Simulation of the Inferior Olive in Arbor

Lennart P. L. Landsmeer Showcase for the Arbor Workshop

The inferior olive model - an example of a model running in Arbor

Central in motor control, learning & timing

Located in the brain stem

Part of the olivocerebellar loop (PF \rightarrow PC –| DCN –| IO –| PC)

RQ: relation between morphological/topological clustering and dynamical clustering

Model part of my master thesis at Erasmus MC Rotterdam and TU Delft under Dr. Mario Negrello



Step 1. Experimental Constraints -> IO Network generation

Geometry





Morphology traight (8)









Network

Key	Data	Reference
Cluster sizes	Cell counts 5-30 Diam 50–250um Took average of 15 cells	Rekling et al. [2012]
Single cell morphology distribu- tions	Distributions (figure 2.1A)	Vrieler et al. [2019]
Cell counts	8666 total, 50.29% MAO (4358), 23.53% PO (2039)	Yu et al. [2014]
Cell counts	3000 PO+dmcc, 3500 DAO, 6500 MAO	Zanjani et al. [2004]
Cell counts	2478 IOPr, 6480 MAO (IOA+IOB+IOC+IOM), IOA 1437, IOArL 224, IOB 2050, IOBe 647, IOC 1485, IOD 2050, IODM 422, IOK 601, IOM 871, IOPr 2478, IOVL 136	Uusisaari (Unpublished)
Axon size	0.5-1um	
Connection counts	Histogram from 4F, WebPlot- Digitizer Median quantiles (0.25, 0.5, 0.75): 10, 14.5, 22: 8 width	Lefler et al. [2020]
Connection counts	Dye counts - 6-20 cells	Leznik and Llinas [2005]
Puffs	Purkinje (GABAergic input) SS and CS spike distribution (Fig- ure 2) after a whisker puff	Romano et al. [2018]
Simple spike firing statistics	Mean GABA firing frequency in awake mice (51.0 ± 2.7) , and 20ms pause duraction after spike.	Shin and De Schutter [2006]

Step 1. Network generation visualized





Step 2. Dynamics (ion channel mechanisms in Arbor)

Subthreshold oscillations

Cluster synchronization

Two spike types (normal & ADP)

Single cell translation done by student Rocher Smol





Step 3. Simulation



Step 4. Results: Effect topology on synchronization

A. Cluster counts B. RDF C. Memory



- 1. Cluster synchronization happens regardless of topological clustering
- 2. But topological cluster does affect memory and cluster shape

Step 5. Local field potentials





Step 5. Local fields potentials: experiment vs model



EXPERIMENT

MODEL

Next up: workshop

Questions? (now or come talk to me at my poster)

Workshop: interactive part

arbor-sim.org



Arbor is a multi-compartment neuron simulation library; compatible with next-generation accelerators; best-practices applied to research software; focussed on community-driven development.



Links

wiki.ebrains.eu/bin/view/Collabs/io-clusters/

Or go to **wiki.ebrains.eu** and search for "Inferior Olivary Nucleus"



arbor-sim.org/playground/

DIY



Methods description (video), https://youtu.be/sovietowszysgs

wiki.ebrains.eu/bin/view/Collabs/io-clusters/



Workflow:

Setup: Import and git clone

Mechanisms: Compile & load NMODL files

Decor: Define which mechanisms go where

Recipe: Putting everything together

Single cell: Simulate a single voltage trace

Network: Simulate an IO network

Visualize: Visualize cluster dynamics

Quantify: Effect topology->synchrony

wiki.ebrains.eu/bin/view/Collabs/io-clusters/



Schweighofer, Nicolas, Kenji Doya, and Mitsuo Kawato. "Electrophysiological properties of inferior olive neurons: a compartmental model." *Journal of neurophysiology* 82.2 (1999): 804-817.

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Setup: obtaining the model

We retrieve the public IO repository here. This contains all code necessary to run the full IO model, b

```
[8]: import os
if not os.path.exists('iopublic'):
    !git clone --depth 1 'https://github.com/llandsmeer/iopublic'
import matplotlib.pyplot as plt
%matplotlib inline
import random, numpy as np
import plotly.express as px
import plotly.express as px
import pandas as pd
random.seed(0)
np.random.seed(0)
import arbor
import networkx as nx
```

Mechanisms: compile & load NMODL files

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Decor: define which mechanisms go where

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Defining the decor: which mechanisms go where?

The decor defines (among other) how our custom IO catalogue mechanisms map onto the morph

```
def decor default(variance=0.2):
    def R(x):
        r = random.gauss(x, x*variance)
        if abs(r) < 0.3 * abs(x): return x</pre>
        return r
    return (arbor.decor()
        .paint('"soma"', arbor.density('na s', dict(gmax=R(0.030))))
        .paint('"soma"', arbor.density('kdr', dict(gmax=R(0.030))))
        .paint('"soma"', arbor.density('cal', dict(gmax=R(0.025)))) # 45
        .paint('"dend"', arbor.density('cah', dict(gmax=R(0.010))))
        .paint('"dend"', arbor.density('kca', dict(gmax=R(0.220))))
        .paint('"dend"', arbor.density('h',
                                               dict(gmax=R(0.015))))
        .paint('"dend"', arbor.density('cacc', dict(gmax=R(0.000))))
        .paint('"axon"', arbor.density('na a', dict(gmax=R(0.200))))
        .paint('"axon"', arbor.density('k', dict(gmax=R(0.200))))
        .paint('"soma"', arbor.density('k',
                                               dict(gmax=R(0.015))))
        .paint('"all"', arbor.density('leak', dict(gmax=R(1.3e-05))))
        .set property(cm=0.01) # Ohm.cm
        .set property(Vm=-R(65.0))
        .paint('"all"', rL=100) # Ohm.cm
        .paint('"all"', ion name='ca', rev pot=R(120), int con=3.7152)
        .paint('"all"', ion name='na', rev pot=R(55))
        .paint('"all"', ion name='k', rev pot=-R(75))
        .paint('"all"', arbor.density('ca conc'))
```

Recipe: putting everything together

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Single cell: simulate a single voltage trace

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Single cell simulation: simulating a single cell

Let's start with simulating a single cell. As expected, subthreshold oscillations are clearly visible



Network: simulate an IO network (pt 1)

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Network simulation: effect of builtin clustering

Now, let's simulate a clustered network. We will have 2 builtin clusters, and simulate 2 networks: one with a high clustering coefficient, one with a low cluster cc

```
def build connection matrix(cluster_coef, ncells, cluster_size):
    'this function defines a IO network with variable amount of clustering'
    if ncells == 1: return np.array([[False]])
    Amask = np.kron(np.eye(int(np.ceil(ncells / cluster size))), np.ones((cluster size, cluster size)))[:ncells,:ncells]
    A = np.random.random((ncells, ncells)) * Amask
    A = (A + A,T)/2
   A = A / A.sum()
    B = np.random.random((ncells. ncells))
    B = (B + B.T)/2
    B = B / B.sum()
    P = cluster coef * A + (1-cluster coef) * B
    np.fill diagonal(P, 0)
   p = np.sort(P.flatten())[::-1]
    p = p[min(ncells * 10, ncells*ncells)]
    return P > p
n, k, k1, k2 = 30, 10, 0.1, 0.9
tstop = 7000
colormap = sum(([i]*k for i in range(int(np.ceil(n / k)))), [])
fig, ax = plt.subplots(ncols=2, figsize=(9, 5))
fig.suptitle(f'Effect of cluster coefficient on network topology (n={n}, k={k})')
```

ax[0].set_title(f'c={k}); G = nx.from_numpy_array(buil_connection_matrix(k1, n, k)) nx.draw(G, ax=ax[0], node_color=colormap) nx.draw(H, ax=ax[0], node_color=colormap)



Network: simulate an IO network (pt 2)

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Visualize: visualize cluster dynamics (pt 1)

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Analysis: Hierarchical Clustering of the Analytical Signal

We have saved the voltage traces in the variables Vhigh and Vlow for respectively the high and low cluser coefficient networks.

First, we calculate the analytical signal (the phases) by filtering using a bandpass filter around the approximate expected STO frequency and then taking the Hilbert transform.



Low cluster coefficient

Visualize: visualize cluster dynamics (pt 2)

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Quantify: effect topology on synchrony

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Let's quantify the agreement between topological and dynamical clusters

Warning! The boxplot shows sampled NMI estimates from the same simulation. This is because Kmeans returns different results based on the initial seed.

from sklearn.metrics:import normalized_mutual_info_score as nmi
true = np.arange(n) // k
def kmeans labels(A):
 return scipy.cluster.vq.kmeans2(np.sin(A1:,3000:]), 3, minit='+', iter=100)[1]
ntrials = 30
WTLhigh = [100*nmi(Ltrue, kmeans labels(Ahigh)) for _ in range(ntrials)]
WTL(true, kmeans labels(Ahigh)) for _ in range(ntrials)]
PL:figur(dpin30)
pl:figur(dpin30)
pl:Linghor((Clustering coefficient')
pl:Linghor((Clustering coefficient')
pl:Linghor(W = stime them toological and dynamical K-means clusters');

NMI estimate between topological and dynamical K-means clusters



Questions? No time!

Come talk to me at my poster