Spatio-temporal activity arithmetics with dopamine and acetylcholine

Introduction

1. Motivation of the occurrence of STAS
    1. ‘temporal activity sequences have been recorded from different brain regions in various tasks’ (see reference 3-11 [review 12] in Spreizer).
        1. Ref 7/8 on decision making
        2. ref 10 for learning (related to dopamine?)
1. Motivation on neurotransmitter (especially dopamine)
    1. Allows for more dynamics as it can appear and disappear on different scales in time and space (reference?)
    2. Dopamine release is patchy (Patriarchi, 37)
2. Motivation on computational simulations of merging these things together
    1. feedforward networks [14] are simplest model for generating STAS [15-17]
    2. A computational model would be the Spreizer model
        1. In contrast to previous research there are no requirements on
            1. Spike frequency adaptation
            2. Spike threshold adaptation
            3. short-term synaptic depression
            4. learning rules
            5. which could also underlie the emergence of STAS (24-26)
3. Thesis: Neurotransmitter such as dopamine add a layer to the network, which allows for dynamic changes of STAS

Material&Methods

Before we can introduce the additional layer to the network, we design a model, that allows and supports the spontaneous emergence of STAS. Hence, this study extends current research, Spreizer et al. (2019) investigated neuronal networks with a ‘leaky-integrate-and-fire’ model, that satisfies this constraint. They set up local recurrent random networks (LCRN) with feedforward networks embedded in them. They developed a connectivity rule, which promote the emergence of STAS. It introduces

inhomogeneities in the spatial distribution of axons. As Spreizer et al. pointed out, two conditions are necessary to ensure the emergence of STAS in a EI-network with spiking neurons: (1) each excitatory neuron projects a small fraction of their axons in a preferred direction ϕ, and (2) ϕs for neurons in the vicinity are similar, whereas ϕs for neurons far from each other are unrelated.

To consolidate the principles and arguments, under which circumstance STAS occur, we exploit a different model.

1. *The rate model (reference required)*
    1. *Advantages*
    2. *Risks*

In order to generate a LCRN with a wide range of possibilities, we aim for a network with a medium number of sequences emerging. Moreover, these sequence ought have medium velocity and tend to change their direction. In the following, we specify the set of parameters to attain a network that elicit the desired properties. An orientation for the parameter, the study of Spreizer et al. provides an analysis of many characteristics resulting from different sets of parameter.

A Perlin configuration with a medium Perlin scale and a shift of one grid point fits the requirements. (refer to Perlin noise, see reference 61 of Spreizer) Additionally, the study provides a framework to tune the external drive with respect to various properties of the network related to STAS.

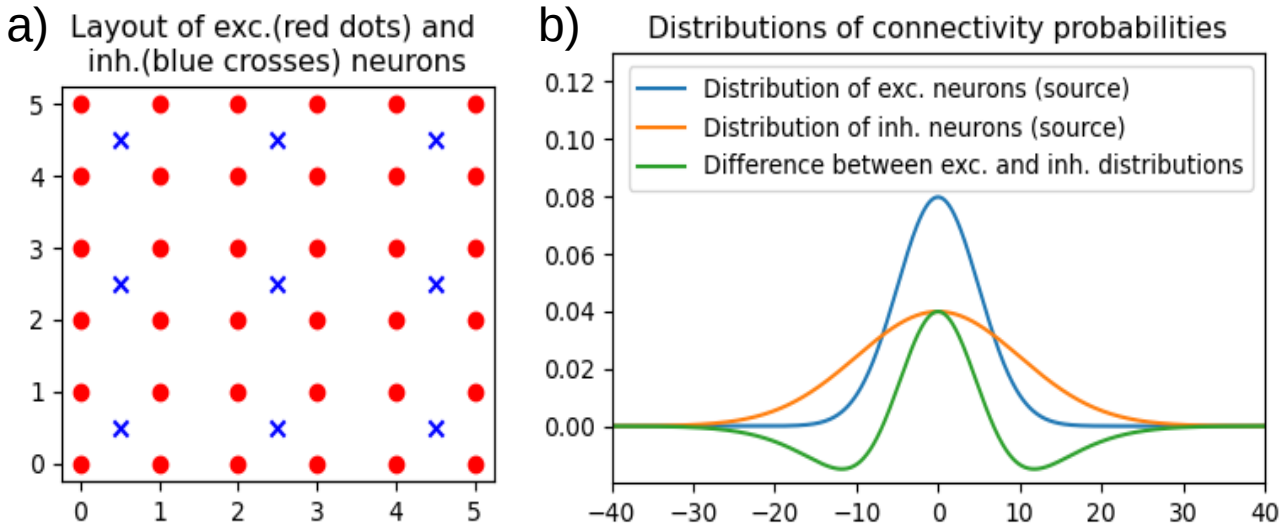

Figure 1: a) Layout of excitatory and inhibitory neurons. b) Distance-dependent connectivity probabilities of a Gaussian distribution (scaled to the grid of excitatory neurons)

Network architecture

In our study, we focus on networks with excitatory and inhibitory neurons (EI-network), since they are common in the brain and seen throughout various brain regions. (reference required, relation to dopamine)

Each neuronal population is arranged on a square grid. The grid is folded to a torus to avoid boundary effects. [See ref. 17 of Spreizer] The excitatory neurons populate a 70x70 grid ($npop_E$ = 4900), whereas the inhibitory population ($npop_I$ = 1225) is arranged on a 35x35 grid. In contrast to Spreizer et al., we

placed the inhibitory neuron as center of four excitatory neurons to avoid an additional asymmetry, due to the equal distance each excitatory neuron has to the closest inhibitory neuron, and vice versa (Figure 1.a).

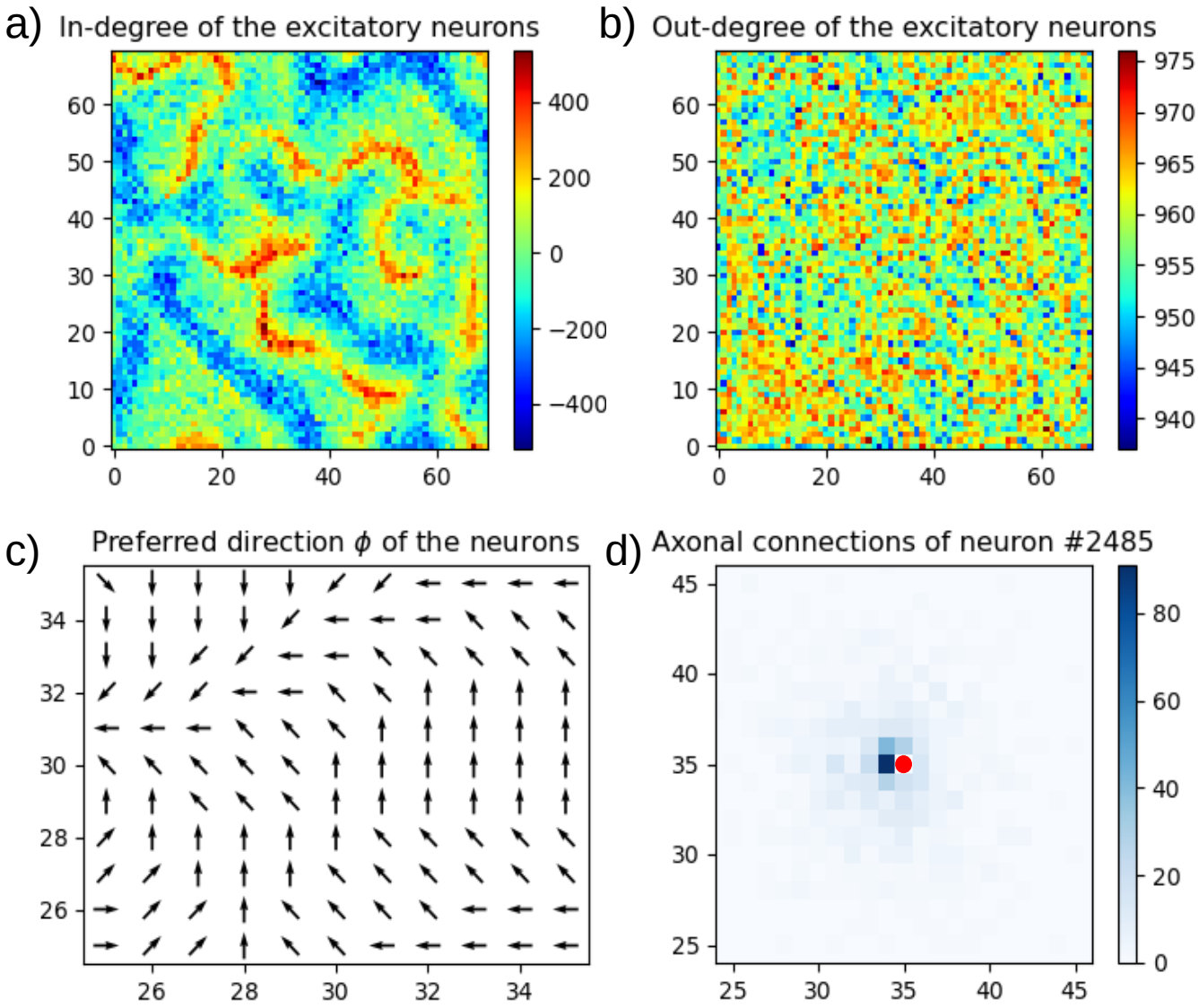

Figure 2: Network configuration: a) Shows the in-degree of the exc. population. Inh. synapses are multiplied with the ratio ($npop_E$:$npop_I$ *= 4:1) and subtracted. b) the out-degree of the excitatory population is shown. c) The preferred direction ϕ is shown. According to the Perlin configuration, adjacent neurons show similar ϕs, whereas neurons far from each other are unrelated. d) The axonal directions of neuron #2485 (red dot) is shown.*

Multiple synapses to a target neuron are permitted, whereas self-connection was excluded. Therefore, each neuron forms up to 980 and 245 synapses to the excitatory and inhibitory population respectively (20% connection probability on average).

Accordingly to Spreizer et al, a distance-dependent connectivity probability is employed to determine the axonal projections. The connection probability depends on the distance between neurons and is

drawn from a Gaussian distribution. The standard deviation of the Gaussian distribution, also called the space constant, is for excitatory neurons σ_E = 5, and for inhibitory neurons σ_I = 5 with respect to the correspondent grid (scaled properly for projections to the other grid) (Figure 1.b). This connectivity method tends to have a high probability of connections within the vicinity, thus they form local recurrent random networks (LCRN). ***(see Spreizer?)***

In contrast to the configuration of Spreizer et al, we used a higher average connection probability, but since the population sizes is much smaller, the total number of connections per neuron is only slightly higher. This high number of connections results in a good representation of the Gaussian distribution, such that the relative differences of synapses between adjacent target neurons is considered to be small.

In line, we introduced the asymmetry of spatial connections from excitatory to excitatory neurons by the algorithm of Spreizer with changes according to our different neuronal grid layout (Figure 2). The algorithm comprises the generation of Perlin noise (size: 4, base: 1), and assigns the preferred direction ϕ of the axonal direction to the neurons of the excitatory population (Figure 2.c). The synapses are shifted by one grid point in the direction ϕ. The Perlin noise and the shift are chosen such that we obtain a balance between the number of generated sequences and the tendency to change their direction. Additionally, the sequences travel with a moderate velocity (Spreizer et al., 2019). Note that the shift of synapses result in the formation of self-connections, due to the constraints, these connections were removed. The resulting network is shown in Figure 2. The in-, and out-degree are shown only for the excitatory population. The in-degree is calculated by the sum of the incoming excitatory synapses **(reference for in and out-degree?)** subtracted the inhibitory synapses, corrected for the ratio between the populations ($npop_E$:$npop_I$ = 4:1). The in-degree show high variations between different locations arising from the fact that the preferred direction ϕ converges in some parts – and diverges in other. The out-degree takes only excitatory-to-excitatory synapses into account. There are neither a high variation, nor regions with high-, or low-out-degree.

The synaptic weight is J_X = 2, and the ***inhibition factor*** is g = 6.5 resulting in excitatory weights of J_E = J_X = 2, and J_I = -J_X x g = -13. To mimic ongoing activity as input to the network, each neuron receives independent, homogeneous inputs from an external drive. This drive is modeled by a Gaussian white noise (μ = 25, σ = 20). The balance of the internal and external drive are critical, and hence are carefully set with respect to the transfer function of the rate model (x_0 = 50, steepness = 0.5, cf. Formula 2)

1. **Inspect the network**
    1. **Seeing regions of high in-degree**
    2. **Seeing regions which projects into the same direction even though they have no high in-degree**
    3. **Expectations of where STAS might occur**
2. **Run the simulations once (baseline)**

1. **Since we do not use spiking neurons, we inspected the activity in time and observed clusters of increased activity, moving across the network.**
2. **This is an exploratory study, so we do not classify the sequences directly (they differ also in size), but for the following, we use the number of sequences passing by as an indicator of the neurons regularly participating a STAS.**
3. **Moreover, this argument as well as the avg. activity holds as basis for the following simulations.**

Results

Discussion

Open Questions

References