NREM and REM: cognitive and energetic effects in thalamo-cortical sleeping and awake spiking model

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November 15, 2022

Abstract

Sleep is known to play a central role in learning and cognition, yet the mechanisms underlying its role in stabilizing learning and improving energetic management are still to be clarified. It is characterized by patterns of cortical activity alternating between the stages of slow wave sleep (NREM) and rapid eye movement sleep (REM). In this work, we investigate the role of sleep-like cycles on a biologically-plausible two-area thalamo-cortical spiking neural network capable of experiencing AWAKE-NREM-REM brain states. We train the network on a handwritten digits classification task and show the beneficial effects of sleep on energy consumption and classification performance, exploiting its effects on internal structure, memory representation and consolidation. We show the ability of sleep to shape the synaptic distribution, thus affecting the neuronal firing rate and creating novel multi-area associations.

1 Introduction

During wakefulness, the perceptual system is continuously subjected to sensory input from different sources and modalities. The involved brain areas process the input in a framework set by previous knowledge (acquired through individual and evolutionary experience), with a crucial role played by the exchange of signals with other brain areas. The ability of the brain to integrate and segregate this information by building a coherent and complete representation of the environment is impressive. Although there is plenty of empirical evidence suggesting that the nervous system uses a statistically optimal approach in combining external information from previous experience with the current, the understanding of how the brain implements these strategies is still in development. In this framework, sleep plays a central role in reorganizing information and optimizing the post-sleep energy required to solve cognitive tasks.

Information is then processed by our brains to generate a subjective, unified representation of the outside world. Indeed, the development of this representation also involves cognitive processes such as learning, decision-making, and selective attention [28]. At the neuronal level, multisensory processing has mainly been investigated in terms of cue integration to provide a more reliable estimate of an object or event compared to modality-specific (stand-alone) cues. Thus, this process leads to behavioral benefits, such as a faster and more accurate response to a given situation [18].

Sleep, on the other hand, is known to be essential in all animal species: young humans spend most of their time sleeping and sleep deprivation is detrimental to cognition [22], making it one of the worst tortures that can be inflicted. Sleep has been proven to exert profound effects on the brain and body, loads of mechanisms are known to be implemented during it, and others are yet to be investigated. Among them,
sleep plays a central role in recovery from brain damage [40] and circuit construction during development [15]; during sleep, regulation of the endocrine and immune systems [3] is also carried out, as well as extracellular clearance of potentially toxic substances [17]. Indeed, one of the characteristics that we are most interested in here is the role of sleep in the consolidation of learned information, in the creation of novel associations, as well as in the preparation of tasks expected during the next awake periods [6, 39]. Mounting evidence is available supporting the SHY (synaptic homeostasis hypothesis) model proposed in [41], suggesting the role of sleep in facilitating recovery of neuronal energy and synaptic resources that have been depleted after prolonged waking [41] [42]. This mechanism implies normalization of the memory representation and optimization of the energetic working point of the system by recalibrating synaptic weights [41] and firing rates [40]. Additionally, the consolidation of memory during sleep can produce a strengthening of associations and qualitative changes in memory representations. Strengthening of a memory behaviorally expresses itself as resistance to interference from another similar task [14, 23] and as an improvement of performance that occurs at re-testing, in the absence of additional practice during the retention interval [15, 44].

Sleep is characterized by unique patterns of cortical activity that alternate between stages of slow wave sleep, nonREM sleep (SWS, characterized by high-amplitude, low-frequency 0.5–4 Hz EEG activity) and rapid-eye movement (REM, dominant theta activity 4–11 Hz) sleep [5]. The temporal sequence of SWS and REM sleep in the normal sleep cycle suggests that these sleep stages have complementary roles in memory optimization: during SWS, system consolidation promotes reactivation and redistribution of selected memory traces for long-term storage, while ensuing REM sleep might act to stabilize transformed memories by enabling undisturbed synaptic consolidation [12]. The activity of the cortical circuits during spontaneous wakefulness, NREM, and REM sleep has been studied with different techniques [46, 31, 25]. In particular, the underlying mechanisms of consciousness during different stages of sleep have been studied in [24, 50, 82] through transcranial magnetic stimulation together with high-density electroencephalography that measures the transmission mechanism of activation of a single cortical area to the rest of the brain. Theoretically, consciousness is believed to require the joint presence of functional integration and functional differentiation, otherwise defined as brain complexity: these studies invariably show that the complexity of the cortical response to Transcranial Magnetic Stimulation combined with electroencephalography (TMS/EEG) collapses when consciousness is lost during deep sleep, anaesthesia, and vegetative state following severe brain injuries, while it recovers when consciousness resurges in wakefulness, during dreaming, in the minimally conscious state or locked-in syndrome [37]. In their work, they show that the fading of consciousness during certain stages of sleep may be related to a breakdown in effective cortical connectivity: there is evidence for a breakdown of effective trans callosal and long-range connectivity during NREM sleep leading to the inability of the cortical areas to interact effectively, in contrast to the persistence or increase in inter-hemispheric and interareal broadband coherence [21]. In this stage, cortical activations become more local and stereotypical, indicating a significant impairment of the intra-cortical dialogue. Dreamlike consciousness, on the other hand, occurs during various phases of sleep, including sleep onset and late night, especially during REM sleep. In these stages, TMS triggers more widespread and differentiated patterns of cortical activation, similar to those observed in wakefulness [26].

Indeed, dreaming sleep experiences and the underlying neuronal mechanisms remain an open question. Several hypotheses and theories have tried to explain the mechanisms and function of dreaming [32]. In this paper, we rely on a specific cellular mechanism proposed in [11], which could explain a top-down component of dreams assuming that dreams are more like imagination, starting from abstract thoughts, concepts, or even unconscious wishes, which are secondarily enriched with sensory precepts. In their work, three different brain states (wakefulness, dreams -REM- and dreamless -NREM- sleep) are defined relying on different roles played by acetylcholine (ACh) and noradrenaline (NA). ACh regulates the transmission of information from the apical integration zone to the soma, facilitating apical drive. NA regulates the extent of spatio-temporal summation of input to the apical dendrites. During quiet and active wakefulness, the apical input amplifies the transmission of relevant information. During dreams, the apical drive transforms contextual guidance into self-fulfilling prophecies. During dreamless sleep, both NA and ACh levels are low, so neurons are in the apical isolation mode. However, more complex combinations of states on the whole brain scale can be observed, such as some areas going to SWS or REM-like states while others are still active in Awake, or the coexistence of SWS and REM activity in different areas (e.g., see [16]). In this work, we will not consider such combinations of different local states.

Here, we present a plastic spiking model capable to express awake-, NREM- and REM-like dynam-
ics relying on the apical drive/isolation principles previously described and matching several experimental observables \[46\]. The model expands the data-inspired thalamo-cortical plastic spiking network models proposed in \[10, 19\], which were able to access only the awake and NREM sleep-like activities. There, the combination of context and perception in a single-area thalamo-cortical model has been exploited, relying on a soft winner-take-all circuit of excitatory and inhibitory spiking neurons, calibrating the circuit to express awake and deep-sleep states with features comparable with biological measures. The capacity of the fast incremental learning model from a few examples, its resilience when proposed with noisy perceptions and contextual signals, and an improvement in visual classification after NREM sleep due to induced synaptic homeostasis and association of similar memories have also been demonstrated in \[10, 19\]. In this work, we pass to a two-area model, mimicking the two hemifields by getting as input two different portions of the external stimulus. The input preprocessing has also been improved, implemented in a foveal-like protocol.

2 Results

The model This work proposes a network structure that takes inspiration from experimentally grounded hypotheses about the mechanisms underlying brain states and cognition. First, the structure of the network is inspired by the hierarchical organizing principle of the cerebral cortex and the supporting cellular mechanisms proposed by \[24, 2\] that are based on the combination of feed-forward signals (from regions lower in the hierarchy) with feedback signals (from other areas) (Fig. 1A, bottom). Furthermore, we relied on the Apical drive/isolation principles \[1\] and the role played by neuromodulators to modulate the capability of the network to express different brain states (awake, NREM, and REM) (Fig. 1A, right). Finally, multi-area interaction and activity in different states (and specifically isolation between areas in NREM stage) have been implemented based on experimental observation in \[37\] (Fig. 1A, top). In this work, we further developed the model proposed in \[10, 19\]. A first novelty is the expression of REM-like dynamics in addition to the NREM and awake regimes demonstrated in the previous models. A second improvement is the integration of the perception of two hemifields capable of reproducing both the NREM and REM sleep-like stages. Each modeled area includes thalamic relay (tc) and reticular (re) neurons in the thalamic layer, as well as pyramidal neurons (cx) and two populations of inhibitory interneurons. The network includes in the cortical layer fast spiking neurons (f-inh), characterized by strong excitatory to inhibitory connections, and slow spiking neurons (s-inh), characterized by weak excitatory to inhibitory connections. There is also a population of excitatory neurons (ro) that forms a higher-level readout layer (Fig. 1B). All neurons are conductance-based Adaptive Exponential Integrate and Fire (Adex), modeled through the NEST simulation engine \[17\], more details in \[4\]. The two areas receive as input two complementary and partially overlapping inputs, projected towards the thalamus through independent Poissonian spike trains. This specific input mechanism is inspired by and to some extent emulates a retinic signal (see \[4\] for more details on input preprocessing of the foveal-like protocol). However, all memory storage and recall mechanisms are quite generic, because each training image is simply associated with patterns of higher activity in th populations and therefore generic and extendable to other sensorial modalities or any cortical area reached by projection of a specific thalamic nucleus. In addition, the extension to a multiplicity of areas working in parallel (that is, at the same level of hierarchy) seems quite immediate.

Apical drive/isolation/amplification principles The network is capable of expressing different brain states: awake-like state (Fig. 1B, left), articulated in a training phase, when memories are stored in the network, and a classification phase, when new stimuli induce activity related to learned memories; REM-like state (Fig. 1B, right), associated with an activity showing a peak around 7.2 Hz; a NREM-like state (Fig. 1B, center), characterized by a slow oscillation state at 1.2 Hz. The transition between different brain-state dynamics is implemented by means of brain-state specific neuromodulation (Fig. 1A, right) and changes in excitatory and inhibitory efficacies (for a more detailed description, see Methods \[4\]). The three implemented states described in Fig. 1B take inspiration from the study by \[1\] summarized in Fig. 1A, left. The awake state emulates the Apical amplification regime, characterized by a selective amplification of information from external stimuli combined with the integration of input from other internal sources. Neuromodulation that regulates the transition between awake and sleep phases, on the other hand, is emulated by modifying the Spike Frequency Adaptation (SFA) and excitation/inhibition mechanisms. During the REM-like phase,
Figure 1: Multi-area thalamo-cortical model and protocol description. A) Ingredients to build the network model. Upper-left: figure adapted from [37] depicting the TMS response in different brain states: wakefulness is associated with spatially and temporally differentiated patterns of activation; NREM sleep with a loss in the ability to engage in complex activity patterns (loss of integration and differentiation/information) and REM sleep with a recovery of recurrent waves of activity associated with spatially and temporally differentiated patterns of activation. Lower-left: figure adapted from [2] depicting a conceptual representation of the back-propagation activated calcium (BAC) firing hypothesis. Pyramidal neurons receiving predominantly feed-forward information are likely to fire steadily at low rates, whereas the simultaneous presence of contextual and perceptual streams changes the mode of firing to bursts (BAC firing). This coincidence mechanism is the same implemented in the previous model [19]. Right: figure adapted from [1] modelling the role of acetylcholine (ACh) and noradrenaline (NA) during wakefulness, dreams and dreamless sleep, introducing the concepts of apical drive, isolation, and amplification. B) Sketch of the structure of the two-area thalamo-cortical model: three layer are implemented: thalamic, cortical and readout. Left) Awake stage mimicking the Apical Amplification mechanism: different portion of the perceptual input is fed independently towards the thalamic layer in each area. In the training phase, also a lateral contextual stimulus is provided to a time-specific subset of ro neurons and to a class-specific subset of ro neurons, mimicking information coming from other higher-level areas in the brain. Center) NREM stage mimicking the Apical Isolation mechanism: no perceptual input is fed into the network and inter-area cortico-cortical connections are cut. Synaptic SDP plasticity is active in intra-area cortico-cortical connections. Each area is thus isolated. Right) REM stage mimicking the Apical Drive mechanism: no perceptual input is fed into the network. Synaptic SDP plasticity is active in both intra-area and inter-area cortico-cortical connections. The internal input directly determines the output of the network. C) Internal composition of the implemented layers: the thalamic layer composed by an excitatory and an inhibitory population (te, re); cortical layer composed by an excitatory population (cx) connected to a fast-spiking inhibitory population (f-in) through strong connections and a slow-spiking inhibitory population (s-in) through weak synapses. The two cx population in each area are reciprocally connected. Cortical areas projected into the readout layer, composed only by excitatory neurons (ro) integrating the information.
Figure 2: **Single NREM-REM cycle and experimental comparison.**

**A)** Rastergram showing the activity of the excitatory cortical network throughout waking state - NREM-sleep - REM-sleep. 

**B)** Time-resolved power spectrum of the simulated network activity during the states experienced by the network; to be compared with fig. 1A by Watson et al. [46].

**C)** Power Spectral Density across simulated brain states, to be compared with fig. 3B in [20]. It should be noticed that during awake state the most of the energy is concentrated in gamma-band; instead, concerning NREM and REM sleep, the chart shows a wide peak in delta-band and a sharp peak in theta-band respectively, consistently with [20].

**D)** State-wise difference of average firing rate. Cumulative firing rate distribution of single excitatory cortical neuron, to compare with Watson et al. fig. 2A and Golosio et al. fig. 2A [10] [11].
Figure 3: Effects of multiple NREM-REM cycles on energetic and classification performance. A) Network performance across brain states. It shows the percentage change in network mean power consumption (purple, see 2) and mean firing rate (light blue) as well as the classification accuracy (orange) during the awake states experienced by the network after sleep stages. The dashed lines (blue, red) show the comparison with the KNN4 classifier (mono-areal, bi-areal, see methods 4). It is worth noting that the classification accuracy is stable, close the theoretical upper-limit, across brain states, whereas network mean firing and power consumption are decreasing. Averages are performed considering 40 balanced training sub-sets. B) Cortico-cortical intra-group excitatory synaptic weights. The blockplot summarizes the dynamic across sleep stages of the intra-group synaptic distribution. Both downscaling and sharpening of the synaptic distribution are shown, leading to network activity and energetic consumption reduction. C) Time-resolved power spectrum of the simulated network activity during awake and sleep stages.
Figure 4: Sleep effects on network firing rate. A) Sleep-induced firing rate homeostasis. The figure should be compared with Watson et al. fig.3B and Golosio et al. fig. 2D [46, 19]. The graph shows the mean activity of the network during two NREM-REM cycles. After each sleep stage the network performed a classification task in order to assess the effect of sleep on the AWAKE network firing rate. The dashed lines indicate the average calculated over the AWAKE stages: pre-sleep (yellow), post-nrem (blue), post-rem (red), post-sleep (purple). Has been measured 5% decrease after two NREM-REM cycles. Averages are calculated considering 40 different training subsets. B) Awake neuron mean firing rate distribution. The panel shows the effect of sleep on the neuron mean firing rate distribution, it can be noticed comparing boxplots that sleep moderate high firing rates and translates the median towards low firing rates.
Figure 5: **Sleep effects on network synaptic structure.** A) Neuron Mean Firing Rate VS Average Output Synapses joint probability distribution. This panel gives an overview of the sleep-induced homeostatic effect on both network firing rate and synaptic structure. It is keen to notice, since the definition provided of synaptic power consumption (see Methods 2), that after sleep the synaptic energy consumption becomes concentrated in the low-firing rate region. B) Sleep effect on the cortico-cortical synaptic matrix. The matrix is rearranged so that memories belonging to same class lie on the diagonal. On the left/right is shown the cortico-cortical synaptic matrix before/after sleep. It can be noticed that after training memories are orthogonal whereas during sleep are developed novel association among neural groups encoding for the same class of memories.
no external perception is provided and an Apical Drive mechanism is emulated: Internal input directly determines the output with an active STDP plasticity within cortical neurons both intra- and inter-area. During this phase, information learnt in both areas is integrated. During the NREM-like phase, no external perception is provided and inter-area cortico-cortical connections are cut: an Apical Isolation mechanism is emulated, inter-area cortico-cortical connections, on the other hand, are active with STDP plasticity.

**Combination of contextual and perceptual signals during the training phase** During the training phase, a set of memories are encoded in groups of cortical neurons (cx) according to an unsupervised protocol through Spike-Time Dependent Plasticity (STDP) mechanisms; during the presentation of the training example, cx neuron receive both the bottom-up perceptual signal from the thalamic layer of the network and a time-specific contextual signal which provides to the cortical layer a pure temporal label, with no info about the label of the class the novel example belong to. This emulates the existence of a time-specific status in other areas in the brain collected by the apical tuft of the cx neuron. Thanks to the action of the STDP plasticity mechanisms, those neural groups that are simultaneously activated in multiple areas by the time-specific contextual label develop two sets of synapses: a) a set of strong intra- and inter-area synapses among themselves, and b) strong connections among the thalamic active pattern and the group of cx neurons facilitated by the time-specific context. At the same time, a supervised training protocol is used to select groups of neurons to represent digit categories in a group of readout (ro) neurons that receive the combination of a bottom-up signal generated by cx neurons in the lower level of the cortical hierarchy and a digital class-specific contextual signal. During the training the STDP dynamics creates stronger synapses both among ro neurons belonging to neurons that will represent a the digit class associated with the digit label and among the ro neurons and active cx neurons. It should be noticed that performance in classification accuracy is measured on the bases of the cx neurons that are trained using the unsupervised protocol while the activity in this ro layer trained using a supervised training are used only for fast check of the in-progress training and to demonstrate the possibility of learning in a hierarchical architecture through context-driven STDP. During the classification phase, new previously unseen perceptual inputs are provided to the network in the absence of any contextual signal: these inputs activate neurons associated with similar learnt memories, stored at the cortical level.

**Aims of the work, while cycling on brain states.** First, we aim to demonstrate that the ThaCo network is capable of expressing AWAKE, REM, and NREM states with features comparable to experimental knowledge and observations. Indeed, in continuity with the model presented in [19], one of the goals of this work is to implement a biologically-plausible model capable to display different “cognitive states”, thus the comparison with experimental outcomes is important to question its plausibility. In this work, we relied mainly on both biological observations made by Watson et al. [46] on the changes of firing rate distributions in awake, sleep and post-sleep phases, and by Rubido et al. [20] for what concerns power spectral density measurements in different brain states. As a second step, we have simulated multiple AWAKE-NREM-REM cycles in order to study the effect of sleep cycles on cognitive and energetics network performance as well as the synaptic structure.

**Comparison with experimental power spectral densities and spectrograms** Fig. 2A depicts the rastergram of the network activity across one NREM-REM cycle. It is worth noting here a different behaviour between simulated brain states: as in AWAKE and REM stages the network experiences high frequency asynchronous activity, during the NREM sleep this is characterized by synchronized global slow-oscillations. Indeed, the time-resolved fast Fourier transform-based power spectrum of the simulated network activity and the Power Spectral Density (PSD) distribution (Fig. 2-B-C) show that during the NREM phase most of the power is concentrated in δ-band with a sharp cut-off at about 10 Hz and that the activity is slightly decreasing in frequency and amplitude with time (Fig. 2-B). On the other hand, the REM activity-power is mainly distributed between 0 – 20 Hz, showing a peak in the θ band, and is followed by the power-law decay consistent with experimental findings [20]. Furthermore, the awake state exhibits a sharp peak in the β band, quite in agreement with what was expected for the task-engaged brain power spectrum [34]. Moreover, the spectrogram of the network activity across the sleep cycle is reasonably in accordance with the one measured over the LFP recorded by Watson et al. in [46], Fig. 1A. Last, in Fig. 2D is depicted the
cumulative distribution of excitatory cortical neurons firing rate in the three different stages, comparable with the ones observed by Watson et al. in 

**Effects of sleep cycles on energetic and classification performances** Here, we discuss the effects of two NREM-REM cycles (Fig. 3C) on the post-sleep energetic and classification performance. The mean firing rate and power consumption (purple and light-blue lines) mark a sharp decrease of about 50% and 5% respectively. This is achieved by means of the cortico-cortical synaptic distribution down-scaling and sharpening performed during sleep, which reduce the overall mean synaptic efficacy and, thus, neural activity resulting in a lower metabolic consumption (Fig. 3B). Furthermore, through each of these stages, the mean firing rate and the power consumption of the network monotonically decreases, without affecting the classification accuracy: multiple NREM-REM cycles, instead of single one, help the network to reach a better operating point, helping the network to perform cognitive tasks reducing the energetic cost required. The network classification performance has been evaluated by comparing it with the K-Nearest-Neighbors algorithm, which provides an upper limit to the classification accuracy of this type of network (see [19] and Methods [4]). As depicted in Fig. 3A, both the classification accuracy (orange line) remains stable close to the theoretical limit imposed by KNN (red dashed line) in sleep (85.5%). Finally, it is worth noting that this paper has been conceived to extend the model to experience REM-like state and to investigate the role of sleep cycles in a non-noisy environment, a case in which classification performance approach the theoretical upper-limit. In this work, we study the effects of sleep on a network trained close to its best theoretical classification performance.

**Effects of sleep on the internal structure: homeostasis & association** This section discusses the homeostatic effect induced by sleep on the firing rate and cortico-cortical synaptic distribution. Fig. 4A reports the mean firing rate dynamics during the awake and sleep stages. This can be compared with what was experimentally performed by Watson et al. [46] in their Fig. 3B, but we extended the study to the evolution during the REM phase. Furthermore, the distribution of the mean neuron firing rate before and after sleep, during the AWAKE phase is reported in Fig. 4B; furthermore, we propose a joint plot that resumes the general homeostatic effect of sleep on both the firing rate and synaptic efficacy (Fig. 5C). Fig. 4A shows the very different mean firing rate dynamics between the network states and allows us to assess a net decrease after sleep. On the other hand, Fig. 4B shows how sleep affects the mean firing rate of neurons, translating the median of the distribution to low firing rate. In Fig. 5C we present the joint probability of the neuron firing rate versus the average output synapses, providing an insight about the neuron mode of firing and power consumption (see Methods) as well as to assess how sleep-induced homeostasis affects such observables. We argue that this kind of plot could help to control the state of the network and have an overview about how neurons communicate within the network. It is worth noting also that the plot depicts how energy consumption is distributed within the cortical population (see Methods [3]), and thus that after sleep, consumption becomes mainly concentrated in the low-firing rate region. Finally, Fig. 5D shows how two NREM-REM cycles affect the cortico-cortical synaptic matrix, it can be noticed that before sleep the matrix is orthogonal, whereas after sleep novel associations are developed within neural groups encoding for the same class.

### 3 Discussion

The beneficial effects of sleep on cognitive performance are experimentally evident [2], even though the mechanisms involved are yet to be understood in their details. There are two major candidates contributing to this phenomenon: the physiological one (sleep-induced restoration of ionic equilibriums and nutrients), and the computational one (reorganisation of memories, firing rates, synaptic weights, and information encoding). In this paper, we explore the last aspect through computational model that captures several aspects of biological networks and brain-state induction, in which cognitive functions and sleep-induced rhythms interact. We consider a spiking network trained to store and classify handwritten digits in a target-based fashion [30, 10, 8]. This strategy allows us to carefully choose the initial internal representation of learned memories, and to evaluate in a controlled way their evolution during sleep phases. This is important to understand how sleep-like dynamics propagates information from one region to another [9], and how
this can be used to efficiently reorganise stored knowledge. In particular, we have extended the thalamo-
cortical spiking model, recently published [10, 19], already able to express AWAKE and NREM states, to
a bi-area model capable of experiencing REM-like sleep and multiple brain state cycles. At the same
time, we aim to characterize such brain states activity by comparing observables such as power spectral density
and neuronal mean firing rate with experimental findings consolidated in the literature [20] [36] and to show
the effect of sleep on network energetic and classification performance during a digit classification task. The
network architecture has been designed to capture the binocular visual information integration, which takes
place in the primary visual cortex during awake-learning through the thalamo-cortical feed-forward stream,
making use of the Apical amplification principle to encode such information into a bi-area cell-assemblies
network. Furthermore, the principles of apical isolation/drive are used to set the cortical neuromodulation
to switch between awake and NREM / REM states and thus to reproduce cortical activity generally in
agreement with the observations of Massimini et al. on the spread of cortico-cortical activity during awake
and NREM/REM sleep [36]. As a result the network has been found able to perform learning and sleeping
cycles holding classification performance close to the accuracy upper-limit for such a network (see par. 4),
decreasing at the same time mean firing rate and synaptic power consumption and keeping cortical activity
coherent with biological recordings (Figs. 2 and 5). Furthermore, we have shown the ability of sleep to shape
cortico-cortical connectivity resulting in the down-scaling and sharpening of the synaptic distribution, and
thus of the mean firing rate, as well as the creation of novel multi-area associations. These results allow us
to argue that NREM and REM sleep cycles are useful in such a network to reduce energy consumption while
reorganizing the synaptic structure of the network. As a future perspective, we propose to better characterise
the opposite effects of homeostasis and association in terms of the entropy of the synaptic matrix: whether
entropy reduction occurs at the synaptic level as a consequence of synaptic downsampling and sharpening,
sleep-induced associations are collaborator with the learning process to produce entropy, thus extending
the state space explorable by the network. It will be interesting to investigate under which conditions the
sum of homeostatic and associative contributions to synaptic entropy is positive or negative. Last, it is
important to notice that the structure of ThaCo, in synergy with the apical amplification mechanism, allows
the network to associate particular percepts with particular thalamo-cortical patterns, endowing the network
with a set of independent neural groups. The groups can interact during both waking and sleeping phase,
automatically evoking specific trajectories in the memory space (for a visual illustration see the figures in
Supp. Mat. Sec. [Winner-Takes-All mechanism]). So, we can say that ThaCo provides a framework in which
mechanisms (supported by neural groups) exist intrinsically [43] and, during both AWAKE, NREM (see
[10] [19]) and REM phases through exogenous or endogenous stimuli, can influence other mechanisms, thus
giving rise to cause-effect complex that consolidate in new accessible mechanisms. In addition, a fundamental
ingredient of ThaCo is integration of information among hemispheres: as in AWAKE and REM sleep Apical
Amplification/Drive support cooperation between brain areas, during NREM sleep Apical Isolation acts in
such a way that information is segregated in a single brain area, hence reducing the state space experienceable
by the network. For these reasons, we argue that ThaCo could provide a framework for testing Integrated
Information Theory (IIT) [43], directly or through measures of the Perturbational Complexity Index (PCI)
[36].

Further optimizations and integration of this work can be done in the perspective of large scale simu-
lations. Based on previous studies of Slow Waves Activity in both spiking [33] and mean-field [7] large
scale cortical simulations, we could improve the present model to exploit the interplay between Slow Waves
propagation and cognitive tasks in larger networks.

4 Methods

Network The network model is represented in Fig. 1. It is a 2-area 3-layer spiking network model.
The two areas receive in input an independent perceptual signal; the thalamic layers are not reciprocally
connected, whereas the cortical layers are connected. The readout layer has a function of integration of the
information coming from the underlying areas and is in common between the two hemicampi. The first layer
in each area, the thalamus, is composed of a population of excitatory neurons and a population of inhibitory
neurons; the cortical layer is composed by a population of excitatory neurons connected to 2 independent
inhibitory populations: one, fast-spiking, with a strong excitatory to inhibitory synaptic connection, and
a second, slow-spiking, with a weak excitatory to inhibitory synaptic connection. The third population, the readout layer, is composed only by excitatory neurons and receives inputs from both cortical layers in the two areas. The described network has been implemented in NEST 3.1 [17, 4] and is made of Adaptive Exponential Conductance Based neurons (Adex) (see Supplementary material 5 for more details on neuronal and synaptic dynamics). All synapses connecting excitatory to inhibitory neurons and vice versa are static in time (i.e. not trainable), others are plastic and described by an STDP dynamics. Specifically, all excitatory-to-excitatory synapses are plastic within the training phase, none are plastic in the classification phase, whereas only cortico-cortical synapses are plastic during sleep-like phases.

**Fast and late inhibition** Within the network, two independent inhibitory populations are identified, acting on different time scales: the fast-spike population is able of fast responding, regularly firing up to 500 Hz for tens of milliseconds, while the slow-spike population responds at around 10 Hz. This choice is motivated because it allows the network to provide time-increasing inhibition to cortical neurons. Therefore, fast-spike neurons are intended to set the excitatory activity level and achieve soft Winner-Take-All (WTA) while slow-spike neurons are used mainly to make the network able to exit memory attractors during REM sleep (See par 4). It is worth noting that these two different behaviors are emulated acting on the inhibitory population excitability only, in order to avoid neural parameters fine tuning. Specifically, a slow and fast response is achieved by properly tuning up the weights of excitatory synapses projecting toward the two inhibitory populations.

**Moving between brain states** In order to switch between brain states, the cortical network is provided with both a thalamic (perceptual) input and a cortical Poissoninan noise, emulating an aspecific stimulus from external brain areas. In addition to this, in order to reproduce a neuromodulation effect similar to the one responsible for apical amplification / drive/ isolation, the cortico-cortical excitability is modulated by changing neural Spike-Frequency Adaptation (SFA), cortico-cortical excitation and inhibition level.

- **AWAKE** In the training phase, contextual signal and thalamic feature-specific stimulus is provided to the cortical network and all cortico-cortical connections are active and plastic (Fig. 6A). This setting should be compared with the Apical Amplification situation. However, during the AWAKE state, cortical activity is elicited by the visual thalamic stimulus only, memory evocation is managed by soft-WTA which allows the network activity to visit different memory-attractors and to take decisions while plasticity is set off (Fig. 6B).

- **NREM** To enter the NREM state, excitatory cortical neurons receive a nonspecific stimulus 1 kHz using a homogeneous poisson noise generator. Also, compared to AWAKE state, cortico-cortical inter-area connections are cut whilst intra-area synapses are up-modulated; the level of SFA is also increased and the synaptic efficacy of both inhibitory populations is decreased, consistent with the apical isolation principle (Fig. 6C). Therefore, potentiated intra-area connections allows the network to exhibit cell-assemblies up-states dynamics controlled by soft-WTA, sustained by fast-spike inhibitors population, and SFA which leads network out of memory attractors. Slow-spike population here only plays a role during cell-assemblies co-activation definitively avoiding the chance of network catastrophic forgetting.

- **REM** The dreaming state is achieved providing two different non-specific stimuli, at 7 Hz and 30 Hz respectively, to cortical neurons. In this case, only inter-area cortico-cortical connections are up-modulated and the SFA level is decreased, in order to emulate the Apical Drive principle. Inhibition changes differently between populations: fast-spike inhibition is depressed, as well as in the NREM phase, while slow-spike inhibition is potentiated (Fig. 6D). Here, the high rate stimulus promotes low gamma activity, while the slow rate stimulus is intended to emulate the interaction with the thalamus, which is known to impart theta rhythms to the cortex during biological REM sleep [13]. As a result, high-rate generator put neurons under-threshold and slow-rate orchestrate the cell-assemblies activation dynamics. It is worth noting that while fast-spike inhibitory population provide soft WTA, slow-spike neurons are fundamental to guarantee exit from up-states, because of low SFA level. Last, the Spike-Timing-Dependent Plasticity time scale has been reduced by a factor of 8 since it greatly enhances REM association performance.
Figure 6: Soft and Hard Winner-Takes-All among different brain states. A) Training phase. The coloured flames aim to depict different levels of neural activity. Due to temporal coincidence of sensory and contextual stimuli, specific neuron groups are selected to encode perceptual information in order to create a multi-area cortical representation of the perception. In this case inhibitory network manage an hard Winner-Take-All (WTA) i.e. only the chosen groups are permitted to activate. B) Classification (AWAKE) phase. The ovals are intended to group cell-assemblies encoding for the same class of the percept. During the classification, only perceptual stimulus is provided to the network. In this scenario inhibitory neurons are administered a soft-WTA, allowing for multiple neural assemblies to respond. Here, since the group activation level is very sensible to the similarity between training set and test-instance (see [4]), it is expected the co-activation of cortical groups corresponding to the class of the perception. C) NREM phase. Aspecific contextual stimulus induce up-state dynamics within the thalamo-cortical network. In this stage inter-area cortico-cortical connections are cut, in order to resemble the apical isolation principle. The fast inhibitory network supports up-states of independent groups in a soft-WTA dynamics, thus avoiding the chance of catastrophic forgetting. D) REM phase. During dreaming state, aspecific contextual stimulus induce a short-up-state dynamics within the thalamo-cortical network. Specifically, whilst the fast inhibitory network provide a soft-WTA, the slow inhibitory network guarantees exit from up-states through an inhibitory strike stopping the group activity. Thanks to the cooperation between the two areas, cortical groups related to the same class are easily coactivated and thus associated.
Preprocessing

As already stated, one of the aims of this work is investigating the cooperation between cortical areas connected through inter-area synapses. To do this, we emulated a few aspects of binocular perception: each area has access to the external perception of only half of the original input, with an overlap in the center. The image data set is composed of MNIST handwritten digits \[11\], in order to implement a two-area perception feature, we improved the preprocessing algorithm already implemented described in \[19\] (pag. 5-6 sup.mat.) in the current work, the salient features of the image are extracted using \textit{Histogram of Oriented Gradient} (HOG) whereby the image has been sampled at different space-scales in order to emulate foveal perception. In addition, the dataset has been rescaled, embedding each image into a background frame.

\textbf{K-Nearest-Neighbour Algorithm}

Thanks to its architecture ThaCo model is able to encode perceptual information into thalamo-cortical and cortico-cortical synaptic matrix in a very general way, using Spike-timing-dependent plasticity (STDP) to capture and condensate temporal correlation, among thalamic pattern activation and cortico-cortical group activity, into new synapses. This provides a framework in which memories written into feature-specific thalamo-cortical connections and cortico-cortical recurrent synapses, developed during the learning phase, are represented as orthogonal cortical states\[19\] promoting at the same time a cooperation among groups coding for those patterns that are first neighbours of the learned ones during a classification supported by a soft-Winner-Takes-All mechanism. In such a way, since cortical group activation is very sensitive to the similarity between thalamic pattern related to memories already learnt and the pattern to be categorized, classification tasks as new-image recognition can be conveniently abstracted as selecting the cortical group whose thalamic activation pattern maximises the dot product with the new thalamic pattern. Therefore, it is quite natural to compare the classification performance of such a network with the weighted KNN algorithm. i.e. the one that weighs the votes nearest neighbours using the inverse of their euclidean distance with the proposed example. The reason for selecting this flavour of KNN is its similarity to the drive that each neural group would exert in a soft-WTA regime. Aiming to take into account binocular perception and biareal processing of ThaCo, we assessed KNN-performance following two different approaches. The first approach KNN-1D considers two sets of perceptual thalamic features related to the left/right (L, R) hemifields. In the KNN-1D case, the weighted KNN algorithm is applied independently to both sets. The winner class is selected according to eq. 1.

\begin{equation}
\text{class}_j = \arg\min \left( \frac{\sum_i d^L_{i,j}}{\sum_i d^L_{i,j}}, \frac{\sum_i d^R_{i,j}}{\sum_i d^R_{i,j}} \right) ; \quad i = 1, ..., n_{\text{ex.,train}} , \ j = 1, ..., n_{\text{ex.,test}}
\end{equation}

where we decided to consider the votes of up to 4 neighbours.

Therefore, KNN-1D selects as winner the class related to the training example which posses the hemifield, is more similar to the classification instance.

The second approach is KNN-2D: features from left and right hemispheres are grouped to classify the new image. This is the case of monocular perception, so we consider it as the upper-limit to ThaCo classification performance. Also, we argue that when ThaCo classification accuracy is close to this limit, the L/R visual hemifield information is integrated as best as possible by the thalamo-cortical network.

\textbf{Synaptic Power Consumption}

Synaptic Power consumption has been assessed as the product between the efficacy of the cortical neuron output synapse and the mean firing rate (eq. 2), averaged on the population of cortical neurons. In this way we can relate it to the metabolic cost required for synaptic metabolism, which is known to represent the main source of energy expenditure for the brain \[27\]. It is important to notice that this definition of power consumption does not consider the amount of energy spent to transmit the spiking information to synapses.

\begin{equation}
P = \frac{1}{n_{\text{neurons}}} \sum_i W_{\text{output},i} \cdot f_{r_i} ; \quad i = 1, ..., n_{\text{neurons}}
\end{equation}
Figure 7: **Neural groups activation: AWAKE** Group activity during awake phase. The rastergram on the left shows 5 seconds of the cortical network activity during the awake stage and spatial magnification. Excitatory population is depicted in black, inhibitory population in blue. In the inset grey horizontal lines delimit neurons belonging to the same class. It is worth noting that the activity of the two cortical areas is strongly correlated, also in this state groups encoding for the same class collaborate and there are frequent coactivation.
Figure 8: Neural groups activation: NREM Group activity during NREM phase. The rastergram on the left shows 5 seconds of the cortical network activity during the NREM stage and spatial magnification. Excitatory population is depicted in black, inhibitory population in blue. In the inset grey horizontal lines delimit neurons belonging to the same class. It is worth noting that in this state groups encoding for the same class are mostly activated individually and the activity of the two cortical areas is decorrelated.
Figure 9: **Neural groups activation: REM** Group activity during REM phase. The rastergram on the left shows 5 seconds of the cortical network activity during the REM stage and spatial magnification. Excitatory population is depicted in black, inhibitory population in blue. In the inset grey horizontal lines delimit neurons belonging to the same class. It is worth noting that, despite the random exogenous stimuli, the activity of the two cortical areas is strongly correlated, also in this state groups encoding for the same class collaborate and there are frequent coactivation.
5 Supplementary material

Winner-Takes-All mechanism In this work, coherently with what described in [19], the network parameters have been set to induce the creation of WTA mechanisms by emulating the organizing principle of the cortex described by [24]. During training, the network is set in a hard-WTA regime (firing rate different from zero only on a selected example-specific subset of neurons), while during classification it works in a soft-WTA regime (i.e., the firing rate can be different from zero in multiple groups of neurons, and the winner group is assumed to be the one firing at the higher rate). Specifically, during training, we set our parameters so that the thalamic signal alone is not sufficient to cause neurons to spike.

AdexNeuron The described network has been implemented in NEST [17, 4] and is made of Adaptive Exponential Conductance Based neurons (Adex) defined by the following equations:

\[ C_m \frac{dV}{dt} = -g_L (V - E_L) + g_L \Delta_T e^{\frac{(V - V_{th})}{\tau_s}} + I_{system} - \omega \]

\[ \tau_\omega \frac{d\omega}{dt} = a (V - E_L) + b \sum_k \delta(t - t_k) - \omega \]

Here, the first equation describes the time evolution of the membrane potential \( V \) and incorporates a spike frequency adaptation mechanism through the term \( \omega \). On the other hand, the second equation captures the essential features of neuronal fatigue that depend on the number of spikes emitted by the neuron itself in the recent past. Moreover, whenever \( V > V_{peak} \) the membrane potential is set to a reset value \( V_{reset} \). Here, \( \tau_\omega \) is the adaptation time constant associated with neuronal fatigue, \( C_m \) the membrane capacitance, \( E_l \) the reversal potential, \( V_T \) the threshold potential, and \( \Delta_T \) the exponential slope parameter. Moreover, \( a \) and \( b \) are the adaptation parameters. The current in the input to the neuron from excitatory and inhibitory neurons \( I_{system} \) can be written as:

\[ I_{system} = g_{ex}(t) (E_{ex} - V) + g_{in}(t) (V - E_{in}) \]

where \( g_{ex} \) and \( g_{in} \) are the time-dependent excitatory and inhibitory synaptic conductances of time-dependent, respectively, shaped according to alpha-function. Assuming that a spike occurs at time \( t_s \), the alpha function for synaptic conductance is defined as

\[ g(t) = \begin{cases} w \frac{(t-t_s)}{\tau_s} e^{-(t-t_s)/\tau_s} & \text{if } t > t_s \\ 0 & \text{if } t < t_s \end{cases} \]

This conductance has a gradual rise and slow decay, reaching its peak at \( t_{max} = \tau_s \). According to this model, the instantaneous current injected by an incoming excitatory synapse spiking at \( t_s = 0 \) is

\[ I(t) = \frac{w}{\tau_s} e^{-t/\tau_s} (E_{ex} - V(t)) \]

STDP The evolution of plastic synapses implemented in this model is described by spike-timing-dependent plasticity (STDP) [29, 38] characterized by the pair-based update law.

\[ \Delta w = \begin{cases} -W_- \cdot \left( \frac{w}{w_{max}} \right)^{\mu_-} \cdot \exp \left( -\frac{t_{post} - t_{pre}}{\tau_e} \right), & \text{if } t_{post} - t_{pre} > 0 \\ W_+ \cdot \left( 1 - \frac{w}{w_{max}} \right)^{\mu_+} \cdot \exp \left( -\frac{t_{pre} - t_{post}}{\tau_e} \right), & \text{otherwise} \end{cases} \]

where \( w_{max} \) represents a limiting value for the weight and \( \alpha \) in \( W^- = \alpha W^+ \) depicts the asymmetry parameter of depressing and increasing synaptic weights. The exponents \( \mu_+ \) and \( \mu_- \) vary in the range [0;1]. In the two extreme cases \( \mu_{+/} = 0 \) and \( \mu_{+/} = 1 \) the model is called additive STDP and multiplicative STDP, respectively. Throughout this work, we use a multiplicative STDP rule. According to Hebb’s postulate, since the weights of all thalamo-cortical synapses are plastic, if both the input pattern and the contextual signal are kept active for a sufficiently long time, the weights of synapses connecting active thalamic neurons to active cortical neurons will grow.
**Model parameters** The table reports all parameters needed to simulate the model in order to reproduce the published results. Parameters not mentioned are the default of NEST. Neuromodulation is fundamental to switch between different states, specifically it is performed by multiplying/dividing (enter, exit) the synaptic distribution for a constant factor. At the following link you can find the code to simulate the model and to reproduce figures: [Github - ThaCo3](https://github.com/ThaCo3).

Table 1: **Model Parameters.** Neuromodulation of the excitatory cortico-cortical synapses is performed multiplying/dividing the synaptic distribution for a constant factor in such a way that the average value of the intra-cellular synapses is scaled down to the value shown in the table.

### Network Parameters

| Connection | $W_0$ | $W_{max}$ | $\lambda_{STDP}$ |
|------------|-------|-----------|------------------|
| $th \rightarrow cx$ | 0.3 | 3.7 | 0.06 |
| $cx \rightarrow th$ | 0.1 | 2 | 0.06 |
| $cx \rightarrow ro$ | 0.1 | 65 | 0.03 |
| $cx \rightarrow exc \rightarrow exc$ | 0.01 | 75 | 0.06 |
| $ro \rightarrow exc \rightarrow exc$ | 0.01 | 2 | 0.009 |
| $th \rightarrow inh$ | 3 | na | na |
| $th \rightarrow exc$ | -1 | na | na |
| $cx \rightarrow inh_f$ | 200 | na | na |
| $cx \rightarrow inh_s$ | 3 | na | na |
| $cx \rightarrow exc \rightarrow inh_s$ | -20 | na | na |

### STDP Asymmetry factor ($\alpha_{STDP}$) 1

### Spike Frequency Adaptation ($b_{SFA}$) 110 (pA)

### Noise Parameters

| Connection | Stage | Rate (Hz) | $W$ |
|------------|-------|-----------|-----|
| $cx \rightarrow cx$ | training | 600 | 500 |
| $cx \rightarrow inh$ | training | 80 | 320 |
| $ro \rightarrow cx$ | training | 80 | 320 |
| $th \rightarrow cx$ | awake | 40 | 400 |
| $cx \rightarrow cx$ | nrem | 1000 | 13.3 |
| $cx \rightarrow cx$ | rem | 7.2 | 13.0 |
| $cx \rightarrow cx$ | rem | 30 | 60 |

### Other Parameters

| | $N^\circ$ classes | 10 |
| | $N^\circ$ training examples | 50 |
| | $N^\circ$ neurons Cell−Assembly | 20 |
| | $N^\circ$ test examples | 210 |
| | Training example presentation time | 1.5 (s) |
| | Test example presentation time | 1 (s) |
| | Training/test rest time | 1.5 (s) |

| Parameter | NREM | REM |
|-----------|------|-----|
| $\langle W \rangle_{th \rightarrow cx}$ (intra) | 50 | 50 |
| $\langle W \rangle_{cx \rightarrow th}$ (intra) | 0.186 | 1.488 |
| $\langle W \rangle_{CA \rightarrow cx}$ (intra) | 59 | as awake |
| $\langle W \rangle_{CA \rightarrow cx}$ (inter) | 0 | 97.5 |
| $cx \rightarrow inh_f \rightarrow exc$ | -0.5 | -0.5 |
| $cx \rightarrow inh_s \rightarrow exc$ | -0.5 | -400 |
| $\lambda$ ($STDP$) $cx \rightarrow cx$ | $3 \times 10^{-4}$ | $3 \times 10^{-4}$ |
| $\alpha$ ($STDP$) $cx \rightarrow cx$ | 3 | 3 |
| $b$ ($SFA$) | 200 | 50 |
| $\tau$ ($STDP$) | as awake | 2.5 |

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