1

STRUCUTRAL ASPECTS

In this chapter we review basic graph theory and explain how these terms are applicable in the context of biological neural networks. We begin with the definition of directed graphs:

1.1 DEFINITIONS & BASICS

References for this chapter: `http://nlab.mathforge.org/nlab/show/graph`, `http://nlab.mathforge.org/nlab/show/quiver`, (Bang-Jensen and Gutin 2008)

Definition 1.1.1 (Directed graphs)**.** A **directed pseudograph** G consists of two finite (, non-empty?) sets V, the *set of vertices* of G, and E, the *set of edges* of G, and two maps

$$s, t : E \to V,$$

the *source* and *target functions* of G. A **directed multigraph** is a directed pseudograph without *loops*, that is the map $d = (s, t) : E \to V^2$ already maps maps to $V^2 \setminus \Delta_V$, where $V^2 = V \times V$ denotes the cartesian product and $\Delta_V = \{(x, x) | x \in V\} \subseteq V^2$ the diagonal. Similarily, a **directed loop graph** is a directed pseudograph where d is injective. Finally, a **simple directed graph** can be defined as a directed pseudograph where d is both injective and already maps to $V^2 \setminus \Delta_V$.

Thus, in simple directed graphs, neither parallel edges nor loops - edges between the same vertex - are allowed, whereas directed multigraphs and directed loop graphs admit one of them respectively.

Say something about what "directed graph" means here.

Given a directed graph G, we denote with $V(G)$ the set of vertices of G and call it the **vertex set** of G. Analogously, the **edge set** $E(G)$ of G denotes the set of edges of G. This means, for a directed graph specified as $G = (V_G, E_G, s_G, t_G)$, we have

$$V(G) = V_G \quad \text{and} \quad E(G) = E_G.$$

A **morphism** $\phi : G \to H$, between two directed graphs $G = (V_G, E_G, s_G, t_G)$ and $H = (V_H, E_H, s_H, t_H)$, consists of a pair of maps $\phi_V : V_G \to V_H$ and $\phi_E : E_G \to E_H$, such that

$$s_H \circ \phi_E = \phi_V \circ s_G \quad \text{and} \quad t_H \circ \phi_E = \phi_V \circ t_G,$$

that is such that the following diagram commutes:

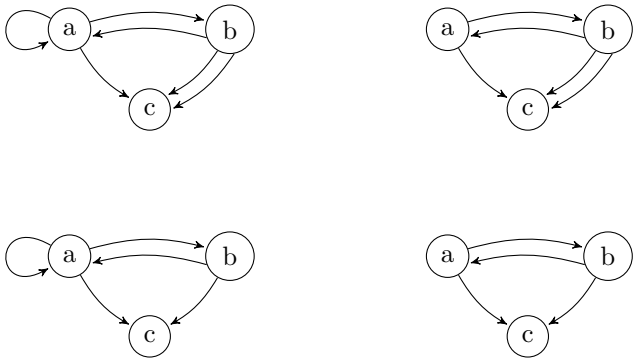
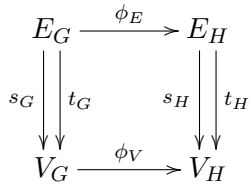


Figure 1: From top left to bottom right, typical examples of the defined graph types: A) directed pseudograph, B) directed multigraph, C) directed loop graph D) simple directed graph.



A morphism $\varphi : G \to H$, between two directed pseudographs G and H is an **isomorphism**, if the maps $\varphi_V : V_G \to V_H$ and $\varphi_E : E_G \to E_H$ are bijective. Two directed pseudographs are called *isomorphic* if there exists an isomorphism inbetween them.

Remark The last definition implies that, if there exists an isomorphism $\varphi : G \to H$, an isomorphism $\psi : H \to G$ can be found. This isomorphism is, of course, easily constructed via $\psi_V : V_H \to V_G, v \mapsto \varphi_V^{-1}(v)$, $\psi_E : E_H \to E_G, e \mapsto \varphi_E^{-1}(e)$.

Definition 1.1.2 (Weighted directed graphs)**.** A **weighted directed graph** is a directed graph G along with a mapping $\omega : E(G) \to \mathbb{R}$, called the *weight function*. Similarily, a **vertex-weighted directed graph** is a directed graph with a mapping $\nu : V(G) \to \mathbb{R}$.

Remark (heavy draft), title: A directed graph category for biological neural networks, in a bordered box?
Certainly, a weighted directed pseudograph is the most fitting mathematical modelling to the biological situation, since self connections and multiple synapse are not only plausibel (source?) but the rule. However there is one abstraction we can make by adding together the synaptic weights - NEST is doing it..
Also think about **inhibitory, excitatory**. Suggestion: edge weights

$\omega : E(G) \to \mathbb{R}^+$ **and** vertex weights $\nu : V(G) \to \{-1, 1\}$. Synaptic weight $\text{syn}(e)$ for edge e is then

$$\text{syn}(e) = \nu(s(e))\,\omega(e).$$

Benefit: Synapse from one neuron are either excitatory or inhibitory but not mixed as in bio.

Equivalent definiton for directed loop graphs A directed loop graph G can be equivalently defined as a pair of finite(, non-empty?) sets V, the *set of vertices* of G, and $E \subseteq V^2$ the *set of edges* of G. For an edge $(x, y) \in E$, we call x the *source* and y the target of the edge (x, y).

Source and target functions are then uniquely determined as the projections on the first and second component, $s = \text{pr}_1, t = \text{pr}_2 : E(G) \to V$. Conversely, the edge set $E(G) \subseteq V^2$ can be determined from the source and target functions as $E := \{(s(e), t(e)) | e \in E\}$. The trivial identities $(x, y) = (\text{pr}_1(x, y), \text{pr}_2(x, y))$ and $\text{pr}_1(s(e), t(e)) = s(e)$ with $\text{pr}_2(s(e), t(e)) = t(e)$ quickly verify the equivalence of the definitions.

Given a directed loop graph G, we often assume the graph to be given in this form and write edges as $e = (x, y)$. Note that this concept is more complicated to introduce for directed pseudographs, since parallel edges e and e' should to be differentiated in the egde set of G, establishing the need for $E(G)$ to be a multi- or indexed set, notions we are trying to avoid in this document.

From now on any *directed graph* is assumed to be a directed loop graph. Although most, if not all, concepts work for directed pseudographs just as well, we want to start to heavily use the canonical edge representation, which when talking about pseudograps makes problems as mentioned before.

More Notation - Check, do I really need this? For a pair of vertex sets $X, Y \subseteq V(G)$ of a directed graph G we write

$$(X, Y)_G = \{(x, y) \in E(G) | x \in X, y \in Y\}$$

for the set of edges with source in X and target in Y. For vertex sets with a single element $X = x$, we also write $(x, Y)_G$ and mean the edges with source x and target in Y.

In- and out-degree For a directed graph G the **in-degree** $d^-_G(x)$ of a vertex x is defined as the number of edges of G with target x, that is

$$d^-_G(x) = |(V(G), x)_G|\,.$$

Similarily, the **out-degree** $d^+_G(x)$ of x is defined as

$$d^+_G(x) = |(x, V(G))_G|\,,$$

the number of edges in G with source x.

Side In some literature about directed graphs (Bang-Jensen), loops are *not* counting towards the in- or out-degree of vertex. In the light of neural network however, we specifically want to count loops as well.

A basic property of the in- and out-degree in directed graphs is that number of in-degrees of every vertex, as well the sum of every out-degree, equal the total number of edges:

Proposition 1.1.1. *In every directed graph G, we have*

$$\sum_{x\in V(G)} d^-(x) = \sum_{x\in V(G)} d^+(x) = |E(G)|.$$

Proof. Since $(V(G),x)_G \cap (V(G),y)_G = \emptyset$ for $x \neq y$, we can write

$$\sum_{x\in V(G)} d^-(x) = \left| \bigcup_{x\in V(G)} (V(G),x)_G \right| = |(V(G),V(G))_G| = |E(G)|.$$

Analogously for the out-degree. □

Walks and distances

Let G be a directed graph (what does it mean here?). A **walk** W in G is an alternating sequence $(x_1,e_1,x_2,e_2,x_3,\ldots,x_{n-1},e_{n-1},x_n)$ of of vertices x_i and edges e_i from G, such that

$$s(e_i) = x_i \quad \text{and} \quad t(e_i) = x_{i+1}, \text{ for } i = 1,..,n-1,$$

that is, such that the vertices are connected by the edges inbetween them. We denote the set of vertices $(x_1,\ldots,x_n)$ of W as $V(W)$ and the sequence of edges $(e_1,\ldots,e_{n-1})$ as $E(W)$ (need it?).

The vertices x_1 and x_n are called the *end vertices* of W and we also say that W is an (x,y)-walk. The **length** of W is defined as the length of the sequence of edges; a walk consisting of only one vertex has length zero. colon, really?

Definition 1.1.3 (Distance)**.** The **distance** of two vertices x,y in a directed graph G (means?), is defined as the minimum length of an (x,y)-walk, if any such walk exists, otherwise $\text{dist}(x,y) = \infty$. In short,

$$\text{dist}(x,y) = \inf\{|E(W)| \mid W \text{ is } (x,y)-\text{walk}\}.$$

$|E(W)|$ is not explained. Necessary?

Proposition 1.1.2. *The distance function* $\text{dist} : V(G)\times V(G) \to \mathbb{N}$ *of a directed graph G satisfies the triangle equality,*

$$\text{dist}(x,z) \leq \text{dist}(x,y) + \text{dist}(y,z), \text{ for } x,y,z \in V(G).$$

Proof. Let x, y, z be vertices in G. If either no (x, y)-walk or (y, z)-walk exists, the inequality holds by definition. Other wise, let W be an (x, y)-walk of minimal length and let U be a (y, z)-walk of minimal length. Certainly, by concatenating W and U we obtain an (x, z)-walk of length $|E(W)| + |E(U)| = \operatorname{dist}(x, y) + \operatorname{dist}(y, z)$, proofing that

$$\operatorname{dist}(x, z) \leq \operatorname{dist}(x, y) + \operatorname{dist}(y, z).$$

□

More to do:

- summarize category of directed (weighted) pseudographs
- weights!
- vertices will also be called nodes and neurons, edges will also be connections or synapses.
- subgraphs
- vertex set, edge set $E(G), V(G)$.
- $\omega(e)$ is weight, connection strength or synaptic weight (as a side remark
- extend to category of weighted directed pseudographs (isomorphisms)
- path
- adjacency matrix
- converses of graph related to opposite category?
- in- and out-degree
- triangle inequality for distance, $\operatorname{dist}(x, z) \leq \operatorname{dist}(x, y) + \operatorname{dist}(y, z)$

1.2 RANDOM GRAPH THEORY

For this chapter, as it is common and practical when talking about random graphs, we move away from the the abstract notion of graphs and their equivalence classes and consider *labeled graphs*, where the edge set of a graph with n vertices takes the form $V = \{1, \ldots, n\}$.

1.2.1 *Erdős-Rényi graphs*

References: Newman, Erdos1960, Erdos1959, Gilbert1959, Wikipedia, (West 2000)

Definition 1.2.1 (Terms used)**.** Graphs with n vertices: $G^n = \{G|G \text{ is graph (means??)}, |V($
$n\}$

Expected number of edges in a directed Erdős-Rényi graph (DERG) $X : G^n \to \mathbb{R}, G \to |E(G)|$, discrete random variable, with probability distribution $G(n,p) = \mathrm{B}(n^2,p)$, binomial distribution. That is, distribution of X via probability mass function $P(X = k) = \binom{n^2}{k} p^k (1-p)^{n^2-k}$. Thus $\mathrm{E}(X)$ equals expect edges in DERG. We have of course, since $G(n,p)$ binomial,

$$\mathrm{E}(X) = pn^2. \text{ (if self} - \text{edges!)}$$

Then, of course, the **mean in-** and **out-degree** is

$$\langle d^{\text{in}} \rangle = \langle d^{\text{out}} \rangle = \frac{\langle |E(G)| \rangle}{|V(G)|} = np.$$

Does this make sense? Define everything properly!!

2

STRUCUTRAL ASPECTS

Subjecting the directionally heterogeneous 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.

2.1 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

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. In the search for structural 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 ??, 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 specifity 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)(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).

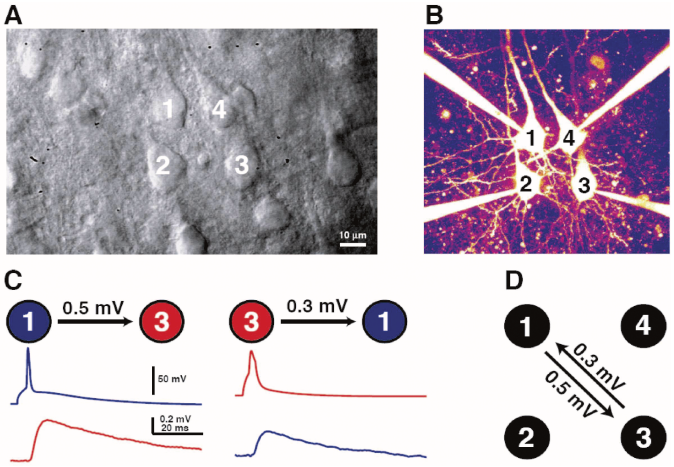


Figure 2: Song et al. use quadruple whole-cell recordings, observing simultaneously the membrane potential of four neurons. **A)** Contrast image showing four thick-tufted L5 neurons **B)** Fluorescent image of the same cells after patching on **C)** Evoking an action potential in the presynaptic neuron causes characteristic membrane potential change in the postsynaptic neuron **D)** Infering 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 directionally heterogeneous network model introduced in ?? 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 ?? 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.

3

NETWORK MODEL

3.1 DISTANCE DEPENDENT CONNECTIVITY

In Gilbert's random graph model $G(n,p)$, (see section ??) the probability of connection p was independently chosen and a fixed value for all vertex pairs. The anisotropic geometric graph model introduced in the last section is itself a random graph model - preferred directions of connections are randomly, uniformly distributed. However, neither is the probability of a connection between a given vertex pair independent of the realization of other edges in the graph, nor is it a fixed value; probability of connection strongly depends on interneuron distance in the anisotropic geometric graph model introduced.

Here, as a first basic result, we analyse the model's distance dependent probability distribution. Where in Gilbert's random graph model the probability p for a edge between nodes v, w to be realized was a fixed value, it is now a function of the distance between the nodes, $d(v,w)$.

In short, we write $p(x)$ to denote the probability that a vertex pair of distance x is connected,

$$p(x) := p((v,w)|\, d(v,w) = x).$$

Theorem 3.1.1. *In the anisotropic geometric graph model distance depend connection probabilities are computed as*

$$p(x) = \begin{cases} 0.5 & \text{for } x \leq w/2 \\ \frac{1}{\pi}\arcsin(\frac{x}{2w}) & \text{for } x > w/2. \end{cases}$$

Proof. To see this, consider a given source vertex v at $(0,0)$ and a possible target w, such that $d(v,w) = x$. We may then express the target coordinates as $xe^{i\varphi}$, $0 \leq \varphi < 2\pi$.

Figure 3 below illustrates for which angles φ the node w becomes a valid target for an edge from v. In the case of $x \leq w/2$,

For a general v make coordinate transformation

□

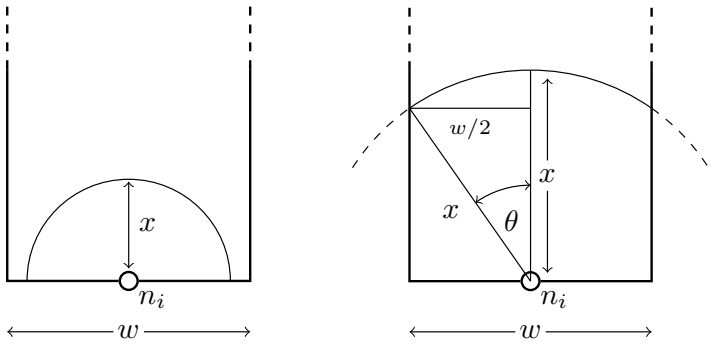


Figure 3

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