (ellipdoid) connections affect the spatial periodicity, so does noise in the neuronal positions
- a network with ellipsoid axons that all show in the same direction preserves the spatial periodicity

Questions

- what about noisy input, mimic Rosenbaum setup with spatially shared input noise
- look at correlations where mean firing is substracted

- better understanding of the necessary input strengths and synaptic weights
- could one study the asymmetry alone by generating two inhibitory populations one with right directionality and with left directionality? how would such a network behave?

Notes on input strength

- when total excitatory drive > inhibitory drive (that is E fire more often than I) , then spatial differences stem from the unequal distribution of inhibition experiment_dict = { "duration": 10000*ms, "excitatory": { "tau": 10*ms, "v_threshold": -40*mV, "v_reset": -75*mV, "tau_refractory": 0.0*ms, "u_ext": 0*mV }, "inhibitory": { "tau": 5*ms, "v_threshold": -40*mV, "v_reset": -75*mV, "tau_refractory": 0.0*ms, "u_ext": -41*mV

  }, "ex-in": { "w": 0.05*mV }, "in-ex": { "w": -0.4*mV }, "initial_condition":{ "excitatory": { "v": '-75*mV+35*mV*rand()'
  }, "inhibitory": { "v": '-75*mV+35*mV*rand()'
  }
  } }

- but this behaviour persists even when E fire less often than I

- more important seems to be, to be in the non-linear regime, where ensembles of excitatory neurons can silence other ensembles experiment_dict = { "duration": 10000*ms, "excitatory": { "tau": 10*ms, "v_threshold": -40*mV, "v_reset": -75*mV, "tau_refractory": 0.0*ms, "u_ext": -0*mV }, "inhibitory": { "tau": 5*ms, "v_threshold": -40*mV, "v_reset": -75*mV, "tau_refractory": 0.0*ms, "u_ext": -35*mV

  }, "ex-in": { "w": 0.4*mV }, "in-ex": { "w": -1*mV }, "initial_condition":{ "excitatory": { "v": '-75*mV+35*mV*rand()'
  }, "inhibitory": { "v": '-75*mV+35*mV*rand()'
  }
  } }

1.5.1 Questions to Farzada

- how well do you think this provides an analogue of the 3d case? how well do these findings apply to the 3d case?
- how can I characterise the network? what input strengths and synaptic weights have to be tested for?
- do you think that this is an interesting network to start with in the circular case?

1.5.2 What is the purpose of the model?

The experimental finding of this unusual axonal morphology (and the non-trivial connectivity rule) stands in contrast to the usual belief of the homogeneous blanket of inhibition. So the model should adress the question how the unusual morphology affects current believes about the role of interneurons and the way they shape network activity.

So I should read up some Yuste work to see how they connect the blanket of inhibition hypothesis with dynamics of networks and the functional role of interneurons.

I still require a starting point, so ideally the network with a spherical axon morphology generating some known and relevant dynamics. Then I could study how deviations in the morphology affect this dynamics.

Possible starting points are - head direction tuning by recurrent inhibition - the shepston paper about the subiculum - the yuste paper about the blanket of inhibition hypothesis - the rosenbaum paper about the effect of spatially structured connectivity on network dynamics especially dynamically balanced states

The first seemed to be hard to connect, because these networks mostly live in feature space and it is not clear how their connectivity fits to the spatial connectivity rules that we had found. However, rethinking what I observed so far, maybe one could use the directionality of the asymmetric neurons to build structurally similar networks, but this is not possible with the symmetric ones in the circular case.

The second and third, I still need to read.

The Rosenbaum paper start at least from a very similar perspective, they look at states a network can be in for given spatial connectivity rules. Their setup is slightly more complex, but it seems to be a valid question to see whether their analysis applies to our network as well. What could be the function? Can I go back to a balanced state with inhibitory axons that distribute inhibition more broadly? Probably not, because their is no recurrent excitation.