Thesis

RELEVANCE OF RHYTHMIC DEPOLARIZATIONS FOR CORTICAL INFORMATION PROCESSING

Energetic Considerations

submitted by

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Declaration of Academic Integrity

I hereby confirm that the present diploma thesis is the result of my own independent scholarly work. I also confirm that in all cases, where material from the work of others (in books, articles, essays, dissertations, and on the internet) is acknowledged, quotations and paraphrases are clearly indicated. No material other than that cited in the reference list has been used. I have read and understood the Medical University's regulations and procedures concerning plagiarism.

Graz, July 27, 2024 Lukas Maximilian Röd m.p.

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Kurzfassung: Im menschlichen Gehirn treten rhythmische Depolarisationen auf verschiedenen zeitlichen und räumlichen Skalen auf. Angesichts des evolutionären Drucks, den Energiebedarf zu optimieren, wird die Hypothese aufgestellt, dass diese Oszillationen genutzt werden, um den Energiebedarf zu reduzieren. Die Betrachtung dieses Phänomens aus einer energetischen Perspektive bietet einen neuen Blickwinkel auf das Thema und kann zum Verständnis des neuronalen Codes im menschlichen Gehirn beitragen. Basierend auf einer umfangreichen Literaturrecherche und der Simulation eines einfachen probabilistischen Netzwerks werden die Energie-kosten für bestimmte Informationsverarbeitungsaufgaben des Gehirns abgeschätzt. Die Phasencodierung einzelner Neuronen liefert eine mögliche Erklärung für die oszillierende Hintergrundaktivität. Auf Netzwerkebene erweist sich die Verteilung der Repräsentation eines Stimulus auf mehrere Neuronen als hocheffizient für probabilistische Low-Cost-Neuronen sowie für die Optimierung der gesamten Repräsentationskapazität eines Netzwerks. Als eine weitere Anwendung der oszillatorischen Aktivität wird die zeitliche Segmentierung von Berechnungen und damit eine kostengünstigere gruppierte Informationsverarbeitung diskutiert. Das Verständnis der in biologischen neuronalen Netzen implementierten Mechanismen ist für die Entwicklung künstlicher neuronaler Netze von großer Bedeutung. Aktuelle neuromorphe Ansätze, d.h. künstliche Systeme, die biologisches Verhalten nachzubilden versuchen, werden diskutiert. Diese Arbeit stellt eine Verbindung zwischen grundlegenden oszillationsbasierten Berechnungen in biologischen und künstlichen Netzwerken her.

Abstract: Rhythmic depolarizations are observed in the human brain at a variety of temporal and spatial scales. Given the evolutionary pressure to optimize energy requirements, it is hypothesized that these oscillations are indeed exploited to enhance its metabolic demand. Investigating this phenomenon from an energetic perspective provides a new outlook on the topic and contributes to the understanding of neural coding. Based on an extensive literature review and the simulation of a simple probabilistic network, energy costs for specific tasks are evaluated. Phase coding of individual neurons is a compelling possible explanation for oscillatory background activity. At the network level, distributed representation of a stimulus over multiple neurons proves highly efficient for probabilistic low-cost neurons, and for the optimization of the representational capacity of a network. An additional role for oscillatory activity was proposed in the temporal segmentation of computations and highly efficient clustered processing. The identification of mechanisms at work in biological neural networks seems to be highly relevant for the development of artificial neural networks. Current neuromorphic approaches are discussed. This thesis links fundamental oscillation-based calculations in biological and artificial networks.

Contents

Abbreviations

1. AP - action potential
2. ATP - adenosine triphosphate
3. CNN - convolutional neural network
4. CNS - central nervous system
5. EEG - electroencephalogram
6. LFP - local field potential
7. TW - traveling waves

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1 Introduction

The human brain consumes a substantial fraction of the available energy for the whole body, corresponding to an energy equivalent of approximately 20W[1]. It relies heavily on the oxidative metabolism of glucose, a multi-step reaction with oxygen and glucose as reactants and CO_2 and water as end-products, making O_2 a good proxy for estimating the absolute energy demand [2]. The brain metabolizes approx. 20% of the total available O_2 in adults at rest, while only contributing 2% to the total body mass [3]. During development, the O_2 consumption is even higher, reaching up to half of all available oxygen in children [4]. The metabolic rates of the whole body (i.e. available energy), stayed more or less constant, while the cerebral demand increased substantially in the course of the human evolution [5, 6]. Each increase in the brain‘s demands resulted in less available energy for other ‘high-cost’ tissues, such as the digestive tract. Inversely, the restricted availability of energy also limits brain size and shapes its architecture and activity [7].
But what is the source of the significant metabolic demand of the brain? We will mainly focus on the vertebrate cerebrum, given that the cerebellum and other CNS regions and invertebrate neurons are likely to follow different rules with strongly diverging energy budgets [8, 9]. Information is encoded in the form of all-or-nothing responses, known as action potentials (APs) or spikes of the nerve cells. They are propagated to other nerve cells via the release of neurotransmitters into the synaptic cleft. Neurons require on one side energy for vegetative processes, such as the replacement of defective proteins, and on the other side signaling-related processes such as the maintenance of their membrane potential, APs, and synaptic transmission. But while only 5-25% of the available energy is spent on housekeeping and vegetative processes, the rest is used for signaling-related activity [2, 8]. Of the non-vegetative energy budget, only 20% is used on the maintenance of the resting potential, and the remainder for the electrical information transmission. Especially the re-polarization after an AP and synaptic transmission are responsible for a large share of the metabolic load, with the Na-K-ATPase alone consuming half of the total energy available to the brain [10, 11]. Electrical signaling is responsible for the majority of the energy expenditure of brain tissue.

One consequence of these high metabolic costs could be a minimization of signaling activity. But interestingly, there is little difference between the brain‘s energy demand during rest and mental activity [12]. Some studies reported an increase of just up to 10% when comparing mental imagery versus rest [13], others even reported no significant increase in O_2 consumption due to a down-regulation of non-active areas [14]. While this observation can partially be attributed to the redistribution of activity (and of available glucose and O_2), a large percentage of the cerebral O_2 and glucose metabolism appears to accrue task-independent. Even after the total removal of input, energy demands remain higher than would be expected based on the assumption that neural activity is held at the minimal possible level. For example auditory suppression, results in a 30-65% reduction of glucose metabolism in the auditory cortex [15]. This remaining base activity can only be reduced by non-physiological measures, such as very deep anesthesia that inhibits neural communication [7, 16, 1, 17, 18, 19].

A potential explanation for the brain's high metabolism at rest can be derived from the spontaneous spiking behavior of nerve cells. Neurons exhibit cyclic synchronous activity, de- and re-polarizing at periodic intervals even without external input. Prove of these oscillations was first reported in the early EEG recordings by the end of the 19th century [20, 21]. Simultaneous postsynaptic potentials of a sufficiently large population of cortical pyramidal neurons cause voltage fluctuations that are measurable across the skull or directly on the cortex. These recordings showed a wave-like pattern at approximately 10Hz over the human occipital (visual) cortex that emerged when the test subjects closed their eyes. This milestone discovery was followed by the identification of a multitude of different frequency bands, covering a spectrum of frequencies ranging from approx. 0.02 to 600Hz [22]. Distinct frequency bands have been linked to different mental states. For example, alpha activity (8-12Hz) was shown to emerge mainly during relaxed wakefulness, faster gamma activity (30-150Hz) was associated with cognitive processing, and delta waves (0.5-4Hz) with sleep. Regarding the number of neurons involved, oscillations range from a single neuron, over inter-area (mesoscopic) to macroscopic synchronization extending over a large part of the cortex [23, 24]. Different pathways and mechanisms have been proposed to be involved in the generation of the synchronized activity, such as the macroscopic recurrent thalamocortical network for alpha, mesoscopic processing for gamma, and the partial synchronization of local gamma for global beta frequencies [25, 26, 27].

Despite their neurophysiological complexity, cerebral oscillations have been studied extensively. A large body of research is devoted to investigating their functional properties and their biological implementation (for a review see [23]). Modulations of oscillatory synchronization, oscillatory amplitude, and frequency have been reported in a multitude of cognitive domains like attention [28, 29, 30], abstraction [31], and movement (e.g. eye movement [32] or reaching tasks [33, 34]), reaction times, and correlate with cerebral blood flow [35]. Synchronous cyclic activity and its respective functions are not restricted to humans but have been preserved through the evolution of mammals [36, 37, 38]. Despite these efforts, the purpose of the oscillations is still an ongoing debate. So far, their functional role could not be identified conclusively and it even can not be ruled out until today that they are merely an epiphenomenon. While this seems unlikely due to research, indicating that even resting-state/background oscillatory activity goes beyond being the result of noise and contains information [39], the question why these patterns would develop in an energy-restricted neural network lacks a satisfactory answer.

Several aspects of this described neurophysiological behavior are surprising at first glance. For decades, the dominant theory of neural transformation of information into electrical signals postulated that they follow a rate-coding regime, thereby transmitting information by means of modulations of the average firing frequency. It was assumed that all relevant information could be deduced from the mean spiking frequency of a sending nerve cell. However the rate-coding theory leaves some explanatory gaps. It remains unclear, why large neural populations should synchronize. Not only a single but million of nerve cells are simultaneously active. This type of spatial correlation and redundancy would be highly inefficient. Furthermore, the maximal information transmission in terms of bits/AP is achieved by neurons firing at significantly faster frequencies (close to 200Hz) and without temporal autocorrelation. Cortical cells, in contrast, fire at a regular and slow rates (as observed during the oscillations) and exhibit a strong autocorrelation and information transmission is minimal. Oscillatory amplitude and cycle length increases with increasing depth of anesthesia (and thereby the absence of consciousness and presumably further cognitive processes) [40, 41, 24]. This indicates that especially slow waves might represent the brain's default activity. In other words, they are the underlying activity that emerges in the absence of current information processing. Given that APs contribute substantially to the brain's metabolic costs, understanding their presence appears to be highly relevant for understanding how biological neural network processes information.

The human brain project was started in 2012 with over 1 billion euros in funding and the ambitious goal to simulate a whole human brain [42]. After 10 years, it ended, having generated multiple interesting results, such as advancing the development neuromorphic computing, new insights into binding theory and phase-dependent synaptic plasticity [43, 44, 45]. Nevertheless, it fell short of major breakthroughs, without being close to the main goal of the simulation of a complete human brain [46]. Regarding energetic considerations concerning cyclic and synchronized neural depolarizations, no fundamentally new explanations were found.

Multiple interconnected driving factors for brain development can be identified: reduction of the number of APs, reduction of individual AP cost, reduction of the total number of neurons, and adaptability (learning). In this work, different aspects of the relationship between neural oscillations and energy efficiency will be explored on various spatial scales. The objective is to identify fundamental principles that are applicable in the context of oscillation-associated information transmission. For this reason, evidence from various frequency bands, neural subpopulations, cortical areas, and species will be gathered. In consequence, the presented results are general, and their applicability to specific subpopulations has to be evaluated individually. The major topic of phase-dependent plasticity and learning is beyond the scope of this publication. Evidence from various modalities such as animal models, human recordings as well as simulation of artificial networks will be presented, to support the claim that oscillations developed due to superior energy cost-benefit properties. First, general principles of information transmission will be reviewed. The aim is to outline several differences between these idealized considerations and neurophysiological findings, in the search for potential explanations for synchronized and periodic neural activity. Second, these principles will be applied to the activity of individual neurons. Third, coding techniques that rely on either the cyclic activity of individual neurons or their environment will be introduced and discussed from the viewpoint of efficiency. Fourth, I will demonstrate how large-scale synchronized oscillations can be exploited at a network level for various tasks like the situational activation of adaptive subnetworks, probabilistic networks, and increase in representational capacity. Fifth, I will show how the discretization of computational steps signal segmentation can be based on synchronized background activity, introducing the notion of sensitivity windows. Finally, I will present findings that imply that spatial aspects of the oscillations contain additional information. On all levels, the possible applications of neural oscillations will be discussed under the light of energy efficiency.

2 Methods

The following major topics were identified as of interest: cerebral energy efficiency, neural coding, and neuromorphic computing. To this end, a narrative literature review was conducted on publications prior to May 2024 to cover these areas. The main literature databases used were PubMed, Google Scholar, and the human brain project publication archive.

Based on the results of this review, a novel mathematical model for probabilistic neural networks was developed. A second model of representational capacity was reproduced based on previous work [7, 4]. The energy efficiency of these models was calculated for various parameter combinations using RStudio (ver 1.3) and with ggplot2 (ver 3.3) for visualization. The precise architecture and parametrization is described in detail below.

3 Results: Oscillation-based Processing

3.1 Information Transmission

Before investigating potential mechanisms at work for neural activity, it is important to understand how information can generally be transmitted between two units. This information theory has a wide range of possible applications, from the description of traditional computer processing to the information content of celestial bodies [47]. In this section, the formalization of information transmission for idealized sending and receiving units will be outlined.

The communication between two units (biological or artificial) can be formalized as the sending and receiving of a string of discrete values. Based on the work of the mathematician Claude Shannon from the 1940th [48], information that can be encoded by one single input symbol that can take one of n different potential values. This corresponds to e.g. reading one letter of a string. The information (or entropy) H of that signal, measured in bits is defined by the Shannon-formula:

$$H = -\sum_{i=1}^{n} p_i log_2(p_i) \tag{1}$$

where s is the probability of the occurrence of the i-th value. Several conclusions that are important in the context of neural coding can be drawn from this formula. First, information can me maximized if all potential values are equally likely. Second, the greater the number of possible values, the greater the entropy. And third, the lower the probability of one specific value, the higher the information. Fewer words start with X than with A in the English language. Thereby, if I read the first letter of a word, I gain more information if it is X compared to A. In other words, an X gives me a better idea of which word I am reading. But as equation 1 estimates the information that any possible symbol of the code can transmit, the sum over all i symbols is calculated.

If the signal is binary, i.e. each input can either be a 0 or 1, In this case, equation 1 can be rephrased as:

$$H_b(s) = -s * log2(s) - (1-s)log2(1-s) \tag{2}$$

where s is the probability of the signal being one of these two values and $s-1$ is the probability of being the other. The maximum information transmission of 1bit per symbol is achieved if $s = 0.5$, so if both values are equally likely (see figure 1). This formula is well suited to approximate the information in neural communication (communication by APs, see section 3.3). Neural activity can be described as a sequence of 0s and 1s (spike train). Every time the neuron fires, it sends a 1, and the other times 0. If during an oscillatory cycle, the firing probability varies systematically, its activity becomes predictable, therefore losing information. In the extreme case of a cell spiking at a perfectly regular interval, $s = 1$ or $s = 0$, and therefore H_b is reduced to 0bits; no information is transmitted. The reason why neural code would be willing to sacrifice the entropy that would be possible with additional symbols will also be discussed in section 3.3.

The equations so far can be applied to single symbols. If I want to calculate the information of a whole spike train [49, 50], it can be done with the formula:

$$H_{train}(X) = -\sum_{x \in X} s(x) log_2(s(x)) \tag{3}$$

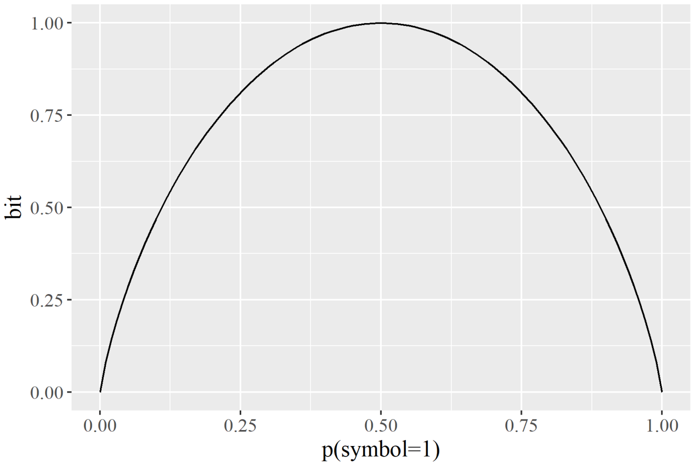


Figure 1: Figure illustrating the relation of symbol probability and information transmission in binary code. It shows that, depending on the probability *p* of one single symbol being a ‘1’ (and the probability of being a ‘0’ 1- *p*), information transmission is maximized if both options (‘0’ or ‘1’) are equally likely. This graph is directly derived from equation 2.

where X is the set of all possible spike trains x, and $s(x)$ the probability of a specific spike train. If a neuron e.g. fires always at the 3rd or 4th position of a 5 time step sequence (with equal likelihood) x can be either 00100 or 00010. The total information for the receiver is $H_{train} = 1bit$, instead of the maximally possible $5bit$ for an unrestricted neuron. Oscillations impose restrictions in regard to spike timing on the cells.

These theoretical considerations can be extended to the spike trains X and Y of two sending neurons with:

$$H_s(X,Y) = -\sum_{x,y} s(x,y)log_2(s(x,y)) \tag{4}$$

where we take the sum over the simultaneous occurrence of all possible spike trains x and y. If X and Y are completely independent, their joint entropy becomes the sum of their single entropies. If they are completely synchronized, as is the case during idealized oscillations, no information is transmitted.

This model has the limitation of describing communication in an idealized setting. Probabilities have to be known at any time, which is highly unlikely for highly complex and variable systems such as the CNS. Nevertheless, information theory generates interesting insights, when applied to biological neural networks.

As a matter of fact, the human sensory system performs at several orders of magnitude lower power than its theoretical potential [51]. Based on these theoretical considerations, we will try to explain, why the brain might diverge from the maximally possible transmission rates.

3.2 Principles of Neural Activity

Before discussing potential neural coding schemes and oscillations on a local (mesoscopic) and distributed (macroscopic) network level, relevant properties of single neurons will be reviewed. Results from single-cell recordings draw a very different picture than neurons being perfectly predictable communication hubs. Indeed, their firing patterns are irregular, variable under identical stimulation, and even present in the absence of current specific stimulation (e.g. [52, 23, 53, 54]). Due to this stochastic and spontaneous activity, it appears that cells metabolize a substantial fraction of the brain's energy budget for activity, without apparent reason to do so. The cause for neurons being willing to 'sacrifice' predictability and expend energy for spiking in the absence of (sensory) stimulation appears to be crucial in explaining the larger-scale communications in the CNS. Two key paradigms that are potentially linked to the brain's energy efficiency are the probabilistic nature of neurons and sparse firing. After outlining these principles, I argue in a next step that, based on these paradigms, large-scale synchronization could either provide the backbone to structure processing or allow distributed representation.

3.2.1 Sparse Activity

As shown above, the concept of constantly firing neurons, responding to every excitatory input with an AP, does not reflect the nature of cortical signaling. In fact, only about 1-4% of neurons are active at any given time [55]. Given that each neuron receives input from an average of over 1000 dendrites [56], the low rate of firing could be based on either a very high spiking threshold or a balanced inhibitory and excitatory input [57, 58]. Even when gamma frequency is externally induced in hippocampal or neocortical slices, pyramidal cells spike in less than 5% of the cycles [23, 59, 60]. The 'sparse' encoding theory of information is supported by intra-cortical recordings from mice, and macaques [61, 62].

Information Rate: At what rate could a digital neuron transmit information and what is the biological reality? Following the information theory [48, 63], the probability of a signal to arrive at a presynaptic terminal is s during Δt being the shortest possible time interval. Following this logic, the highest information density can be achieved at $0.5s$. A reasonable estimate for Δt of cortical neurons corresponds to the 2,5ms refractory period, and thereby a maximum possible firing frequency of 400Hz [4]. At 200Hz the data rate would be the highest, with $1 bit/\Delta t$ or $200 bit/s$. This theoretical value is opposed by significantly lower in vivo measured firing rates, being closer to 4Hz [7]. When $s = \Delta t * Frequency$ and equation 2, at these physiological rates $s = 0.01$ the bandwidth corresponds to 32bit/s (or 0.08bit/Δt).

Cost of Information: Why should the brain work at a significantly slower pace than possible? In contrast to digital components, for the energy requirements of sending either a 0 or 1 are nearly the same, it is significantly more expensive for a neuron to be active, as opposed to being at rest. The factor $r = \frac{Energy\ when\ active}{Energy\ at\ rest}$ can vary significantly, depending on the location of the neuron, but is most likely in the range 10-200 [4]. Following reverse reasoning, the r that minimizes the energy demand for a certain spike probability can be calculated with the equation $r = \frac{log2(s)}{log2(1-s)}$ [4]. If maximizing the function $H(s)/E$, where E is the total required energy, different values for the optimal frequency emerge for different r. This gives an explanation, of why neurons might fire in the observed frequency ranges. Nevertheless, it leaves the reason for the regularity and synchronization open. In the next sections, I will highlight several differences regarding neural firing activity and will present several coding schemes for single neurons in order to provide answers to these questions.

Neural Sparseness: As shown above, this low-frequency approach is not optimal in terms of transmission speed but is essential for energy efficiency. For retinal neurons, a direct link between transmission rate or maximum bandwidth and energy demand has been demonstrated [64]. It can be extrapolated that the average cortical bandwidth is closer to an energy optimum when firing less frequently.

On the downside, a large number of of inactive neurons (and glia) increases the housekeeping costs as well as the costs for the maintenance of the resting membrane potential. The latter is responsible for over 1/4 of the brain's total energy consumption [55]. But, even when taking 'resting cost' into account, theoretical work has shown that weakly active neurons are indeed more energy efficient than high-frequency approaches [4]. In summary, the firing frequency is the result of balancing resting against messaging costs.

3.2.2 Probabilistic and Spontaneous Activity

A large body of data suggests that the brain is based on stochastic rather than deterministic communication mechanisms over a wide range of spatial and temporal scales [65]. Even in the absence of stimulation, neurons fire at variable intervals [66, 67]. Neurons in visual cortex V1, for example, fire spontaneously (i.e. without sensory stimulation) on average 7 times per second [68], whereas other cortical neurons generally have a base activity closer to 1-4Hz [69, 7]. Not surprisingly, spontaneous activity has been shown to be associated with large-scale oscillations, with neurons firing most of the time at a low frequency, with occasional peaks of activity [70, 71].

Potential explanations for the spontaneous activity are the probabilistic nature of individual cell components such as ion channels (varying numbers of ions migrate through an open channel [52, 72], ion pumps (a stochastic process governs the transport of ATP to the ion pumps [73], neurotransmitter release (not every AP results in a release and the number of vesicles that is released is random [53, 74, 75] and variable blood supply [76]. The stochastic behavior of these individual components can add up to chaotic dynamics within a cell [77, 78].

One obvious explanation of why the CNS would allow for such unreliable reactivity of its cells is found when analyzing the energy costs of predictability. While each of the individual components could be implemented in a more reliable (closer to deterministic) manner, this would entail vastly increased energy costs. At a fundamental level, there is a direct relationship between the thermodynamic cost and the probability of a calculation being correct [79, 80].

In physiological terms, the link between signaling cost and signal quality can be illustrated with the example of axonal channel density (the number of ion channels along the membrane). While information density and signal-to-noise ratio are highest in cells with a high number of voltage-gated ion channels, the number of channels that maximizes energy efficiency is significantly lower [81]. The negative correlation between energy efficiency and information rates follows the ‘law of diminishing returns’; every additional energy expenditure will yield a smaller increase in information rate.

Apparently, only in 25 to 50%, an AP causes the release of neurotransmitters at a presynaptic terminal[7]. Especially, if several synapses exist between sending and receiving neuron, as these ‘synaptic failures’ reduce the energy expenditure per bit (probable values for the connections between two neurons range between 1 and over 6) [63]. Even though up to 75% of the preterminal information is ‘lost’, this effect can frequently be compensated by alternative synapses. It was suggested that this low release probability in addition can serve as a filter, in order to prevent an overload of a single cell, given that each neuron receives usually input of several thousand synapses together with noise [63, 82].

These examples illustrate, how probabilistic behavior is implemented at virtually all temporal and spatial scales (see [81] for a review). An apparent advantage is a significantly augmented energy efficiency, but comes with the cost of less reliable individual components of the neural network.

Noise: Low-cost neurons come at the expense of less predictable behavior due to intrinsic noise, and higher susceptibility to extrinsic noise (for an overview of different sources of noise in the CNS see [83]). Above, the stochastic or noisy firing behavior of single cells was discussed. But if each cell produces a stream of noisy output and receives at the same time input over thousands of dendrites[56], it is constantly bombarded with network noise. Even the sensory input is noisy. If it comes for example to auditory tasks, very often in natural scenes, the target signal is mixed with a variety of irrelevant sounds (such as traffic, birds, construction work, etc). In consequence, noise is relevant in virtually all processing stages.

Stochastic Resonance: The incorporation of intrinsic/neuronal noise and integration of external/sensory noise can be utilized to conserve energy and heighten sensitivity [54, 84]. This phenomenon of stochastic resonance can be observed in nonlinear systems (such as low-level sensory neurons), with a weak, periodic, and stochastic/noisy input signal. The undistorted signal would remain under the detection threshold but can surpass it due to the added noise.

Counter-intuitively, in these systems, the signal-to-noise ratio is superior in the presence of noise [54]. This is the case, because noise adds up to a low-intensity signal, enabling them to surpass the detection threshold (see figure 2). While theoretical frameworks illustrate that

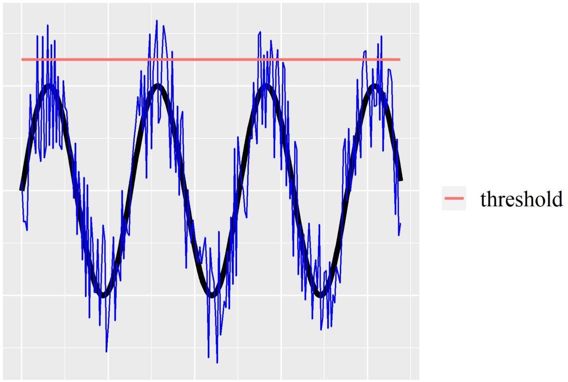


Figure 2: Illustration of the enhanced signal detection in stochastic resonance. The black line indicates a periodic and weak signal that can not surpass the detection threshold. If noise is added (blue line), it can be detected in various instances. The three necessary requirements are met: non-linear detection (all-or-nothing), weak and periodic signal as well as noise that is strong enough.

neural signaling is by several orders of magnitude less energy efficient than theoretically possible in a noise-free environment, a different scenario emerges in its presence [84]. Artificial neural networks designed to reassemble biological networks were shown to display self-sustaining gamma oscillations in the presence of specific input noise levels [85]. These networks were able to detect periodic sub-threshold signals that would typically remain undetected. The periodic input is amplified by the background noise. This improves signal detection (see [51] for a simulated illustration).

Since cortical neurons are subjected to constant noise, the periodicity of input in the form of oscillatory activity could potentially serve as a basis for the network to distinguish between random background firing and actual signals. The extent to which the brain takes advantage of this phenomenon and its impact on the evolution of the brain is yet to be established.

3.2.3 Oscillations as Consequence of Neural Nature

Based on the discussed nature of neurons, oscillations can be essential for cortical processing in two ways. Either they are a byproduct that is exploited for calculations that are performed by neurons that do not follow this periodic pattern, or they represent the signal itself.

In the former case, it could be argued that in addition to being the 'cheaper' coding method, the sparse and probabilistic firing behavior of cortical neurons can generate additional value. Synchronization allows the formation of large-scale oscillations, providing the backbone for new coding schemes, such as phase coding. There are several possible mechanisms by which

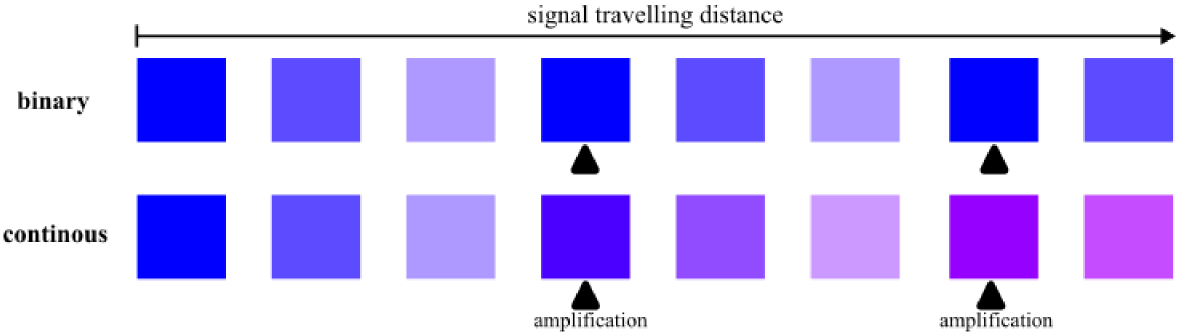


Figure 3: Illustration of the signal distortion with traveling distance. Both signal types (binary and continuous) are impacted by noise (red) and loose signal strength (opacity). The binary signal can take only the values blue or red. The continuous signal can also take every value in between. The signals get amplified at specific points along the path. In these instances, the binary signal can be reset to its original value (blue). This can not happen for the continuous signal, because the original value is not known at the amplification terminal.

synchronized activity emerges from stochastic noise. Specific neuronal subpopulations may act as pacemakers, as has been shown for the well-studied alpha oscillations of the visual cortex [25]. However, even in the absence of regular periodic stimulation, physiologically coupled neurons with noisy synaptic input will reach a state of synchronous activity driven by a mechanism known as coherence resonance [85]. This synchrony then could give rise to the measurable, large-scale oscillations in the EEG, once enough cells are involved to generate measurable currents. This can be exploited to segment the non-noise calculations (see 3.5) or enable the brain to implement additional coding schemes (see 3.3.2).

On the other hand, the oscillations might represent the signal itself. This cyclic coordinated activity arises when multiple neurons are involved in the representation of one state or coherent concept. In order to be recognized as belonging together (elicit an appropriate downstream response), their activity has to be coordinated. In this scenario, if multiple neurons represent one single feature, they allow for a reliable interpretation of their activity despite highly variable responses of individual cells (see 3.4.2). Furthermore, the activation of situational and flexible subnetworks is possible as discussed in 3.4.5. Notably, the usage of periodic, synchronized activity as either signal or background activity is not mutually exclusive and could be implemented by the same networks.

3.3 Neural Information Transmission

The first step in order to discuss how larger structures of the human brain communicate is to explore different possibilities for how single neurons encode information. Understanding these basic building blocks of cerebral activity is essential, to the question of how complex information can be encoded and processed. Theoretically, neurons could either communicate in a graded or binary fashion. In the former case, neural responses encode information as a continuous signal, e.g. in terms of an ion gradient at an electrical synapse. In the latter case, each input signal that surpasses a specific threshold will elicit a full response, while other signals will cause no reaction. At each time point in the binary setting, the activity of a single cell transmits one single binary value (active or inactive, 1 or 0), while graded responses allow for theoretically nearly unlimited information (assuming a receiver with sufficiently high sensitivity). Therefore, these responses would in ideal environments allow for significantly higher transmission rates with potentially superior energy efficiency in terms of ATP/Bit, but come at the cost of signal decay correlating with communication distance (see figure 3), therefore making it susceptible to accumulating noise [64, 81]. Since the identification and description of the intricate interplay of opening and closing ion channels that leads to the described electrical spike studied by Hodgkin and Huxley in the giant squid axon in 1952 [86], it is widely accepted that neurons incorporate, with few exceptions, a binary, AP-based form of communication.

In the following section, different analog options of how the brain could potentially encode information based on these binary building blocks will be explored. After general considerations about neural transmission, the classical idea of (oscillation independent) rate coding will be outlined. Second, alternative neural coding mechanisms that rely on oscillatory background activity, namely temporal coding, the logical XOR-operation, and stochastic resonance will be presented.

3.3.1 Traditional View: Rate Coding

Recordings of real 'analog' neurons' firing behavior oppose theoretical considerations of digital neurons. How can information alternatively be transcribed in a sequence of spikes, or spike-train? Following the traditional view, the main carrier of information in neurons was considered to be their firing frequency. This relation was first described in 1926 by Edgar

Adrian [87], who reported that the spike rate of sensory fibers innervating a muscle correlated with the weight hanging from this muscle. Due to the fact that single-cell responses vary between trials, their activity is treated as stochastic. To read a 'rate code' spike train, Δt (the duration of each basic building block of the code) is defined significantly longer than the duration of a single AP. Reasonable estimates for Δt are in the range of $100 - 500ms$ [88]. Under steady input, a neuron spikes at a regular rate without noise and irregularly after adding noise to the input [51]. The total number of APs is counted within one interval, but the precise timing of individual APs is disregarded as noise.

There is ample evidence that the CNS applies rate codes in a substantial number of situations. Neuronal populations that exclusively rely on rate coding have been identified in numerous studies (e.g. [89, 90]).
The major advantage of rate coding is that it is relatively robust against noise, in contrast to a digital train of 0s and 1s that is easily distorted. This can be illustrated by an example, like the 4-bit digital binary code 0101, encoding the decimal number 5. If now a single bit of the digital code is changed to 1101, the decimal becomes 13. Or if the spike train is temporally shifted, the distorted signal looks like 1010, corresponding to the decimal 10. Minor variations of the code cause a significant change in content. Potential sources of noise and uncertainty have briefly been discussed in section 3.2.2. In contrast to this, as a rate-coded signal is averaged over the interval, it does not matter at what time the individual APs arrive within these time frames as long as their total number stays the same. Considering the spike trains above, shifting the spikes by one time unit from 0101 to 1010 does not change the result (two spikes in average), and switching one bit from 0 to 1 will only cause a minor change in the result (either two or three).

Nevertheless, there are several reasons to call into question, rate coding as the only paradigm at work. In many situations, processing speed is essential. Indeed, object recognition tasks can be performed in less than $1/5$ second [91, 92, 93, 94]. This time allows for one 'feed-forward' cascade in the visual cortex, but not for integration windows required for rate coding at several processing steps. Even more so, all information contained within the precise timing of individual spikes within one interval is ignored. Assuming that all probabilities are equal, equation 3 shows that a rate-coded four-digit spike train yields only 2,3bit (instead of 4). This difference increases for longer Δt. If $\Delta t = 500ms$, i.e. 125 elements a $2,5ms$, the entropy only increases to 7bits (instead of the maximally possible 125bits). That all of the additional information within each interval would be lost seems implausible, given that the input of each cell is intricately balanced even at the millisecond level, supporting a control of its spiking behavior [57, 58]. This raises the question of what possible mechanisms could be used to increase the efficiency and robustness against noise. Several mechanisms have been identified that can be applied to maximize the information gain. Indeed, estimates range from 1 to 10 bits that can be transmitted with each individual spike [95, 96]. For these reasons, several potential other coding mechanisms have been proposed.

3.3.2 Background Oscillation Based Coding

Logical operations: A standard threshold neuron is capable of performing three elementary logical actions: AND, OR, and NOT [97]. A fourth logical operation, XOR or ‘exclusive or’, which is true (elicits an AP) exactly one input is true, requires multilayer networks with these neurons. It has been demonstrated in artificial networks that inherently oscillating single neurons can execute this supplementary logical operation where standard threshold neurons failed [98].

Although conceptually engaging, it is uncertain whether this serves as a driving factor for generating large-scale neural oscillations, considering that other potential implementations of the XOR gate have been discovered in the brain. In the human cortex, dendrites within the L2/3 layer demonstrate atypical, graded instead of binary response properties, allowing for the mentioned operation to be implemented within a single layer [99].

In comparison, oscillating neurons possess the advantage of being adaptable to various operations depending on the background activity phase, while neurons with non-linear dendritic response properties are hard-coded. This flexibility comes at the cost of repetitive activation, due to continuous de- and re-polarization. Overall, it is unclear whether the oscillatory properties of neurons are utilized in the human brain to achieve further logical operations on a larger scale.

Temporal Coding: The term temporal coding refers to neurons or neuronal populations that react in terms of spike timing, rather than frequency modulation [100, 101, 102, 91]. The precise timing of an AP in relation to the stimulus onset (latency coding) or background activity (phase coding) contains the information. As the latter requires a structured background activity, it appears to be an interesting candidate for the explanation of neural oscillations.

In animal models, the timing of a spike in relation to the oscillation phase has been demonstrated as crucial for multiple cognitive domains such as short-term memory [103], object categorization [91], proprioception [104] and spatial orientation [100]. The most renowned example of phase coding neurons are the place/grid cells, a subpopulation of the hippocampus responsible for spatial orientation. These neurons commence firing when the test animal enters a particular area of the experimental maze but do so at specific times in relation to the ongoing background theta oscillations. As the rats traverse the fields, the phase at which the neuron fires shifts depending upon the precise location within the field (i.e. the distance to the center) [100, 105]. One spike contains information about the current presence in a specific place field (present/absent), as well as localization within the field (timing of the spike). Phase coding has been demonstrated across different oscillatory frequencies (such as delta, gamma, and theta) in various brain regions in both animals and humans [36].
Temporal coding can be captured in the information theory framework. Assuming for example a background theta frequency of 6Hz, a single AP can occur at 70 different discrete timepoints during each cycle. As a result of equation 3 over 6bits/spike can be achieved. Strictly speaking, background oscillations are no necessary prerequisite, but might serve as a reference value. Given that the exact timing of an AP might vary, the results could be more robust. Assuming that each spike encodes the number corresponding to the background activity level in percent. If the spike train is shifted by one time step the decoded result might change from 1 to 0.99. This is a relatively small change in comparison to the changes that a shift would cause in a conventional binary code (for an example see section 3.3.1).

Temporal coding allows neurons to increase information entropy, and thereby coding efficiency. It has been demonstrated in-vivo that retinal cells can transmit considerably more information based on stimulus-to-spike-latency than possible by rate coding alone [101] and the metabolic costs are lower for gamma phase coding in the cortex than in rate coding [106]. In addition, neural populations can discriminate stimuli with a higher temporal resolution than can reasonably be expected in a rate-coding paradigm [107].

One essential prerequisite for effective temporal coding is the exact timing of individual neural activity. Given the relatively slow latencies of the ion channels involved in the development of an AP, this would not be expected. But indeed, extremely high temporal precision was demonstrated in the mammals' auditory [108] and visual [109] cortex, and even areas that are higher up in the hierarchy as the medial temporal lobe [110, 109]. In all of these examples, neurons showed stimulus-locked spiking behavior with as little as a few milliseconds variance. The previous examples are based on a rhythmic, high-amplitude background activity.

It was demonstrated that the mammalian brain processes the neurophysiological capability to implement temporal coding, and does so for a variety of tasks. Yet, there are several limitations to this type of information coding. On the one side, it requires an ongoing background activity, to give a temporal frame for the 'signal'-activity. Given that this activity is highly regular and synchronized, it can not encode information on its own but contributes to the metabolic demands. Furthermore, precise timing is crucial. Even though neurons are capable of this precision, as shown above, this is only possible at an increased metabolic rate (see section 3.2.2). In consequence, it remains task and network-specific whether the increased coding efficiency of 'coding' neurons outweighs the additional cost of precision and background activity.
The concept of temporal coding remains controversial beyond energetic considerations [23, 111, 112]. Simple models of coupled oscillators that are used to study the behavior of self-sustained periodically active systems are highly sensitive to phase perturbations. In addition, individual hippocampal place cells display considerable variability between trials, and only the simultaneous firing patterns of multiple cells allow a reconstruction of the current location of the animal [23, 113]. The probabilistic spiking pattern of neurons, together with multiple sources of internal and external noise, represent limitations of this coding scheme.

In consequence, temporal coding is only one aspect of a broader picture. Rate and temporal code are not mutually exclusive in the mammalian cortex and links between them have been reported. They have even been shown to be implemented by the same neurons (e.g. 85% temporal and 15% rate code in specific populations of the rat somatosensory cortex)[114, 51]. It has been argued that they encode distinct aspects of sensory inputs

[115, 102]. For example, information about an individual stimulus was proposed to be coded by frequency, while the accurate timing of an AP corresponds to the surroundings of the stimulus [116]. Another possibility for certain tasks is that phase coding enhances the accuracy of the rate code, as demonstrated for spatial orientation [117]. A potential different link between rate and temporal code has been suggested by [118]. The authors proposed that based on asymmetric firing patterns of hippocampal neurons that oscillatory inhibition indeed enables the conversion from rate to temporal code. In summary, there exists a diverse array of neural populations that exhibit differing coding abilities, some limited to rate coding, others limited to phase coding, and yet others that rely on both coding schemes. To mitigate the problem of noise limiting temporal precision, one possible solution is to activate multiple neurons simultaneously, encoding the same information and accessing the average firing times through population coding (see section 3.4.2).

3.4 Distributed Representation

In most cases, a stimulus will elicit responses from various neurons within one cortical area, and distant regions. The processing is ‘distributed’, if multiple neurons are responsible for the encoding of a feature, object, or scene.

In the following section it will be discussed, how the integration of this activity can be accomplished. The general concept of population codes is outlined and its potential energy efficiency is illustrated with a model of a probabilistic neural network. As the model investigates the network behavior at a very short time scale and disregards spatial considerations, these will be outlined. A second network-energy-efficiency model will be portrayed, incorporating the representation of stimuli at longer time scales as well as the representational capacity of a network. Ultimately, considerations regarding the distributed representation in complex networks will be presented.

3.4.1 Neural Binding Mechanisms

If multiple neurons react to an input and contribute to its representation, their activity has to be registered as connected to assure appropriate further processing. But how can the cumulative activity of many neurons be decoded? Two complementary binding strategies have been proposed: synchronization- and convergence-binding.

Synchronization Binding: Synchronous firing, achieves grouping due to increased saliency and thereby, increased impact on downstream areas, enabling it to induce effective sensory integration [23]. The process of synchronization can happen quickly, in the up to a few milliseconds [119, 120, 121]. This has the advantage of being highly flexible. Weak synaptic links and indirectly coupled neurons are sufficient for this process [38, 122]. Cyclic repetitive activation may be the most cost-effective means of achieving this type of flexible synchronization. Following this reasoning, observable oscillations can arise resulting from the binding process of neural populations. As a negative consequence, the signaling costs rise due to the necessity of multiple spikes of the contributing neurons until simultaneous activity is attained.

Convergence Binding: In the case of convergence binding, the activity of neurons can be integrated, if their axonal tracks have a common integrative target. In theory, no repetitive spiking is required for integration. This has the advantage of potentially reducing signaling energy costs. This disadvantage is that each potential distinct object requires a different convergence unit and already ‘wired’ connections, causing an increased number of axonal and dendritic tracts (see [123]). Novel and unanticipated combinations could not be encoded in neural activity.

But even when adopting a conversion binding approach, the activity of the individual cells has to be temporally coordinated. The intervals for integrating population rate code can range from 20 to 200ms, corresponding to theta to gamma frequency [124, 115, 125]. These long integrative time windows are opposed by neurophysiological recordings. Koenig et al. [126] argue that cortical neurons mainly serve as coincidence detectors and do not integrate input over longer intervals. This conclusion is based on findings that integrative windows of neurons in the cat and monkey visual cortex are significantly shorter than the inter-spike interval. To achieve successful stimulation, signals have to arrive within a relatively short period. In line with Koenig et al.´s results, several other authors reported that for APs to be most effective, they have to arrive in a few ms (≤ 5) time window at a common downstream target [23, 127, 110]. In consequence, if a large number of neurons is responsible for encoding a specific stimulus, synchronous activity (but not necessarily repetitive) activity can be measured in extra-cortical recordings. This is in line with results from the human brain project [44], suggesting that intra-area frequency coupling is a consequence of the connectivity between the cortical areas and not the cause for binding. As long as the sending population oscillates, the receiving one does so as well.

Criticism: It has to be noted that synchronization (and convergence) binding is not undisputed [43]. The criticism is based, amongst other reasons, on weak gamma-coupling over long distances [128, 129] and threshold variability for coincidence detection [130].

Given that gamma synchronization is only strong for a couple of mm, the authors [43] argue that efficient binding over longer distances can not be achieved. This conclusion is based on EEG, and microelectrode recordings from multiple units. Given that with increasing distance, it is reasonable to expect a reduced number of neurons participating in the population coding for the current stimulus. It does not contradict however the assumption that local binding is achieved by gamma-band synchronization at the local level and may be sparse to a point of undetectability for longer distances. It has been proposed that alpha oscillations take the role of long-distance binding.

Furthermore, the authors argue that between areas, there is a threshold variability of integrating neurons. If the firing threshold is too low, they cannot act as coincidence detectors (opposing the notion of convergence binding as well). A single excitatory stimulation, or even spontaneous membrane potentials can suffice to elicit a response. However, this is not convincing, as not every neuron has to act as an integrating unit. It suffices that certain specialized cells fulfill this role.

The authors [43] suggest instead that cells are bound into one object once they surpass a specific firing frequency. Among the general limitations of rate codes (see section 3.3.1), only one object can be represented at each time point. However, attention can be divided among multiple objects [131, 132]. Following the rate-coding regime, this can only be achieved if only one object is represented at each time frame, and attention quickly switches between objects. In consequence, alternating periods of high and low frequency can be measured for the individual neural populations. Attentional switches are linked to episodic memory [133] which is inextricably linked to hippocampal theta oscillations [134]. If attentional switches between frequency-bound populations occur therefore regularly, measurable large-scale oscillations arise. In contrast to synchrony binding individual cells are not required to be as tightly temporally correlated to other cells, but the measurable brain activity on a low (EEG) spatial resolution can be similar.

Oscillations as Consequence from Binding: While there is evidence for both, convergence- as well as synchronization-binding, the majority of synaptic input for cortical cells originates from cells bound by simultaneous activity [110]. Given their different advantages, the binding methods could be responsible for distinct tasks. Specific ‘hard-wired ’convergence units could become active for common or intra-area input while binding by synchrony is responsible for novel, unexpected, and local input. Critics of these binding schemes raised some valid points. But even when adopting a frequency-binding approach, oscillations can arise from this binding process, despite a different underlying mechanism. All three binding theories result in oscillations.

3.4.2 Population Coding

Due to the probabilistic nature of neurons, and intrinsic and extrinsic noise, each AP carries a level of uncertainty. To reduce uncertainty at higher cognitive and behavioral levels, the activity of an ensemble of nerve cells can be aggregated. If multiple cells respond to one feature, single cell variance gets averaged out and the results become more reliable. This technique is known as population coding.

It was demonstrated in cats’ visual cortices by [124] that LFPs of neurons in visual cortex exhibited peak activity when a visual stimulus matched a preferred direction, but showed graded responses depending on the degree of match between stimulus and preferred orientation. Interestingly, despite the high degree of variability in single-cell activity, the precise reconstruction of the correct stimulus was achievable through the summation of weighted direction vectors (activity level x preferred direction) of the whole population. This illustrates how rate and population coding combine to reduce the impact of noise. However, population coding is not limited to rate codes. Its feasibility combined with temporal codes has been shown [135]. Population coding has been demonstrated at various temporal and spatial scales, ranging from microscopic (few mm) to macroscopic (involving distant cortical areas) cell assemblies [136].

Beyond increased resilience against noise, population code renders neural networks robust against pathological changes in the network structure. The human brain can tolerate cell loss due to disease to a certain extent. If calculations are distributed over a larger population,

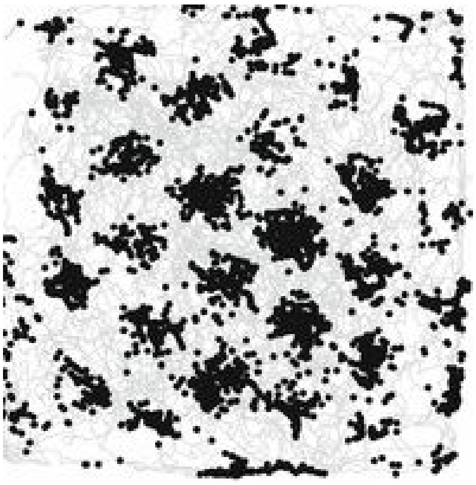
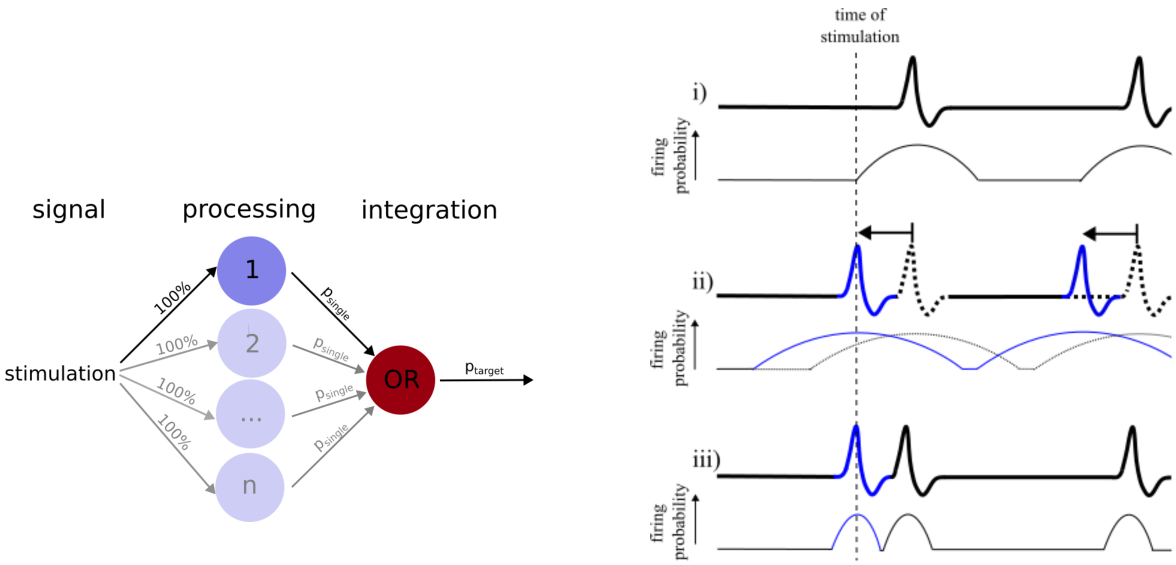


Figure 4: Activity of a multi-peaking grid cell as the rat moves along the gray path. Adopted from Micro-, Meso- and Macro-Dynamics of the Brain, Buzsáki G, Christen Y, editors.Cham (CH): Springer; 2016.(open access)

humans can under certain circumstances lose a surprisingly large fraction of their cortex without severe reduction of their cognitive capacity.

One obvious disadvantage of population codes is that they require the activity of multiple neurons instead of one. If the synchronization is achieved by oscillation, they are activated multiple times, instead of once. Given the high energy costs of APs, they reduce the potential savings of stochastic low-cost neurons. In section 3.4.3, a simple model simulates the energy costs of these networks. To create noise-resistant networks with cells that each respond only to a specific dimension of a stimulus, the total number of required cells multiplies manifold as opposed to single-cell coding. This results in higher resting energy costs and spatial requirements. Mechanisms to reduce the absolute number of neurons while maintaining the representational capacity have been identified. This reduction is possible due to a property known as multi-peaking, which allows cells to maximally respond for different inputs. For example, entorhinal grid cells exhibit multi-peaking by firing when the rat enters one of various locations that are arranged in a grid-like formation, rather than one single specific region (see figure 4). Therefore, the potential distinct representations increase exponentially with the number of neurons [137], resulting in a decrease in overall cell count and consequently energy requirements. A basic model of cell count and metabolic costs is presented in chapter 3.4.5).

Population codes provide robustness and even allow a reduction in cell count based on multi-peaking neurons. Yet, the process of synchronization-by-oscillation and the necessity



(a) Diagram of the probabilistic network model

(b) Theoretical considerations regarding the energy costs of probabilistic neurons

Figure 5: Figure illustrates the concept of the modeled probabilistic neural network. 5a illustrates the basic model architecture. Upon arrival of an appropriate signal, 1 to n neurons are stimulated. Each cell responds with an AP with a probability of p_{single}. These responses target a single integrative neuron that implements an OR operation (responds if at least one cell fired). The probability of a response of the whole network is denoted by p_{target}. 5b justifies the non-linear relation between spiking cost and probability. In i) the spike train is not altered, and energy costs are identical to background activity. In ii), highly probabilistic neurons allow for a shift of the spike train. The additional costs are relatively small, at the cost of increased uncertainty. The highly deterministic neurons in iii) do not allow for a temporal shift, resulting in the highest possible energy costs, as an additional AP is triggered.

of multiple simultaneous spikes imposes a metabolic burden.

3.4.3 Modeling Probabilistic Neural Populations

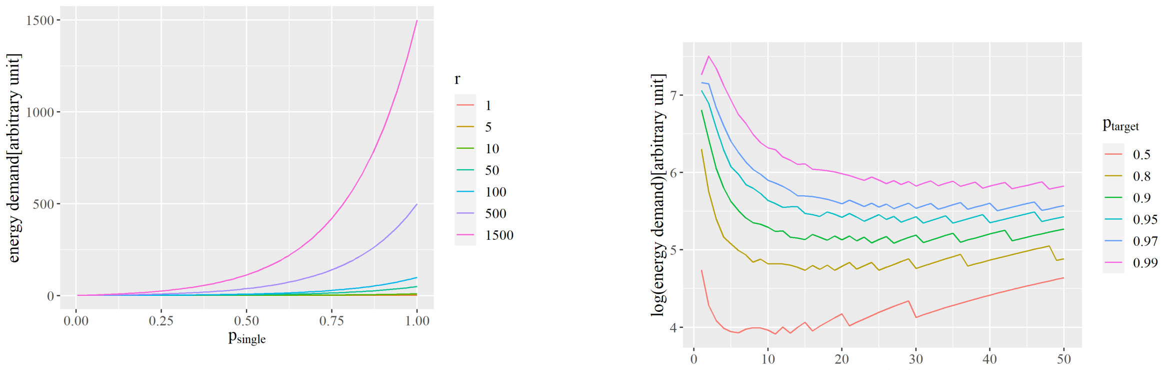
To demonstrate the concept of a probabilistic and signaling-cost constrained network, a simplistic concept was developed in the scope of this thesis. This reductive model illustrates, how the distribution of a neural code across multiple probabilistic neurons can augment energy efficiency. It describes the energy use of a neuron or neural network, at which an input signal is present at one single discrete time point (Δt) that requires its forwarding. This is achieved, if the modeled network becomes active (see figure 5a). Because the exact activity pattern within the network is disregarded as noise and there is one single binary output, the maximum possible rate of information transmission is limited to 1bit/Δt.

Parameters - Probabilistic Model: Several simplifying assumptions will be made: an approximately exponential relation between the firing probability of a single neuron (p_{single}) , and its energy consumption is postulated (see figure 6a). The actual ATP consumption of the spike itself will be very similar in every case. However, the total additional energy costs over a longer time window is not, as the spike can be shifted to the right timing, depending upon its probabilistic base activity (see figure 5b). Additionally, a single neuron response is presumed sufficient for the population to be counted as the appropriate reaction of the population.

A physiological spontaneous release rate of cortical neurons will be approximately 1.2Hz [69]. With a Δt of 2.5ms, the probability to be spontaneously active at each Δt is therefore $s = 0.003$. This is the basic state of each neuron and corresponds to the lowest energy consumption. Different relations $r^m = \frac{Energy\,Cost\,to\,Spike}{Baseline\,Energy\,Cost}$ between minimal and maximal costs ranging between $r = 1$ to $r = 1500$ are explored. The cost of activity can be approximated based on the base spike probability s with the formula $r = (2 * s)^{-\frac{1}{0.7}}$ based on [4]. For $s = 0.003$ subsequently r 1500 (and $s = 0.01$ the energy optimal r 250) . In this scenario it is 1500 times more expensive to spike at a specific time with 100% probability as opposed to 0.3% baseline probability. With exponentially increasing energy costs, the probability of an AP at the right time increases.

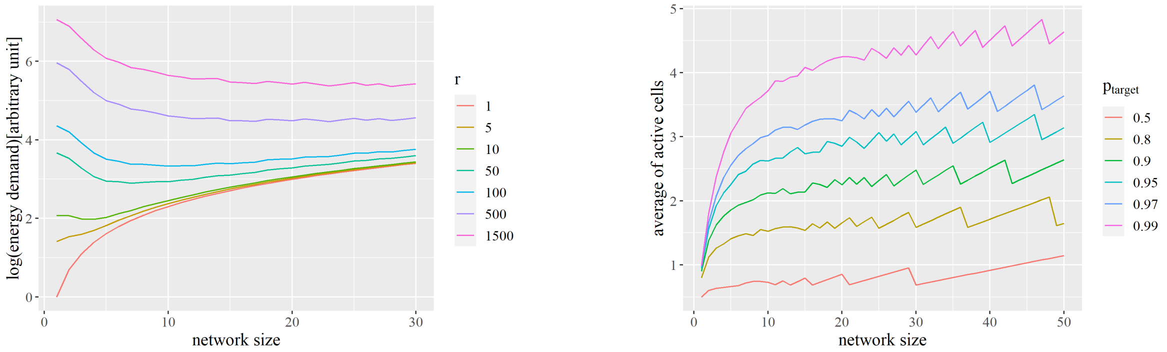
To approximate the necessary energy demand of each cell, their firing probability (p_{single}) was increased stepwise, until the accuracy of the entire network surpassed the specific target accuracy (p_{target}). The total costs resulted from the energy demand of each cell and the network size. This was done for all potential combinations of parameters. As this model merely serves illustrative purposes, no statistical comparison was performed.

Results - Probabilistic Model: Assuming that one cell's AP is sufficient to elicit a response cascade, the total energy costs in relation to the cell number that encodes for a stimulus are shown in figure 6. Notably, the energy-optimal probabilistic representation of a stimulus is achieved for nearly all parameter combinations by a population of neurons, instead of single cells. The results remain robust for various combinations of these parameters (see figure 6c and 6b). In consequence, the distributed representation will cause the simultaneous activity of multiple neurons, if $p_{target} > 0.8$ (see figure 6d).



(a) Predicted costs of a single neuron in the network in relation to firing probability $psingle$

(b) Costs of the whole population in relation to target probability (p_{target})



(c) Costs of the whole population in relation varying with different r-values

(d) Average number of active cells (y-axis) in relation to the network size (x-axis)

Figure 6: Figure shows the energy costs of a probabilistic neural network comprising of 1 to n cells. Energy costs are estimated in a relative (arbitrary) unit. In 6a, different potential trajectories of the energy costs of an AP in relation to p_{single} are shown. The minimal relative energy costs of each cell is defined as 1 at the minimum response probability of $s = 0.003$ and r value corresponds to the maximal possible costs at $p_{single} = 100\%$. 6b shows the costs of the model depending on different target response probabilities p_{target}. The effect of different energy cost trajectories of single cells on the costs of the whole network with a target accuracy of $p_{target} = 95\%$ is displayed in 6c. 6d shows the number of active neurons, depending on the network size (neurons) and p_{target}. For higher target accuracies, the likelihood of multiple neurons being active simultaneously is high, especially for highly distributed representations.

Discussion - Probabilistic Model: In conclusion, if a neural population incorporates multiple probabilistic cells instead of one, interesting features emerge. The costs of the representation of a stimulus can be reduced if it is distributed across several units/neurons. These results can be extrapolated to more realistic/complex settings. It might be beneficial if the receptive fields of neurons overlap. If an appropriate stimulus is shown, several neurons are likely to fire at the same time. If a network has to encode complex objects, comprising several distinct features, hundred or thousand cells might fire simultaneously. Oscillations can arise in two ways from this. Either the processing of stimuli occurs in periodic time windows (see section 3.5.2, or the synchronization process for weakly wired neurons is oscillation-based (see section 3.4.1)

These results can easily be extended from a binary setting to analog neurons that encode a signal with an increase of firing frequency above a certain threshold (see 3.3.1). As the code remains binary (either below or above the threshold), only some parameters have to be adjusted. With longer Δt representing integrative windows for the rate code, instead of minimum AP duration and s representing the probability of a neuron spontaneously exhibiting a spike frequency above threshold.

This model has several obvious limitations. The assumed maximum r value of 1500 is significantly higher than in measured physiological recordings. Nevertheless, even if lower r values are applied in the model, no significant change in results due to the exponential nature of the energy-cost to probability relation emerges. Even when setting r as low as 10, the finding that energy optimal representation is achieved when distributing a signal across several neurons remains consistent. The thermodynamic energy costs are inseparably linked to the probability of a calculation being correct [79, 80]. The exponential relation between the correct timing of a spike and its energy cost seems plausible and was demonstrated for electronic circuits [138], but remains to be tested for biological components. In addition, the energy costs for larger populations are likely to be an underestimation, as it seems likely that one cell alone actually might not be enough to initiate a proper downstream response, especially in larger populations. A reasonable approach would be to adjust the number of cells that have to be active to sufficiently represent a state to somewhere around 2-16% of all available neurons [4]. Furthermore, resting costs have been disregarded so far. At very short Δt, they become neglectably small but gain influence if energy budgets are assessed for longer periods, especially in sparsely active networks. So far, the number of neurons that is ideal to represent one single state and not the number of neurons that is necessary to represent all potential states was evaluated. The overall representational capacity will be addressed in section 3.4.5.

Despite these simplifications, the model nicely illustrates how it might be energy optimal to distribute computations over several probabilistic, instead of one deterministic neuron. As a natural consequence of this behavior, the likelihood of multiple neurons being active simultaneously rises with growing cell number (see figure 6d). If multiple neurons are responsible for encoding individual features, complex stimuli in consequence could cause a large-scale synchronized activity.

3.4.4 Spacial Limitations

On the one hand, the demands for the developing fetus during gestation for the mother's metabolism [64, 139] and maintenance after birth [6] have been shown to restrict brain size. The number of central nervous system cells is fundamentally linked to metabolic requirements. Given a neural density in primates that is relatively constant, independent of the brain size, the number of neurons can be estimated to correlate with the size of the human brain [140].

On the other hand, as humans adopted upright bipedal motion, the diameter of the birth canal decreased. This limits the size of a newborns head and in consequence its brain volume. Given that the neurogenesis after birth is marginal [141], this represents an additional limiting factor.

Consequently, over the last 100,000 years, the human brain volume decreased despite significant intellectual and cultural progress [142]. This suggests that space-saving techniques are in operation to achieve a high computational power with fewer neurons.

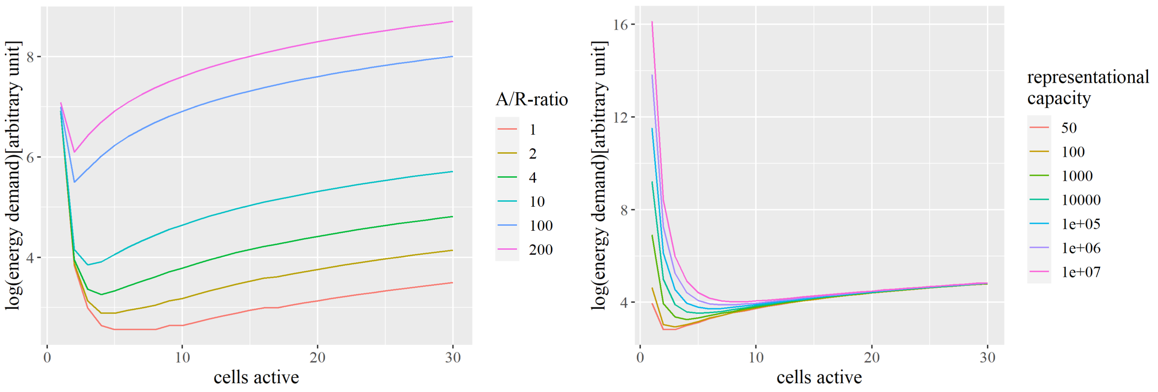
Energetically speaking, smaller brains have two evolutionary advantages: a lower cell count (resulting in lower 'resting' costs) and shorter distances between cortices (resulting in lower signaling costs). The significance of short messaging distances is emphasized by the efficiently optimized mesoscopic [81, 143] and macroscopic wiring [144, 81]. Although the majority of synaptic connections are local [145], long-distance connections consume the majority of the available metabolic energy budget. When partitioning the energy budget of the human brain, it is estimated that long-distance communications consume approximately 20 times more energy than local computations [146].

In summary, the energy expenditure associated with the number of cells can be lowered through a decrease in the overall cell count or a reduction in long-range communication (signaling reduction and increased efficiency). The data backing the idea that the brain utilizes oscillatory activity to implement these techniques to reduce energy consumption will be analyzed alongside potential limitations.

3.4.5 Modeling Representational Capacity

Many neurons (especially on low sensory levels) are broadly tuned, meaning that they exhibit a graded response to a variety of potential stimuli [110]. To generate a precise representation of a complex real-world object, the integration of the response of multiple nerve cells is necessary (see section 3.4.2). While each cell encodes a basic property, like the orientation of an edge, color, contrast, etc., the whole object can be reliably constructed from group activity. The various possible combinations of these 'basic' neurons allow for a high number of objects that can be coded. These combinations are possible within and across different sensual modalities. This reduces the total number of required neurons.

How many neurons are energy-optimal to represent different objects or states in the brain? In other words, how many cells have to be active at any time point to achieve the highest representational capacity, i.e. the number of distinct states that can be encoded by a system, relative to its ATP consumption? A basic example, modeled in analogy to [7, 4], illustrates how distributed coding across multiple cells reduces energy demands. The following considerations and data represent a replication and minimal extension of the original model in the scope of this thesis. To simplify the calculation, it is assumed that all neurons of the example act as homogeneous binary signaling devices. This population can represent 2^n different states or bits, where n is the size of the population. If the number of cells that is active at each time point is restricted to a cells, this number reduces to $\frac{n!}{a!*(n-a)!}$. To encode 1000 different network states (representational capacity) with a single neuron each, 1000 cells are necessary (i.e. only one specific neuron is active during each state). Using two neurons for each state reduces this number to 46 cells ($\frac{46!}{44!*2!} = 1035$ distinct combinations). If states are represented by three active neurons, only 20 cells are necessary ($\frac{20!}{17!*3!} = 1140$ distinct combinations), and so forth. A population reaches the highest representational capacity if 50% of its neurons are active at each state [63].



(a) Costs for different A/R-ratios (b) Cost for different representational capacities

Figure 7: Figure shows the logarithm of energy costs for networks in relation to the number of active cells, including resting costs of nonactive neurons. In 7a, the costs of a network with a fixed representational capacity of 1000 are illustrated. Colors indicate different $A/R-ratio$ (cost of activity versus rest). In 7b, the A/R-ratio is fixed to $4/1$. The color of the line indicates the networks' representational capacity. These plots were created by stepwise increasing the number of total cells until a target representational capacity was reached. Energy costs could be deduced from the number of active and inactive cells, as well as the A/R-ratio.

When examining the representational capacity under energetic constraints, the metabolic demands are defined by the number of cells and the difference between activity and rest. In universal terms, one cell's energy costs are A in the active state and R in the resting state per second. In the one-neuron-scenario, each second 999R+1A, in the two-neurons scenario 44R+2A, and in the three-neurons scenario 17R+3A are 'spent' per second. Over a wide range of A/R ratios as well as possible states, the energetic cost of distributed representation remains 'cheaper' compared single-cell representation. Figure 7 shows the predicted costs for a broad range of representational capacities and A/R-ratios.

But how can the activity of multiple distinct neurons be recognized as belonging together? The most probable method for multiple neurons to represent a state is simultaneous activity (e.g. [126, 147, 148]). Numerous approaches to achieve synchronous activity are viable (e.g. a single, powerful input signal), but oscillation-based synchrony is the most energy-efficient [38, 149]. If the neural population representing a state is large enough, it becomes a potential candidate to explain the large-scale cyclic activity detected in EEG.

Distributing the calculations across a neural population, reduces not only the necessary cell number (and thereby the size of the brain) but more importantly also minimizes its metabolic demand.

Higher temporal resolution require higher frequencies and increase A, thus promoting more sparse coding; fewer neurons are active for each state[7]. Numerous studies of multiple sensory modalities indicate that information is encoded sparsely [150, 151, 152]. However, this model does not consider the distance between neurons and their firing frequency, which have a considerable impact on signaling cost, i.e. increasing A. It is significantly higher for distant cortical areas, resulting in a severe penalty for long-distance synchronization and favoring local computations instead.

In summary, the composition of neural representations represents a compromise between signaling cost and distance on one side and resting cost and temporal resolution on the other. Under all modeled parameter combinations, the distribution across multiple neurons surpasses the efficiency of single-neuron representation. Oscillations can arise as a consequence of the synchronization process that is necessary for the grouping of the activity.

3.4.6 Distributed Processing in Complex Networks

Perceptual Grouping: As described by 'Gestalt'-psychologists, humans tend to bind different sensory features into one coherent object [23, 153, 154, 155, 124]. This phenomenon can be observed within one sensual modality, for example when adjacent contours with similar contrast that move in the same direction are perceived as one object. Across-modality perceptual binging occurs, if for example the lip movement of a speaker matches the auditory input [153, 156]. In this case, there is activity in two distinct cortex areas that is perceived as one object. This mechanism can on the one side enhance object recognition and is on the other side responsible for the perception of specific illusions (such as the illusion of biological motion [157]). The concept of distributed stimulus representation forms the basis of the feature binding theory. In contrast to traditional hierarchical models of cognition, which assume a convergence of sensory information in a higher region, empirical findings suggest that synchronization at lower levels may be sufficient to represent a stimulus.

The simultaneous activity enables the linking of single features into a coherent object. Demonstrated by Gray and Singer's work in the early 90s [124], individual neurons that fire simultaneously can represent various aspects of a stimulus that are bound into a coherent percept. Early multimodal integration has been demonstrated across multiple brain areas and modalities [158, 153, 155]. If a congruent auditory and visual stimulus is presented, the synchrony in the gamma band between the corresponding cortices is significantly increased, while the amplitude of oscillations in the corresponding auditory and visual areas remains unaffected [159].

One driving force might be a reduction of neurons needed for computation, as in theory no convergence units are required, thus reducing total resting costs. To create a distinct representation of an object, it may be sufficient to synchronize the corresponding sensory neurons without requiring a higher-order ‘integrative’ layer.

Dynamical Networks: Beyond the representation of low-level sensory information, it has been argued for a broader understanding of flexible patterns of neural coherence that allow task-specific activation of variable subnetworks [160]. A large range of neural populations can be activated without the energy-consuming and slow process of synaptic plasticity, but by means of synchronization (see section 3.4.1). This can be modulated in a top-down manner to select the necessary networks for the given task. Cortico-spinal synchronization has been demonstrated even in the anticipation of motor tasks [161]. This flexibility, again, allows for a reduction in the number of neurons, because individual cells can be used in a variety of computations and are not limited by their axonal wiring.
The notion of anticipatory coherence is intriguing, yet presently lacks support from a wider range of modalities.

3.5 Background Oscillation Based Segmentation

The previously discussed applications of repetitive cyclic activity addressed the potential for the direct encoding of information. Another train of thought bases on the assumption that (some) oscillations do not intrinsically contain information, but are a necessary backbone/ structuring processing. It does not specify how the information is processed. The ‘true’ calculations can but do not have to be oscillation-based.
In the following, the advantages of temporally clustered processing on a cellular level will be demonstrated with the concept of sensitivity windows that can facilitate this. Furthermore,

the concept of predictive coding will be presented. Research, indicating how this concept can benefit from structuring oscillations will be outlined. Finally, I will demonstrate, how oscillations can provide spatial information in the form of frequency-dependent directionality and traveling waves.

3.5.1 Bursts: Clustered Information Processing

Instead of processing information at a continuous/'tonic' rate at the level of single cells, a significant part of the signal transduction is condensed into short time windows with multiple consecutive APs [162, 163, 164]. Surprisingly, data from simulations suggests that the total energy costs (in terms of ATP consumption) of these bursts with multiple spikes are indeed comparable to solitary spike [165], while at the same time transmitting more information. In addition to the time of an event, bursts encode information via size (number of spikes) and even precise 'intraburst' spike intervals [164]. According to the burst coding hypothesis, bursts and tonic/single APs are interpreted as distinct events [162] with different behavioral consequences [163] and encode different aspects of a stimulus [164]. Post-synaptic excitability is increased during these bursts, making each spike more likely to trigger a response [166]. Clustered spikes are involved in a wide range of processes, including long-range synchronization in the beta and gamma bands [167] and the modulation of synaptic plasticity [168]. Bursts operating with similar energy demands as single APs, will therefore result in an increased energy efficiency. As a result, a substantial part of the processing is clustered at short intervals. If these intervals occur periodically, as suggested in the following section, it might be a potential candidate for explaining the emergence of oscillations.

3.5.2 Sensitivity Windows

To achieve effective signaling, sending neurons must ensure that receiving neurons are currently capable of processing the input. If the receiving cell is still re-polarizing from a previous AP or hyper-polarized from inhibitory input, the probability that an input signal will trigger the appropriate response is greatly reduced. This presents a crucial constraint for mesoscopic, and even more so for costly long-distance, communication. One proposed mechanism for ensuring that action potentials reach their intended target in a state of readiness is the concept of sensitivity windows that are generated by the background oscillations [169]. Signals that reach their target during the trough of the cycle can be processed and

integrated with other input that reaches the neuron in the same time window. Signals that arrive outside of these intervals are disregarded as noise. To communicate efficiently, distinct neural populations must synchronize [36].
Empirical evidence for sensitivity windows comes, among other areas from the auditory system, where playback of a 3 Hz tone elicited a synchronous delta wave in the auditory system [170]. The detection of a sound gap correlated most significantly with the phase of the cortical delta oscillation at which the gap occurred, rather than with the sound wave phase. This indicates that the auditory cortex has specific sensitivity windows, which correspond with the cyclic background activity.

While having several advantages, the concept of specific sensitivity windows of clustered information processing falls short of the optimization of information transmission. As discussed in section 3.1, messages with the highest possible information have to have equally high probabilities for spiking versus non-spiking at every moment. Given that the likelihood of activity is not equal for all time steps during periods of sensitivity windows versus non-sensitive phases, the information gained is suboptimal.

It is hard to estimate the precise energy savings from assuring the reception (and processing) of a signal in comparison to the cost of reduced entropy. In conclusion, the concept of sensitivity windows remains appealing, but convincing evidence that they are a driving force for neural activity patterns remains to be found.

3.5.3 Predictive Coding

Predictive coding refers to a concept that addresses the question of how the brain filters relevant information for further processing [171, 172, 173, 65, 174, 175]. This filtering is in itself a mean to save energy, as irrelevant sensory input is disregarded and does not initiate a chain reaction of neural activity. Predictive coding does not per se depend upon oscillations. Therefore, a brief overview of its concept will be given. Subsequently, data is presented that suggests that cyclic background activation can indeed augment this process.

The brain is subject to a constant stream of noisy sensory input. Every calculation has to be performed under a certain degree of uncertainty. Preselecting input that provides new information and deriving the true signal from the distorted input poses a significant challenge. The predictive coding paradigm suggests that neuronal activity implements a mechanism known as Bayesian inference. It posits that a neuron/network incorporates a ‘prior belief’ or expectation about the state of the environment [175]. New input is compared to the prior. If they are identical, no action is triggered. If they diverge, the input is sent further up in the neural hierarchy and the ‘posterior belief’ of the current level is updated and becomes the new ‘prior‘ for the next input. This paradigm can be applied at various levels of the cerebral hierarchy.

The certainty of the posterior belief depends on the certainty of the prior belief and the ambiguity of the input. If the prior belief is strong, the posterior belief will be mainly influenced by the prior state instead of the signal, and vice versa.

Predictive coding can save energy in two ways. By preselecting input with a high information gain and by integrating prior knowledge at various processing stages, limiting the impact of noisy input. In consequence, neuronal efficiency can be enhanced.

At the cellular level, predictive coding can be illustrated by the behavior of sensory rods and cones in the retina. These cells are constantly exposed to photon noise. Stimulated cells exert an inhibitory effect on adjacent cells (‘lateral inhibition‘) [176]. The degree of inhibition will correspond to the average noise level neighboring cells are experiencing. This can be seen as ‘prior‘. Only input deviating from this level will trigger a response. If a cell is now subjected to multiple successive photons, it will adapt (update the ‘posterior‘) and become less reactive to upcoming stimulation.

Evidence for predictive coding was found on various levels of the cerebral hierarchy. Stochastic inference does even translate to the level of human behavior, as test subjects exhibit in various tasks probabilistically optimal reactions [171, 172, 173]. Similarly, it has been proposed that cortical neurons can efficiently receive input mainly when their neighbors are inactive, as is the case at the drought of an oscillation (see section 3.5.2).

The concept of predictive processing also translates to artificial systems. It was demonstrated that complex probabilistic information can be stored in realistic cortical models [65]. Recurrent neural networks with restricted energy supply develop comparable predictive capabilities, with inhibitory units weakening unsurprising input [177].

But how does this coding concept relate to cerebral oscillations? The separation of the processing steps as well as the enhancement of the inference itself have been proposed as potential links. Given that predictive relies on separate processing steps, continuous input needs to be discretized. Analogous to sensitivity windows at the network level, the drought period during oscillations could be used for sampling, i.e. signal discretization. Within each cycle of the background activity, it was shown that the distribution of neural activity, remains mainly constant, and switching occurs preferentially at phases of low firing frequency of the population [65, 178]. The oscillatory cycles can provide a time frame for the inference process and enable switching to the next step. The positive and negative phases of an oscillatory cycle relate to the different inference steps of mixing (combination of 'prior' and signal) or consolidation (formation of 'posterior') [65, 171]. Oscillations have been observed in specific probabilistic inference networks, ('Hamiltonian Monte Carlo'), and have been found to improve computations, suggesting the importance of oscillatory activity in information processing in neural networks. These excitatory-inhibitory Monte Carlo network models were designed to mimic the visual cortex. They were able to handle continuous, ambiguous input and showed to be by an order of magnitude more efficient and faster than their non-oscillating counterpart [174]. The authors' explanation for this observation is that the oscillating network efficiently explored various possible interpretations of the input.

Following these arguments, the maintenance of background oscillations could support the brain's predictive inference operations. However, a conclusive evaluation of the increased metabolic load caused by the sparse waves versus the energy savings from better processing has yet to be carried out. Consequently, the potential evolutionary advantage remains conjectural.

3.6 Oscillation Based Spatial Information

3.6.1 Frequency Dependent Directionality

The direction of messaging is associated with the frequency band. In cortical processes, the gamma band is primarily involved in feed-forward or local processes (e.g. [179]), whereas beta oscillations are mainly involved in feed-backward information flow [180, 181]. This dichotomy is also reflected in the cortical architecture. The superficial layers L2/3 transmit feed-forward signals at gamma frequency, and the deeper layers L5/6 transmit feedback signals at beta frequency [23]. Frequency-dependent directionality was detected even within a single cortical area. Gamma and theta oscillations carry forward information, while alpha [24] and beta [182] oscillations provide local feedback information in the monkey's visual cortex.

From a network perspective, this frequency-dependent directionality could serve two functions: providing robustness against noise and signal filtering. As retrograde beta messaging mainly consists of long-distance connections, and the traveling distance of an action potential(AP) constitutes an essential energy cost factor [123], the brain needs to ensure that these APs are most robust against noise. By this theory, neural connectivity models have demonstrated increased resilience to synaptic noise when synchronizing in the beta band [23, 66, 183]. While higher frequencies are more vulnerable to noise, they permit quicker interactions with higher temporal resolution. By selecting the appropriate frequency channel, the CNS ensures that long-distance connections, which are rare and energy-demanding, reach their intended target without distortions. Gamma oscillations, which have a higher computational power, are used for less energy-expensive but more complex mesoscopic connections.

The second function of frequency specificity may involve neural frequency filtering. The use of different frequencies may assist in addressing the correct cell population. Neurons have been shown to implement high- and low-band frequency filters, which causes them to respond only to a narrow range of stimulation [38]. This mechanism may be involved in separating various feed-forward and feedback streams.

The extent to which frequency-filtering neurons are necessary for the control of targets in the CNS has yet to be determined. As previously mentioned, multiple cortical layers are implicated in local, feed-forward, and feedback processing. Therefore, directionality may be hard-wired, providing the advantage that repetitive or cyclic activity is unnecessary and singular activation is sufficient. This option would decrease repetitive AP energy costs, but it may be slightly less flexible. The significance of these findings for cerebral evolution is still uncertain. Several other mechanisms exist to ensure that long-distance signals reach their intended target undistorted, without relying on different frequency bands. These include specific neural 'highways', i.e.myelinated fibers.

3.6.2 Traveling Waves

So far, the concept of the discussed oscillations was stationary, meaning there is no systematic mesoscopic spatial variance of activity. Novel imaging techniques, such as voltage-sensitive dyes, have led to an increased interest in the phenomenon of traveling waves (TWs) [184, 24, 185, 186, 187, 37, 188, 189]. These new observations contradict earlier assumptions as oscillations detected in various brain regions are not static, but instead propagate across the cortex. TWs were previously undetectable on EEG and fMRI recordings due to inadequate spatial or temporal resolution, respectively.

The observed waves travel in a posterior to anterior trajectory during the state of wakefulness [184], while at sleep, this direction is reversed [24, 188]. The traveling speeds range from 0.1 to 0.85m/s in demyelinated fibers on a mesoscopic scale, and up to 10m/s in myelinated fibers on a macroscopic scale [24, 184]. TWs were found to be involved in visual and olfactory perception, spatial orientation, and predictive of observable behavior [184, 185, 186, 187, 37].

In addition to the potential benefits of steady-state cyclic activity, TWs offer several advantages. These include intrinsic logical operations, enhanced information transfer, and spatial/temporal segmentation of neural representations.

Collision-based computations may provide an efficient means of implementing basic logical operations (see figure 8). All four basic logical operations can be carried out through the interaction of two waves, such as OR using superposition, or XOR that corresponds to the annihilation of two waves [190]. Promising results from artificial neuromorphic systems show that computations based on wave interactions can be realized [191]. However, only a small portion of cerebral computations can utilize collision-based computations, due to their need for dense waves with a significant percentage of neurons participating in each cycle [24]. As cortical neurons underlie the sparseness regime, with only a small portion of neurons active at the peak, waves will pass through each other, or interact in unpredictable patterns.

TWs are capable of carrying additional information. Research shows that TWs in the beta spectrum encode information through amplitude and latency, frequency and are phase-locked to stimulus onset [192]. This corresponds to stationary beta and theta waves encoding information through amplitude, frequency, and phase [193, 194]. However, wave statistics of

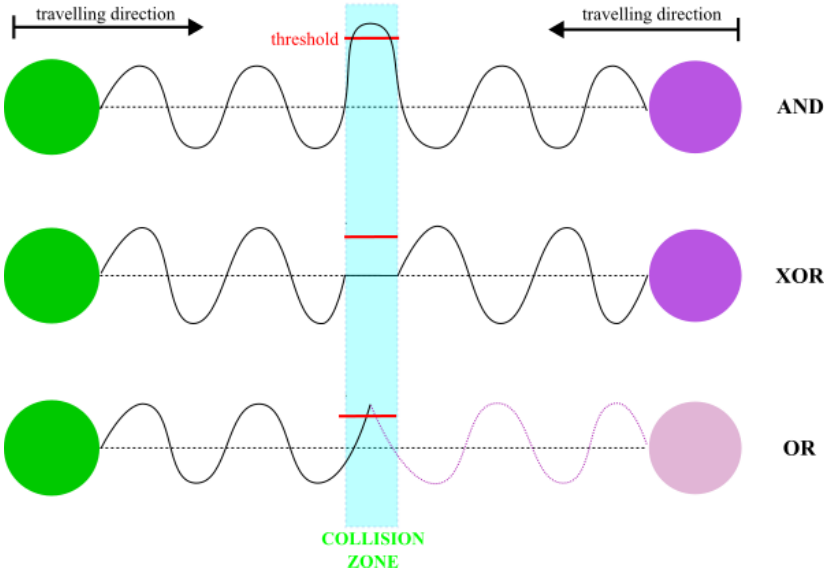


Figure 8: Figure illustrates the concept of collision-based logical operations. TWs from the left (green) and right (purple) sender move towards a common collision zone in the middle. The waves interact here with each other and stimulate a receiver (in the collision zone). In the case of the AND operation, the TWs get amplified, so that they can surpass a threshold, they could not surpass alone. In the case of the XOR-operation, if both senders are active, their signal gets canceled out, because they arrive out-of-phase. Each signal would be able to surpass the threshold alone. The same is true for the OR-operation, with the difference that if both senders' signals arrive in-phase at the collision zone. Not displayed is the NOT-operation.

TWs can be used to determine the signal origin [24]. Comparing a cell's input to the activity of its neighboring cells (orientation and curvature of the wave) allows to reconstruct the direction, traveling speed, and origin of the wave. The spatiotemporal structure provides additional information without any additional cost.

In line with the principles of predictive coding and sensitivity windows, the TWs have the potential to separate different processes temporally and in addition spatially, as has been shown for alpha and theta waves [184, 178, 195, 196, 197]. Following this logic, it is only possible to perform calculations at the trough of the background TW. The order of involved cortical areas is determined by the motion of the TW. At the peak, a reset occurs. Indeed, research has demonstrated that while alpha waves travel across the cortex, gamma oscillations are phase-locked to the troughs of these TWs[189]. Therefore, the higher cognitive functions relating to faster frequencies rely on the time frames generated by the slower alpha TWs.

At the time being, the possibility remains that TWs are a mere epiphenomenon. While the potential computational roles of TWs are intriguing, their importance for the functionality of the CNS on a larger scale has still to be established.

4 Discussion

4.1 Oscillation-based Enhancement of Efficiency

Cyclic neural depolarizations are a ubiquitous phenomenon in the human cortex. Due to the repetitive and synchronized activity, a large number of neural spikes is triggered. These contribute substantially to the brain's energy budget, while their precise function remains unclear. Based on reported findings from various sub-disciplines in neuroscience, several mechanisms that rely on neural oscillations were presented. Two simple models were analyzed to evaluate the energy demands of distributed networks. One new model of a probabilistic neural network was designed for this thesis, and one model of the representational capacity of a network was adapted with minimal changes.

In conclusion, none of the presented theories alone provides a satisfactory answer to the question of the existence of neural oscillations. There is strong evidence that the cortex implements phase codes that convey information in the form of the precise timing of an AP in relation to the background activity. However, temporal codes are only responsible for a fraction of the information transfer and coexist together with rate codes. Therefore, they alone are unsatisfactory as the sole explanation for cerebral oscillations.

On a network level, it was demonstrated that the distribution of activity across several multi-receptive, broadly tuned, and probabilistic neurons is superior to the activity of a few sharply tuned, deterministic neurons in terms of energy efficiency. If the representation of single states is accomplished by a larger number of active cells, the total number of required cells (active and inactive) can be reduced along with the size of the brain and its energy budget. Oscillations are most likely the responsible mechanism for coordinating the activity of these cell ensembles. The distributed representation of natural scenes provides a compelling explanation for the coordinated activity of up to several thousand nerve cells. Nevertheless, it falls short of explaining the simultaneous activity of millions of neurons that is measured in the EEG.

Other advantages of neural oscillations such as the segmentation of the signal for probabilistic inference, or the generation of sensitivity windows for effective clustered signaling are compelling. However, non-oscillation-based mechanisms to achieve signal discretization, such as simple pacemaker neurons, or a linear network architecture could achieve the same goal. Conclusive evidence that cyclic signal segmentation is indeed a driving factor of network functionality remains to be given.

While no single approach suffices to explain cerebral oscillations as a whole, their combination might. While there appears to be no universal answer for the ‘oscillation’-phenomenon, distinct mechanisms for various circumstances could be at work. Strongly simplified, low frequency, sparse macroscopic frequencies could provide a structure for calculations, high-frequency dense oscillations could be involved in the ‘proper’ data processing. The oscillations-specific task depends upon the spatial expanse, the cortical region, the frequency band, and temporal development.

This thesis provides a broad, multidisciplinary perspective on the field of neural oscillations. Compared to previous work, it provides an extensive overview of various theories on many temporal and spatial scales. Furthermore, it was possible to demonstrate with the help of a simple probabilistic network developed for this thesis the cost efficiency of stochastic neurons. Mediated by oscillatory synchronization, this offers a compelling new cause of neural cyclic activity. The reported explanations supply a basis for the mechanisms at play in the human cortex. In addition, they provide valuable approaches for cost-efficient artificial computations.

4.2 Biological and Artificial Computations

Classical binary processors are the core element of man-made computers. These are in some aspects superior to biological networks. Relevant time intervals in CPUs are by several orders of magnitude faster than in the brain. The clock-rate of a modern processor is in the range of nanoseconds, while it takes APs several milliseconds to enfold. This is a striking 10^6 fold difference. None of the analogue coding schemes discussed above comes close to potential digital information processing speeds [51].

This striking difference in processing speed becomes relativized when considering the capability of simultaneous processing. Neural networks are capable of parallel processing, as the separate physiological processes will unfold without the necessity of supervision. Each computer core on the other hand has to do one calculation at a time. Despite efforts to exploit parallel processing by building multi-core computers, the number of different cores for private users usually ranges in the single-digit field, with some research systems incorporating up to several million cores [198]. The approximately 100 billion neurons of the human brain [199], could incorporate millions to billions of simultaneous processes (in the most extreme scenario, each neuron serves as an individual processing unit). The decentralization of computations has, in addition to parallel processing, another advantage: robustness against local malfunctions. Humans can compensate for the loss of substantial fractions of their neurons due to disease or accident.

While classical computers excel at processing speed and precision, they struggle when it comes to dealing with ambiguous and complex information, creativity, and energy requirements [200]. Even though the CNS consumes a substantial proportion of the total available energy to the body, this is put into perspective when looking at the absolute numbers. The total energy consumed by it per day can be covered by eating one chocolate croissant (412kcal). A conventional laptop consumes in comparison the equivalent of at least 10 croissants per day. The blue brain project made attempts to simulate neural activity on a small region of a rat's cortex (a cortical column) [201]. The IBM processor with 16 thousand cores needed 100s for each second of simulated activity. Upscaling of this simulation to the whole human brain would consume an equivalent of close to 60 million chocolate croissants per second of brain activity.

Recently, artificial neural networks such as ChatGPT have gained the public interest. But already before this, convolutional neural networks (CNNs) were applied successfully for e.g. image recognition. These CNNs normally implement a comparably simple network architecture. They are strictly linear, with each layer supplying the input for the next and converging the input in one single output. This approximates early visual processing of the brain. In specific tasks, CNNs already surpass the image classification performance of humans. For example, in an ECG-based myocardial infarction task, the AI performed significantly better than physicians [202]. This shows, how neural networks (biological and artificial or biological) excel in the handling of highly complex and ambiguous stimuli.

The mentioned artificial networks remain 'simulations' on classical processors. For this reason, their energy costs remain high, and large-scale simulations, such as the human brain project, fell short of the expectations [203]. Opposed to simulation, emulation bases on reproducing the nervous system's properties by incorporating components that reassemble in their behavior biological counterparts. Instead of describing a neuron's properties with mathematical equations, networks of 'artificial neurons' can be constructed. Starting with the work of Carver Mead 1989 [204], the idea of artificial neural networks incorporating biological principles has gained increased interest. Since then, several large-scale neuromorphic systems have been developed and tested [200]. In terms of speed, they are comparable to biological networks. However, despite surpassing conventional neural networks in energy efficiency, each connection stays 10^3 fold more energy expensive than in the human cortex. Other wave-based neuromorphic approaches were able to re-demonstrate up-to brain-like efficiencies, but remain up-to-date a proof of concept [205, 191]. It has to be seen, whether these concepts can be applied in large-scale systems. Despite promising results, neuromorphic systems remain at an experimental stage.

4.3 Limitations

Several limitations apply to the conclusions of this thesis. These are based on the selection of studies and the scope of the thesis.

One major field that is frequently associated with cerebral oscillations is memory consolidation. This includes long-time memory [206, 207, 208] as well as episodic/working memory [32, 209]. Little data is available regarding the energy efficiency of learning in large-scale biological networks.

Publications discussed in this paper are mainly based on finding in the mammalian endbrain, and early sensory cortices in special. This limits possible inferences mainly to sensory processing. In other parts of the CNS as the cerebellum e.g., the functionality differs substantially. Its largest share of the energy budget is, for comparison, required for housekeeping and the resting membrane potential [8] instead of signaling.

Results from animal and human studies as well as data acquired in a variety of cortical areas were gathered and presented. Within and across species there is a large variety of AP-shapes with several orders of magnitude difference in their energy efficiency [9]. These considerations influence the energy budget and operating principle of the CNS.

Furthermore, the cortical neuronal populations have been regarded as mostly homogeneous, with similar response properties and connectivity of their cells. However, inter- and intra-area differences in response properties of neurons within the human cortex are substantial [95, 210, 211]. The existence of two different populations of neurons, one being energy efficient but slow, the other expensive but fast was suggested.

In addition, different oscillation frequencies are linked to different cognitive processes (e.g. [76, 170, 184, 189, 110]). These differences were disregarded, as the goal of this thesis is to identify fundamental mechanisms of oscillation-based energy enhancement.

The presented model that links the energy efficiency to the distribution of activity over multiple stochastic low-cost neurons, is based on an exponential cost-to-probability function. The precise nature of this connection lacks biological proof, or mathematical proof-of-concept.

However, the presented oscillation-based computation mechanisms do not have the aspiration to be universally valid. This thesis aims to provide general mechanisms that are applicable to energy-limited systems. These can provide a basis for future exploration of the functionality of individual cortical areas, neural populations, and frequency bands.

4.4 Conclusion

Several oscillation-based mechanisms that apply to energy-restricted systems were discussed. While none of these provides a satisfactory universal answer for the existence of cerebral cyclic activity, their combination does. Distinct, frequency-specific applications appear to be at work for meso- and macroscopic oscillations. These include temporal coding, coordination of distributed representation, and signal segmentation. The presented theories allow a better understanding of the functionality of the cortex. Furthermore, they provide new impulses for man-made computation systems. In the last decade, noteworthy progress has been made in designing energy-efficient systems. However, the energy efficiency of biological neural networks remains unmatched. Despite several limitations, distributed and probabilistic networks have a substantial potential to save energy. An objective for future work remains to investigate the exact cost-to-likelihood relation of an AP. The next step is the implementation of probabilistic large-scale systems that can perform classification tasks.

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