Nonrandom connectivity in local cortical circuits from anisotropic axon morphology

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Introduction

Experimental results indicate that connectivity in cortical circuits is highly nonrandom:

1. Reciprocally connected pairs appear more often than expected by chance [1, 2]
2. Certain triplet motifs of neurons are strongly overrepresented [1]
3. Clusters of neurons show more often a high degree of connectivity than predicted from spatial connectivity [2]

Recently, these characteristics have been found in detailed reconstructions of cortical circuits [3] and it was shown that generic network models can account for some of these features [4]. However, it remains unclear what properties of a cortical circuit affect the connectivity such that the structures above emerge. Here we propose a simple network model based on the stereotypical anisotropy of axon morphology (Fig. 1).

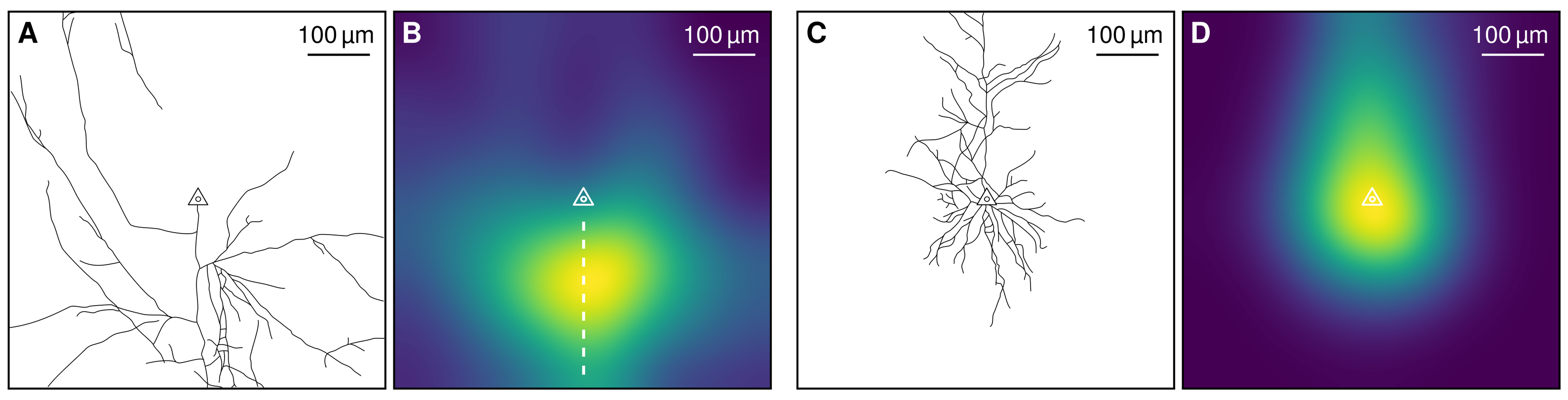

Figure 1: Projections of thick-tufted layer V pyramidal cells in the rat somatosensory cortex (manually traced from [5]) **A** Axon morphology of a single cell (left), branch density heatmap of axons for 5 neurons with the soma aligned at the center. **B** As in A, but for dendrite.

Model

Motivated from the observed anisotropy in axonal morphology (Fig. 1) we formulate the *anisotropic network model*: $N = 1000$ neurons are distributed uniformly at random on a square of length 296 µm. Each neuron is assigned a random direction $\alpha \in [0, 2\pi)$ and connections are established to target neurons lying within in a corridor of width $w = 74.6\,\mu$m (Fig. 2A). Here, the width w was tuned to obtain a network connection density of $p = 0.116$ as found in [1].

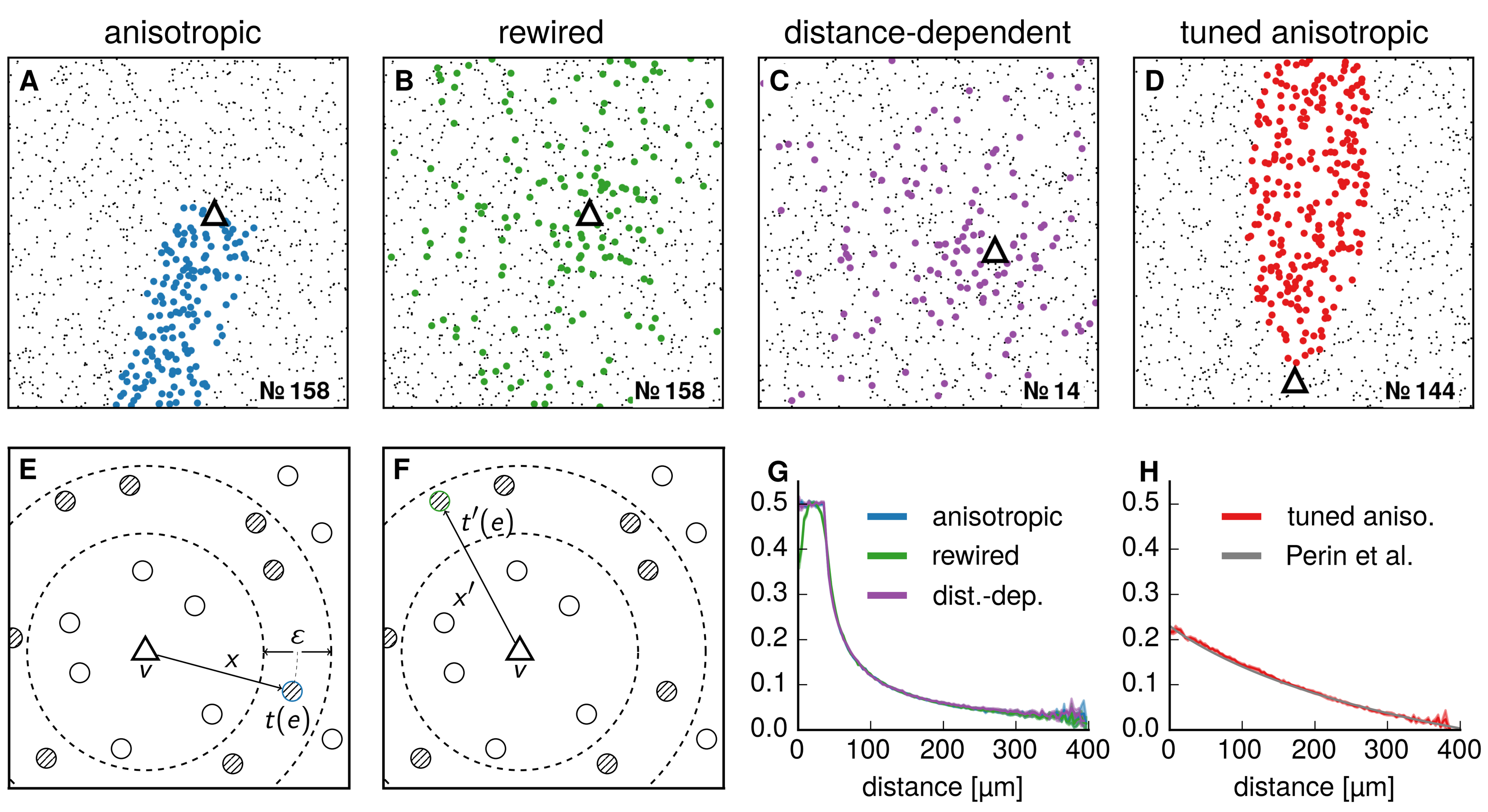

Figure 2: Network models. **A-D** Targets of a single neuron (Id in bottom right corner) for the different network models. **E-F** Rewiring algorithm. **G-H** Distance-dependent connection probabilities.

The *rewired network* (Fig. 2B) is obtained from the anisotropic network by randomly picking new targets that differ in distance to the source neuron maximally by ϵ from the original target (Fig. 2E-F). The *distance-dependent network* (Fig. 2C) is a randomly connected graph where the probability of a connection to exist depends on the distance between the nodes, using for example the profile of the anisotropic network (Fig. 2G). Finally, the *tuned anisotropic network* (Fig. 2D) is similar to the anisotropic network with the difference that the corridor is shaped in such a way that the distance-dependent connection probability found in [2] is obtained in the network (Fig. 2H).

Results

In both anisotropic and tuned anisotropic networks, reciprocally connected pairs occur more often than in a random network with the same connection density (Fig. 3A).

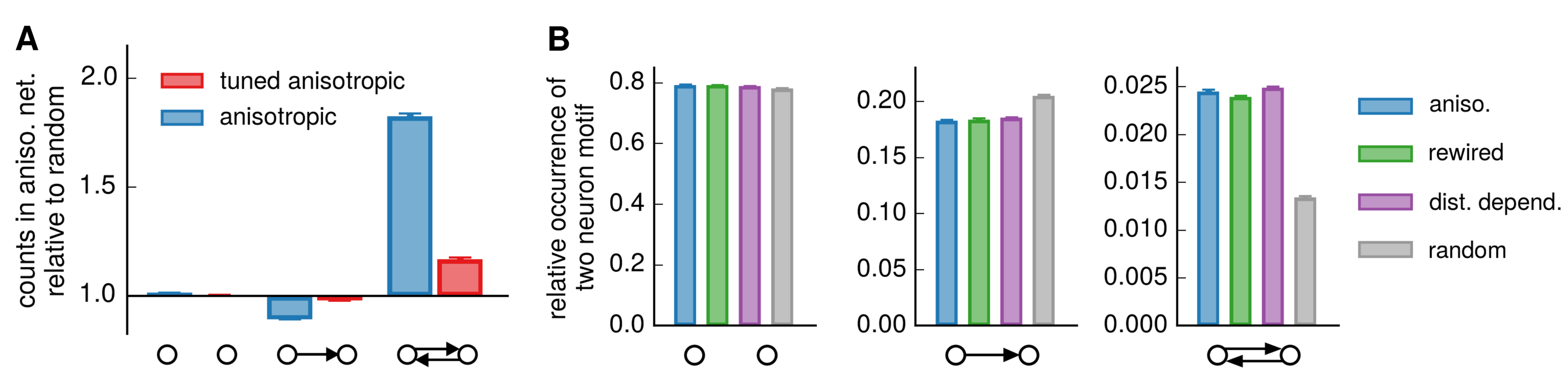

Figure 3: Unconnected, unidirectional and bidirectional neuron pair occurrences in the network models

However, is this due to anisotropy? Indeed, we find almost identical pair counts in rewired and distance-dependent networks (Fig. 3B). The overrepresentation of reciprocal connections in the data of Perin et al. [2] is not explained by distance-dependency, so that there could be other pair-symmetric irregularities in the connection probabilities that cause the overrepresentation [6].

Next we tested the occurrence of three neuron patterns as reported in [1]. We found that in alignment with experimental results, certain motifs are strongly overrepresented in the anisotropic networks (Fig. 4). Here, it is indeed anisotropy that causes the motifs to appear more often – the motif overrepresentations are drastically reduced in rewired and distance-dependent networks.

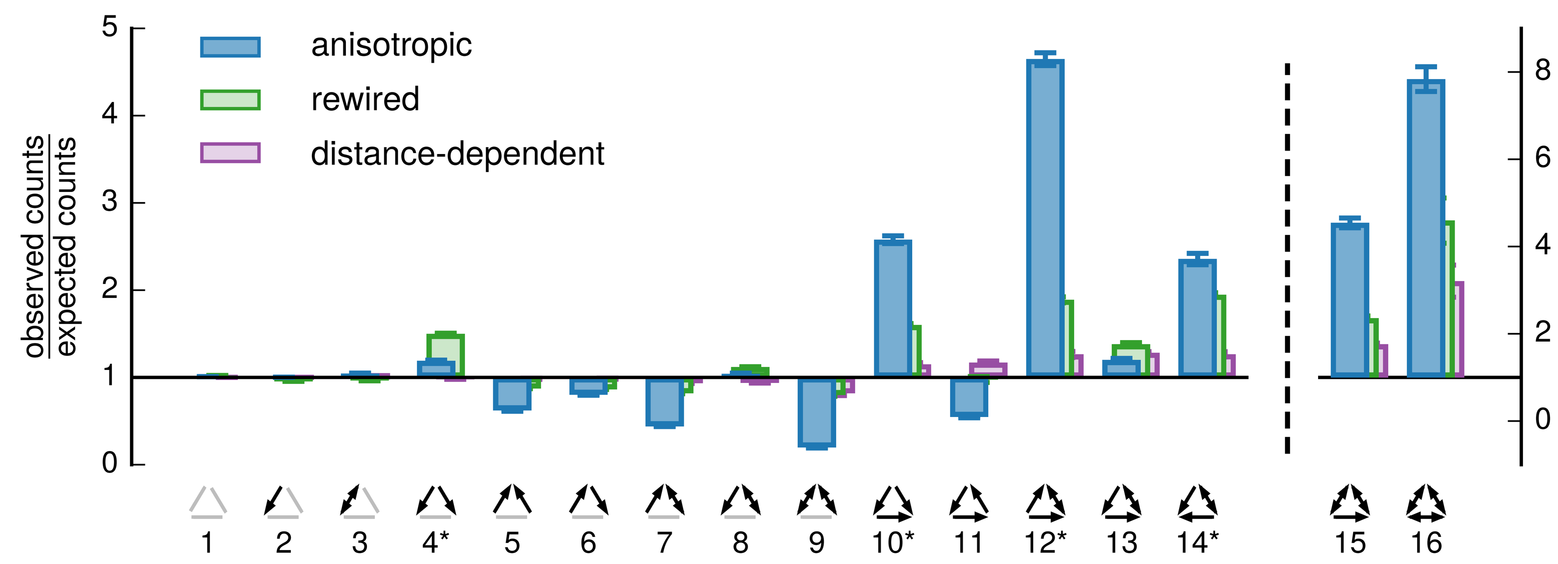

Figure 4: Occurrence of three neuron patterns relative to expected counts from pair statistics. Motifs indexed with * were reported to be overrepresented in [2].

Perin et al. [2] reported that in somatosenory cortex of rats, groups of neurons more often show a high connection density than expected from the measured distance-dependent connection probabilities. Both anisotropic and tuned anisotropic networks also showed this effect in groups of 3, 6, 8 and 12 cells (Fig. 5).

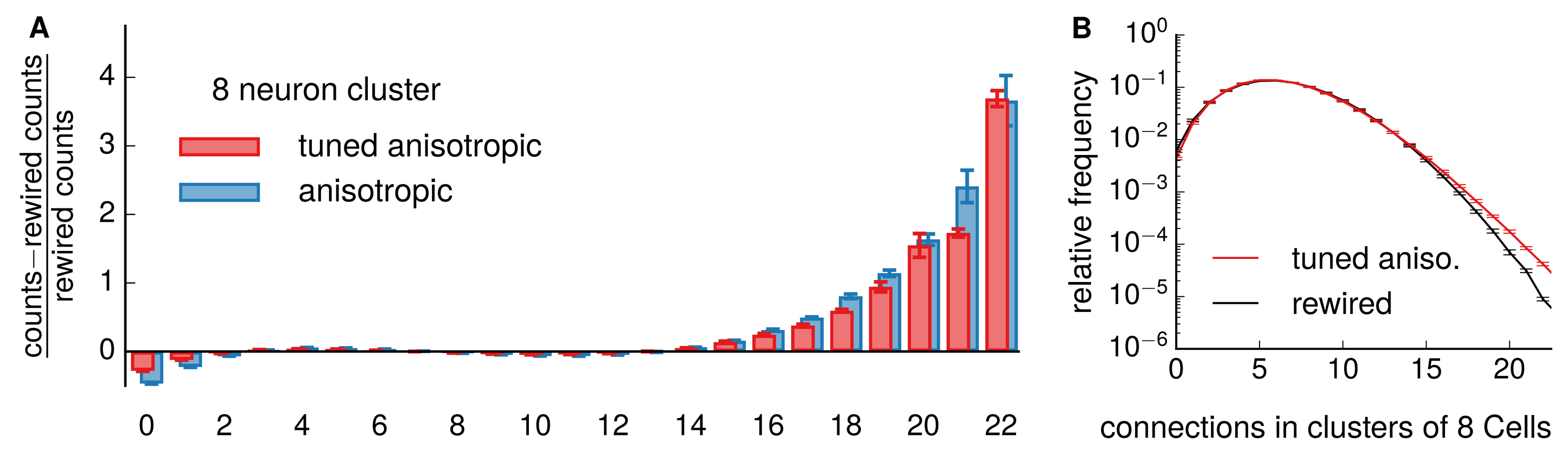

Figure 5: For groups of 8 cells a high number of connections appears more often in anisotropic and tuned anisotropic networks than in their rewired versions. **A** Relative difference in occurrence. **B** Frequency of number of connections in tuned anisotropic networks and their rewired version.

What other network connectivity properties does anisotropy affect? By only partially rewiring anisotropic networks, we found that the distribution of shared inputs to a random pair of neurons is shaped by anisotropy (Fig. 6A-C). In anisotropic networks unconnected, unidirectionally connected and reciprocally connected neuron pairs have distinctly different in-neighbour distributions, which is not the case for distance-dependent networks (Fig. 6D-E).

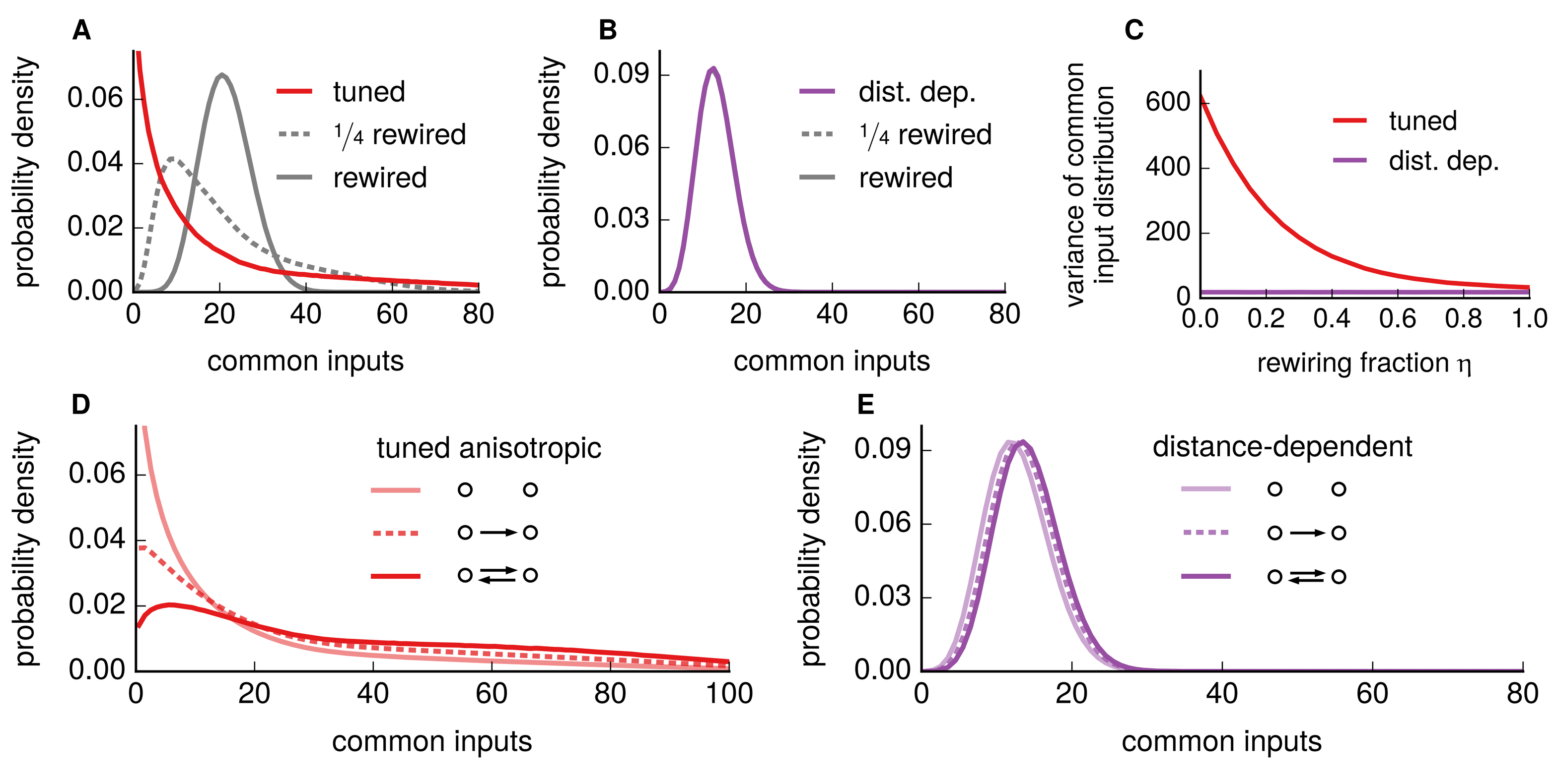

Figure 6: Anisotropy in spatial connectivity affects the distribution of common inputs. **A** Common in-neighbours to a random neuron pair in tuned anisotropic networks, partially rewired networks and fully rewired networks. **B** Common in-neighbour distribution in distance-dependent networks and rewired versions. **C** Variance of common in-neighbour distribution in tuned anisotropic and distance-dependent networks as a function of rewiring fraction η. **D-E** Common input distribution of unconnected, unidirectionally and bidirectionally connected neuron pairs in anisotropic tuned and distance-dependent networks.

Key points

- Anisotropy in spatial connectivity as result of stereotypical anisotropy in axon morphology
- Nonrandom connectivity patterns identified in anisotropic network model suggest that prominent connectivity structures of cortical circuits might arise from neuron morphology
- Common input statistics particularly affected by anisotropy: Induces broad distributions and significant differences between connected and unconnected neuron pairs

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