

STRUCTURAL ASPECTS

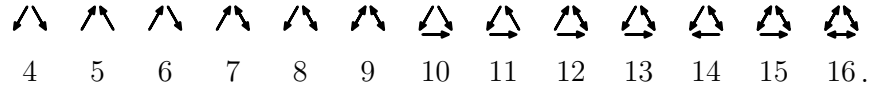
Subjecting the anisotropic network model to a critical examination of its structural features, we identify prevalent patterns of connectivity and relate theoretical and computational results to findings from experiments in the rat's cortex.

1.1 MOTIFS

In this chapter we analyze the structural. The term motif refers to... . Studies of [Song et al. \(2005\)](#) and [Perin et al. \(2011\)](#) show stuff. Per-nice2011, Sporns , Zhao2011.

Here we investigate the occurrence of three-neuron patterns in anisotropic networks. Song et al. (2005) reported a characteristic, highly non-random motif distribution of pyramidal cells in the rat's visual cortex (layer 5), a result later confirmed by Perin et al. (2011) in their experiment in the rat's somatosensory cortex (layer 5). Repeating the experiment *in silico* for the different networks subject to this study, we find similar, characteristic motif distributions strongly influenced by the anisotropy in connectivity.

There are 13¹ non-isomorphic 3-motifs in simple directed graphs. In reference to Song et al.'s result, the patterns are labeled 4 to 16,



Let X be a random variable that maps three random vertices $v_1 \neq v_2 \neq v_3$ in a graph G to the $n \in \{4, 5, \dots, 16\}$ labeling the isomorphism class of the full subgraph with vertex set $\{v_1, v_2, v_3\}$ in G as above if the subgraph is connected, and let X map to $n = 0$ otherwise. A first idea of how to compute the distribution of X is by inferring the probabilities of motif occurrence from the two-neuron connection probabilities from Section ?? . In anisotropic networks we found that the probabilities of occurrence are

$$\begin{aligned} p_u &= 0.791336 && \text{for unconnected pairs,} \\ p_s &= 0.184151 && \text{for single connections and} \\ p_r &= 0.024513 && \text{for reciprocal connections.} \end{aligned}$$

From these we may, for example, calculate the probability of occurrence for motif 8,

$$\mathbf{P}(X = 8) = 6 p_u p_s p_r,$$

where the factor 6 is determined by the number of different *labeled* graphs belonging to the isomorphism class. The distribution of X for the remaining motifs is given by

$$\begin{aligned} \mathbf{P}(X = 4) &= 3p_s^2 p_u & \mathbf{P}(X = 9) &= 3p_r^2 p_u & \mathbf{P}(X = 13) &= 6p_s^2 p_r \\ \mathbf{P}(X = 5) &= 3p_s^2 p_u & \mathbf{P}(X = 10) &= 6p_s^3 & \mathbf{P}(X = 14) &= 3p_s^2 p_r \\ \mathbf{P}(X = 6) &= 6p_s^2 p_u & \mathbf{P}(X = 11) &= 2p_s^3 & \mathbf{P}(X = 15) &= 6p_s p_r^2 \\ \mathbf{P}(X = 7) &= 6p_s p_u p_r & \mathbf{P}(X = 12) &= 3p_s^2 p_r & \mathbf{P}(X = 16) &= p_r^3. \end{aligned}$$

¹ There are 16 non-isomorphic simple directed graphs with 3 nodes. Three of those graphs are unconnected (cf. Davis 1953, N. J. A. Sloane. The On-Line Encyclopedia of Integer Sequences, <http://oeis.org>. Sequence A000273).

Does this distribution accurately reflect the occurrences of three-neuron motifs in anisotropic or even distance-dependent networks? Here we take the distribution determined from the two-neuron probabilities as a reference to analyze occurrences of three-neuron motifs in our sets of sample graphs. Counting the occurrences of patterns in we find that there are significant over- and underrepresentations in anisotropic as well as distance-dependent networks, relative to our expectation (Figure 1.1). We find, for example, that in anisotropic graphs pattern 12 occurs almost 5 times as often as we would have expected from the two-neuron probabilities, whereas the counts for pattern 11 only make up less than 30% of the occurrences expected.

*distribution from
neuron-pairs as
reference*

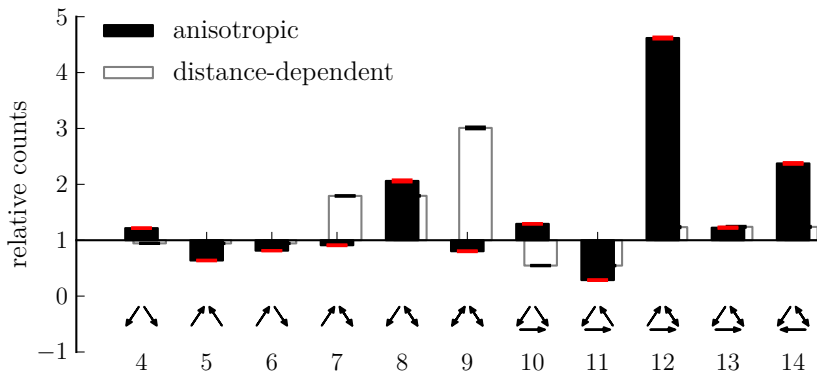


Figure 1.1: Relative occurrence of three-neuron patterns Extracting the counts of three-node motifs in anisotropic (filled bars) and distance-dependent networks (unfilled bars), the quotient of the obtained count with the number of occurrences expected from the two-neuron connection probabilities in the networks (cf. Section ??) shows the over- and underrepresentation of specific motifs in the network (red and black errorbars are SEM). In anisotropic networks pattern 12, for example, appears around five times more often than we would expect from the occurrence two-neuron connections. The relative counts for anisotropic networks resemble the findings of Song et al. (2005) and differ significantly from the counts in distance-dependent networks, implying that anisotropy has a strong influence on the relative occurrence of three-neuron patterns. (4839ce41)

Comparing the relative counts for motifs in anisotropic graphs with those in comparable distance-dependent networks, we identify a strong influence of anisotropy in connectivity on three-neuron motif occurrence (Figure 1.1). In their experiments, Song et al. and Perin et al. find an overrepresentation of motifs 4, 10, 12 and 14. In anisotropic networks increased counts of motifs 4, 8, 10, 12, 13 and 14 were recorded. However, motifs 8 and 13 are overrepresented in distance-dependent networks as well, leaving the reported motifs 4, 10, 12 and 14 as motifs that are overrepresented due to anisotropy. To analyze this effect

*anisotropy
strongly affects
3-motif occurrence*

closer, we also compare three-neuron counts before and after rewiring in anisotropic networks (Figure 1.2).

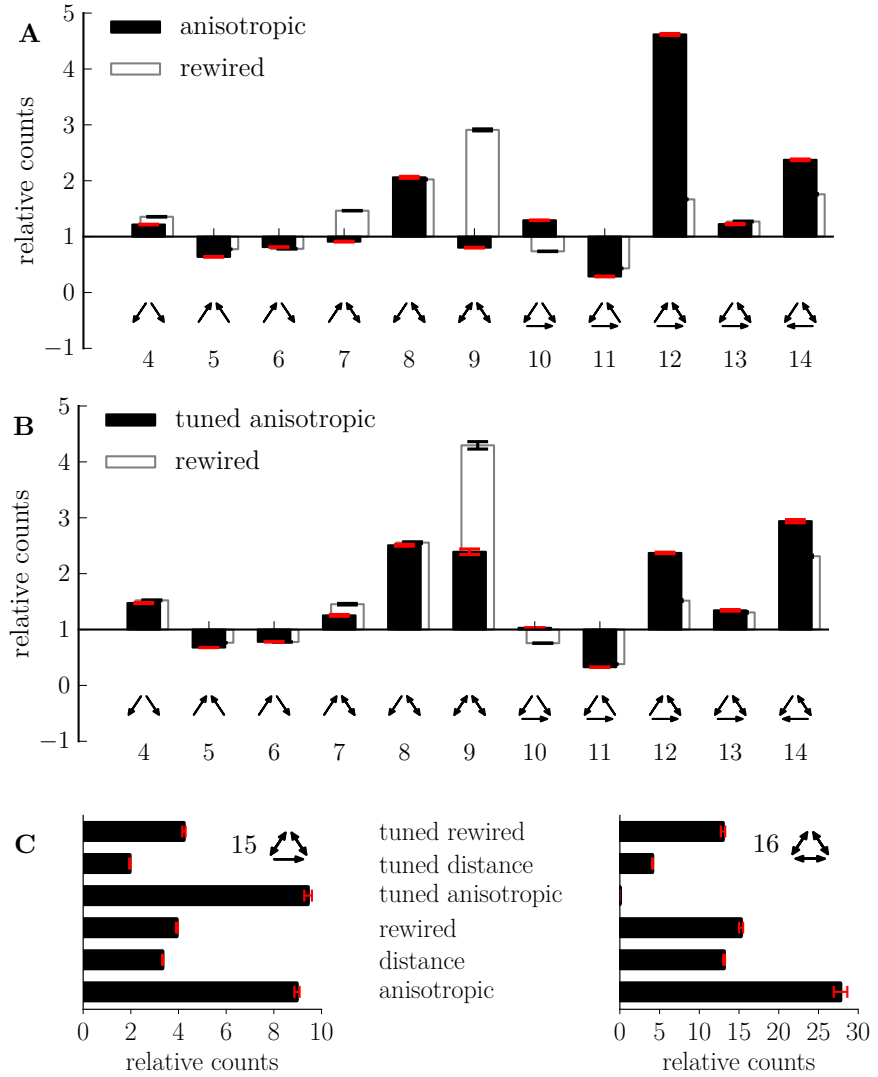


Figure 1.2: Three-neuron motif occurrence in different network types **A)** Comparing counts in anisotropic sample graphs with their rewired counterparts. **B)** Three-neuron motifs occurrence in tuned anisotropic networks (cf. Section ??) with their rewired counterparts. For this two-neuron connection probabilities were extracted as in Section ?? and motif probabilities were calculated analogously to anisotropic networks. **C)** Relative counts for the high edge count motifs 15 and 16 for different network types, errorbars SEM. (4839ce41)

Considering motif occurrences in anisotropic as well as tuned anisotropic networks, we once again confirm the overrepresentation of motifs 4, 10, 12 and 14. However, increased counts of pattern 4 are observed in the rewired networks as well, leading to the conclusion that increased occur-

rence in this motif is only implicitly affected by anisotropy. Motifs 10, 12 and 14 however show significant overrepresentation even over their rewired counterparts in anisotropic as well as in tuned anisotropic networks.

The overall motif distribution shows itself stable under changes in the distance-dependency with the notable exception of motif 9, that shows underrepresentation only in anisotropic but not in tuned anisotropic or any distance-dependent network type. Analyzing the occurrences of motifs 15 and 16 with a high edge counts (Figure 1.2 C) we find that anisotropy has strong influence on both motifs, with motif 15 being significantly overrepresented in anisotropic networks. Motif 16 shows a highly increased occurrence in anisotropic networks, however tuning causes the loss of this feature in the network connectivity.

Summarizing the above observations, we find that anisotropy in connectivity induces increased occurrence of motifs 10, 12, 14 and 15 in the network, reflecting experimental results in the rat's cortex. While over- and underrepresentation observed in local cortical circuits can be indirectly linked to anisotropy for some motifs (4, 9), it does not accurately reflect observed counts for other motifs (8) and shows instability under manipulation of distance-dependency in some patterns (9, 16).

results summary

Edge counts in neuron clusters

In motifs consisting of 3 to 8 neurons, Perin et al. (2011) reported a striking statistic from their experiment with pyramidal cells in the rat's somatosensory cortex, layer 5: Counting the number of edges appearing in a cluster of n neurons, they find that clusters with relatively high edge counts appear significantly more often than expected from the network's distance-dependent connection probabilities alone. Do anisotropic networks exhibit a similar feature?

Recruiting the collection of sample graphs once again we analyze the occurrence of edge counts in clusters of n neurons in the different network types. In the main process, after randomly sampling n pairwise different vertices S_n , the motif H in G with vertex set $V(H) = S_n$ is identified and its number of edges $|E(H)|$ is recorded. Repeating this sufficiently often (order 10^6) we obtain edge counts for clusters of 6, 8 and 12 neurons in the anisotropic- and tuned anisotropic networks as well as in their rewired counterparts. Then, showing the difference between counts in the anisotropic networks and counts in the rewired networks, normalized by the rewired counts, we identify an overrep-

resentation of high edge counts in the neuron similar to Perin et al. (Figure 1.3).

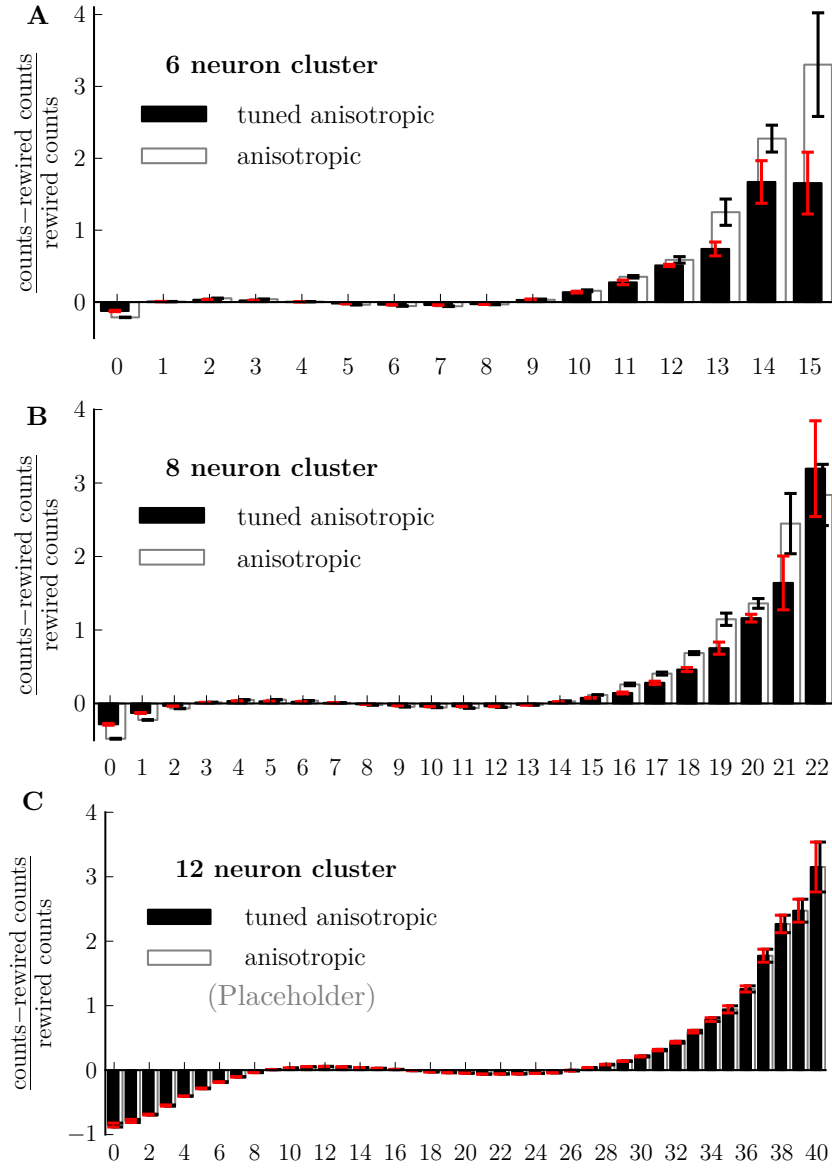


Figure 1.3: High edge counts are overrepresented in networks with anisotropy The number of edges in random clusters of 6, 8 and 12 neurons were recorded in the anisotropic and tuned anisotropic networks, as well as in their rewired counterparts. Visualizing the normalized difference between counts in the anisotropic and rewired networks, shows an overrepresentation of high edge counts in networks with anisotropy in connectivity.

Tuning the networks distance-dependency appears to have no affect as overrepresentations in anisotropic and tuned anisotropic are essentially

Anisotropic networks inherently carry a connection principle that goes beyou

we find that this effect is even stronger in comparison with distance-dependent networks (Figure 1.4).

Here

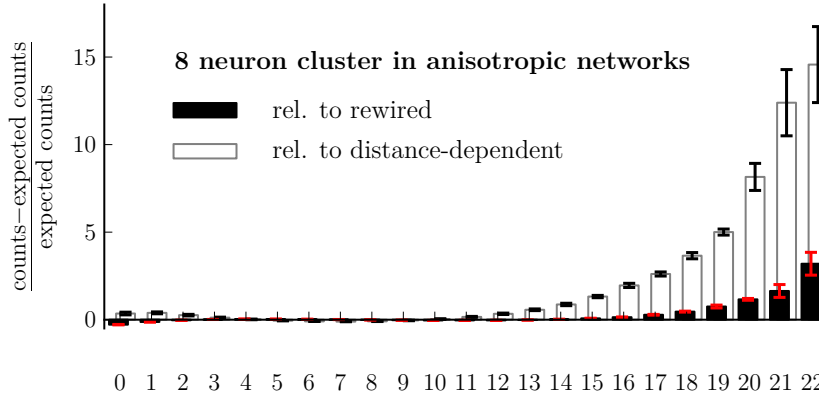


Figure 1.4: Stronger overrepresentation of clusters with high edge counts with distance-dependent networks as reference
 Showing we find that the overrepresentation of motifs with high edge counts is stronger (7c826e10)

1.2 COMMON NEIGHBOR RULE

In their study, Perin et al. follow their report of increased edge counts in neuron clusters with the observation of a “common neighbor rule”. Relying once again on their data in the rat’s somatsensory cortex, Perin et al. find that not only do neuron pairs with a high number of common neighbor count appear significantly more often than expected, but also that such pairs display a higher probability of being connected. In fact, the relationship between pair connectivity and number of common neighbors appears to be linear. Perin et al. also report that this effect is most pronounced when only considering common in-neighbors, that is other neurons that are projecting to both neurons in the pair.

common neighbor rule as underlying principle?

Here we also investigate our networks for the existence of such a common neighbor relationship. Simultaneously recording connection probabilities and the number of common neighbors between pairs of neurons, we find inherent dependencies between the two quantities in all network types (Figure 1.5).

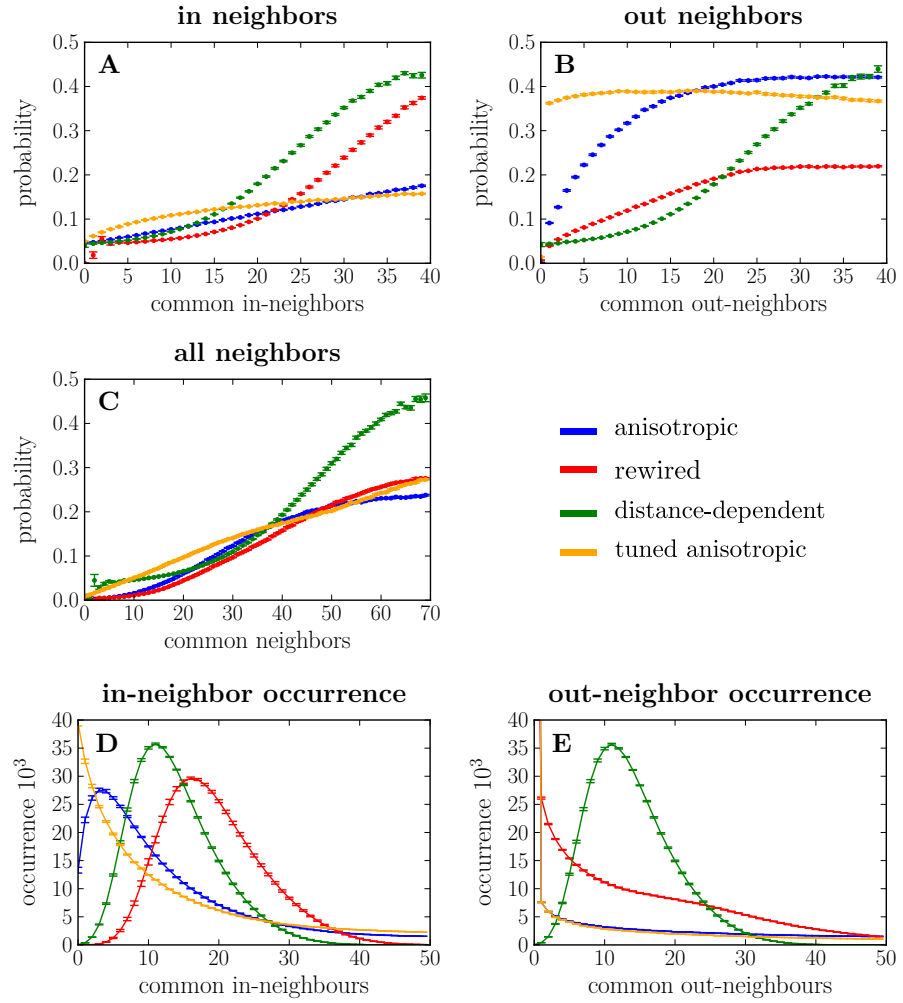


Figure 1.5: Distance-independent overrepresentation of reciprocal connections (something)

Analyzing the results, we immediately note the sharp difference between in- and out-neighbors in their effect on connection probabilities in anisotropic networks, as well as in rewired networks. Only in distance-dependent networks it appears that in- and out-neighbors can be considered equivalent in their influence on connection probabilities (Figure 1.5 A-B). Furthermore, while the distribution of the number of common neighbors is consistent in distance-dependent networks, the other network types display a characteristic distribution of common out-neighbors (Figure 1.5 D-E). This observation clearly relates to the drastically different out-degree distributions in the different networks found in Section ??.

Both for in- and out-neighbors, we find characteristic curves describing their influence on connection probabilities. The in-neighbor profiles split into two categories: While networks with anisotropy in connectivity (blue, orange) display a constant increase, distance-dependent

network types (red, green) show a sigmoidal shared input-connection probability curve (Figure 1.5 A). We thus find a strong influence of anisotropy on the shared input relationship, inducing a common neighbor rule characteristically different from isotropic, distance-dependent networks.

anisotropy induces characteristic common neighbor rule

Does this anisotropy-induced rule reflect the findings in cortical networks? Perin et al. report a linear common neighbor relationship, finding a stronger effect when considering only in-neighbors. Imposing the common neighbor rule on *in silico* networks reflecting a distance-dependency as determined *in vivo*, Perin et al. were then able to reproduce the observed overrepresentation of high edge counts in neuron clusters, identifying the common neighbor effect as an underlying connection principle inducing increased high edge counts in clusters comparable to the profiles shown in Figure 1.3. Showing not only the presence of such an edge count overrepresentation in anisotropic networks, but also finding that only networks featuring anisotropy display an approximately linear relationship between common inputs and connection probability, we identify anisotropy in connectivity as a candidate for an underlying connection principle motivated from neuronal morphology, to induce a common neighbor rule, that may be at the heart of many of the non-random connectivity statistics observed in local cortical networks.

anisotropy as underlying connection principle!

Extending the analysis of shared inputs in the different network types, we further observe that anisotropy affects the number of common in-neighbors typically observed itself (Figure 1.5 D). We specifically find that increases anisotropy in connectivity induces an increased variance in the distribution of common inputs of a random neuron pair (Figure 1.6). Such increased variance may provide an important advantage in the processing of information, allowing a heightened functional specificity in the network, where many neurons do not share many common inputs, enabling a high variety of functionality, and where few neuron pairs have a high number of shared inputs, strengthening their correlation and thus their capacity to relay related information.

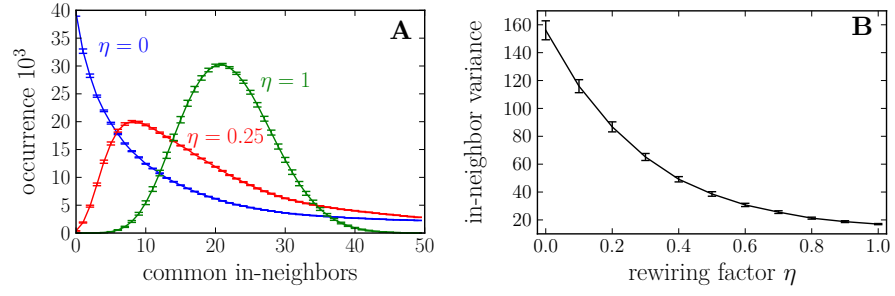


Figure 1.6: Anisotropy increases variance of common input distribution Recording common in-neighbor counts for random neuron pairs in tuned anisotropic networks and their rewired versions reveals increased variance in networks with a high degree of anisotropy. **A)** Common in-neighbor distribution for original tuned anisotropic networks ($\eta = 0$, blue) and rewired versions with $1/4$ of all edges rewired ($\eta = 0.25$, red) and completely rewired ($\eta = 1$, green). (5841710e) **B)** Variance of the common in-neighbor distributions declines with increasing rewiring factor η ; highest variance is found in networks with the highest degree of anisotropy ($\eta = 0$). Errorbars SEM. (ffcefe9b)