On the 'Dynamic Brain' Metaphor

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Abstract. Dynamic system theory offers conceptual and mathematical tools for describing the performance of neural systems at very different levels of the organization. Three aspects of the dynamic paradigm, namely neural rhythms, neural and mental development and macroscopic brain theories and models are discussed.

Keywords: neurodynamics, rhythms, neural and cognitive development, hermeneutics, brain imaging

1. Introduction

Metaphors provide concepts and relationships between these concepts to understand the mechanisms of phenomena, and proved to be useful to analyze biological systems [87]. The brain, the metaphorical brain, as it is suggested by Arbib, [3] has been described by different metaphors. First, there are the technical brain analogies: technical devices, as telegraph circuits, holograms and of course computers have been offered as metaphors and/or models of the brain. Second, theoretical notion of physics from quantum physics to thermodynamics served as analogies for characterizing neural functioning of the physical brain. Third, there is the notion of the computational brain [27]. More precisely, the metaphor has two directions ("brain as a computer" versus "computer as a brain"). Fourth, the philosophical brain has been approached by a variety of theories, each finally labeled as either monist or dualist, but none of them proved capable of meeting the strict criteria which the neurosciences seem to offer. In an earlier paper [40] we argued that the philosophical tradition of hermeneutics, i.e., the "art of interpretation", which is a priori neither monist nor dualist, can be applied to the brain. Playing with the idea that the "technical" or "device approach" to the brain and the "philosophical approach" can be reconciled, it was concluded that the brain is a physical structure which is controlled and also controls, learns and teaches, process and creates information, recognizes and generates patterns, organizes its environment and is organized by it. It is an "object" of interpretation, but also it is itself an interpreter. The brain not only perceives but also creates new reality: it as a hermeneutic device.

In the core of that analysis was the *dynamic* character of the brain. More specifically, brain activities can be understood from different perspectives, such as the thermodynamics of open systems, control theory, learning machines and algorithms, self-organizing systems and theory of information storing, processing and creating devices, etc.

The importance of the analysis of dynamic patterns of neurons and cell assemblies was emphasized by a conference organized by Aharon Katzir Katchalsky ([72]), and an influential booklet was published after he died at the Tel-Aviv airport in 1972 by a terrorist action. After Katchalsky death, the "dynamic brain paradigm" though was not abandoned, it was faintly mostly by the revival of the computationalist approach.

However, the concepts and techniques of the dynamic approach to the brain (and even to the mind) has been revitalized. This renaissance has at least two different roots.

First, just from the seventies the mathematical theory of dynamic system itself, and also its applications, related to several disciplines such as catastrophe theory [113], theory of dissipative structures [83] and of synergetics [62], has been emerged and had a massive influence on theory formation. Each of these (neostructuralist) theories form a subclass of the so-called nonlinear science using such keywords, as oscillations and fluctuations, bifurcations and phase transitions, chaos, strange attractors and fractals, morphogenesis and multistability, just to mention some of them. Second, experimental methods have been developed to monitor spatiotemporal phenomena at different levels of neural organization: from single cells by microelectrode techniques, from neural networks by using multielectrode techniques, and from neural centers and the whole brain by applying brain imaging methods.

In this paper, we give a non-technical review of three aspects of the "dynamic brain" paradigm.

First, **neural rhythms** are discussed. Neural rhythms can be found in very different phylogenetic scales. They occur in elementary neural networks, and are the building blocks of central pattern generating and motor pattern generating devices. Cortical structures produce oscillation with a wide range of frequencies, from less than 1Hz oscillation to very high frequency activities with several hundred Hz. Specifically, the occurrence of synchronized rhythmic activities in different neural centers generated great excitments, since they have been supposed
to be the neural substrates of many cognitive function, including consciousness.

Second, the relationship between neural and mental development is briefly reviewed. Selectionism and constructionism are theoretical frameworks to describe developmental processes. Selectionism was suggested mostly in biological context, while constructivism has its tradition related to mental development. Roughly speaking, the crucial difference between the two approaches is, that the second one assumes a more active role of the structured environment than the first one. The hermeneutic approach, which reconciles the "device approach" and the "philosophical approach" emphasizes that the brain is not a passive transformer, but it can establish mental constructs called reality. In addition, mental activity can influence neural development.

Third, the routes to formulate a macroscopic dynamic brain theory and models to serve as a framework of recent and future brain imaging method are analyzed. Global brain activity depends on the interaction of different levels of neural organization, from multicompartamental neurons via networks through large-scale brain areas. The main conceptual and technical challenge is to bridge the gap between brain imaging data and the underlying neural activity. To make large-scale and long-term realistic neural simulations there is a need to find a compromise between the biophysically detailed multicompartamental modeling technique, and the sometimes oversimplified network models. Statistical population theories offer a good compromise. Ventriglia [121, 122] introduced a kinetic theory for describing the interaction between a population of spatially fixed neurons and a population of spikes travelling between the neurons. In our group [45, 61, 10] a scale-invariant theory (and software tool) was developed, which gives the possibility to simulate the statistical behavior of large neural populations, and to monitor synchronously the behavior of an "average" single cell. There is a hope that activity propagation among neural centers may be realistically simulated, and the neural mechanisms of human cognition can be better understood.

Dynamic and computationalist paradigms are, however, not reconcilable. The term computation can be extended to dynamical systems ([82, 101], or more precisely it was shown that dynamical systems are able to process, store and - related to chaotic behaviour - even create information, e.g. ([82, 101, 117].

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By reviewing and evaluating in this paper the "dynamic brain" paradigm, we make it clear that, whatever useful this is concept, we don't consider it as the "final metaphor". Concepts like chaos, unpredictability, circular and network causality, information, emergence, complexity etc. led to the limits to dynamic structuralism. The hegemony of the Newtonian paradigm, has been weakened by the physics and chemistry motivated neostructuralist theories such as the theory of dissipative structures, and of synergetics. In spite of their ambitious endeavors, and undeniable success, no theory of brain and theory of evolution can be given within a pure structuralist framework. Brain theory and evolutionary theory are the prototypes of the 'science of complexity' and they ought to be "poststructuralist" [39, 41, 40].

The dynamic paradigm is certainly cannot be isolated from the classical structural and functional approaches. Arbib et al 1997, [4], Arbib and Érdi (in press) [5] shows how the integrated structural, functional, and dynamical approach can unify theoretical frameworks and experimental data.

2. Neural rhythms: how and why?

2.1. CENTRAL PATTERN GENERATORS AND MOTOR PATTERN GENERATORS

The generation and control of movement is certainly a fundamental dynamic activity of the nervous system. A theory should describe the transformation from neural activities to muscle contraction and behavior. Mostly simple, stereotyped movements, and elementary rhythmic behaviors, as breathing, feeding, and locomotion have been studied.

The current metaphor to study motor behavior is motor program [32]. The term "program" should be understood in a rather abstract way. It produces biologically relevant behavioral output patterns to external stimuli, or even in the absence of input.

A central pattern generator (CPG) is a network of neurons that produce rhythmic behavior in the absence of sensory input. Relatively simple invertebrate systems, such as the crustacean somatogastric ganglion, are capable of generating temporal patterns independently of peripheral reflex loops. The network structure and the transmitterology of this system has already been quite thoroughly uncovered. The fundamental temporal patterns can be explained by coupled oscillator
models.

At a higher phylogenetic level, the locomotion of lower vertebrates, such as tadpole and lampreys, has been studied. Motor patterns underlying locomotions are produced by a spinal circuit. Not only the neural circuitry, but also the transmitters and the membrane properties are largely known [98]. Animal locomotion, even at higher phylogenetic level, maybe generated and controlled by a central pattern generator. However, the total motor pattern generator involved various feedback loops which use sensory input to adjust the motor pattern to current circumstances. Multi-legged animals exhibit several distinct patterns of leg movements; these basic patterns called gaits (e.g. walk, run, hop for humans; trot, canter, gallop for horses. Quadrupedal locomotion, may be controlled by at least four coupled oscillators [30].

The general, model-independent properties of symmetrically coupled oscillators have been studied by group-theoretical methods. These oscillators have been identified with locomotor central pattern generators. Six symmetrically coupled oscillators have been considered as models of CPGs in insects, and the transitions between the gaits were modeled as symmetry-breaking bifurcations [28]. In particular, the relationship between the different network structures of the symmetrically coupled oscillators and the possible rhythmic patterns (associated to gaits) which they can generate were derived and listed. The symmetries of quadrupedal animal gaits have also been analyzed [29]. The analysis showed that minor modification in the network structure may imply a significant effect on the resulting gait. It is not easy to localize central pattern generators. By making symmetry analysis of animal gaits information about the possible network structure of CPGs can be obtained. Since the same network may produce different rhythmic patterns depending on the parameter values, the same locomotor central pattern generator may produce and control very different gaits.

There is a changing view on CPGs (see e.g. [73]). First, it seems to be evident, that though even single cells can produce in certain cases complex temporal behaviour, the coordinated and controlled patterns are emergent network properties. In addition, the networks are not so rigid, or hard-wired: chemical modulators by modifying membrane properties may produce drastic changes in the behavior of the system, and even the network itself can be rearranged.

The understanding of the physiological control of motor activities [81] is in the overlapping area of biology- and technology-oriented re-
searches. The motor control system send motor command to the object to be controlled (often called as plant, since the terminology comes from engineering). A biological motor system should adopt a control strategy to respond to changes in the sensory inputs and internal goals. Different types of control strategies, such as feedforward, feedback and adaptive control are known. If the control signal does not depend on the output of the system, it is called as feedforward controller. The oculomotor system is an example of this control. If the action of the controller depends on the deviation of the output signal of the plant from a reference value, it is a feedback controller. Physiological systems use extensively feedback control, and it was one of the key concepts which played an important role in the emergence of cybernetics [94]. Adaptive control strategies based on the observation of the system at a longer time scale that it is necessary to feedback control. Therefore the control signal is generated after having some measure of the average performance of the plant. Adaptive control systems may adjust the parameters of the system, and even changes in the reference values can be adaptively controlled. Not only engineering-oriented methods are used to understand motor control, but there are serious research works with the intention to ultimately create autonomous humanoid robots [97]. This paper asks whether "Imitation learning is the route to humanoid robots?"

The acquisition of motor behaviour [14] is certainly a very characteristic part of the dynamic brain paradigm. Learning of such types of skills, as walking and swimming the subject needs feedback information about its performance. Learning in neural networks can be classified as supervised, reinforcement, or unsupervised learning [65]. Unsupervised learning, in which a cell's connections change according to some built-in measure of performance (so that a measure of similarity acts as a fixed built-in supervisor) is distinguished from supervised learning, in which the environment-teacher specifies the correct classification, and instructs the system by some error-correcting mechanism. In reinforcement learning, the learner does not get complete teacher information, but instead receives a "reward/punishment" or "reinforcement" signal depending on the quality of the output. It was suggested [11] that reinforcement learning is an indispensable, but not the only, algorithm for motor learning, for improving performance.
2.2. Cortical rhythms: neural substrates and functional significance

Global brain states, in both normal and pathological situations, may be associated with spontaneous rhythmic activities of large populations of neurons. Experimentally, these activities may be detected by recording both from large neural assemblies (as in the electroencephalography (EEG) or from a single neuron of the cell population. Here we discuss, the thalamocortical and hippocampal rhythms and their relationship to mental states.

2.2.1. Thalamocortical oscillators
The thalamocortical system, a massive reciprocally connected systems of the thalamus and the cerebral cortex, controls the transition of the brain from the aroused state to the state of sleep (and back). The thalamus is assumed to be the ultimate source of neocortical rhythmicity, and it is the major gateway for the flow of information toward the cerebral cortex. The underlying thalamic oscillation is not generated by single "pacemaker" cells but seems to be a "network property" ([20]). Both the aroused and the sleeping brain exhibit particular dynamic activity patterns. The aroused brain is characterized by high-frequency rhythms, while during sleeping the dominant spatiotemporal pattern is synchronized low-frequency activity. These patterns are generated in the thalamus and the cortex, which are intimately interconnected by reciprocal projections. The detailed analysis helps to classify the different rhythms, and to understand the mechanisms and functional consequences of rhythm generation. Thalamocortical oscillations can be demonstrated both at the single-cell and network levels, and the interplay between them should be better understood [108]. The interaction among simple single cell oscillators through synaptic coupling may lead to more complex temporal patterns. Awakening, i.e. the transition from the sleeping to the aroused state, is associated with change from high-amplitude EEG oscillation to low-amplitude fast rhythms. The process of awakening associated with desynchronization is activated by the neuromodulators of various ascending systems.

In the early stage of quiescent sleep, the high-frequency (20 to 80 Hz, mainly around 40Hz) gamma rhythm of the aroused state is reduced to the "spindle waves" which occur at a frequency of 7 to 14 Hz. Deepening of sleep implies the appearance of slower frequencies (0.1 to 4 Hz) in the EEG. The sleep state associated with rapid eye movements (REM sleep) is characterized by abolition of the low frequency oscillations (and an increase in cellular excitability). Transition from quiescent sleep
to REM sleep is also activated by the ascending modulatory system, specifically by cholinergic activation.

Delta oscillations are most likely generated by intracellular mechanisms, they are also visible in the EEG because of the existence of some efficient synchronization mechanisms (locally, by axonal collaterals of thalamocortical neurons, or by connection from the reticular nucleus or from the cortex). It should be remarked, however, that there is a significant difference between the delta rhythms of single thalamic cells and the EEG delta waves, since the former are regular, while the latter show polymorphic irregularities.

Spindle oscillation is considered from behavioral physiological point of view as the physiological correlate of drowsiness, and the early stage of sleeping. In the EEG records it appears as a high amplitude waxing-and-waning field potential wave with 7-14 Hz frequency. These oscillations are grouped in sequences that last from 1 to 3 s, and that recur every 3 to 10 s. There is a long history behind spindle oscillation researches going back at least to Bremer, [17]. Inhibitory coupling may have an important role in its generation [34]. Specifically, the mechanism for waxing-and-waning is not well understood. It was speculated [108] that the waxing stage “could be generated by a recruitment of neurons through divergence of axonal connections between reticular and thalamocortical neurons as well as through the effects of cortical pyramidal cells that are entrained in the oscillation and impinge back onto reticular thalamic neurons...”. The waning is explained by a shift in the properties of the ionic conductances and/or by the failure in operation of the pacemaking reticular thalamic nucleus.

Thalamocortical gamma oscillation was found both in animal and human studies. Specifically, magnetoencephalographic (MEG) measurements [95, 77, 70] showed gamma oscillation, evoked mostly for auditory stimuli.

2.2.2. Hippocampal rhythms
Two main, normally occurring, global hippocampal states are known: the rhythmic slow activity, called the theta rhythm with the associated gamma oscillation, and the irregular sharp waves (SPW) with the associated high frequency (ripple) oscillation. A pathological brain state, associated with epileptic seizures, the epileptiform patterns are also frequently occur in the hippocampus.
The **theta rhythm** is a population oscillation with large (1 mV) amplitude and with 4-12 (Hz) frequency. It was found to occur whenever the animal engages behaviors as walking, exploration, or sensory scanning, as well as in REM sleep [19]. Single-cell physiological studies showed different relations between the behavior of individual cells and the theta rhythm. Pyramidal cells in the hippocampus proper generally discharge with a very low frequency (0.01-0.5Hz), although spatially sensitive ”place cells” show firing at 4-8Hz when the rat is in its place field, and the position of the animal within a cell’s place field may be correlated with the phase of its firing relative to the theta rhythm. Phase precession [85] expresses a ternary relationship between the position of an animal, single cell activity of place cells and temporal patterns of the local field potential. Specifically, spikes of place cell appear at progressively earlier phases of the theta rhythm as the animal traverse the place field of the cell. Based on this phenomena it is reasonable to assume the existence of *phase coding*.

Theta rhythm can also be phase-locked to sensory stimuli. Buzsáki et al. (1994) [21] speculated on the double functional role of hippocampal theta rhythm. First, a large-scale oscillation in the entorhinal-hippocampal network induced by the septum is maintained by phase-locking. Second, since the majority of the pyramidal cells are silent during theta, and their membrane voltage is kept close to but below the threshold, relatively few excitatory synapses are sufficient to discharge them. In addition, theta is involved in generation of LTP (long-term potentiation), which is supposed to be the cellular basis of memory formation.

The theta rhythm is thought to be generated extrahippocampally, but data have been accumulated to support the view that it has even internally generate components. The main source is the septo-hippocampal pathway. It has a cholinergic component, but it is not the only one to contribute to the generation of theta rhythm: atropin, a muscarinic antagonist of ACh, does not entirely abolish the rhythmic slow activity. The GABAergic component of the septal afferents modifies the activity of the principal cells by disinhibition and is also involved in the generation of theta rhythm. These GABA-ergic cells are located mostly at the border of the medial and lateral septum, and terminate on the GABA-ergic interneurons of the hippocampus, and on the non-GABA-ergic supramammillary cells, which are known to project to the septal complex and the hippocampus.
Results of in vitro experiments modify this view. Population oscillation at the theta frequency can be induced pharmacologically by carbachol in hippocampal slices. Based on these and similar findings it was suggested that theta rhythms may be generated not (only) extrahippocampally, but also by the intrinsic membrane properties of the neurons of the CA3 region. The underlying single-cell firing patterns, however, may be different for in vivo and in vitro carbachol-induced oscillation: the pyramidal cells fire at a much higher frequency than in vivo. Some observations suggest a presence of two, relatively independent, theta generators in the hippocampus, which are mediated by the entorhinal cortex and the CA3-mossy cell recurrent circuitry, respectively. The CA3-mossy cell theta generator is partially suppressed by the dentate gyrus interneuronal output in the intact brain. Resonant properties of the CA1 neurons were found in vitro in the theta frequency range ([75]).

**Gamma oscillation** is in the 20 - 80 Hz frequency range. The mechanisms underlying gamma oscillations are not fully understood. Studies on the hippocampal formation have suggested that field oscillations in the gamma frequency band reflect synchronous IPSPs on the somata of principal cells. Synchronized population oscillation may emerge in networks of interneurons connected by GABA-A synapses even when individual cells fire at remarkably higher frequencies [127, 124]. Alternative hypotheses suggested that the origin of the synchronized gamma activity may be in single cell level ("chattering cells") [59].

Gamma oscillations, either spontaneous or stimulus evoked, have been found in different sensory as well as in motor cortices. Synchronized gamma oscillations was found in the olfactory system [50], and in the visual cortex [58, 35] and many other later. Synchronized gamma oscillation as a putative mechanism of feature binding and even consciousness was a hot issue in the last decade [31, 102]. Fast oscillation (20-80Hz) in cortical regions were thoroughly surveyed by Traub et al., [115].

**Sharp waves** (SPWs) have a very large amplitude (up to 3.5mV), their duration is 40-120ms, and their frequency can be between 0.2 and 5 Hz. Though maximal SPW frequencies do overlap theta frequencies, theta waves are much more regular than SPWs. SPWs also have behavioral correlates: they occur during awake immobility, drinking, eating, face washing, grooming and slow wave sleep [19].
During SPWs, pyramidal and inhibitory cells fire with increased frequency. Furthermore, there is a partial synchronous cellular activity of both pyramidal and inhibitory neurons. The degree of synchrony is, however under the threshold for induction of epileptic seizure. The amplitude and frequency of SPWs can be increased by high-frequency stimulation of the commissural system and the Schaffer collaterals, suggesting that such stimulation enhances the efficiency of the excitatory synapses. The activity of neurons in the deep layers of entorhinal cortex are also correlated with SPWs.

SPWs are thought to be formed by internal intrahippocampal processes. One important precondition for SPW generation is the occurrence of a population burst in a small set of CA3 pyramidal cells. Their synchronization is mediated by excitatory synaptic connections [18].

The largest degree of synchronization occur in the adult hippocampus during the irregular sharp wave in physiological conditions. CA3 pyramidal cells have recurrent excitatory connections which terminate within the CA3 region. The autoexcitation due to these connections produces large excitatory postsynaptic potentials (EPSP) which are propagated to the CA1 region through the Schaffer collaterals. Inhibitory connections control the population activity in both regions.

While sharp waves were found in rat hippocampus during consummatory behaviors and slow wave sleep, there is a normal human EEG phenomenon called small sharp spikes (SSS), which is thought to be analogous to SPW, since it also results from partial synchronous cell firing.

Not only "normal", but also epileptiform SPWs can occur. The latter are characterized by larger than 4 mV amplitude, and/or their pattern is less irregular. Their duration is shorter than during normal SPWs. Epileptogenesis from the perspective of the dynamical system theory will be discussed after several paragraphs.

**High frequency** ("ripple") (200 Hz) network oscillations are displayed in CA1 pyramidal cells in conjunction with sharp wave bursts [129]. Similar types of high frequency oscillation were recorded from the entorhinal cortex and hippocampus of patients with mesial temporal lobe epilepsy. The lower frequency oscillation (80-160 Hz) was regarded as a human equivalent of normal ripples in the rat. The higher frequency oscillation (250-500 Hz) was found in the epileptogenic regions and may reflect pathological hypersynchronous population spikes of bursting pyramidal neurons. Sleep is characterized by a structured
combination of neuronal oscillations. In the hippocampus, slow-wave sleep (SWS) is marked by high-frequency network oscillations, neocortical SWS activity is organized into low-frequency delta (1-4 Hz) and spindle (7-14 Hz) oscillations. The existence of temporal correlations between hippocampal ripples and cortical spindles are also reflected in the correlated activity of single neurons within these brain structures. This coactivation of hippocampal and thalamocortical pathways may be important for the process of memory consolidation, during which memories are gradually translated from short-term hippocampal to longer-term neocortical stores [16].

Single pyramidal cells discharge at a low frequency are phase locked to the negative peak of the locally derived field oscillation. CA1 basket cells increase their firing rate during the network oscillation and discharged at the frequency of the extracellular ripple. These findings indicate that the intracellularly recorded fast oscillatory rhythm is not solely dependent on membrane currents intrinsic to the CA1 pyramidal cells but it is a network-driven phenomenon dependent upon the participation of inhibitory interneurons. One of the hypotheses was, that fast field oscillation (200 Hz) in the CA1 region reflects summed IPSPs in pyramidal cells as a result of high-frequency barrage of interneurons [129]. These specific currents responsible for the ripple are believed to be synchronized somatic IPSPs interrupted by synchronous discharges of CA1 pyramidal neurons at every 5-6 msec. Concurrent with the hippocampal sharp wave, ripples are present also in the subiculum, parasubiculum, and deep layers of the entorhinal cortex, but the ripple frequency is fastest in the CA1 region. Recent experimental and computational simulation results suggest that ripple oscillation may be mediated by direct electronic coupling of neurons, most likely through gap-junctional connections [115].

2.3. Epilepsy: Dynamic Models of Generation and Control

Epilepsy is a typical example of dynamical diseases. A dynamical disease is defined that occurs in an intact physiological system yet leads to abnormal dynamics. Epilepsy itself is characterized by the occurrence of seizures (i.e. ictal activities). During epileptic seizures oscillatory activities emerge, which usually propagate through several distinct brain regions. The epileptic neural activities generally displayed in the local field potentials measured by local electroencephalogram (EEG).

Epileptic activity occurs in a population of neurons when the membrane potentials of the neurons are "abnormally" synchronized. Both
experiments and theoretical studies suggest the existence of a general synchronization mechanism in the hippocampal CA3 region. Synaptic inhibition regulates the spread of firing of pyramidal neurons. Inhibition may be reduced by applying drugs to block (mostly) GABA-A receptors. If inhibition falls below a critical level, complete synchrony occurs. Collective properties of networks of pyramidal cells modulated by inhibition have been studied successfully by [114]. As we already know, a certain degree of synchrony is necessary for normal theta and SPW behavior, and the transition between normal and abnormal degrees of synchrony is not clear. Rather arbitrarily, activity has been considered epileptic if more than 25% of the cells fire during 100ms. In vitro models of epilepsy [114] offer a means to study the cellular mechanisms of the different types of epileptic phenomena by combined physiological and simulation methods. Several in vitro models of seizures have been developed, including electrical stimulation, low calcium, low magnesium and elevated potassium levels.

Dynamical system theory offers a conceptual and mathematical framework to study epileptogenesis [114, 78, 79, 10]. Analytical studies based on bifurcation theory should clarify the possible operating modes of a given neural network. The balance between excitation and inhibition is certainly one important control parameter, and its change may imply transition between the regimes. Epileptic activities may be considered as chaotic processes [8]. There has been some hope that technique of controlling chaos may offer new therapeutic and diagnostic tools for controlling epileptic activities [100].

2.4. Computational modeling: alternative strategies

Structure-based bottom-up modeling has two extreme alternatives, namely multi-compartmental simulations, and simulation of networks composed of simple elements. There is an obvious trade-off between these two modeling strategies. The first method is appropriate to describe the electrogensis and spatiotemporal propagation of the action potential in single cells, and in small and moderately large networks based on data on detailed morphology and kinetics of voltage- and calcium-dependent ion channels. The mathematical framework is the celebrated Hodgkin-Huxley model [66] supplemented with the cable theory [92, 93]. Neural simulation softwares such as NEURON [63, 64], and GENESIS [125, 15] have been constructed to simplify the efficient simulation of neurons with branching patterns. The second offers a computationally efficient method for simulating large network of neurons where the details of
single cell properties are neglected. There is a series of cell models with different level of abstraction. While multi-compartmental models take into account the spatial structure of a neuron, neural network techniques generally based on integrate-and-fire models. The latter is a spatially homogenous, spike-generating devices. For a review of “spiking neurons”: [55].

Depending on its structure, an autonomous NN may or may not exhibit different qualitative dynamic behavior (convergence to equilibrium, oscillation, chaos). Some architectures show unconditional behavior, which means that the qualitative dynamics does not depend on the numerical values of synaptic strengths. The behavior of other networks can be switched from one dynamic regime to another by tuning the parameters of the network. One mechanism of tuning is synaptic plasticity, which may help to switch the dynamics between the regimes (e.g. between different oscillatory modes, or oscillation and chaos, etc. ...)

The description of large population of neurons requires a different methodological approach, namely the application of population theories. This description is discussed in subsection 4.3.2. on Dynamic approach to brain imaging: macroscopic brain theories and practice.

3. Neural and Cognitive Development

3.1. SELECTIONISM, INSTRUCTIONALISM, CONSTRUCTIVISM, HERMENEUTICS

The relationship between neural and mental development is debated in terms of selectionism, instructionalism and constructivism [107, 37, 91]. Selectionism [107] is based on (i) the generation of variabilities, (ii) the interactions of neural elements with environment, (iii) the selective amplification of certain neural elements. Instructionalism offers a unidirectional mechanism for learning, when information passes from the "teacher" to the "student". Constructivism emphasizes the importance of environmental driven development, and even learning is, at least partially, self-directed.

3.2. DEVELOPMENTAL NEURAL EVENTS

Developmental events are usually classified (rather mechanistically) as progressive (or additive) and regressive (or subtractive) events. Brain development emerges as the combination of progressive and regressive
events. Progressive events are the birth and proliferation of neurons, the migration of the neurons from the proliferative zone to their final destination, the sprouting and extension of long-range axonal connections and short-range dendritic branching, and the changes at the synaptic junction.

One of the dogma's in neurosciences is that no neurons are formed postnatally. This widely held belief has been challenged. Extensive evidence accumulated that certain brain areas (mostly hippocampus) retain the capability to generate new neurons in adulthood [60].

Different mechanisms of regenerative events coexist: cell death, axon retraction, axon regrowth and synaptic pruning are characteristic examples.

3.3. THE SELECTIVE STABILIZATION HYPOTHESIS

Ontogeny and plasticity of neural structures, as well as their learning capability, should be considered as dynamic processes and generally they have to be explained by common or similar mechanisms. The postnatal ontogenetic development of the nervous system is determined by the interaction of the innate genetic program and environmental factors, since the information content of the genome does not seem to be sufficient to determine the precise formation of the topographic maps.

To find a compromise between the nativist (or preformist) and empiricist points of view the selective stabilization hypothesis [25, 26, 23] was offered, as a third option. According to the former, the neuronal network is specified genetically, while the latter emphasizes (indeed overemphasizes) the role of the activity of the system to specify its own connectivities. The main conceptual advantage of the selective stabilization hypothesis is that it offers a gene-saving mechanism for specifying ordered neural structures.

Recent debates about the scope and limits of selectionist theory of neural development (see e.g. [89, 106, 24, 90] have been organized around the mechanism of the formation, elimination and stabilization of synaptic connectivity patterns. In particular, one crucial element of the debate is the effect of activities. While the earlier selectionist view stated that "activity does not create novel connections, but rather, contribute to the elimination of the pre-existing ones" [24], arguments for showing the indispensable role of electrical activity both in network
development and in adulthood have been summarized by [119, 120]. Activity-dependent mechanisms have a major role in cortical formation. It was suggested [99] that (i) a neural circuit within the immature retina is responsible for generating specific spatiotemporal patterns of neural activity; (ii) spontaneous activity generated in the retina is propagated across central synapses; and (iii) even before the photoreceptors are present, nerve cell function is essential for correct wiring of the visual system during early development. Since spontaneously generated activity is known to be present elsewhere in the developing CNS, this process of activity-dependent wiring could be used throughout the nervous system to help refine early sets of neural connections into their highly precise adult patterns. In any case, neural selectionism offers a beautiful, though not the only, metaphor to formulate neural development.

3.4. Self-organization: Development and plasticity of ordered structures

The emergence of complexity through self-organizing mechanisms has been studied on both the ontogenetic and the phylogenetic time scale. Thinking in terms of dynamical concepts, ontogenetic development is associated with the temporal change of state due to interaction among the state variables (when these are considered to include the synaptic weights of our neural network), while phylogenetic evolution can be visualized as bifurcations in a parameter space which characterizes a whole range of evolutionary possibilities: continuous changes in the control parameters may lead to a discontinuous change in the state space. Ontogenetic development and phylogenetic evolution are closely related as dynamic processes [57]. In particular, development of individuals of a population can explain elementary evolutionary changes, and individual life histories can be modified by certain "evolutionary feedback" mechanisms. Self-organization phenomena are related to normal ontogenetic development and plastic behavior occurring at different hierarchical levels of the nervous system. An important question here is the balance between determinism and randomness in the nervous system.

Many examples from embryology, anatomy, and physiology suggest that the brain cannot be considered as a purely deterministic system, and probabilistic concepts have a role in our understanding of the formation and operation of some neural structures. A family of apparently random behaviors has been identified with chaos and reduced
to deterministic mechanisms, but irreducibly stochastic elements are also important both in neural signal analysis and in modeling neural ontogeny and performance.

In the theory of dynamic systems, it turned out that in certain situations (mostly in the neighborhood of instability points), the effect of the fluctuations cannot be averaged out. On the contrary, they may cause drastic effects even at the macroscopic level. The theory of “noise-induced transitions” [67] showed that fluctuations may operate as “organizing forces”. Speaking somewhat more technically, noise may cause instability of the deterministic attractors and a stochastic model might exhibit properties qualitatively different from those of the deterministic model. These phenomena are illustrated in simple (and now already too simple) models of the ontogeny of ordered neural structures, both retinotectal connections [46, 47] and ocular dominance columns [9, 48]. Our simulation experiments showed that whereas a purely deterministic synaptic modification (“learning”) rule generated at best only locally ordered structures, taking into account a small additive random term even globally ordered structures were generated. Intuitively the role of environmental noise is to destabilize the metastable states. Activity-dependent self-organizing mechanisms, where environment may play active, constructive role in structure formation, may have a very important role in neural development. The same algorithms was able to describe not only the normal ontogeny of ordered structures, but the plastic response of the system for partial lesions.

There are many evidences now that cortical circuits of the mammals are reorganized by experience throughout the whole lifetime. There are different mechanisms of this plasticity. Plasticity changes with the age, and it certainly the largest during the critical period, when there is the dendritic and synaptic growth. Structural changes correlate with behavioral changes. It is possible to partially restore lost plasticity by recreating the developmental conditions that favor maximal plasticity [74]. Now there is hope that knowledge on plasticity can be utilized in clinical practice [69]. It was shown [33] that not only bottom-up but top-down processing may have an effect on neural plasticity.
3.5. **Downward causation, constructivism, the cognitive-neural interaction, and hermeneutics**

*Downward causation* is considered, when higher-level emergent patterning exerts influence on the dynamics of the lower-level constituents of a self-organizing system. Specifically, the application of the concepts to the brain-mind problem, i.e. that mental agents can influence the neural functioning, was suggested by Sperry [104, 105]. Sperry was criticized by stating that the postulate that physiological mechanisms of the brain are directly influenced by conscious processes is unclear [36, 111]. Alternatively, it was cautiously suggested that the nervous system can be considered as being open to various kinds of information, and that there would be no valid scientific reason to deny the existence of downward causation, or more precisely, a two-way causal relationship between brain and mind [109].

Modeling cognitive development, including language acquisition has been attempted using connectionist approach (for the connectionist perspective on development see [37]). The authors acknowledge the role of biological forces in determining behavior, but these forces should interact with their environment. They argued that interactions occur at all, even genetic, levels.

Cognitive developmentalists study development in the light of the nativism – constructionism dichotomy [71]. The nativist view [49] neglects the developmental aspects of the mind, and modularization is a dynamic process. The traditional constructivist approach [88] emphasizes

the domain-specific aspect of the development. Domain-specificity means that a certain (cognitive) module deals exclusively with a single information type (e.g. fly detection in the frog, face recognition etc.)

Analyzing the neural and mental development we stated [43] that (1) environmental influence is necessary for normal development; (2) selectionist mechanisms of neural development are based on the interaction between the innate genetic program and environmental factors; (3) mental development is involved not only in the representation but also in the creation of reality; (4) the human brain, which is a structurally and dynamically complex device, not only perceives but also creates reality: it is a hermeneutic device [40].
4. Dynamic approach to brain imaging: macroscopic brain theories and practice

4.1. Brain-imaging methods

Non-invasive brain-imaging techniques will have a major role in relating neural structures and function. Present techniques have two groups. The basis of the classification are the physical quantities the imaging is based. First, electric and magnetic signals generated by the neural tissue are used. These methods, such as EEG and MEG, record often outside from the scalp, so generally they provide a spatial resolution around 1cm, while the temporal resolution is in the region of milliseconds. Second, neural activity is estimated based on measurements of hemodynamic and metabolic events. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) produce data with several millimeter resolution, and the time resolution is on the order of few seconds for fMRI and to tens of seconds for PET. The electrophysiological methods serve better dynamic temporal information but only at a few brain centers, while the PET/fMRI methods give information about the brain regions and the strengths of interconnections among them during the performance of cognitive tasks. The combination of techniques is useful: first the brain regions to be involved in some cognitive task have to be determined, than the detailed dynamics of this site can be measured by EEG.

4.2. EEG and neurodynamics

The traditional view was that the source of the EEG, i.e. field potentials generated by the extracellular current flow, is the synaptic activity. Buzsáki and Traub (1997) [22] concluded that, at least in principle, "...every event associated with membrane potential changes of individual cells (neurons and glia) should contribute to the perceptual voltage variability of the extracellular space...". EEG reflects well the the two brain states (aroused and sleep) discussed in Chapter 2.2.1.

Dynamical system theory helped to connect large-scale neurodynamic behavior to EEG recording and cognition [52, 128, 84, 76]. Some dichotomies related to modeling electrocortical activities have emerged [42].
4.2.1. Attractor neural networks vs. biologically motivated models
"Computation with attractors" became a paradigm which suggests that dynamic system theory is a proper conceptual framework for understanding computational mechanisms in self-organizing systems such as certain complex physical structures, computing devices, and neural networks. Its standard form is characterized by a few properties. Some of them are listed here: (i) the attractors are fixed points; (ii) a separate learning stage precedes the recall process whereby the former is described by a static 'one-shot' rule; (ii) the time-dependent inputs are neglected; (iv) the mathematical objects to be classified are the static initial values: those of them which are allocated in the same basin evolve towards the same attractor, and can recall the memory trace stored there. In an extended form, not only fixed points but also limit cycles and strange attractors can be involved. A continuous learning rule may be adopted but, in this case, the basins of the attractors can be distorted which may even lead to qualitative changes in the nature of the attractors. Wright & Liley argued cautiously that biologically motivated models of the cortex can be interpreted as special cases of attractor neural networks. More realistic models, which take explicitly into account the continuous interaction with the environment, however, are nonautonomous in mathematical sense [44, 2]. Such systems do not have attractors in the general case. Consequently, attractor neural network models cannot be considered as general frameworks of cortical models.

4.2.2. Near-equilibrium vs. nonequilibrium processes
On the one hand, Nunez and Wright & Liley basically state that EEG is interpreted as a near-equilibrium process. On the other hand, Freeman's approach has been motivated by the theory of nonequilibrium thermodynamics [83] and of nonequilibrium phase-transitions [62]. The term, near-equilibrium" does not have a precise definition, and it is really recommendable to avoid it [116]. From purely physical point of view the brain is a thermodynamics based non-thermodynamic system. It was pointed out [38], how nonequilibrium thermodynamics can be extended to "higher than molecular" hierarchical levels. A certain type of well-defined "near-equilibrium" phenomena, as random fluctuations around equilibrium or stationary states, could and should be treated as special cases of nonequilibrium (stochastic) processes.

4.2.3. Linear versus nonlinear dynamics
In Nunez's model, the EEG is treated as a linear wave process, while Freeman [51, 103] adopted a nonlinear model of the cortex. The terms "linear" and "nonlinear" are mathematical concepts that have multiple
meanings. We have to be cautious, how to use them. In Freeman’s model, for example, (i) the static transfer function (wave-pulse relationship) is a nonlinear function; (ii) the differential equations for describing the activity of lumped cell aggregates are also called nonlinear. There is no formal connection between the two types of nonlinearity. The transition between linear and nonlinear equations is, however, possible. To mention a relevant example, in the the case of discrete state space stochastic processes, the differential equations for the absolute probability are linear, but nonlinear equations for the expectation can be derived from them. These derived equations govern situations qualified experimentally as “nonlinear phenomena”.

4.2.4. Stochastic vs deterministic chaotic time series
On one hand, classical signal analysis considers EEG records as realization of (often stationary) stochastic processes, and spectral (and later also wavelet) analysis has been the conventional method to extract the dominant frequencies and other parameters of the rhythms.

On the other hand, the occurrence of chaotic temporal patterns has been reported at different hierarchical levels of neural organization. Chaotic patterns can be generated at the single neuron level, due to the nonlinearity of voltage-dependent channel kinetics of the ionic currents, at the multicellular network level, due to the interactions among neurons, and at the global level in consequence of spatiotemporal integration.

Dynamic system theory offered a conceptual approach to EEG signal processing, different from the classical analysis. Time series, even irregular ones, are considered as deterministic phenomena generated by nonlinear differential equations. Though the methodological difficulties of interpreting the calculated quantities (Lyapunov exponents, fractal dimensions, entropies etc.) to characterise neurological categories are now acknowledged [86], we cannot deny that the application of dynamic system theory brought a new fresh air to the methodology of processing of neural signals.

Despite the existence of improved statistical methods to discriminate between noise and chaos, it is still hard to uniquely decide whether electrocortical recordings should be considered as purely random or deterministic chaotic patterns.
4.2.5. Local (microscopic) and global (macroscopic) scales
The adjective "local" means point-like here, and "global" may be interpreted as the whole. Obviously, local descriptions may have very different (and relative) meanings, even if we do not go below the single cell level. A single neuron, which is certainly a sub-microscopic unit relatively to Freeman's microscopic model, may be described by a spatially extended (global) model by using multicompartamental technique. But Freeman's model for neuron populations is local, since the whole population is lumped into a "point". In addition to speaking about "local" and "global", [53] we should remember the whole hierarchy of the neural organization. A step in this direction is the statistical theory of neural fields for describing the global brain activities in terms of interacting sub-fields (see Section 4.3.2).

4.3. PET, fMRI: from statics to dynamics

4.3.1. Structural modeling
PET and fMRI studies serve average activity data calculated for volume units (voxels). A voxel of the present techniques is large compared with even a cortical modules. (A cortical module contains several thousands neurons). Voxels showing correlations in blood flow during a specific cognitive task are assumed to be functionally connected. Interacting brain regions form a functional network. Structural modeling provides the numerical values of correlation coefficients between brain regions by assuming linear relationship between these active areas. More precisely, while functional connectivity reflects temporal correlations between remote neurophysiological events, effective connectivity characterizes the influence one neural system exerts over another [54].

The present evaluation techniques are based on statistical analysis (such as correlation, regression, principal component and independent component analysis). A more sophisticated, still static, technique, called covariance structural equation modeling (CSEM) was also introduced and applied for a number of specific cognitive tasks. This method, combines anatomical and hemodynamic-metabolic data and was qualified ([68]) as a system-level neural modeling.

A real large-scale neural modeling technique, which connects neural activity to PET data, was introduced by Arbib et al [6], and was applied to primate grasp control [7]. The key hypothesis to establish a synthetic PET is that counts acquired in PET scans are correlated with the synaptic activity within a region. Simulated PET activity was computed by integrating the absolute value of the total synaptic
activity over the time course of the study within the different areas. To model the saccade generation several regions, such as basal ganglia, frontal eye fields, posterior parietal cortex, visual cortex, and superior colliculus have been involved.

Recently (Fifth International Conference on Functional Mapping of the Human Brain, http://www.apnet.com/hbm99/methphyscog.htm) there is an increasing tendency both to improve the temporal resolution of the experimental devices, and to new techniques of the evaluation. Among others the use of nonlinear dynamics was demonstrated in the human brain using PET and transcranial magnetic stimulation [80]. Unstable cortical states are accompanied by increased rCBF in a well-defined, discrete set of areas. This may reflect increased synaptic activity due to increased network firing rate near the transition point. There seem to be methods to detect cortical instabilities (which may lead to neuropsychiatric disorders), and analyze them by the methods of dynamic system theory. To connect neural mechanisms to dynamic cognitive networks [56] is still a long way. There is a need for mesoscopic level neural simulations to bridge the gap between microscopic single cell activities and macroscopic brain states.

4.3.2. Statistical approach to large-scale and long-term neurodynamics
Just as collective phenomena emerging in physical systems made from large number of elementary components (spins, molecules, etc.) are treated by statistical mechanics, so, analogously, have statistical dynamic theories of neural populations been established [126, 1, 96], and [121, 122, 123]. Neuronal population theories established earlier have used oversimplified single-cell models. One important example is the lack of ability to generate bursts mode. Our kinetic population model [10, 61] has common principles with multicompartmental models in that both models are built from anatomical and physiological data on cell types, network connectivities, unitary synaptic functions. There is, however, a methodological difference between the two approaches. For two reasons, our model does not contain the details of single cell events (but benefits from the results of single cell modeling!). First, even if we believed that without very detailed biophysical description of single cell events the understanding of the functional organization of the whole hippocampus was impossible, we could neither find sufficient elementary data to build the model, nor the large-scale and long-term simulation could be done, even by supercomputers. Second, and more importantly, the statistical theory we apply is based on the hypothesis that the behavior of large neuron populations can most adequately be
described by the methods of statistical neurodynamics.

In this framework (i) the activity (different levels of subthreshold membrane potential/refractory state) distribution of groups of otherwise not distinguished neurons is considered, and the subpopulations of neurons communicate via packets of impulses (action potentials) which they can emit and absorb; (ii) neurons and impulses (action potentials) form two distinct populations. (iii) The neurons, both excitatory and inhibitory ones, occupy fixed positions in the space, and their state is characterized by probability density functions over two continuous variables: their membrane potential and internal calcium concentration. (iv) The impulses can move from the point of emission (a neuron) to the point of absorption (another neuron) either by homogeneous spreading (random connectivity) or along prespecified paths (specific connectivity), carrying a quantum of excitation or inhibition (depending on the character of the emitting neuron). The absorption of impulses by a neuron implies: (A) change of the membrane potential; (B) firing of the neuron with a probability determined by the value of the membrane potential; (C) emission of new impulses as a result of firing.

To have a statistical description of the system, a few distribution functions are defined: the expected number of (excitatory and inhibitory) impulses and neurons, also for neurons being in refractory state. To take into account the actual connectivity structure of the system, a set of absorption coefficients and emission coefficients are given. These values define the strength and efficacy of the excitatory and inhibitory effects at each point of the neural system. Further parameters incorporated into the model give the possibility to take into account other specific biological details such as impulse generation from external source, spontaneous decay of subthreshold excitation, refractory period, synaptic delay etc. To evaluate and to visualize the simulation experiments, some macroscopic variables are defined. These macroscopic variables are: the local density of impulses, the local mean net excitatory effect, and the local mean subthreshold excitation. Several normal epileptic activities, as synchronized population burst and synchronized synaptic potential (the analogue of SPW in slices) and the propagation of the stimulus have been simulated, while the behavior of an “averaged” single neuron was also shown [61, 10, 12, 13]. It is clear that simulations can be extended for describing activity propagation among several neural centers.
5. Conclusions

Dynamic system theory offers a conceptual and mathematical framework to analyze spatiotemporal neural phenomena occurring at different levels of organization, such as oscillatory and chaotic activity both in single neurons and in (often synchronized) neural networks, the self-organizing development and plasticity of ordered neural structures, and learning and memory phenomena associated with synaptic modification.

The basic principle of neural functions is stated to be its self-organizing character [112, 110]. The emergence of complexity by self-organizing mechanisms has been demonstrated both on ontogenetic and phylogenetic scale. According to embriological, anatomical and physiological studies, the wiring of neural networks is the result of the interplay of purely deterministic and random mechanisms. Fluctuations may operate as "organizing forces" in accordance with the theory of noise-induced transitions. Self-organizing developmental mechanisms (considered as "pattern formation by learning") are responsible for the formation and plastic behaviour of ordered neural structures.

It is often said in a colloquial sense that the brain is a prototype of complex system. [41]. Several different notions of complexity may be more formally related to neural systems. First, structural complexity appears (i) in the arborization of the nerve terminals at the single neuron level, (ii) in the complexity of the graph structure at the network level, and (iii) in the systems of networks forming closed loops of closed loops. Second, functional complexity is associated with the set of tasks performed by the neural system. Third, dynamic complexity can be identified with the different attractors of dynamic processes, such as point attractors, closed curves related to periodic orbits, and strange attractors expressing the presence of chaotic behaviour.

The notion of dynamical hypothesis appeared even in cognitive science [118] stating that cognitive agents are (i) dynamical systems, (ii) best understood scientifically as dynamical systems.

The understanding of neural organization requires the integration of structural, functional and dynamic approaches [4]). Structural studies investigate both the precise details of axonal and dendritic branching patterns of single neurons, and also global neural circuits of large brain regions. Functional approaches start from behavioural data and provide a (functional) decomposition of the system. Neurodynamic system
theory offers a conceptual and mathematical framework for formulating both structure-driven bottom-up and function-driven top-down models.

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