

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 visual cortex.

1.1 INTRODUCTION

Investigation of the brain's connectivity is an ongoing endeavour. Concurrent collaborative efforts like the Human Connectome Project [HCP], the Open Connectome Project [OCP] and the Allen Brain Atlas [ABA], intent on mapping the 'wiring' of the brain, as well as the continued development of experimental techniques and computational resources, demonstrate the great interest in advancing this field.

HUMAN
Connectome
PROJECT
humanconnectome.org

*Open Connectome
Project*
[openconnectome-
project.org](http://openconnectome-project.org)

ALLEN BRAIN ATLAS
brain-map.org

Research in brain connectivity spreads over the whole scale of the brain; from the mapping of fiber pathways between brain regions at the macroscopic level, to the synaptic connections of individual neurons on the microscale, researchers are trying to identify the links that enable the brain its characteristic cognitive abilities. connections, these links are of anatomical nature. However, statistical dependencies and causal relationships between the distinct computational units in the brain are being researched with equal emphasis (Sporns 2007).

Connectivity in the context of the directionally heterogenous geometric networks introduced in Section ??, refers in this chapter to structural links. So far, we have only briefly mentioned that the network's nodes should be interpreted as individual neurons; to allow for a discussion of functional relationships between nodes, we have yet to provided a physical description of a neuron's function. As such, we will here explore the network's structural connectivity, modeling synaptic contacts between axon and dendrites of individual neurons.

Synaptic Connectivity

In the local cortical circuits the anisotropic geometric model was derived from, synaptic connectivity is a major mode of configuration. In those networks, connectivity has been determined to be neither completely random nor exclusively specific [Source]. Recurring patterns of connectivity have been identified by several reports (Sporns and Kötter 2004; Song et al. 2005; Perin et al. 2011).

The impact of this structural specificity discovered in local networks is shown to be significant; while the linking of network structure and network dynamics remains an active field of research, several studies were able to employ computational and theoretical models to establish such a connection. A study by Zhao et al. from 2011, for example, demonstrates how second order connectivity statistics affect a network's propensity to synchronize (Zhao et al. 2011). In the same year, Alex Roxin reported on the influence of in- and out-degree distributions on dynamics of neural network (Roxin 2011). Later, Pernice et al. were able to link structural connectivity to spike train correlations in neural networks (Pernice et al. 2011).

Mapping synaptic connectivity in experiments

Experimentally, paired intracellular recordings are used to determine synaptic connectivity in cortical slices. Using two electrodes, one inserted in the cell and one outside the cell, a single intracellular recording allows for measurement of a cell's membrane potential (Brette and Destexhe 2012, Chapter 3; Weckstrom 2010). Simultaneous recordings from multiple neurons are then able to infer synaptic connectivity by evoking an action potential through current injection in one neuron and observing the change of membrane potential in the other cells (Song et al. 2005).

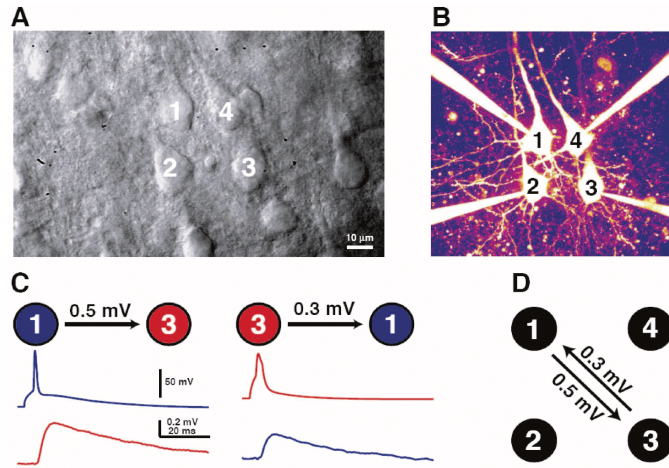


Figure 1.1: Song et al. use quadruple whole-cell recordings, observing simultaneously the membrane potential of four neurons. **A)** Contrast image showing four thick-tufted L5 neurons **B)** Fluorescent image of the same cells after patching on **C)** Evoking an action potential in the presynaptic neuron causes characteristic membrane potential change in the postsynaptic neuron **D)** Inferring synaptic connectivity from the EPSP waveform observed in C). Image from (Song et al. 2005).

While techniques for paired intracellular recordings are rapidly developing, their ability to capture connectivity patterns of large networks is yet very limited. To this date, the connectome of *C. Elegans* remains the outstanding exception of a connectivity configuration that has been fully mapped [Source]. Even in the state-of-the-art experiment conducted by Perin et al., using a setup capable of recording up to twelve neurons simultaneously, the authors note that an investigation of degree distribution was not carried out, due to lack of sufficient data (Perin et al. 2011).

Exploiting the benefits of a geometrical model

Working with a geometrical network model and its computational implementation, such restrictions disappear; the full information about the network, in form of its connectivity matrix, is given at point in time and can be easily queried for. Experiments that may take days to perform *in vivo*, can be completed in a matter of seconds *in silico*. As such, geometrical models lend themselves to extensive examination of their structural aspects.

*Extrapolation vs.
reduction*

In trying to exploit these advantages, two approaches present themselves. One may construct a network model that extrapolates the known biological configuration; a full structural examination of these networks could possibly expose relevant patterns not yet observed. For this approach a sophisticated understanding of the biological configuration is critical. Neuron morphology, however, is difficult to describe and extract.

For this analysis we suggest a reductionist approach. Having motivated an abstract model reflecting a cortical network's directional heterogeneity, we distinguish emerging patterns of connectivity, specific to directionally heterogeneous networks, from results, that only indirectly stem from the network's anisotropy, in the hopes to be able to characterize the significance of directional heterogeneity in structural connectivity of cortical circuits.

Structural aspects of the heterogeneous model

In this chapter we subject the anisotropic network model introduced in Section ?? to a critical analysis of its structural aspects. General network topology, as well as specific modes and patterns of connectivity, are to be identified and laid out for comparison with findings in biological neural networks.

*employing
anisotropy
measure*

In an effort to map out structural features that can be directly associated with the network's directional heterogeneity, it is crucial to differentiate such findings from results that are only indirectly caused by the network's anisotropy. To this end, already in Section ?? we developed a measure to quantify the degree of anisotropy prevalent in a given network; throughout this chapter we will now frequently employ this measure to determine which structural aspects are originating from the network's heterogeneity, and which aspects are to be attributed solely to the network's distance dependency.

Accordingly, results from this investigation are categorized in two sections: The first section, 'Section 2', describes structural aspects that can not be directly attributed to the model's anisotropy. The second section, 'Section 3', then presents results that are truly features of network's directional heterogeneity.

1.2 DEGREE DISTRIBUTION

The in- and out-degree of vertex in a directed graph describes the number of incoming and outgoing connection from and to other vertices (cf. Definition ??). As a fundamental concept in graph and network theory, the degree distribution is integral in the categorization of networks and allows for the estimation of graph properties.

Degree distribution was shown to have strong impact on the dynamics of neuronal networks models commonly used in computational neuroscience research (Roxin 2011). Increasing in-degree variance for example could be connected to the appearance of oscillations in the network. Extracting degree distributions from biological networks however, remains a challenge as many neurons need to be tracked simultaneously to obtain enough data to confidently estimate degree distributions.

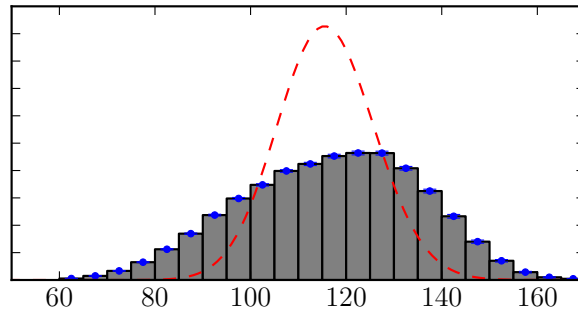


Figure 1.2: In-degree distribution in anisotropic networks shows comparably high variance and is skewed to the left From 250 anisotropic networks in-degree distributions were extracted and are shown in a normed histogram plot, errorbars SEM. Comparison with the binomial degree distribution (red) of a Gilbert random graph model with matching parameter set ($N = 1000$, $p = 0.116$) shows higher variance of in-degrees in anisotropic networks (sample variance = 344.54, variance of binomial distribution $Np(1 - p) = 102.44$.) Skewness to the left of the sample is -0.1763 . (9326138e)

Here we analyze in- and out-degrees in the anisotropic network model. First we find that compared to the binomial in-degree distribution of a Gilbert random graph model, in-degrees of vertices in anisotropic networks display higher variance and their distribution is skewed to the left (Figure 1.2). However, this specific in-degree profile is not an intrinsic property of anisotropy, as the distribution remains stable under manipulation of the anisotropy degree and closely matches the profile of a purely distance-dependent network (Figure 1.3). This result agrees

with findings of Perin et al. (2011, Fig. S3), who were able to recreate degree distributions from their experiment with layer V thick-tufted pyramidal cells in neonatal rats from the extracted distance-dependent connection profiles alone.

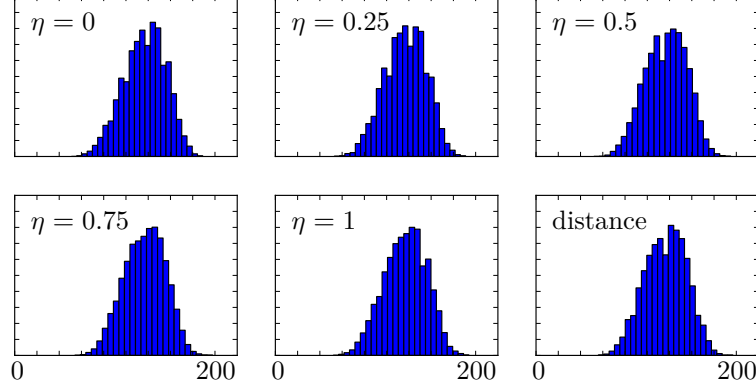


Figure 1.3: In-degree distribution not affected by varying degrees of anisotropy In-degree distributions from the 25 sample graphs (ref ??) and their rewiring stages are plotted in normed histograms and listed from rewiring factor $\eta = 0$ (original anisotropic) to $\eta = 1$ (completely rewired, maximal isotropy). Comparison shows that varying degrees of anisotropy do not influence the degree distribution, in fact in-degree distributions match with the degree distribution of an equivalent distance-dependent network shown bottom-right (77995b6b).

While the out-degree distribution of vertices in the anisotropic network also shows itself stable under rewiring, its distribution is drastically different from the out-degree distribution in a comparable distance-dependent network (Figure 1.4). The asymmetric, long-tailed distribution is identified as an artifact of the anisotropic network’s spatial confinement; a neuron, closely located near a surface edge, might have an axon projection out of the square causing minimal out-degree or, projecting through the entire length of the surface, may have maximal out-degree. Approximating the expected number of outgoing connections for a vertex in an anisotropic network of size N , side-length s and axon width w as

$$N \frac{wl}{s^2},$$

with parameters $N = 1000$ and $\frac{w}{s} = 0.252$, we obtain an upper bound for the expected out-degree,

$$N \frac{wl}{s^2} \leq N \frac{w}{s} \sqrt{2} \approx 350.$$

If $f(l)$ is the probability density function to find axon length l for a random node v in the anisotropic network model, the out-degree distribution is then approximated by

$$\Pr[d_{\text{out}}(v) = N \frac{wl}{s^2}] = f(l), \quad (1.1)$$

see also Figure 1.5.

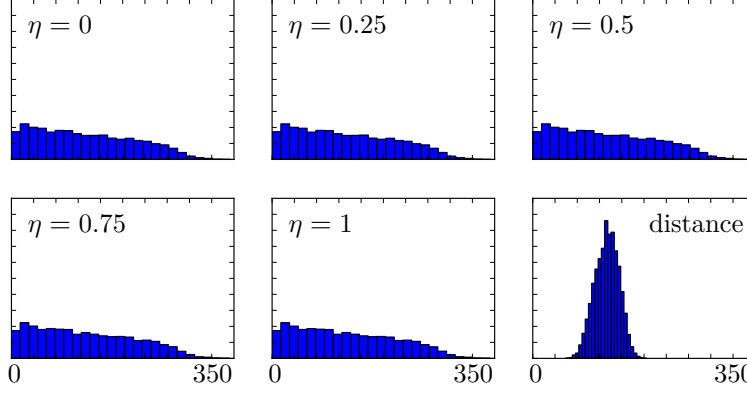


Figure 1.4: Out-degree distribution not affected by varying anisotropy but highly different from distance-dependent networks Out-degree distributions from the 25 sample graphs (ref ??) and their rewiring stages are plotted in normed histograms and listed from rewiring factor $\eta = 0$ (original anisotropic) to $\eta = 1$ (completely rewired, maximal isotropy). While varying degrees of anisotropy do not influence the degree distribution, the characteristic out-degree profile is drastically different from the distribution found in equivalent distance-dependent networks (77995b6b).

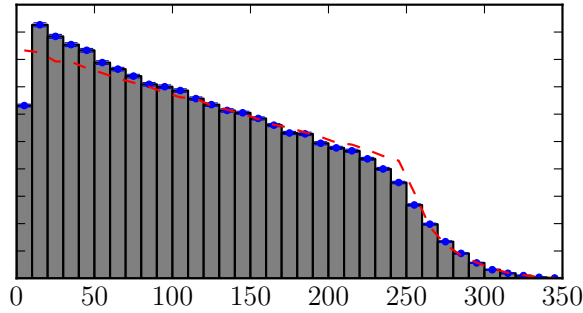


Figure 1.5: Characteristic out-degree distribution as an artifact of network's boundaries From 250 anisotropic networks out-degree distributions were extracted and are shown in a normed histogram plot, errorbars SEM. The characteristic distribution is identified as an artifact of the network's spatial confinement; using equation 1.1 the out-degree profile is approximated (red) by the distribution of axon lengths in the anisotropic network (019555b0).

1.3 SMALL WORLD PROPERTIES

Sporns papers

1.4 MOTIFS

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