Nonrandom connectivity in local cortical circuits from anisotropic axon morphology

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Abstract

Nonrandom connectivity patterns have been repeatedly found in local cortical networks, but it remains unclear which connection principles underlie this form of network organization. Here we present a simple geometric random network model that reflects an anisotropy

Suggesting that features of the pyramdial neuron's stereotypical morphology can be the cause for such non-randomness, a simplistic geometric random network model is introduced reflecting "anisotropy in neural connectivity", the observation that synapses of cortical pyramidal cells tend to cluster around the main axon's projection. Analysis of the network's connectivity reveals patterns closely resembling the findings in cortical circuits. Characteristic neuron morphology must therefore be considered as an important aspect of the underlying connection principles in the cortex. Reflecting network non-random network connectivity faithfully, the proposed model offers itself for further investigation of the consequences of patterns consequences in networks dynamics and learning.

Introduction

The network structure has large effect on functional properties of the network such as correlations [1]

While morphology is generally diverse , pyramidal cells in the layer 5 share characteristics (Fig 1).

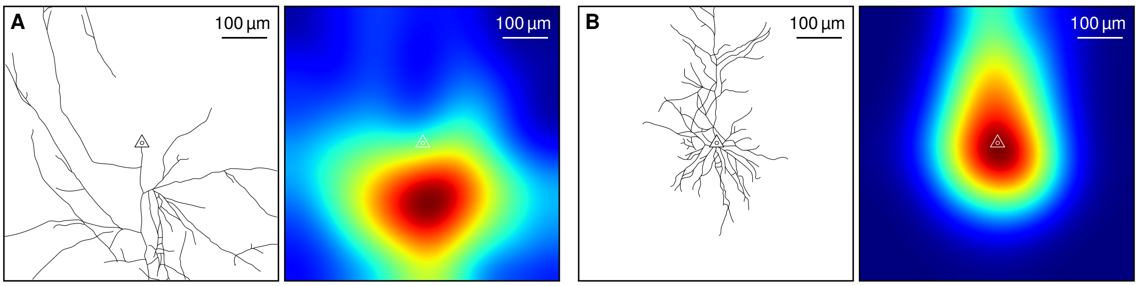

Figure 1: **Stereotypical morphology of layer 5 pyramidal cells** Morphology of projected [2]

Methods

Anisotropic network model

Here we consider a network model

The model is implemented as an adapted version of a two-dimensional directed random geometric graph: additionally to the random position on the unit square, each node is assigned a uniformly distributed axon projection angle a. For each vertex v, directed connections are then established to nodes with distance $\leq \frac{w}{2}$ to the projection ray originating from v with angle a (Fig. 2 A). This *anisotropic network model* is determined by two parameters; network size N and the "axon width" w.

Rewired networks

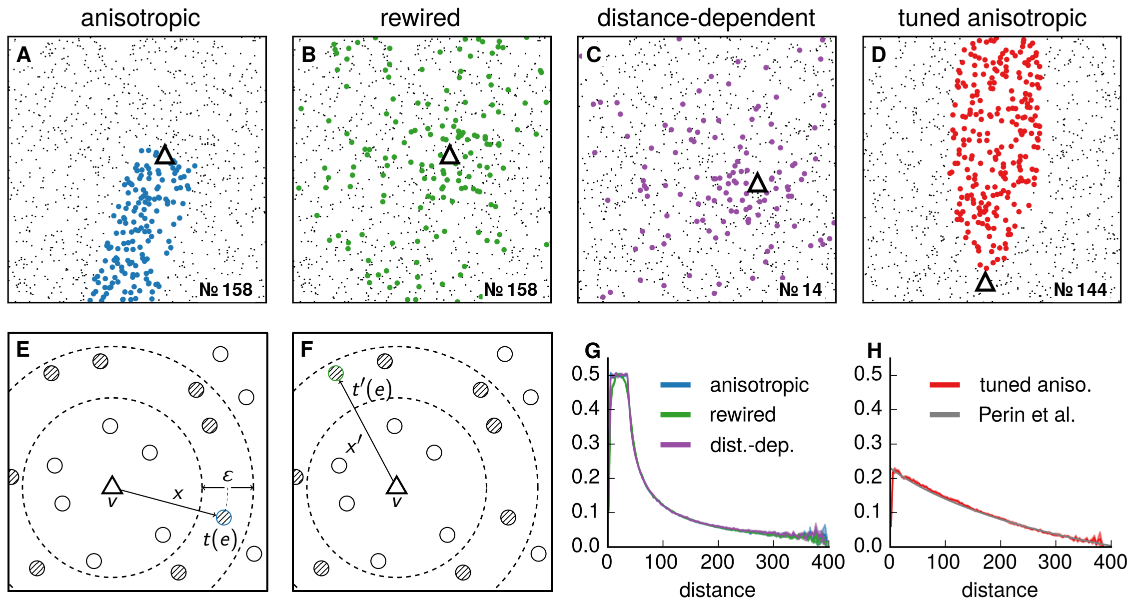

Figure 2: **Network models A–D**. Graphic representation of the different network types. For each model the full network area is shown and the $N = 1000$ neuron locations are indicated as gray dots. For a single cell (triangle, node number shown in bottom right corner) target nodes of its outgoing connections are marked in color, revealing the typical connectivity in the model. **E–F**. Visualization of the rewiring algorithm for a single edge between two neurons of distance x. First, possible targets within distance $x \pm \varepsilon/2$ are identified (hatched nodes). Then, from the possible targets one node is chose at random and the rewired edge projects from the original source vertex v to the new target $t'(e)$. **G** Connection probability between two nodes dependent on their distance matches in the networks from A,B and C. **H** Distance-dependent connection probability profile of the tuned network, matched to the findings of Perin et al.

In order to understand which structural features are shaped by the anisotropy in the network, it is necessary to have a reference network that doesn't feature anisotropy, but is otherwise equivalent to the anisotropic model. For this we introduced a rewiring algorithm on networks that preserves first-order connectivity statistics as well as the distance-dependent connection probability profile. In this process each connection with a spatial distance x between source and target, is rewired to a new random target that differs not more than ε from x in spatial distance to the source vertex (Fig. 2 E-F). The resulting network has greatly reduced anisotropy in connectivity, resembling that of a distance-dependent network (supporting information).

Mention the outcome of the rewiring. Some very edges are lost in the process!

By rewiring only a section of all connections, a *partial rewiring* produces a state that retains some anisotropy...

The relative width of the rewiring parameter was chosen as $\varepsilon/E = 0.05$ (??) to achieve an effective rewiring while closely maintaining the distance-dependent connection probability distribution of the original networks (see SI ??).

Distance-dependent networks

To record in how far the rewired model resembles networks implemented purely from a distance-dependent. In order to test for this a standard distance-dependent was implemented as well.

Tuned networks

Finally,

Results

Standard network measures

Degree distribution Neither in-degree nor out-degree distribution is affected by anisotropy/rewiring, but out-degree distribution shows artifact that makes it different from distance-dependent networks.

Small-world properties

Two neuron connections

We tested whether reciprocally connected neuron pairs

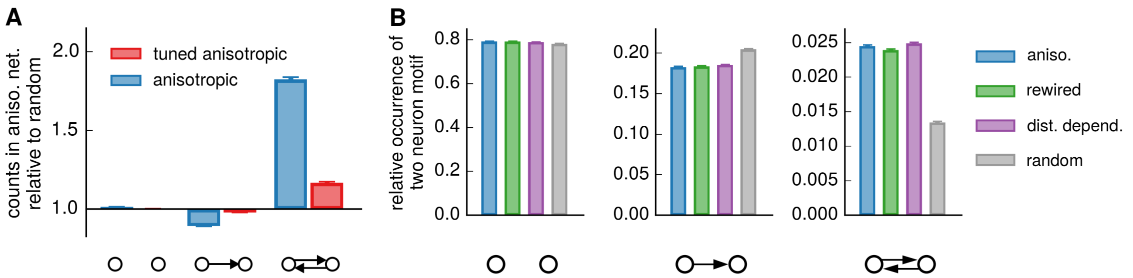

Figure 3: **Overrepresentation of two neuron connections not is not induced by anisotropy** A-B: While general overrepresentation is found, no significant difference to the rewired mode is identified C-E: Overrepresentation as found by Perin et al. is distance-independent and is not affected by anisotropy

Three neuron motifs

To expose the effect of anisotropy in connectivity on the statistics of the occurrence of motifs composed of three neurons, in each of the three graph types (anisotropic, rewired, distance-dependent) a sample of 3 graphs was taken and in each of those graphs the motifs of 300000 random triplets of neurons were registered. The observed occurrence of three-neuron motifs distinctly differed from what one might expect from relative frequencies of connections in neuron pairs: Assuming independence, the expected relative frequency of the 16 different motifs were calculated from probabilities p_u, p_s and p_r from above **??**Displaying the relative counts (counts extracted from graphs divided by counts expected from neuron pair statistics) in Fig. 4, we find that anisotropy has significant impact of distribution of motifs.

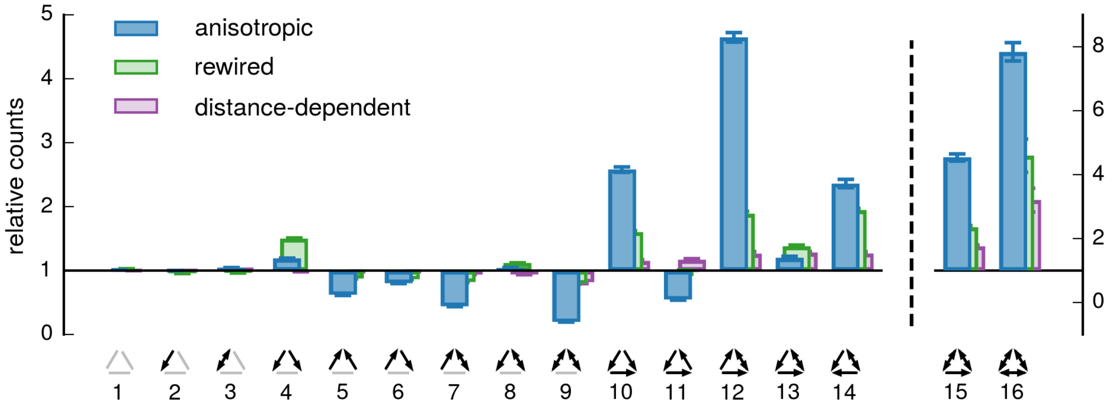

Figure 4: **Over- and underrepresentation of three-neuron motifs due to anisotropy** Counting the occurrences of three-neuron motifs in anisotropic, rewired and distance-dependent networks, we find that

The strongest deviations were observed in motifs 8,10,12,14,15 and 16 (overrepresented) and motif 9 ?? (underrepresented). Rewired and distance-dependent networks show a deviation from the expectation as well, however, the effect is much stronger in anisotropic networks

Interestingly, this effect is much stronger than in distance-dependent, where one might expect significant over- and underrepresentations as well. Finding two connected pairs in a triplet indicates a spatial closeness, that can be transferred to third pair as well - thus one should find a higher connection chance. We find that in comparable distance-dependent networks, only

Neuron clusters

Specifically, the high edge counts in neuron clusters *does not* depend on how anisotropy was implemented (tuned or normal)!

While rewiring, some connections have been lost (numbers!), that means some of the overrepresentation might be due to that as this relationship is strict (no new connections get introduced). It was shown that small deviations *can* have a significant effect - see for example 85c70a9f_1v1. However, in average no such is noticeable as expected.

The significant overrepresentation from rewired to distance-dependent is something important to think about. It kind of destroys the point I'm trying to make: Anisotropy makes all the things! So, it's very important to understand: Is it really true that the rewired-distance effect is strong? (So far this has been only tested for one case: 8counts) Then, it's crucial to understand where this difference is coming from. What aspect is in rewired, but not in distance, that produces this?

Common Neighbor relations

Discussion

Conclusion

Acknowledgments

[3]

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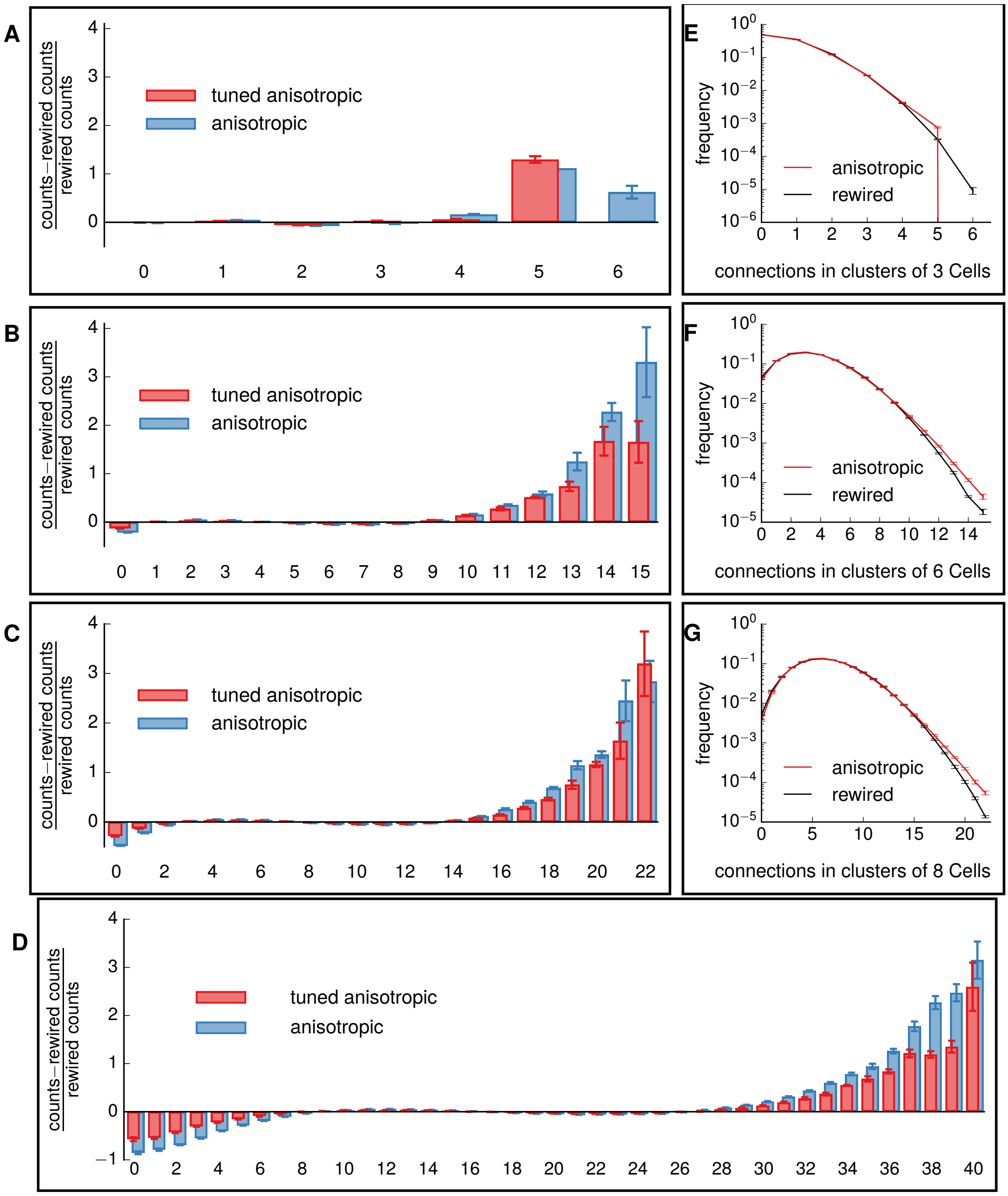

Figure 5: **LOOK AT DIMENSIONS (PLOSMAIN) BEFORE MAKING FIGURE Strong influence of anisotropy on the neuro cluster counts** A-C: Important: No 3 neuron motifs with 6 edges in tuned anisotropic graphs registered