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# Multi-Scale Causation in Brain Dynamics

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**Abstract–** For any complex system, consisting of several organizational levels, the problem of causation is profound. Usually, science considers upward causation as fundamental, paying less or no attention to any downward causation. This is also true for the nervous system, where cortical neurodynamics, or even higher mental functions of the brain are normally considered causally dependent on the nerve cell activity, or even the activity at the ion channel level. This study presents both upward and downward causation in cortical neural systems, using computational methods with focus on cortical fluctuations. We have developed models of paleo- and neocortical structures, in order to study their *mesoscopic* neurodynamics, as a link between the *microscopic* neuronal and *macroscopic* mental events and processes. We demonstrate how both noise and chaos may play a role for the functions of cortical structures. While microscopic random noise may trigger meso- or macroscopic states, the nonlinear dynamics at these levels may also affect the activity at the microscopic level.

## 1. Introduction

The human brain is a complex system whose activity is reflected by a highly complex neurodynamics. This dynamics is characterized at a macroscopic level by oscillations, chaos and fluctuations, apparent in EEG and depending on underlying neural processes, external stimuli and various neuromodulatory mechanisms. The different organisational scales of the brain, from ion channels to neurons to networks, are coupled via specific processes, each with a characteristic time scale.

Denis Noble has argued [1] that there is no privileged level of causality in biological systems. Supposedly, "higher levels in biological systems exert their influence over the lower levels. Each level provides the boundary conditions under which the processes at lower levels operate. Without boundary conditions, biological functions would not exist" [1]. The current work addresses this issue, with the aim of elucidating the causal pathways in brain dynamics, where downward causation from larger to smaller scales could be regarded as evidence that multilevel 'both-way' causation occurs. While the outset for Noble's argument is the single (heart) cell with respect to its molecular constituents, the same arguments should apply to cortical networks and its cellular constituents.

We use computational models of different brain structures, both of paleocortex and neocortex, to investigate how cortical neurodynamics may depend on structural properties, such as connectivity and neuronal types, and on intrinsic and external signals and fluctuations. We also investigate to what extent the complex neurodynamics of cortical networks can influence the neural activity of single neurons [2].

Our results are suggestive for the neural mechanisms underlying EEG and the spatio-temporal patterns of activity associated with perception and cognitive functions, as well as for the dynamical effects of arousal and attention on cortical neurons. Our studies are also aiming at a greater understanding of the interplay between order (e.g. in terms of regular oscillations) and disorder (noise and chaos) in neural information processing. In a larger context, this kind of studies should be relevant for our understanding of the intricate inter-relation between neural and mental processes, which will be elaborated on in the Discussion section.

## 2. Cortical Network Models

### 2.1. Paleocortical Model

Our paleocortical model, which mimics the structures of hippocampus and the olfactory cortex, has network units with a continuous input-output function, corresponding to the average firing frequency of neural populations, which we compare with EEG and LFP data [3]. There are three cortical layers, with network units corresponding to populations of *feedforward* inhibitory interneurons, excitatory pyramidal cells, and *feedback* inhibitory interneurons, respectively. All connections are modeled with distance dependent time delays.

The time evolution for a network of $N$ neural units is given by a set of coupled nonlinear first order differential delay equations for all the $N$ internal states, $u$. With odour signal, $I(t)$, noise $\xi(t)$, characteristic time constant, $\tau_i$, and connection weight $w_{ij}$ between units $i$ and $j$, separated by a time delay $\delta_{ij}$, we have for each unit activity:

$$\frac{du_i}{dt} = -\frac{u_i}{\tau_i} + \sum_{j\neq i}^{N} w_{ij} g_j[u_j(t-\delta_{ij})] + I_i(t) + \xi(t) \qquad (1)$$

The input-output function, $g_i(u_i)$, is a continuous sigmoid function:

$$g_i = A \cdot Q_i \left\{ 1 - \exp\left[ - \frac{\exp(u_i) - 1}{Q_i} \right] \right\} \quad (2)$$

The gain parameter $Q_i$ determines the slope, threshold and amplitude of the curve for unit *i*. This gain parameter is associated with the level of arousal/attention as expressed through the level of acetylcholine. *A* is a normalization constant [3].

### 2.3 Neocortical Model

In our model of visual cortex, we use spiking model neurons, since we want to compare our results with observed data, as spike triggered averages of local field potentials. All model neurons satisfy the following Hodgkin-Huxley equation:

$$\begin{aligned} CV' = & -g_L(V+67) - g_{Na} m^3 h (V-50) - g_K n^4 (V+100) \\ & - g_{AHP} w (V+100) - I^{syn} + I^{appl} \end{aligned} \quad (3)$$

where $V$ is the membrane potential and $C$ is the membrane capacitance. $g_L$ is the leak conductance, $g_{Na}$ and $g_K$ are the maximal sodium and potassium conductances, respectively. $g_{AHP}$ is the maximal slow potassium conductance of the afterhyperpolarization (AHP) current, which varies, depending on the attentional state. $I^{syn}$ is the synaptic input current, and $I^{appl}$ is the applied current. The variables *m, h, n* and *w* are calculated in a conventional way, and described more thoroughly in [4].

In each of the three (lumped) layers of the local area network, there are four types of interactions: 1) lateral excitatory–excitatory, 2) excitatory–inhibitory, 3) inhibitory–excitatory, and 4) inhibitory–inhibitory, with corresponding connection strengths, which vary with distance between neurons.

## 3. Simulation Results

### 3.1. Bottom-up: Noise-induced State Transitions

Noise appears primarily at the microscopic (subcellular and cellular) levels, but it is uncertain to what degree this noise normally is affecting meso- and macroscopic levels (networks and systems). Under certain circumstances, microscopic noise can induce effects on mesoscopic and macroscopic levels, but the role of these effects is still unclear. Evidence suggests that even single-channel openings can cause intrinsic spontaneous impulse generation in a subset of small hippocampal neurons [5].

For a constant, low-amplitude random input (noise), the three-layered cortical network model is able to oscillate with two separate frequencies simultaneously, around 5 Hz (theta rhythm) and around 40 Hz (gamma rhythm). Under certain conditions, such as for high *Q*-values, the system can also display chaotic-like behaviour, similar to that seen in EEG traces. In associative memory tasks, the network may initially display a chaotic-like dynamics, which then converges to a near limit cycle attractor, representing a stored memory (of an activity pattern) [6, 7].

Simulations with various noise levels show that spontaneously active neurons can induce global, synchronized oscillations with a frequency in the gamma range (30-70 Hz). Even if only a few network units are noisy, i.e. have an increased intrinsic random activity, and the rest are quiescent, coherent oscillatory or pseudo-chaotic activity can be induced in the entire network, if connection weights are large enough. The onset of global oscillatory/chaotic activity depends on, for example, connectivity, noise level, number of noisy units, and duration of the noise activity. The location and spatial distribution of these units in the network is also important for the onset and character of the global activity. For example, as the number or activity of the noisy units is increased, or if the distance between them increases, the oscillations tend to change into irregular patterns. In Fig. 1 we show that global network activity can be induced if only a small fraction of the network units are noisy (spontaneously active), and the rest are silent. After a short transient period of collective irregular activity, the entire network begins to oscillate, and collective activity waves moves across the network. Similar effects can be obtained with regular oscillatory activity of a few network units (See [8] and references therein).

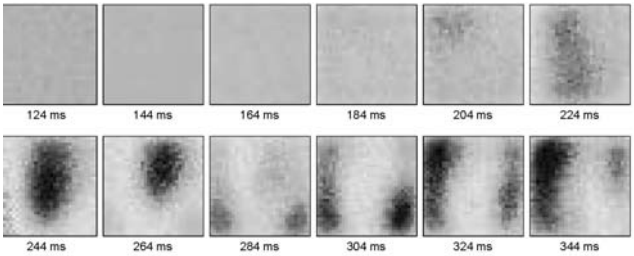


**Figure 1.** Spontaneous random activity in the network may suddenly result in complex global activity patterns. The frames show snapshots 20 ms apart of the neural activity of the excitatory layer of the three-layered paleocortical network model, going from upper left to lower right.

### 3.2. Top-down: Network Modulation of Neural Activity

The neural activity at the microscopic level of single neurons is the basis for the neurodynamics at the mesoscopic network level, and fluctuations may sometimes trigger coherent spatio-temporal patterns of activity at this higher level. Irregular chaotic-like behaviour can be generated by the interplay of neural excitatory and inhibitory activity at the network level. This complex network dynamics, in turn, may influence the activity of single neurons, causing

them to fire coherently or synchronously. This downward causation is complementary to the upward causation previously in focus.

### *3.2.1 Neromodulated Oscillations*

The cortical neurodynamics observed in e.g. LFP and EEG studies may be (partly) controlled by neuromodulators, such as acetylcholine (ACh) and serotonin (5-HT). Such agents can change the excitability of a large number of neurons simultaneously, or the synaptic transmission between them. ACh is also known to increase the excitability by suppressing neuronal adaptation, an effect similar to that of increasing the gain in general. The concentration of these neuromodulators seems to be directly related to the arousal or motivation of the individual, and can have profound effects on the neural dynamics (e.g. an increased oscillatory activity) and on cognitive functions, such as associative memory [2, 9].

We use both our paleocortical and neocortical models for investigating how the network dynamics can be regulated by neuromodulators, implemented in the models as a varied excitability of the network units and modified connection strengths. The frequencies of the network oscillations depend primarily upon intrinsic time constants and delays, whereas the amplitudes depend predominantly upon connection weights and gains, which are under neuromodulatory control. Implementation of these neuromodulatory effects in the models cause dynamical changes analogous to those seen in physiological experiments.

### *3.2.2 Attention-modulated Neurodynamics*

Related to the level of arousal, and apparently also under neuromodulatory control, is the phenomenon of attention, which plays a key role in perception, action selection, object recognition and memory. The main effect of visual attentional selection appears to be a modulation of the underlying competitive interaction between stimuli in the visual field. Studies of cortical areas V2 and V4 indicate that attention modulates the suppressive interaction between two or more stimuli presented simultaneously within the receptive field [10]. Visual attention has several effects on modulating cortical oscillations, in terms of changes in firing rate [11], and gamma and beta coherence [12].

The inter-scale network interactions of various excitatory and inhibitory neurons in the visual cortex generate oscillatory signals with complex patterns of frequencies associated with particular states of the brain. Synchronous activity at an intermediate and lower-frequency range (theta, delta and alpha) between distant areas has been observed during perception of stimuli with varying behavioral significance [13,14]. Rhythms in the beta (12-30 Hz) and the gamma (30-80 Hz) ranges are also found in the visual cortex, and are often associated with attention, perception, cognition and conscious awareness [13,15]. Data suggest that gamma rhythms are associated with relatively local connections, whereas beta rhythms are associated with higher level interactions.

Our simulation results show reduced beta synchronization with attention during a delay period (under certain modulation situations), and enhanced gamma synchronization, due to attention during a stimulation period (Fig. 2). In comparison with an idle state, where the dominant frequencies are around 17 Hz, the dominant frequency of the oscillatory synchronization and its STA (spike triggered averages) power in the "attended-in" group, $A_{in}$, is decreased, by inhibition of the intra-cortical synaptic inputs. This result agrees qualitatively with experimental findings that low-frequency synchronization is reduced during attention [3].

It is apparent that many factors play important roles in the network neurodynamics. These include 1) the interplay of ion channel dynamics and neuromodulation at a micro-scale, 2) the lateral connection patterns within each layer, 3) the feedforward and feedback connections between different layers at a meso-scale, and 4) the top-down and bottom-up circuitries at a macro-scale. The interaction between the top-down attention modulation, and the lateral short distance excitatory and long range inhibitory interactions, all contribute to the beta synchronization decrease during the delay period, and to the gamma synchronization enhancement during the stimulation period in the $A_{in}$ group.

The top-down cholinergic modulation tends to enhance the excitability of the $A_{in}$ group neurons. The Mexican hat shape lateral interactions mediate the competition between $A_{in}$ and $A_{out}$ ("attended-out") groups. Other simulation results demonstrate (not shown) that the top-down attentional/cholinergic effects on individual neurons and on the local and global network connections are quite different. In particular, the higher beta synchronization of the $A_{in}$ group is much stronger than that of the $A_{out}$ group.

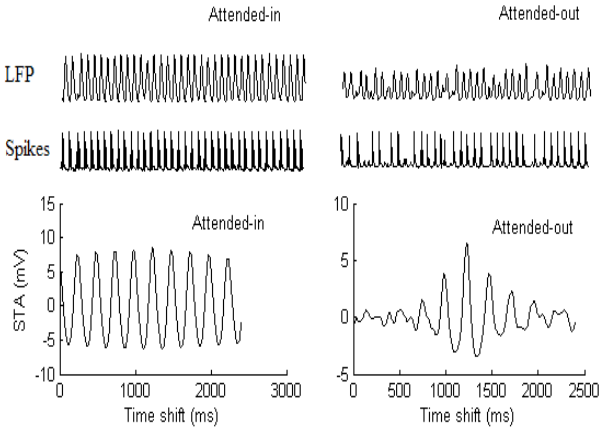


**Fig. 2.** Cholinergic modulation effects during a stimulus period. The activity of cortical neurons in attention (left) and out of attention (right). Local field potential (LFP), spikes, and spike triggered averages (STA) of attended-in and attended-out groups are shown, and calculated for the superficial layer of the six-layered neocortical network model.

## 4. Discussion

Our simulations have demonstrated how events and processes at the microscopic level of single neurons can influence the mesoscopic neurodynamics of cortical networks, which in turn are associated with cognitive functions at the macroscopic level. It is apparent that internal noise can cause various phase transitions in the network dynamics, that may have effects on higher level functions. For example, an increased noise level in just a few network nodes can induce global synchronous oscillations in cortical networks and shift the system dynamics from one dynamical state to another. This in turn can change the efficiency in the information processing of the system. We have previously demonstrated that system performance can be maximized at an optimal noise level, analogous to the case of stochastic resonance, and that spontaneous activity can facilitate learning and associative memory [7,16]. Thus, in addition to the (pseudo-) chaotic network dynamics, the noise produced by a few (or many) neurons, could make the system more flexible, increasing the responsiveness of the system and avoiding getting stuck in any undesired oscillatory mode [8,17].

In addition, we have demonstrated how neuromodulation, whether related to the level of arousal or as a consequence of attention, can regulate the cortical neurodynamics, and hence the activity of its constituent neurons. The firing patterns of single neurons are thus, to a certain degree, determined by the activity at the network level (and above). For example, neurons in visual cortex may fire synchronously and in phase, as a result of cholinergic modulation during attention, which is confirmed by both experimental studies and computer simulations.

The objective has been to investigate how structure is related to dynamics, and how the dynamics at one scale is related to that of another. In this endeavour, we believe computational models of cortical structures can complement experimental studies in order to study the causal relationship between activities at different spatial and temporal scales.

It is apparent that the intricate web of inter-relationships between different levels of neural organization, with inhibitory and excitatory feedforward and feedback loops, with nonlinearities and thresholds, noise and chaos, makes any attempt to trace the causality of events and processes futile. In line with the ideas of Noble [1], it seems obvious that there is, in general, both upward and downward causation in biological systems, including the nervous system. This also makes it impossible to say that mental processes are simply caused by neural processes, without any influence from the mental on the neural. On the contrary, these aspects of the human brain-mind relation seem complementary, and open up for a greater understanding of such ideas as “mind over matter”, placebo effects, free will, etc.


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