

Nonlinear Dynamics of the Rhythmical Activity of the Brain: Summary of the Thesis

In this Chapter, we present a brief survey of the main results exposed in this dissertation¹. We follow the order given in the previous Chapters and we refer to the same figures. We also assume that the reader is familiar with the techniques of linear stability analysis as well as neurophysiology.

Introduction

The first recording of the electrical activity of the brain is due to Caton [55] in 1875. By placing recording electrodes at the surface of the rabbit's cortex, he reported "weak currents which direction varies spontaneously". From the same experiment in simian's cortex he also observed *oscillations* of the current. It must be emphasized that the early recordings of brain activity are already accompanied by the description of rhythmical activity. In 1929, Berger publishes the first recording of the electrical activity at the level of the human scalp, which he calls electroencephalogram (EEG). He also notes that the EEG displays prominent oscillatory behavior, which may be subject to important changes during the various behavioral states.

The pioneering steps of researchers such as Du Bois Reymond, Hermann, Bernstein, led to the discovery of the cellular origin of this electrical activity in the neurons. These cells are characterized by a resting potential, which is maintained by differences in the concentration of ions, such as Na^+ , K^+ , between the intra- and extra-cellular space. Later, the remarkable work of Hodgkin, Huxley and Katz [137, 138, 139, 140] uncovered the mechanisms of neural excitability. They showed that the permeability of several ionic channels is voltage-dependent and that this property is sufficient to reproduce the excitable behavior of neurons.

They also provided a set of differential equations [141], which were deduced from simple kinetic considerations, and which parameters were fitted to experimental data. They succeeded to explain their experimental results using this set of equations. Many of the most recent advances in neural modeling are still based on the Hodgkin-Huxley formalism.

Today, the knowledge of the physiology of neurons has led to the understanding of

¹A full PDF copy of the thesis (in french) is available at <http://cns.iaf.cnrs-gif.fr>

many other phenomena at the cellular level. However, in spite of the large amount of “microscopic” data, our understanding of “macroscopic” brain phenomena, such as the collective rhythms, distributed neural activity or information, are still poorly understood. This suggests that the classical approach of neurophysiology might be inadequate for studying such phenomena.

The study of self-organized and collective phenomena was studied by Nicolis and Prigogine [223]. These authors described how in nature a collection of particles – or cells – interacting with simple laws could generate collective behavior, such as rhythms, spatial structurations, ... It appears that the presence of nonlinear interactions between the constituents of the system contributes to the emergence of such structured and coherent behavior. These considerations have been applied to many biological fields such as morphogenesis [18, 285] or biochemical systems [114].

In parallel to the apparition of the concept of self-organization, a new branch of physical sciences has emerged these last decades, aiming at the description of the various dynamical phenomena in natural as well as mathematical systems. This so-called “nonlinear physics”, “theory of dynamical systems”, or more commonly “nonlinear dynamics”, bases its description of dynamical phenomena on differential equations and partial differential equations. The solutions of these equations are classified into stationary states, limit cycle oscillations, chaotic dynamics, ... The basis of the stability of these solutions was introduced through notions of a geometrical character. In particular, the *phase space* is a compact representation where each axis is spanned by an independent variable of the system. In this space, each point constitutes a possible state for the system and if a subset of points is stable, we call it an *attractor*. Among many attractors, let us recall that a stationary state will appear as a single point, called *fixed point*; a periodic oscillatory state will be represented by a closed curve, called a *limit cycle*; etc (cfr. refs. [37, 126, 258]).

One of the successes of this type of formalism was to establish an appropriate framework for the description of chaotic or weakly turbulent phenomena. Physicists and mathematicians, such as Smale, Landau and Lifshitz, Lorenz, Ruelle and Takens, have studied a particular class of systems which presents an internal instability, and they finally introduced the concept of *deterministic chaos*. Although they were first conceived as models for weak turbulence, chaotic systems were rapidly extended to many fields.

In parallel to the development of this theory, methods appeared to estimate key dynamical parameters from experimental time series. This constitutes a very important step for the nonlinear sciences, as these methods have allowed to verify experimentally the predictions of theoreticians [1]. In particular, these methods allows us to characterize the dynamics of complex systems by analyzing experimental data recorded as a series of measurements in time of a relevant and easily accessible variable of the system.

The object of this thesis is to describe the different types of rhythmical activity of the brain in the framework of nonlinear dynamics. In a first part, the Chapter 2 describes the different methods used in Chapter 3 to analyze various EEG rhythms in the framework of nonlinear dynamics. In a second part, we introduce a model of the brain rhythmical activity. In Chapter 4, we present a simple model which considers the main cellular types of the cerebral cortex. The stability of stationary and periodic solutions is described. In Chapter 5, the interaction between this model and a thalamic oscillator is considered. The model is then analyzed using the methods from nonlinear dynamics. Finally, in Chapter 6,

we introduce a model of the various rhythms at the level of the thalamus, as well as their control by the brain stem.

Methods of nonlinear dynamics

In Chapter 2, we give a brief overview of the different techniques of nonlinear dynamics used for analyzing a time series. This time series may be obtained either from an experimental measurement or from computer simulations of differential equations.

In Section 2.1, we describe the various techniques used for the reconstruction of phase portraits from a time series. The technique of singular value decomposition is also briefly introduced and its application to the construction of noiseless phase portraits is emphasized.

We discuss the concept of self-similarity and fractal dimension in Section 2.2. Different definitions of the dimension, such as the Hausdorff dimension, the correlation dimension, the generalized dimensions, the semilocal dimension and the topological dimension are reviewed here. We discuss how the fractal dimension may be used to characterize a chaotic signal and how the concept of determining the dimension from a time series may be helpful to quantify a complex signal and possibly identify the presence of deterministic chaos. The requirements of these algorithms concerning the length and the stationarity of the time series are also discussed.

In Section 2.3, the algorithms for estimating the Lyapunov exponents are presented. We discuss how the concept of sensitivity to initial conditions may be used to characterize a time series and to identify a chaotic system.

The Section 2.4 is devoted to the application of symbolic dynamics in chaotic systems. We introduce a method to obtain a symbolic sequence from a time series and to evaluate the order of the Markov process associated with this sequence. This information is also useful to characterize the dynamical complexity of the system.

Other methods such as autocorrelation and crosscorrelation functions, mutual information and Fourier transforms are presented in the last section of this Chapter.

Nonlinear dynamics of the EEG

The characterization of different types of rhythmical activity using human EEG recordings constitutes the aim of the Chapter 3. The various methods from nonlinear dynamics are applied to EEG signals in order to evaluate whether they can be described in the framework of nonlinear dynamics. The methods introduced in Chapter 2 are applied here to the EEG during various behavioral states and the reliability of the algorithms as well as the biological relevance of the results are discussed.

In Section 3.1, we describe the recording and digitalization techniques used for assessing EEG data.

In Section 3.2, we show EEG recordings obtained during the various stages of sleep, the awake state as well as during pathologies. It is seen that although indisputable periodicities appear in some of these recordings, the EEG is generally characterized by an

aperiodic time evolution.

The main results of Chapter 3 appear in Section 3.3. The methods described in Chapter 2 are applied to the various EEG signals and a particular importance is given to the verification of the reliability of these algorithms, as well as the role of the different parameters. The values obtained by different laboratories are compared to our results.

The power spectrum is currently used to quantify the EEG [47]. In Section 3.3.1, we show that for an “awake eyes open” EEG, the spectral structure of the EEG is indistinguishable from that of a stochastic process. On the other hand, for some stages, important peaks emerge from a continuous background. We evaluate this structuration of the power spectrum by measuring the spectral range of the various EEG rhythms. It appears that the spectral range of awake eyes open or REM sleep is very broad, and becomes more and more restricted to a few peaks as the level of arousal decreases (successively: awake eyes closed, sleep stage II, sleep stage IV). For pathologies, the EEG activity is restricted to very few peaks.

The reconstruction of the phase portraits show similarities between the different procedures used (Section 3.3.3) and the singular value decomposition technique (Section 3.3.4) provides smoother trajectories. An obvious structure emerges from these phase portraits during some typical rhythmical activity, such as the alpha rhythm (awake eyes closed), or during pathologies.

In Section 3.3.5, we describe the evaluation of the correlation dimension from the different EEG rhythms. We show that, provided sufficient care is taken concerning the choice of the parameters of the method, reproducible results can be obtained. The apparent discrepancy between the results of different authors can be attributed to an underestimation of the dimension when using time series of a limited number of points (cfr. Fig. 3.18). However, the inherent error of this method leads us to consider that only the relative values between different behavioral states are meaningful. From a set of EEG signals of different individuals, we observe that, as the level of arousal of the brain decreases, the dimension also decreases, attaining values close to 4 for the deep sleep (stage IV). The dimension attains the lowest values for pathologies, which are the closest to periodic phenomena.

The evaluation of the topological dimension (Section 3.3.6) reveals that, for some pathological EEG, the dimension may take values which depend on the specific region considered on the attractor. The evaluation of the semilocal correlation dimension (Section 3.3.7) shows that these EEG attractors may be decomposed into several regions, which corresponds to specific events in the signal, such as spike, waves, ... In this case, the semilocal correlation dimension gives an estimate of the temporal coherence of these specific events. The relatively low semilocal dimension of the EEG spikes suggests that they constitute a sub-dynamical system which temporal coherence is higher than the remaining parts of the system.

In Section 3.3.8, we transform the dynamics of interspike intervals of the EEG into a sequence of symbols. The evaluation of the order of the associated Markov process shows that this sequence is far from being random. The successive EEG spikes are therefore not produced randomly but seem to obey unknown, but well-defined dynamical laws.

Another characteristic feature of chaotic systems is the sensitivity to initial conditions. As illustrated in Section 3.3.9, this sensitivity is also found in EEG attractors. The spectrum of Lyapunov exponents was evaluated by Gallez and Babloyantz [106] and provides

a quantification of this property. The positive exponents found confirms the chaotic nature of the EEG. Moreover, they could evaluate the Lyapunov dimension which confirms the values of the correlation dimension.

As a conclusion to this Chapter we formulate the following remarks:

1. The algorithms from nonlinear dynamics suffer from a relatively high sensitivity to the parameters if they are badly chosen. We show that, when applied to sufficiently long and stationary time series, these methods provide reproducible results. The discrepancies in the literature originate from the use of too small data sets [23]. However, the intrinsic variability of the values obtained by these methods leads us to consider the results published with great care. We think that our results are meaningful only when comparing the relative values obtained in different states.
2. EEG signals appear extremely complex and aperiodic, but for appropriate recording conditions, these signals are assimilable to stationary processes [20]. The dynamical nature of the EEG appears when treating the latter as a time series. The values of the correlation dimension [22, 23, 25, 28, 30, 84] of the Lyapunov exponents [106], the broad band spectra [25], the vanishing autocorrelation, as well as symbolic dynamics [78] constitute serious indications for the presence of deterministic chaos during some stages of the EEG. In the case of the Creutzfeldt-Jakob (CJ) disease, the signal is stationary and each of the above-mentioned methods could be applied successfully [28].
3. These techniques allow to classify the EEG rhythms along the criteria of nonlinear dynamics. A hierarchy of states emerges from this analysis [25]. Following the decreasing level of arousal, one considers successively the following states: awake eyes open, REM Sleep, awake eyes closed, sleep stage II, sleep stage IV and pathological states. We observe that, as the level of arousal decreases, the correlation dimension, therefore the temporal coherence of the EEG, also decreases while prominent peaks progressively emerge from the power spectrum. Following the same hierarchy, the EEG becomes closer to limit cycle oscillations, its main frequency decreases and its amplitude increases. The sleep stage IV represents the highest degree of temporal coherence of a normal brain, with the lowest correlation dimension, the highest amplitude and the lowest mean frequency. Epileptic petit-mal seizures show similar properties as the CJ disease.
4. An important property is suggested by these results. If one assumes that the EEG amplitude is a good measure of the synchronization between cortical neurons², then the nonlinear dynamical analysis provides evidences that the increase of synchronization between neurons as the level of arousal decreases is also accompanied by an increase of the coherence. This indicates that when the cortical neurons augment their tendency to fire in synchrony, they also tend to oscillate more regularly.

During the following part of this work, we consider these results as a constraint for model construction. We propose a model of cortical and thalamic oscillatory activity,

²experimental evidences of this assumption are given in Section 5.1.1

which intend to explain the origin of the regulation of the coherence of the global activity of the brain.

Stability analysis of a cortical neural network

In Chapter 4, we describe the collective dynamics in a model of the cerebral cortex. In Section 4.1, we introduce a two dimensional network of excitatory and inhibitory neurons. The equations describing each individual neuron are based on the electrical analogue of the membrane. The connectivity extends to the proximate cells and the proportion of inhibitory and excitatory cells mimics that of the cerebral cortex. However, the connectivity patterns are identical for each neuron (uniform connectivity), therefore the equations remains relatively simple and allow mathematical treatment.

The uniform solutions constitute the basis of our analysis. We show that uniform solutions are the solutions of a reduced system of two neurons with self- and inter-connections (Section 4.2). We calculate the fixed points of this system and evaluate their stability using linear stability analysis techniques applied to delay equations. We determine the conditions of occurrence of periodic oscillations, which arises from a Hopf bifurcation and disappear following a homoclinic bifurcation.

The stability of the fixed points of the network is considered in Section 4.3. By the use of Fourier transforms and from the evaluation of the stability frontier of the system, we can predict the stability of the uniform resting steady state of the network, as a function of size and connectivity. We show that destabilization occurs for the less densely connected systems and for the largest sizes. Moreover, the stability of the fixed points in the network is the same as that of the reduced system of two neurons.

When destabilization of the uniform steady state occurs, the network may show spatially uniform oscillatory solutions (synchronized or “bulk” oscillations). In Section 4.4, we introduce a method for calculating the stability of the bulk oscillations. We show that for sufficiently large networks, bulk oscillations may be unstable.

For networks where the steady-state solutions and bulk oscillations are both unstable, the system may show spatiotemporally non uniform solutions. In Section 4.5, we use numerical simulations to analyze this type of dynamics. The simulations confirm the results of the stability analysis described above. For networks of large number of neurons with local connectivity, spatiotemporal chaos may appear. This type of dynamics occurs spontaneously for a large range of parameters. Several properties also suggest that the apparition of spatiotemporal chaos might be related to homoclinic phenomena.

The properties of spatiotemporal chaos are described in Section 4.6. We show that, analogously to hydrodynamic turbulence, “neuronal turbulence” is characterized by a loss of spatial correlations, at least one positive Lyapunov exponent and an increase of the transport properties.

As a conclusion, we stress the following points:

1. The stability analysis of the uniform steady state of the network shows that the fixed points and their stability properties are the same as that of the reduced system of two neurons. These results can be applied to other systems as well.

2. The stability analysis also shows that the apparition of oscillations in networks of excitatory and inhibitory cells is due here to the interaction between excitatory and inhibitory synaptic connections. To observe oscillations, the presence of both excitation and inhibition is a necessary condition but also, important synaptic weights are required.
3. For locally-connected networks of a large number of neurons, bulk oscillations becomes unstable and spatiotemporal chaos may appear. It should be emphasized that this type of “turbulent” behavior appears spontaneously in a system where there is no spatial inhomogeneity.
4. The bifurcation diagram of the network shows a structure very similar to the reduced system of two neurons (Fig. 4.35). This property greatly facilitates the search for oscillatory solutions in the network, because they always appear in the same range of parameters as in the reduced system.

Spatiotemporal chaos appears as one of the most representative type of spontaneous dynamics in networks of a large number of neurons. In the remaining part of this work, we will assume that spatiotemporal chaos constitutes the spontaneous state of the cerebral cortex. This state will be referred as “desynchronized”.

Synchronization of cortical neurons

In Chapter 5, we describe the properties of synchronization in a network of cortical neurons submitted to a periodic input. Such a system represents the thalamo-cortical interaction during the various behavioral states. As described in Section 5.1, we assume that the various rhythms of the cortex are the result of oscillatory activity in the thalamus, which is communicated to the cortex via thalamo-cortical connections. The experimental basis of this model are discussed in Section 5.1.1.

The cortex is represented by the model described in Chapter 4 and the two-variable model of Rose and Hindmarsh [250] is used as the thalamic oscillator. Field potentials are calculated from the network according to the formalism of Nunez [227].

The properties of the synchronization of the network are described in Section 5.2. Before the onset of the oscillator, the network displays desynchronized type of behavior. As the thalamic oscillation sets in, although a small minority of cortical neurons have been chosen to receive connections from the thalamic oscillator, the vast majority of the cortical neurons may be entrained into coherent behavior.

In a first step, we describe the spatial properties of the synchronization for two basic frequencies of the thalamic oscillator (Section 5.2.1). Snapshots of the system indicate that during synchronization, the activity of the network “pulses” between depolarized and hyperpolarized states at a frequency close to the thalamic frequency. However, although the system shows an obvious increase of spatial coherence compared to the desynchronized state, the activity patterns still remain chaotic.

From the comparison of the two different thalamic frequencies with cross-correlation functions, a remarkable property appears. The slowest oscillations seem to induce synchronized activity which is spatially the most coherent.

The temporal properties of this system are described in Section 5.2.2. In this case, we use the average membrane potential and the field potentials, which both represent a global activity of the network. Taken as a function of time, these variables may be considered as time series and the methods of Chapter 2 can be used. The average potential and the field potentials indicates an aperiodic activity with some periodicities. The higher amplitude for the slow thalamic oscillations indicates that the degree of synchronization is higher. The evaluation of the correlation dimension and of the Lyapunov exponents indicates that these aperiodic activity stem from deterministic chaos. Moreover, the dimension is lower for the slow rhythm.

In Section 5.2.3, we investigate the role of the thalamic frequency on the coherence of the collective oscillations in the cortex. The correlation dimension is evaluated for thalamic oscillations of various frequencies. We show that the dimension increases approximately linearly with the thalamic frequency.

Field potentials of the network are compared to the EEG in Section 5.2.4. We show that at the onset of the thalamic oscillator large amplitude oscillations appear, in a manner similar to the onset of synchronized rhythms in the EEG.

As a conclusion to this Chapter, we discuss the following points:

1. The model presented here considers the collective rhythms in a network representing the cerebral cortex. Two main hypotheses constitute the basis of this model. First, we assume the cortical rhythms depend on the presence of a periodic input from the thalamus. Although experimental evidence [271] suggests a participation of the cortex as the generator of some of these rhythms, numerous evidences indicate an essential role for the thalamus [272]. Second, we assume the spontaneous dynamics of the cortex is desynchronized in the absence of the thalamic oscillator.
2. As thalamic oscillations set in, the cortical activity is entrained into more coherent behavior [79]. Although cortical neurons are more phase-locked, the global activity has the properties of spatiotemporal chaos. The average activity of the system shows deterministic chaos of rather low dimensionality. Therefore, the periodic activity communicated by the thalamus to the cortex seems to increase the spatiotemporal coherence but the system remains chaotic.
3. The frequency of the thalamic oscillations appears as an essential element in the control of the spatiotemporal coherence of cortical activity [80]. The slower rhythms induce greater spatial coherence in the electrical activity of cortical neurons. The correlation dimension, which measures the temporal coherence of the system, is shown to increase linearly with the frequency of the thalamic oscillator.
4. As for EEG recordings (see Chapter 6), the evaluation of the correlation dimension, the spectral range and the amplitude of the field potentials allows to establish a classification of the different rhythmical states of the model [80]. It appears that in the absence of pacemaker activity, the system is of low amplitude and of high dimension. These properties resemble to those of the beta rhythm or REM sleep. In the presence of the pacemaker, the model show oscillations of various amplitude. These

properties are similar to those of the alpha rhythm. For slow pacemaker oscillations, the amplitude is higher, the spectral range smaller, and the dimension is the lowest. These properties have been encountered before for the delta waves (sleep stage IV). However, although it is clear that EEG rhythm are more complex than the rhythms of this simple model, there exists clear dynamical analogies between this model and the real networks of neurons.

5. A more serious question arise about the nature of EEG itself. Although EEG stems from the electrical activity of a very large number of spatially distributed and interconnected neurons, the exact relationship between this global activity and the cellular events is not yet completely elucidated. Therefore the nature of the dynamics assessed from the EEG, although related to the cortical events, does not say much about the exact nature of distributed activities at the cellular level. Granted that the underlying dynamics of the EEG is governed by deterministic chaos, it is important to understand the meaning of this finding at the cortical level. From a dynamical point of view, it is tempting to suggest that the various behavioral states of the human cortex follows dynamics similar to the one depicted in our model. Thus the temporal chaos seen from time series analysis could be the manifestation of spatiotemporal-like chaotic activity at the cortical level. Low dimensional chaotic attractors would then arise when larger and larger patches of neuronal population synchronize for longer and longer times.

We must keep in mind that the main parameter of this model is the frequency of thalamic oscillations. The thalamus is considered here as a simple oscillator. A more satisfying model of the thalamo-cortical interaction necessitates a more elaborate model of the cerebral cortex and of the thalamus which takes into account the reticular activating system. The dynamics of the thalamic oscillations is more specifically described in Chapter 6.

Oscillatory modes of the thalamus

In Chapter 6, we focus on the oscillatory properties of the thalamus. Contrary to the other Chapters, where the main approach was to assess the collective properties of neural systems, we consider here the intrinsic properties of thalamocortical (TC) neurons, briefly reviewed in Section 6.1.

Several models of the oscillatory behavior of thalamocortical (TC) neurons are introduced and are based on recently published voltage-clamp data of intrinsic ionic conductances. A Hodgkin-Huxley-type kinetic scheme is used for the low-threshold Ca^{2+} current I_T , the anomalous rectifier I_h , the various voltage-dependent K^+ currents designated globally as I_M , and the Ca^{2+} -dependent K^+ current $I_{K[Ca]}$. Some simulations are performed in the presence of the fast Na^+ - K^+ -mediated action potentials. The kinetic models for these currents are described in Section 6.2.

In Section 6.3, we describe the various types of oscillatory properties of this model of TC neurons. The combination of the various currents is considered step by step and the properties are compared to experimental data. The main results can be summarized as follows:

1. The association of I_T with the leakage current gives to the TC cell the ability to generate a low-threshold spike in response to the release from inhibition. These two currents may account for the two modes of firing of TC cells: burst firing and repetitive firing (Section 6.3.1).
2. The combination of I_T with I_h and the leakage current produces spontaneous oscillations of the membrane potential. These so-called pacemaker oscillations possess voltage-dependent properties very close to those seen from TC neurons. Moreover, the simulation shows that the oscillatory process is mainly generated by the activation variables of I_T (Section 6.3.2).
3. For slower time constants, the interaction of the same currents leads to the production of spindle-like oscillations. These oscillations are based on the coexistence between a stable stationary state and limit cycle oscillations. However, the properties of these oscillations does not match experimental data (Section 6.3.3).
4. Addition of I_M gives rise to spindle-like oscillations in a range of parameter values compatible with experimental data. The voltage-dependence of these oscillations agree well with experimental data. Moreover, blockage of the noninactivating K^+ current transforms the spindle-like oscillations into pacemaker oscillations. This constitutes a testable prediction of the model (Section 6.3.4).
5. The mechanisms of the spindle-like oscillations are investigated by treating I_h activation as a parameter. We have found that a subcritical Hopf bifurcation underlies the alternance between silent periods and oscillatory periods, which characterizes the spindle sequence (Section 6.3.4).
6. The same type of oscillations are observed if I_M is substituted by the Ca^{2+} -dependent K^+ current $I_{K[Ca]}$. Pacemaker and spindle-like oscillations have very similar properties in the presence of this current (Section 6.3.5).
7. The transition between these oscillating states can be achieved by modulation of I_h . In this case, for increasing I_h strength, the cell is shown to be either in a hyperpolarized resting state, in an oscillating state, show spindle-like oscillations or enter into a depolarized resting state. The mechanism of the coexistence between these states is investigated using (Section 6.3.6).

After this investigation of the properties of single thalamic neurons, we introduce in Section 6.4 a model of the thalamic reticular (RE) nucleus on the basis of the intrinsic properties described Section 6.3. However, as RE neurons appears electrophysiologically close to TC cells, we describe these cells by a formalism involving the two currents I_T and I_h . These RE neurons are incorporated into a network with local inhibitory connections, which mimics that of the RE nucleus [272].

The properties of such a network are those of a multi-frequency pacemaker. First, spatiotemporally coherent oscillatory activity can be obtained in this system. The oscillations are of a frequency comparable to that of the isolated cell. Second, for increasing values of

\bar{g}_h , rhythms of increasing frequency can be observed in the network. For too small or too high values of \bar{g}_h , the system shows a resting state.

In conclusion, we investigate the dynamical properties of TC cells by a combination of numerical and dynamical analysis. The various currents I_T , I_h , and an outward current which may be either I_M or $I_{K[Ca]}$, are responsible for the coexistence between several oscillatory states. By treating the slow current I_h as a parameter, we show the dynamical basis of these oscillatory states. This allows to suggest the following role for each current [82].

1. The low-threshold calcium current, I_T , has been shown to be responsible to burst firing. The same current also appears to have a determinant role in the production of pacemaker oscillations.
2. The anomalous rectifier I_h contributes to the genesis of pacemaker oscillations and to spindle-like oscillations.
3. A depolarization-activated slow outward current, which might be muscarinic, Ca^{2+} -dependent ($I_{K[Ca]}$), or any other type of noninactivating potassium current, allows I_h to participate actively in the generation of spindle-like oscillations.
4. I_h has also a determinant role in the control of the type of oscillatory state of the TC cell by the brain stem. For increasing I_h strength, the model show the TC neuron is either in a hyperpolarized resting state, in an oscillating state, exhibit spindle-like oscillations or enter into a depolarized resting state.
5. Our simulations also show that decreasing the depolarization-activated slow outward current may transform spindle-like oscillations into pacemaker oscillations. If this prediction reveals to be correct, it gives a second potential pathway for the control of the state of thalamic neurons.
6. The model of the RE nucleus indicates that from a network based on neurons which possess the two currents I_T and I_h , various types of collective oscillatory behavior can be observed [81]. The most important property of this system is the remarkably efficient control of these oscillatory states by the modulation of a single conductance, \bar{g}_h . Modulating this parameter entrains transitions between resting states (“re-lay”), slow oscillations or fast oscillations. In TC cells, this parameter was shown to be under the influence of brain stem afferents [213]. If the presence of this current is confirmed in RE cells, our model shows that the brain stem possesses, via I_h , a simple and efficient way to control thalamic rhythms.

Conclusions

We give here a brief summary of the conclusions outlined in Chapter 7. We discuss first the approach used through this study. Then, we compare the results obtained in the model to the properties of the EEG. Finally, we give a summary of the biological and physiological implications of our results as well as their relation with current hypotheses.

Approach used

In this study, we have used recent methods from nonlinear dynamics to analyze and quantify the various rhythmical activity of the EEG and of a model of thalamo-cortical interactions. These methods give access to the phase space of an experimental system and this provided a quantitative ground for the comparison between model and experimental data. The apparition of these methods constitutes therefore an event of a considerable importance for the construction and analysis of models.

We have always put emphasis to ensure the stability of our results by using numerous values of the parameters. Different schemes of connectivity were used in the model of the cortex, and different kinetic schemes were taken for modeling thalamic currents.

Granted the great variability which usually characterizes biological systems, the parameters and the feedback or activation functions estimated from experiments may be subject to several different interpretations. Therefore, it is of great importance to prove that a given model is not sensitive to the particular choice of these functions and parameters. If the solutions are still observed from small changes in the structure of the equations, then these solutions are *structurally stable* [126]. This important property is sometimes neglected in the modeling approach in biology. Presenting so-called “computer models” without taking care of the structural stability of the results is of poor value.

In addition to structural stability, which concerns the stability of the solutions in the framework of a specific model, it is essential to ensure the validity of the model in the biological context. An efficient mean is to search for predictions which could be tested experimentally. This approach constitutes the basis of the development of most of the areas in physical sciences, which have progressed through the interaction between experimentalist’s observations and theoretician’s predictions. Granted the important development of biological modeling studies, we could assist to a similar scenario in neurophysiology in the next decades.

Comparison between the model and EEG data

During some behavioral states, the EEG seems to obey chaotic dynamics of rather low dimension. It is remarkable to observe that very few degrees of freedom characterize a signal generated by millions of variables. We note here that the same property is observed in the model. Some 500 differential equations also give rise to low dimensional chaos. This property might be due to the process of averaging.

The comparison between the nonlinear properties of EEG signals shows that their temporal coherence seems to be related to the level of arousal of the brain. The synchronization of neurons is therefore accompanied by the apparition of more periodic activity. This property is also encountered in the model, where we show that the most synchronized states corresponds to spatiotemporal chaos with a more regular and low dimensional activity.

The physiological role of chaos was investigated by many authors. We consider here chaos as an observable property of the collective activity of the brain and we use this property as a constraint to model construction. From the model, we could show a similar hierarchy of rhythmical states as that observed from EEG analysis: desynchronized states are of low amplitude and are high dimensional. The synchronized rhythms are character-

ized by periodicities in the average activity and by a low dimension. The slow rhythms appear as the lowest dimensional, while the amplitude of the field potentials is the highest.

Physiological role of the thalamocortical rhythms

At the cellular level, the origin of the rhythmical activity may be twofold. First, oscillations may arise from the interaction between excitatory and inhibitory processes, such as in our model of the cortex. Second, rhythmical activity may appear following the interplay of voltage-dependent conductances, such as in TC cells. In this case, oscillations are an intrinsic property of the neuron.

Still at the cellular level, we could show that the modulation of a single conductance is sufficient to control the spectrum of oscillatory states of the thalamic neurons. The same conductance also appears to control the *frequency* of oscillatory states in a network of thalamic reticular neurons. As this conductance is known to be regulated by brain stem afferents, this property allows the control of the oscillatory state of the thalamus by a simple and efficient way.

This modulation of the frequency of the thalamus by the brain stem may serve as the basis of the control of the different rhythmical activities of the brain during the various behavioral states. As suggested by our model, the frequency of the external pacemaker (thalamus) seems to have a determinant role in regulating spatiotemporal coherence at the cortical level. Since the model of the thalamic reticular nucleus suggests that the pacemaker frequency can be regulated by brain stem afferents, these two models put together give a possible scenario for the control of cortical coherence by a single parameter.

The coherence of collective oscillations may play an important physiological role. As suggested by Buzsaki [54], highly synchronized activity might be involved in the reinforcement of synaptic weights in the hippocampus. If this scheme also holds for the entire cerebral cortex, then the slow synchronized rhythms, such as delta waves, could provide the basis of the stabilization of information acquired during the awake state.

Addendum

The thesis was successfully defended on March 13 (private defense) and March 20 (public defense), 1992. The members of the Jury were Agnès Babloyantz, Yves Burnod (invited member), Jacques Demongeot (invited member), Jean-Louis Deneubourg, Grégoire Nicolis, and Ilya Prigogine. The grade was “*La Plus Grande Distinction avec Félicitations du Jury*” (Greatest Distinction with Congratulations of the Jury).

A copy of the full thesis (written in French) is available at <http://cns.iaf.cnrs-gif.fr>

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Bibliographie

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