Chapter 3: The Connected Brain:

Network and Communication

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In our exploration of the brain, we have examined its size, its convolutions, and the geometric marvels that define its structure. Yet, these anatomical features alone cannot explain the remarkable abilities of the human mind or the intricate behaviours of other species. To understand how the brain operates, we must shift our focus from the static geometry of its folds to the dynamic connectivity of its components. The brain is, at its core, a network—a web of interconnected neurons that communicate through intricate pathways of electrical signals to achieve all aspects of cognition. These networks, much like the complex systems governing transportation, communication, or the internet, exhibit principles that transcend their individual components, giving rise to emergent phenomena.

Networks in neuroscience offer a framework to understand how information flows through the brain, how regions interact to produce coordinated activity, and how disruption in these interactions leads to dysfunction. By representing the brain as a network (aka as a graph in mathematics)—where nodes correspond to neurons or brain regions and edges represent connections or interactions—we can apply mathematical tools from graph theory to characterize its topology. Is the network organized hierarchically or modularly? Does it follow small-world principles, allowing efficient communication across distant regions? These questions are not merely theoretical; they underpin our understanding of cognition, learning, memory, and even consciousness. In this chapter, we shall explore the mathematics of networks and how they provide a lens to study both the remarkable capabilities of the brain and the vulnerabilities that arise from its intricate connectivity.

3.1 Networks everywhere

From the tangled web of blood vessels in an organism to the sprawling infrastructure of highways connecting cities, networks are ubiquitous in both nature and human design. In its ideal form, a network is defined as a collection of **nodes**, representing the fundamental units of the system, and **edges**, which encode the relationships or interactions between these units. For instance, in a social network, individuals are nodes, and the edges connecting them may represent friendships or professional ties. In the World Wide Web, web pages form the nodes, and hyperlinks are the edges facilitating navigation between them.

Mathematically, a network is defined as a set $\mathcal{N}$ of N nodes labelled 1 to N and a set of edges

$\mathcal{E}$ connecting them. For instance, Figure 3.1 shows a simple network with

$$\mathcal{N} = \{1, 2, 3, 4, 5, 6\}, \tag{3.1}$$
$$\mathcal{E} = \{(1, 2), (1, 5), (2, 5), (2, 3), (3, 4), (4, 5), (4, 6)\}, \tag{3.2}$$

Where the pair $(1, 2)$ means that node 1 and node 2 are connected.

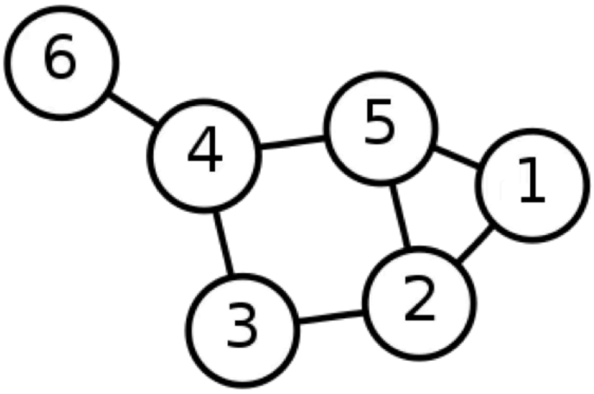


Figure 3.1: A simple network with 6 nodes and 7 edges.

3.2 Connectomes

At the heart of neuroscience lies an ambitious question: can we fully map the wiring diagram of the brain? This map, known as the connectome, captures the complete set of neurons (nodes) and their synaptic connections (edges) in an organism. The connectome is akin to a country map, where each city represent neurons and the roads linking them represent synaptic pathways. Much like a map will give you the best way for people and goods and people to move, the connectome reveals how signals flow through the nervous system, orchestrating behaviour and cognition. While the idea seems straightforward, the task of creating a connectome is immensely challenging, requiring unprecedented levels of precision and resolution. In this Section, we will explore the concept of the connectome, the methods used to map it, and the broader implications of decoding the wiring diagrams of living organisms.

3.2.1 The worm turns

The full connectome of the humble worm *Caenorhabditis elegans* stands as the first and, for many years, the only example of a complete neural wiring diagram. With its 302 neurons and 7,725 synaptic connections, C. elegans was chosen for its simplicity and ease of study, a scientific marvel, especially when compared to the billions of neurons found in more complex organisms. Yet, mapping even this modest network was an extraordinary feat. Researchers spent over a decade reconstructing the connectome using thousands of electron microscopy images, painstakingly tracing each neuronal process and synapse by hand. This endeavour, completed in 1986, marked a monumental milestone in neuroscience, laying the foundation for connectomics as a field. Despite its simplicity, the C. elegans connectome continues to inspire new discoveries, offering profound insights into the relationship between neural architecture and behaviour.

3.2.2 The fly

In 2024, neuroscience achieved another landmark breakthrough with the publication of the full connectome of the fruit fly, *Drosophila melanogaster*. With an astonishing 139,255 neurons (nodes) and 54.5 million synaptic connections (edges), this connectome is by far the most detailed neural wiring diagram ever produced for a complex organism. Drosophila holds a special place in biology as a model organism, celebrated for its genetic tractability and well-studied behaviours. The connectome now offers a comprehensive blueprint of its nervous system, linking neural architecture to the circuits underlying sensory processing, motor control, learning, and memory.

Mapping the Drosophila connectome was a Herculean task, requiring cutting-edge technologies and an international collaboration spanning several years. Using high-resolution electron microscopy, researchers captured terabytes of data from thousands of ultra-thin brain slices. Advanced machine learning algorithms were employed to reconstruct neuronal pathways, while painstaking manual curation ensured the accuracy of synaptic connections. The result is not merely a map but a treasure trove of data, revealing the brain's intricate modularity and hierarchical organisation.

3.2.3 The human

Unlike smaller organisms such as C. elegans or Drosophila, where a connectome can be painstakingly reconstructed using electron microscopy, the sheer complexity of the human brain makes it impossible to obtain a full connectome. Yet, we can look at the problem from a different perspective that only relies on non-invasive imaging techniques. One of the most powerful methods for this purpose is **diffusion tensor imaging** (DTI), a specialised form of magnetic resonance imaging (MRI) that tracks the diffusion of water molecules within the brain. Since water preferentially diffuses along the direction of axonal fibers, DTI allows us to infer the pathways of white matter and reconstruct a map of the brain's structural connections.

The process of obtaining a structural connectome using DTI involves several steps. First, high-resolution MRI scans capture the brain's anatomy, while DTI sequences measure the diffusion of water in three dimensions. These measurements are represented as *tensors*—mathematical entities that generalises the notion of *vectors* and describe the direction and magnitude of diffusion at each point. Fiber-tracking algorithms then use these tensors to estimate the trajectories of axonal bundles, reconstructing the brain's white-matter tracts. The net result is a graph where the nodes correspond to distinct brain regions (defined by cortical parcellation schemes) and the edges represent the strength or density of the connections between them. While DTI is not without limitations—such as its inability to resolve crossing fibers or infer synaptic connections—it remains a cornerstone of human connectomics, providing a macroscopic view of how structural networks support brain function.

3.3 Network and matrices

Now that we have shown how to obtain connectomes, we need to find ways to analyse them to obtain meaningful information about their architecture. The first step is to transform networks into matrices (think of them as just table of numbers).

To translate a network into an **adjacency matrix** A, we follow a systematic process to represent the connections (edges) between nodes numerically in a matrix form. Here's how it works, step by step:

1. **List the nodes**: We assign a unique label to each node in the network. In this example, the nodes are labeled $\{1, 2, 3, 4, 5, 6\}$.
2. **Create a matrix grid**: Construct a square matrix where both rows and columns correspond to the nodes. For a network with N nodes, the adjacency matrix will be $N \times N$.

3. **Mark the connections**: For each edge in the network, place a 1 in the matrix at the intersection of the row and column corresponding to the connected nodes. Since the network is *undirected*, ensure that the matrix is symmetric by placing a 1 in both (i, j) and (j, i). If there is no edge between two nodes, place a 0.

Let's try on our example shown in Figure 3.1. The adjacency matrix for this network is constructed as follows: There is an edge between nodes 1 and 2, so we mark $A_{1,2} = 1$ and $A_{2,1} = 1$. Similarly, other edges are added symmetrically for all pairs in $\mathcal{E}$.

The resulting adjacency matrix is:

$$A = \begin{bmatrix} 0 & 1 & 0 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 1 \\ 1 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix}$$

If we are given an adjacency matrix we can always obtain the corresponding network: Each row and column corresponds to a node, numbered 1 to 6 in our case. A 1 in position (i, j) indicates that there is an edge between nodes i and j. The matrix is symmetric because the network is undirected, meaning connections between nodes are bidirectional.

Using the same procedure we can obtain the adjacency matrix from dTI brain data as shown for the case of a parcellation with 83 nodes in Figure 3.2. The particular adjacency matrix that we use for our simulations is obtained from the tractography of diffusion tensor magnetic resonance images of 418 healthy subjects of the Human Connectome Project and is based on the Budapest Reference Connectome v3.0 (Szalkai et al., 2017). The original graph contains 1015 nodes and 37,477 edges and it is further reduced here to a graph with N= 83 nodes and 1,130 edges (see [1] for details).

Remarkably, we already see a lot of structure in this matrix. For instance, we see two big blocks along the downward diagonal that look similar. It corresponds to the two brain hemispheres. Indeed, while the two hemispheres are a bit different, they mostly mirror each other. Hence, we expect to have the same overall connectivity in each one. We also see that there are few connections between the two hemispheres (which are contained in the two big blocks on the upward diagonal), another typical feature of the human brain.

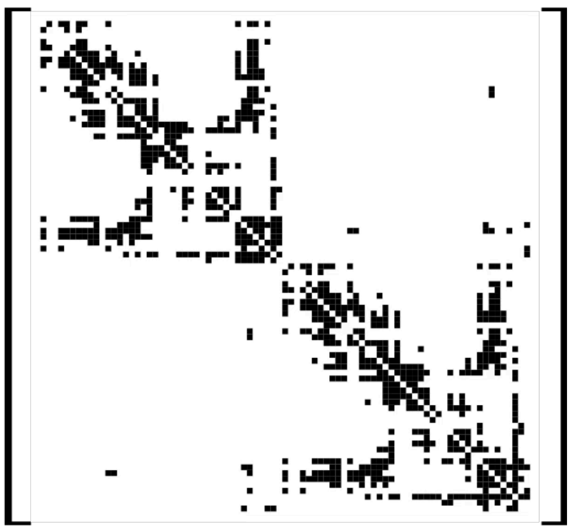
$A =$ 

Figure 3.2: The adjacency matrix of the brain for an atlas with 83 different nodes.

This adjacency matrix provides a compact and precise representation of the undirected network, capturing all its edges and nodes. More importantly, it can be used to compute important quantities related to the network as we shall now see.

3.4 Many paths

In graph theory, a path of length 2 between two nodes consists of exactly two edges, connecting the nodes via an intermediate node. For an undirected network, the adjacency matrix A provides a convenient way to calculate the number of such paths. By squaring the adjacency matrix, we can determine all paths of length 2 between any pair of nodes in the network.

When we compute the square of A, denoted as $A^2 = A \times A$, the entry $(A^2)_{ij}$ (rows i and column j) represents the total number of distinct paths of length 2 between nodes i and j. Indeed, each entry of the matrix product sums over all possible intermediate nodes that form a path of length 2. Mathematically, the entry A^2_{ij} is given by:

$$(A^2)_{ij} = \sum_{k=1}^{N} A_{ik}A_{kj}, \qquad i, j = 1, \dots, N.$$

It is a routine operation on a computer that only takes a few nanoseconds for small matrices. For example, consider a network with six nodes and the adjacency matrix:

$$A = \begin{bmatrix} 0 & 1 & 0 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 1 \\ 1 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix}.$$

To find all paths of length 2, we compute A^2 by multiplying A by itself:

$$A^2 = \begin{bmatrix} 2 & 1 & 2 & 1 & 0 & 0 \\ 1 & 3 & 1 & 2 & 1 & 0 \\ 2 & 1 & 2 & 1 & 0 & 0 \\ 1 & 2 & 1 & 3 & 1 & 0 \\ 0 & 1 & 0 & 1 & 2 & 1 \\ 0 & 0 & 0 & 1 & 1 & 0 \end{bmatrix}.$$

Reading the entry (1,3) of this matrix we find $A^2_{13} = 2$, which means there are exactly two distinct paths of length 2 connecting node 1 to node 3, passing through intermediate nodes 2 and 5, something that can be easily checked by inspection of the network.

This approach is particularly useful for networks where direct enumeration is computationally impractical. For instance, it would be unthinkable to work out by inspection all paths of length 17 between two nodes even for a small matrix like the one in our example. A quick computation on a computer gives

$$A^{17} = \begin{bmatrix} 29376 & 36640 & 26437 & 29638 & 38019 & 11866 \\ 36640 & 42570 & 36691 & \mathbf{32788} & 51262 & 16887 \\ 26437 & 36691 & 19334 & 31668 & 29587 & 8171 \\ 29638 & 32788 & 31668 & 24304 & 43534 & 14781 \\ 38019 & 51262 & 29587 & 43534 & 44392 & 12751 \\ 11866 & 16887 & 8171 & 14781 & 12751 & 3382 \end{bmatrix}$$

and we find, for instance that there are 32,788 paths of length 17 between node 2 and node 4 (row 2, column 4, indicated in bold).

3.5 Hubs and clubs

Another important notion about network is the notion of degree

3.5.1 Degree

In a graph, the **degree** of a node represents the number of edges connected to that node. It provides a simple measure of how connected that node is within the network. It is simply the count all of edges incident to a given node. For our example, the node 2 is connected to node 1,3, and 5. Hence node 2 has degree 3.

Mathematically, the **degree of a node** i can be computed directly from the adjacency matrix A. To find the degree of a node, we sum the entries in the row (or equivalently the column, since the matrix is symmetric for undirected networks) corresponding to that node:

$$\text{degree}(i) = \sum_{j=1}^{N} A_{ij} = A_{i1} + A_{i2} + \ldots + A_{i,N-1} + A_{iN}.$$

As an example, we can compute the degree of node 2

$$\text{degree}(2) = A_{21} + A_{22} + A_{23} + A_{24} + A_{25} + A_{26} = 1 + 0 + 1 + 0 + 1 + 0 = 3,$$

3.5.2 Hubs

In the world of networks, a **hub** is a highly connected node that plays a critical role in holding the network together. Think of a hub as a major airport in a global flight network. While smaller airports connect to just a few nearby destinations, major hubs like Heathrow link to many cities worldwide, ensuring efficient travel between distant locations. Similarly, in a network, a *hub is a node with a high degree*, meaning it has a large number of direct connections to other nodes. In social networks, the “influencers" are hubs as they are connected to many others, spreading information quickly, even though not always correctly. In biological networks, hubs can represent proteins or genes that interact with numerous others, making them essential for the system’s stability and function.

Mathematically, we identify hubs by examining the degrees of the nodes in the network. Nodes with degrees significantly higher than average are considered hubs. For example, in a network where the average degree is 3, a node with a degree of 10 would likely qualify as a hub. These hubs often serve as shortcuts, allowing information or resources to move efficiently across the network.

However, hubs also have vulnerabilities. In a flight network, disrupting a major hub like Heathrow could severely affect global air traffic. Similarly, in other networks, targeting hubs can lead to cascading failures. This makes hubs both powerful and fragile, emphasising their importance in understanding and maintaining the structure and function of networks.

3.5.3 Rich clubs

Imagine a group of influential people—celebrities, politicians, or business leaders—who not only have many connections but are also closely connected to one another. This elite circle, where the most connected individuals form their own tightly-knit group, is known as a **rich club** in the world of networks. Just as hubs are the nodes with the highest number of connections, a rich club refers to a subset of hubs that are disproportionately well-connected among themselves. An example of such a structure is shown in Figure 3.3.

In networks, rich clubs often emerge in systems where cooperation or coordination among the most important nodes is beneficial. For instance, in the internet's network of servers, the richest nodes—those with the most connections—frequently link directly to one another, creating a highly efficient backbone for data flow.

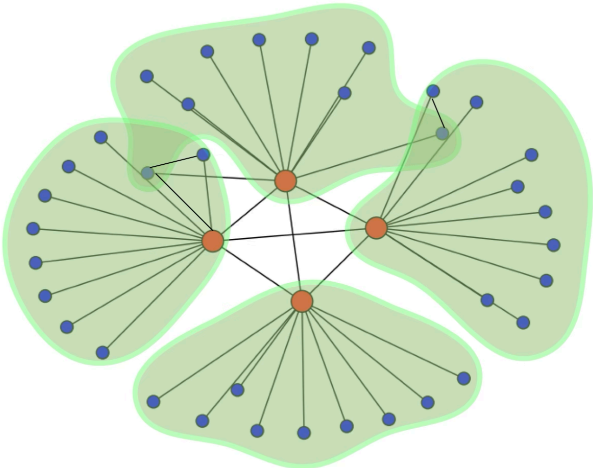


Figure 3.3: An example of a networks with hubs, clubs, and communities. The nodes in red are hubs. They have high degrees (many more connections to other nodes than on average). They are also connected with each other making them a **rich club**. The nodes of lower degrees they are connected to form a **community**.

Mathematically, a rich club is identified by analysing how densely the high-degree nodes are interconnected. If the connections between hubs are significantly more frequent than what would be expected in a random network, we say that a rich club exists. This can be quantified using a "rich club coefficient", which measures the density of connections among the top $k\%$ of nodes ranked by degree. A high coefficient indicates that these elite nodes are not just hubs but are also preferentially linked to each other.

Rich clubs play a critical role in the resilience and efficiency of networks. Their interconnectivity creates robust pathways for communication, allowing information to flow even if some nodes are removed. However, this same feature makes them vulnerable to targeted attacks; disrupting a rich club can have far-reaching consequences for the entire network.

In the human brain, neuroscientists studying the connectome have identified rich clubs structure, with regions like the precuneus, superior frontal cortex, and thalamus, which play pivotal roles in integrating sensory input, attention, and executive control. These regions work together to distribute information efficiently across the brain, much like a network of highways linking major cities. However, rich clubs also highlight the brain's vulnerabilities. Damage to these regions—due to injury or diseases like Alzheimer's—can severely disrupt global communication, leading to widespread cognitive impairments.

3.6 Small-worldness

When we think of communication in a network, we want to be able to connect two nodes in a network by a short path with few edges overall. To formalise such an idea, we need two introduce two notions.

First, the **average path length** tells us how many steps, on average, it takes to travel between two nodes in the network. First, we find the shortest length between two nodes and construct a distance matrix D, where the entry d_{ij} represents the shortest path length between nodes i and j. The distance matrix for our example is:

$$D = \begin{bmatrix} 0 & 1 & 2 & 2 & 1 & 3 \\ 1 & 0 & 1 & 2 & 1 & 3 \\ 2 & 1 & 0 & 1 & 2 & 2 \\ 2 & 2 & 1 & 0 & 1 & 1 \\ 1 & 1 & 2 & 1 & 0 & 2 \\ 3 & 3 & 2 & 1 & 2 & 0 \end{bmatrix}.$$

To compute the average path length, L, we sum all the finite entries in D and divide by the total number of node pairs ($N \times (N-1)$). For our network, we have

$$L = \text{Average Path Length} = \frac{\sum_{i \neq j} d_{ij}}{6 \times 5} = \frac{5}{3}.$$

A short average path length means the network is efficient, allowing information, traffic, or signals to travel quickly. In the brain, for example, a short path length ensures that different regions can communicate rapidly, supporting high-level cognitive functions. For our 83 node network, we have $L = \frac{10490}{6806} \approx 1.54$. On average, it takes about 1.5 steps to go from any 2 nodes.

Second, the **clustering coefficient**, C measures how tightly nodes are grouped together. It answers the question: If two of my friends are connected to me, are they also connected to each other? A high clustering coefficient indicates that nodes tend to form tightly knit groups, like neighborhoods in a city or specialized regions in the brain. In the brain's connectome, clusters often correspond to areas working together on specific tasks, such as processing visual input or coordinating movement.

Mathematically, it amounts to find all the triplets of nodes that are connected among the nodes that have at least 2 neighbours. For our graph, 5 nodes are connected to 2 nodes but there is only 1 triplet (nodes 1,2,5), hence we have $C = 1/5$.

Now, let's combine these two ideas to explore **small-worldness**. A network is said to have "small-world" properties if it combines a short average path length (like a highway system connecting distant cities) with a high clustering coefficient (like neighborhoods where everyone knows everyone else). Small-world networks are efficient, striking a balance between local specialization and global integration. This property is found in many real-world networks, including social networks and the internet.

In neuroscience, small-worldness helps explain how the brain operates with both speed and precision. Local clusters of neurons can specialise in specific functions (a process called *segregation*), while global connections between clusters ensure coordination across the brain (or *integration*). This small-world structure is thought to be critical for processes like memory, learning, and adaptability.

Epilogue

The use of networks in neuroscience has revolutionised how we understand the brain, providing a new fundamental tool and theoretical framework to study its complexity. One of the most significant achievements is the discovery of the brain's "small-world" architecture—a design where local clusters of neurons handle specialised tasks while global connections between clusters enable efficient communication across the brain. This insight helps explain how the brain achieves both speed and adaptability, allowing us to think, move, and react in real time.

Networks have also shed light on the concept of hubs—highly connected brain regions that act as control centres, coordinating information flow. For example, regions like the precuneus and thalamus are critical hubs for integrating sensory input and executive functions. By mapping the brain's structural and functional networks, researchers have identified disruptions in connectivity patterns that are linked to conditions such as Alzheimer's disease, autism, and schizophrenia. These discoveries have opened new avenues for diagnostics and therapies, making network neuroscience a cornerstone of modern brain research.

Yet, there are two important aspects of brain networks that we have not discussed. First, the brain is a dynamic organ where change is the only constant. While the structural networks are static, the way information flows is dynamics. To capture this dynamic, there is another type of networks that encode how different parts of the brain interact with each other, the *functional network* that we will encounter in our next lecture. A second important feature is that what makes the brain so efficient also creates potential weaknesses. We will see in future lectures that some neurodegenerative diseases hijack the axonal highway to spread efficiently through the brain.

Further reading

The ideas of using graph theory and networks to study the brain are so powerful and successful that there are many great books available to learn more about it, both technical and popular science. Here are a few.

- *Networks of the Brain* (2016) by Olaf Sporns, one of the leaders of the field is a technical but very readable book [4].
- *Sync: The emerging science of spontaneous order*(2004) by Steven Strogatz recounts in wonderful terms the genesis of the discovery of small-worldness [5].
- The 1998 paper by Duncan Watts and Steven Strogatz is a must-read classic. It is one of the most cited papers of mathematics, yet it is very clear and readable [6].
- As the title suggests *Connectome: How the brain's wiring makes us who we are* (2012) is all about the progress in connectomics. [3].
- *The entangled brain: How perception, cognition, and emotion are woven together* (2022) by Luiz Pessoa is well written and informative presenting a more in-dpeth analysis of brain networks than most books [2].

References and Further Reading

[1] Sveva Fornari, Amelie Schäfer, Ellen Kuhl, and Alain Goriely. Spatially-extended nucleation-aggregation-fragmentation models for the dynamics of prion-like neurodegenerative protein-spreading in the brain and its connectome. *Journal of Theoretical Biology*, 486:110102, 2020.

[2] Luiz Pessoa. *The entangled brain: How perception, cognition, and emotion are woven together*. MIT Press, 2022.

[3] Sebastian Seung. *Connectome: How the brain's wiring makes us who we are*. Houghton Mifflin Harcourt, 2012.

[4] Olaf Sporns. *Networks of the Brain*. MIT press, 2016.

[5] Steven Strogatz. Sync: The emerging science of spontaneous order. 2004.

[6] Duncan J Watts and Steven H Strogatz. Collective dynamics of ‘small-world’networks. *nature*, 393(6684):440–442, 1998.