1 STRUCTURAL ASPECTS

Connectivity in local cortical circuits exhibits a salient feature: Examining the occurrence of connections in neuron pairs, studies have repeatedly found that bidirectionally connected neuron pairs appear much more frequently than expected from the network's overall connection probability. In layer 5 of the somatsosensory cortex studies from Markram (1997) and Perin et al. (2011) have found an overrepresentation of reciprocally connected pairs of thick tufted pyramidal cells, an observation that has also been reported in layer 2/3 (Holmgren et al. 2003) and layer 5 (Song et al. 2005) of the visual cortex. The overrepresentation of bidirectionally connected pairs is significant, Song et al. for example found such pairs represented four times the expected amount.

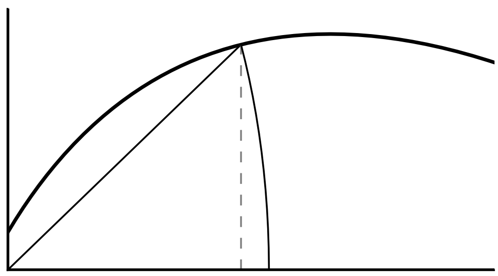

Figure 1.1: Here we examine anisotropy in connectivity as a possible candidate for an underlying principle explaining the characteristic two neuron connection distribution. In random networks, the chance to encounter a specific mode of connection in a random pair of neurons be can easily be computed from the overall connection probability p.)

The underlying connection principle imposing this overrepresentation on the network however remains unclear. Song et al. discuss the possibility of known learning rules to explain their findings, leaving a definitive answer open to further investigation. More recent studies find overrepresentation of reciprocally connected pairs *in vitro* resulting from functional specificity (Ko et al. 2011) and *in silico* from dense neuron clustering rules (Klinshov et al. 2014), identifying specific network characteristics that may contribute to the reported overrepresentation *in vivo*.

Here we examine anisotropy in connectivity as a possible candidate for an underlying principle explaining the characteristic two neuron connection distribution. In random networks, the chance to encounter a specific mode of connection in a random pair of neurons be can easily be computed from the overall connection probability p. For this let X be the random variable of the number of edges between two different vertices in a Gilbert graph $G(n,p)$ with $n \geq 2$. As the edges are independently realized, resulting in a simple directed graph, we have

$$\begin{aligned} \mathbf{P}(X=0) &= (1-p)^2 && \text{unconnected pair,} \\ \mathbf{P}(X=1) &= 2p(1-p) && \text{single connection,} \\ \mathbf{P}(X=2) &= p^2 && \text{reciprocal connection;} \end{aligned} \tag{1.1}$$

in short $\mathbf{P}(X=k) = \mathcal{B}_{2,p}(k)$ for $k \in \{0,1,2\}$ and $\mathbf{P}(X=k) = 0$ otherwise. Using this probability distribution as the expectation for connectivity of neuron pairs in the various network types, a numeric analysis of the anisotropic sample graphs reveals that bidirectionally connected pairs appear almost twice as often as expected from the overall connection probability ($p = 0.116$) and equations 1.1, similarly as reported by Song et al. (Figure 1.2 A). However, comparing the pair probabilities in anisotropic networks with the probabilities in their rewired counterparts, we find that anisotropy does not influence the occurrence of two-neuron motifs (Figure 1.2 B) In fact, expected connections in neuron pairs are identical in distance-dependent and rewired anisotropic networks (**??**).

We further support this observation by computing the probability distribution for the expected number of edges between to random vertices in the anisotropic graph model. For this we assume that only the distance-dependent connection probability $C(x)$ determines the occurrence of edges in vertex pairs in the anisotropic graph model. Then, using the probability distribution $f(x)$ for the a random neuron pair to be at distance x, we calculate

$$\begin{aligned} \mathbf{P}(X=0) &= \int_0^{\sqrt{2}} (1-C(x))^2 f(x)\,dx, \\ \mathbf{P}(X=1) &= \int_0^{\sqrt{2}} 2C(x)(1-C(x)) f(x)\,dx \quad \text{and} \\ \mathbf{P}(X=2) &= \int_0^{\sqrt{2}} C(x)^2 f(x)\,dx. \end{aligned}$$

Inserting the distance-dependent connection probabilities $C(x)$ in the anisotropic graph model as computed in Theorem **??** and the probability distribution $f(x)$ from Theorem **??** we obtain

$$\begin{aligned} \mathbf{P}(X=0) &= 0.791336 && 0.7907 \pm 0.0008 \\ \mathbf{P}(X=1) &= 0.184151 && 0.1846 \pm 0.0007 \\ \mathbf{P}(X=2) &= 0.024513 && 0.02462 \pm 0.00009, \end{aligned}$$

perfectly matching the probabilities extracted from anisotropic sample graphs in the right column (error SEM, `c5f1462b`). Noting that distance-dependency alone is sufficient to accurately predict edge probabilities in neuron pairs in the anisotropic network model and combined

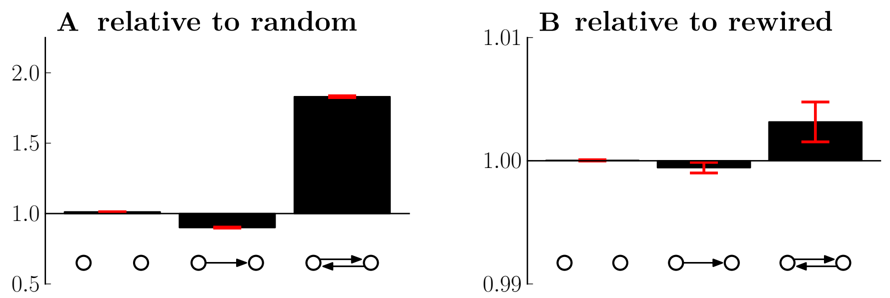

Figure 1.2: Overrepresentation of reciprocal connections in anisotropic networks due to distance-dependent connectivity Extracting the counts of unconnected, one-directionally and bidirectionally connected neuron pairs in the anisotropic sample graphs, overrepresentation of reciprocally connected pairs is identified as a feature of the network's distance dependency as opposed to anisotropy in connectivity. **A)** Showing the quotient of the counts for the three pair types, extracted from the set of sample graphs, with the number of expected pairs in Gilbert random graphs $G(n, p)$, where $n = 1000$ and $p = 0.116$ were matched to the sample graph parameters. While single connections appear less often than in Gilbert random graphs, reciprocal connections are significantly overrepresented. Errorbars SEM. **B)** Comparing appearance of connection pairs in the anisotropic sample graphs with their respective appearance in the rewired sample graphs, we find that eliminating anisotropy does not significantly change the counts for the connection types, indicating that anisotropy does not influence two neuron connection probabilities. Errorbars SEM. (`c5f1462b`)

with the observations in Figure 1.2, we conclude that varying degrees of anisotropy do not affect the occurrence of neuron pair motifs.

Does however distance-dependency affect the connections in neuron pairs? Finding in matching probabilities in (rewired) anisotropic and distance-dependent networks, we relate the observed overrepresentation (Figure 1.2 A) to distance-dependent connection probabilities.

that distance-dependency Song et al. as well as Perin eta al. report that distance-dependency is not the cause for overrepresentation. To test this tuned networks! Fig A remains unexplained, tune to be able to reproduce.