Frustrated Chaos in Biological Networks

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Summary

The behaviour of three biologically inspired networks is investigated: Immune Idiotypic Network (IIN), Hopfield Network (HN) and Coupled Map Lattice (CML), mainly the effect on the dynamics induced by connecting the network in a frustrated way. Frustration occurs when the global structure is such that local connectivity patterns responsible for stable behaviour are intertwined, leading to mutually competing attractors and chaotic itinerancy among brief appearance of these attractors. Frustration un-stabilizes the network and provokes an unpredictable "wavering" among the stable dynamic regimes which characterize the same network when it is interconnected in a non-frustrated way. As the main contribution of this paper, an immune idiotypic network in which the prevailing behaviour is oscillatory is studied in details. It is shown how connecting an elementary three-clone network in a frustrating way transforms the oscillatory regime into a chaotic one. This chaotic regime is further analysed and several interesting aspects are discussed such as the variable homogeneity, the intrinsic chaotic itinerancy among brief oscillatory regimes and the strong unpredictability. In addition, dynamical regimes obtained by frustrating the connectivity of HN and CML are presented and the similarities as well as the differences with the INN dynamics are emphasized. Common to all these networks is the description of the frustrated chaos as a succession of attempts to relax the network into one of the oscillatory regimes given by a weaker and non-frustrated connectivity, an impossible achievement making the dynamics rambling over brief but repelling orbits.

1. INTRODUCTION

Suppose a generic biological network of N connected Boolean units which can be in either one of two states. Suppose that the network is further constrained such that two units being connected means that the unit 1 in one state can only co-exist with the unit 2 in the anti-state (i.e. the two units are connected in an inhibitory way). A 2-unit network can only settle in two possible configurations. Now take a 3-unit network and connect the units in an open chain fashion: the unit 1 is connected only to the unit 2 which in turn is connected only to the unit 3. There again two configurations are possible with the 1-2 couple as well as the 2-3 couple containing two units settled in reverse states. Each couple per se complies with the local effect of the connection: the state/anti-state pair.

As shown in fig.1, the problem gains interest by closing the chain i.e. connecting the unit 3 back to the unit 1. We now have three couples: 1-2, 2-3 and 1-3 which must each independently complies with the imposed constraint: the state/anti-state pair. As a matter of fact no global configuration turns out to be possible: the couples mutually compete for reaching their state/anti-state configuration. Expressed in a different way, there are three possible stable configurations: “1 in state-opposition with 2 and 3”, “2 in state-opposition with 1 and 3” and “3 in state-opposition with 1 and 2” which compete for “taking possession” of the network. Looking at the Moebius triangle in fig.2 you’ll observe a very similar type of impossible global configuration despite three possible local coupling. In the modeling of spin glasses, this well-known phenomenon has been originally designated by the term “frustration” (Toulouse, 1977). The presence of loop containing an odd number of inhibitory bounds is responsible for preventing spin glasses from relaxing to their minimal energy level, and thus for enlarging the set of higher energy levels, intermediary and less stable, among which the network can choose to relax.

<INSERT FIGURE 1>

<INSERT FIGURE 2>

The effect of frustration has been detected and analysed in different types of biological networks: Boolean net (Thomas, 1991), Hopfield net with fixed point dynamics and with oscillatory dynamics (Amit, 1989; Atiya & Baldi, 1989; Hirch, 1987; Marcus & Westervelt, 1987; Sherrington, 1990) and network of oscillators (Daido, 1992; Omata & Yamaguchi, 1988). The dynamical sensivity to this structural aspect seems to be ubiquitous in biologically-grounded networks of ordinary differential equations. In some cases the presence of frustration has been positively assessed as enlarging the repertoire of equilibrium configurations (Amit, 1989; Sherrington, 1990) while in some others the same phenomenon has been perceived as something to prevent due to the instability it induces in the network.

On the whole the responsibility of loops with an odd number of inhibitory links for bringing forth instability in systems with desired homeostatic properties is nothing new but so far this instability has always been restricted to the appearance of oscillation (which can be seen as another type of stable regime) in homeostatic systems. This paper will address the next qualitative jump: no longer how frustration un-stabilizes a fixed point attractor to give oscillation, but rather what happens when the system to be frustrated presents an inherent oscillatory dynamics. If the frustrated network dynamical regime always increments its degree of complexity with respect to the non-frustrated one: from monostability to bistability (Omata & Yamaguchi, 1988), from fixed point to oscillations, the presence of chaos is likely to be the natural consequence of frustrating an oscillatory network. This is indeed what is observed in the simulation of an idiotypic immune network (described in the next section) in which the dynamics of a couple of units is naturally oscillatory, with the first unit oscillating in counterphase with the second one. Here again there is no difficulty to anticipate the global behaviour of a network composed of three units interconnected in an open chain (1<-->2<-->3). Unit 1 and unit 3 will oscillate together both in counterphase with unit 2. Even if the three units are interchangeable in principle, the fact of not having the same local connectivity i.e. only unit 2 has two connections, makes immediate their differentiation in the dynamical behaviour.

Now frustrate the system just as before and close the chain by looping back unit 3 to unit 1 (1<-->2<-->3<-->1). What is the resulting dynamics? In the computer simulations, the very regular oscillations observed in the open chain situation are substituted by a strongly erratic dynamics where any periodicity has disappeared. The network behaves as if "aiming" to match the open chain situation but with the two units association characterizing the regular behavior of the open chain continuously changing in a seemingly random way the units it is composed of. Although a simple observation of the simulations indicates the attraction effect exerted by the oscillatory regime i.e. the system is wandering in an erratic way around all the possible configurations giving oscillatory regimes, no periodic behaviour similar to the open chain case can be sustained for more than one or two cycles.

The next section will present an analysis of this dynamics in order to conclude on the chaotic nature of the regime. Besides original aspects of this chaos will be further investigated by means of a power spectrum analysis and first return maps, but also by a symbolic dynamics analysis. We believe this frustrated chaos to be more appropriately characterized by an unpredictable wavering among brief appearance of repelling orbits. Although such a characterisation of chaotic regimes is rather classical (Grebogi et al., 1988; Lathrop & Kostelich, 1989; Kaneko, 1994), the originality here lies in the identification of these orbits as the stable regimes of the “non-frustrated” network. Still a matter for conjecture, the unpredictability might be a direct consequence of the fractal nature of the basins of attractions of the cyclic regimes around which the system wanders. In section 3 and 4, two related dynamics respectively obtained in Coupled Map Lattice and Hopfield networks will be presented and discussed in a more sketchy way. Although these dynamics are likely to be obtained by means of some form of frustrated connectivity, in both cases the phenomenon is less salient, less “pure” and eventually less easy to characterize.

2. FRUSTRATED CHAOS IN IDIOTYPIC IMMUNE NETWORK

The possibility that frustration turns an homeostatic idiotypic network into an oscillatory one was already observed with circumspection by Hiernaux (1977). He believed that this remarkable sensitivity of the dynamics of the network to its connectivity ought to make questionable the idiotypic network structure of the immune system, another negative perception of the frustration effect. In this section, the next qualitative transition will be investigated: from oscillations to chaos. The system of coupled ODE’s showing this interesting frustration induced phenomenon was originally meant to study the dynamics of one particular IIN first proposed by Varela et al. (1988), Stewart and Varela (1990) and largely studied and described in the literature (Bersini & Calenbuhr, 1995; De Boer & Perelson, 1991; De Boer et al., 1993; Perelson, 1990; Stewart & Varela, 1990; Varela et al., 1988; Varela & Coutinho, 1991).

The interest for the dynamical behaviour of the IIN arose from the observation that the concentration of natural antibodies displays fluctuation patterns that are believed to be related to the connectivity of the immune cells instead of the result of encounters with external antigens. Moreover these antibodies in normal and auto-immune individuals have been shown to fluctuate in a different way, and this might hypothetically suggest to relate these two states with different structures of connectivity and to explain the disease by a structural alteration. Up to date, the most interesting dynamical pattern exhibited by the network simulations is an oscillatory regime (some of the fluctuation patterns observed in biological experimental data have in fact a strong oscillatory tendency (Varela & Coutinho, 1991)) in which the units always split into two groups oscillating in counterphase. As a consequence, this type of network turns out to be susceptible to a frustration phenomenon that we indeed observed in the presence of odd loops.

Since among all biological networks the idiotypic network must be one of the less familiar and also because the remaining part of the paper concerns more original work, its modeling deserves to be described into sufficient details (a much more detailed description can be found in (Calenburh et al., 1996). The IIN model under study contains n units (i=1..n) (such an unit is often called a clone in the immune literature). In contrast with other more familiar biological structures like neural networks, a unit is representative of two different immune cells: the antibody f_i and its associate producer the B lymphocyte b_i. On account of the very high specificity of B lymphocytes which only produce antibodies sharing this same specificity, an unique index i serves as reference mark to one type of antibody and its B lymphocyte associate producer. For each clone i, the system of ODE's accounts for B lymphocyte proliferation and maturation, antibody production, the formation and subsequent elimination of antibody-antibody complexes, the natural "death" of antibodies and B lymphocytes and finally a supply of B lymphocytes (named the "source") coming from the bone marrow. Antibody-antibody and antibody-B lymphocyte interactions are determined by a so-called affinity matrix m, which is symmetric and reflects the network structure of the model. An entry m_{ij} is called the affinity between clone i and j and, for the present study, only takes value 1 if affinity exists between clone i and j and 0 if not. The evolution in time of the concentration of the clone i two immune actors f_i and b_i is described by the two differential equations:

$$\frac{df_i}{dt} = -k_1\sigma_i f_i - k_2 f_i + k_3 \mathrm{mat}(\sigma_i) b_i \qquad (1)$$

$$\frac{db_i}{dt} = -k_4 b_i + k_5 \mathrm{prol}(\sigma_i) b_i + k_6 \qquad i = 1..n \qquad (2)$$

k_1 to k_6 are six time constants. The extent to which two clones interact in the network is thus determined by m and the concentration of the antibodies. The integral impact of the whole network on a specific clone i is measured by a value σ_i which is called the field: $\sigma_i = \sum_{j=1}^{j=n} m_{ij} f_j$ (3)

mat and prol are two log-normal functions which determine how B lymphocytes maturate and proliferate upon activation by the field:

$$\mathrm{mat}(\sigma_i) = \exp\left\{ - \frac{\ln(\sigma_i/\mu_m)}{s_m} \right\}^2 \qquad \mathrm{prol}(\sigma_i) = \exp\left\{ - \frac{\ln(\sigma_i/\mu_p)}{s_p} \right\}^2$$

The parameter values for the simulations described in this paper are:
$k_1 = 0.0016[\mathrm{conc}^{-1}\mathrm{d}^{-1}]$; $k_2 = 0.02[\mathrm{d}^{-1}]$; $k_3 = 2.0[\mathrm{d}^{-1}]$; $k_4 = 0.1[\mathrm{d}^{-1}]$; $k_5 = 0.2[\mathrm{d}^{-1}]$; $k_6 = 0.1[\mathrm{d}^{-1}]$; $\mu_m = 80[\mathrm{conc}]$; $s_m = 0.5$; $\mu_p = 120[\mathrm{conc}]$; $s_p = 0.5$.

The biological motivations behind such a modeling is outside the scope of this paper (see (Varela & Coutinho, 1991) for these motivations). Also the value for each parameter was determined in agreement with biological data which need not be discussed here. Basically the parameters were tuned so as to obtain an oscillatory behaviour for the simplest possible network containing 2 complementary clones with the affinity matrix given by: $\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}$

It is worth saying that some stability analysis and bifurcation diagram have been drawn by various authors for this model or very related ones (De Boer et al., 1993; Stewart & Varela, 1990). For instance DeBoer, Perelson and Kevrekidis (1993) have shown that for a very similar model limited to a two-clone idiotypic network, the dynamical regimes can be of any classical type: fixed point, oscillation and Lorenz type of chaos. The focus of this paper is aside from this parametric type of bifurcation analysis but rather, by maintaining all parameters constant, is concentrated on examining the sensitivity of the dynamics to connectivity alterations. Thus this is the reason why in this paper we limit the parametric exploration to the obtainment of limit cycle behaviour for the 2-clone network, the starting point of our study. As shown in (Stewart & Varela, 1990) this oscillatory behaviour is very robust and strongly prevails for a large range of parameter values.

In order to produce frustration in the structure of connectivity, attention will be paid only to affinity matrix which reflects the complementarity of the clones (two complementary clones which can be seen as two opposite spins), thus in the absence of self-affinity (m_{ii}=0) and with affinity restricted to complementary clones (m_{ij}= m_{ji} and can only take value 0 or 1). Such a structure will indeed lead to the open and closed chains which are precisely our objects of interest.

In fig.3, simulations are shown for the network sizes 2 and 3 with indicated for each case the corresponding affinity matrix. Only the temporal evolution of the antibody concentrations is shown. The figure clearly shows the periodic nature of the regime obtained for both the 2-clone and the non frustrated 3-clone situation. Interestingly enough the 3-clone open chain situation is very close to the 2-clone situation when substituting one of the clones in the 2-clone case by a couple of them in the 3-clone case.

<INSERT FIGURE 3>

It is remarkable to see for the 3-clone situation and for whatever number of clones in general how much the 2-clone dynamics prevails and the attractive effect it exerts on all other configurations. In the 3-clone open chain situation described by six differential equations the network behaves nearly in the same way as in the 2-clone case with clones 1 and 3 oscillating in perfect synchronization so as to form a double-clone equivalent to one of the two clones in the 2-clone case (except for the amplitude which is not surprisingly half the value). Since taken individually clone 1 and 3 are in a situation indistinguishable from the 2-clone situation i.e. they present affinity with one and only one clone (i.e. clone 2), they tend to behave just like in the 2-clone situation with as direct consequence their mutual coupling and the appearance of the double-clone.

When closing the chain (1<-->2<-->3<-->1) and so doing obtaining a frustrated triangle, the periodic regime switches to an aperiodic one. Since now, taken individually, each clone presents the same local connectivity (they are all connected to two neighbors) and then appears indistinguishable from the others (as will be confirmed below), none of them can assume the privilege to oscillate alone (then differently) in counterphase with the double-clone. Accordingly, the double-clone is continuously and erratically changing the nature of its members. This perfect clonal equivalence is obviously a very basic reason and original feature of the complicated regime which typifies the closed chain case. As expected this type of aperiodicity disappears for four clones and in general for an even number of clones. In the 4-clone either closed or open chain, the two double clones oscillate in counterphase, in contrast with the 5-clone closed chain where the aperiodic regime reappears. In fig.4, the time-dynamics of the second antibody is plotted against the first one both for the 3-clone open chain and the closed one. By simply looking at the figures, it is easy to understand the nature of the frustrated attractor as a dynamical regime which randomly wanders around the cyclic attractor (with the three possible compositions). Indeed this latter is clearly perceivable in the background of the chaotic attractor.

< INSERT FIGURE 4>

The IIN as a whole does not naturally self-sustain its frustrated configuration and shows a strong tendency to eliminate one of its clones so as to return to a non-frustrated configuration. When decreasing either the degree of maturation k_3 or the source term k_6, the system tries to suppress one of its clones in order to reach the 2-clone configuration. For instance, when decreasing k_3 the suppression occurs during longer intermittent periods. The frustrated network displays stages of pure oscillatory behaviour whose duration can be roughly said inversely related to k_3. Intermittently, these oscillations are interrupted by chaotic bursts due to the resurgence of the eliminated clone.

We have extended the observation of how chains of interconnected clones (only the closest neighboring elements of the diagonal of the connectivity matrix are non-zero) behave up to 19 clones. As we expected, first return maps and the calculated power spectra indicate the presence of chaos for any odd loop while even chains are responsible for oscillatory behaviour. More surprisingly, for 19 clones connected in a loop, two oscillatory attractors were found in addition to the frustration chaos. In general increasing the number of clones connected in a loop seems to favour the presence of oscillatory regimes and to decrease the size of the basin of attraction of the frustration chaos.

Always aiming at a better characterization of how the three-clone dynamical regimes scale up when increasing the network size, together with Vincent Detours (Detours et al., 1994) we have recently launched a systematic study largely inspired from Kauffman's NK analysis for Boolean networks (Kauffman, 1992) where N is the number of clones and K the radius of interaction (i.e. each clone has affinity with its K neighbours on the list of N clones). The NK analysis reduces to the chain analysis described above for K=1 and the network is fully connected for K=N. A complete study of the results is under progress but so far some general tendencies can be drawn. Chaos is found for most of the N-K values and a significant outcome appears to be the fragmentation of the network into clusters of 2,3 or sometimes 4 activated clones separated by resting clones. Clusters of 2 and 4 clones are oscillating and clusters of 3 clones shows the frustration chaos presented above. The clones within the clusters fluctuate with an average of fi=40 whereas the resting clones separating the clusters fluctuate around mean concentration three orders of magnitude less. However as a very preliminary conclusion of this NK analysis, the omnipresence of chaos reveals the high probability of the presence of frustration and its destabilizing effect within a large range of networks.

The main question to be addressed in this paper is the nature of the 3-clone closed chain regime and of the, generally speaking, frustrated chaos. The computer experiments of the dynamics show strong evidence of an aperiodic behaviour. A simple reasoning may help to eliminate some well-known possible regimes intermediary between chaos and periodicity like a toroidal attractor. Indeed this type of attractor is generally due to the merging of distinct periodicities, each associated to different variable activities. However, an essential characteristic of the 3-clone closed chain is the perfect equivalence among the three clones. It is indeed this structural equivalence which is responsible here for inducing the frustration phenomenon and the resulting aperiodicity. Structural equivalence means that the three units evolve in time in the same mathematical way and are similarly connected to two of their neigbours. Why then should three equivalent units, similar in their dynamics and their connectivity, behave in a different way? As a consequence it is unlikely that this irregular behaviour be attributed to a toroidal attractor characterized by an heterogeneity in the dynamics of its associated variables. In fig.5, the power spectrum given by the dynamics of one clone is displayed. The presence of a continuous broad band which can, in a certain range of frequencies, be described by a law proportional to $1/f^{\delta}$ is a good indicator for a chaotic regime.

<INSERT FIGURE 5>

In fig.6 first return maps are shown for two of the three clones antibody concentration. Their perfect similitude is remarkable (also for the third which is not displayed here), confirming the homogeneity of the variables discussed above. Furthermore, the obtained map is here again very characteristic of a chaotic regime with the presence of several regions of high density. These regions might be associated with the different oscillatory attractors the network is continuously trying to reach and help in understanding the chaos here as an unpredictable wavering among the cycles obtained when “un-frustrating” this same network.

< INSERT FIGURE 6>

The computation of the 6 Lyapunov exponents gives $\lambda_1 = 0.018$ for the greatest one (using Wolf et al’s (1985) classical algorithm) and the exponents sum turns out to be negative. This is clear evidence for a stretching-and-folding type of chaos despite the difficulty to detect the divergent and convergent directions when all variables behave in a same way. One possible intuitive explanation would be that the divergence occurs when the dynamics leaves a cyclic intermittent period to be trapped into another one, while convergence occurs during the brief trapping into the repelling orbits.

The IIN frustrated chaos is a succession of attempts to decouple the system in two groups of oscillators, an impossible achievement making the dynamics rambling over very brief and successful configurations. Since each cyclic behaviour presents fractal basin boundaries, the wavering among these cyclic attractors is beyond all predicitability. It is impossible to predict when a point in the phase space will be attracted by one of the cycles since the attractive regions have frontiers themselves impossible to draw with finite precision. Also important differences can be pointed out with the standard type of intermittency since intermittent oscillatory phases, as short as they appear to be, always concern a 2-clone version of the network to contrast with classical intermittent regimes which involve all the variables in an indifferent way.

Symbolic dynamics is being more and more proposed to extract invariant grammatical and statistical characteristics from time series (Ebeling, 1991; Hao, 1991; Nicolis and Prigogine, 1991). It is generally achieved by dividing the phase space into a finite number of partitions and by labeling each partition with a symbol. Then a symbolic string is generated by following and marking how the trajectory circulates over the partitions. Since in our model, the symbolic analysis was easy to conceive, we decided to rely a lot on these statistical tools for characterizing the chaotic regime. Symbolic strings were generated just by spotting the clone whose antibody concentration exceeds the concentration threshold of 150 (like indicated in fig.7).

< INSERT FIGURE 7>

Since there are three clones: 1,2 and 3, the resulting long string produced by the dynamics were constituted by the three possible digits. However the most accurate results were obtained with strings (of length up to 20000) composed of only two letters just by spotting the clones 1 and 2 when they crossed the concentration threshold. A statistical analysis revealed that the generation of the string could be matched with great accuracy by a third order Markov process (Bersini & Calenbuhr, 1995). Such a small order can be taken as the signature of a strong chaotic behaviour (Ebeling & Nicolis, 1991; Nicolis & Prigogine, 1990). Furthermore up to words of length 10, the Shannon entropy for subwords of length n (1,..,10): $s(n)=-\sum_i p_i \log p_i$ (with p_i the probability of occurrence of the ith subword of length n) scales linearly with the length of the subwords: another strong indication not only of the chaotic nature of the regime but of a fully developed chaos contrasting with weakest types like type 1 intermittency (for a detailed discussion on this type of analysis see (Ebeling & Nicolis, 1991; Nicolis & Prigogine, 1990).

Finally the most striking characteristic of this statistical analysis (for both two and three letters alphabet) is the equality of the probability of occurrence of two subwords when the substitution in the first subword of all the appearance of one of the three digits by another one (and vice versa) gives the second subword (Bersini & Calenbuhr, 1995). For instance for subwords of two letters and indicating by Pr the occurrence probability: Pr(11) = Pr(22) = Pr(33) and Pr(12) = Pr(21) = Pr(13) = Pr(31) = Pr(23) = Pr(32). In the same way, for subwords of length 5 we had Pr(12123) = Pr(21213) =

Pr(31312) = ... This equality together with the possibility to superimpose the three first return maps confirms the total equivalence and "interchangeability" of the clones.

3. FRUSTRATED CHAOS IN COUPLED MAP LATTICE

Chaotic itinerancy has been first observed and described by Kaneko (1994) in CML. Similarly to the frustrated chaos, the dynamics wanders around various quasi cyclic attractors in a very unpredictable way. Each attractor is characterized by several clusters of units which fluctuate in a synchronous way. Chaotic itinerancy refers to the continuous alteration of these clusters which continuously modify their composition and dynamics. Ordered states characterized by this spontaneous clustering are intermittently replaced by highly chaotic states. Since this phenomenon is reminiscent of what happens in the IIN, it is worth investigating whether an elementary 3-unit CML could reproduce the type of dynamics observed in IIN ? CML equations can be written in a network form as:

$$x_i(t+1) = (1-\varepsilon)f(x_i(t)) + \frac{\varepsilon}{n-1}\sum_{j=1}^{n} w_{ij} f(x_j(t)) \quad \text{with } f(x) = 1 - ax^2 \qquad (4)$$

When tuning ε to 0.1 and a to 1.65, a non-frustrated three-unit CML ($W=\begin{bmatrix}1&1&0\\1&1&1\\0&1&1\end{bmatrix}$) behaves in the way indicated by fig.8 (only two units are shown since one is indeed a double-unit). Like in the IIN case, a double-unit seems to regularly oscillate in counterphase with the single one, and, again like in the IIN case, the effect of frustrating the network by closing the chain ($W=\begin{bmatrix}1&1&1\\1&1&1\\1&1&1\end{bmatrix}$) is to un-stabilize the network (also shown in fig.8).

< INSERT FIGURE 8>

Similarly to the IIN case, the double unit is continuously and erratically changing the nature of its members. This indeed might consist of the most elementary instance of chaotic itinerancy in a CML. However a fundamental difference has to be pointed out with IIN. The non-frustrated 3-unit CML does not behave in a purely periodic way like the figure 9, plotting unit 2 against unit 1 both for the non frustrated and frustrated cases, clearly shows. Actually, the open-chain dynamics is quasi-periodic. The only apparent effect of frustration is to increase the degree of chaoticity of the already chaotic non-frustrated system. Here by degree of chaoticity, we intuitively mean the chaotic attractor apparent diffusion in the phase space.

< INSERT FIGURE 9>

In CML chaos does not turn to be the sole effect of frustration (like for IIN) but there exits some intrinsic chaoticity due to the dynamical nature of the units. In fact everything that happens in CML happens in an un-stabilizing chaotic sea and it is very hard to obtain a pure periodic behaviour like for the non-frustrated HN and IIN. Also the chaotic itinerancy is not only caused by the perturbing effect produced by the other competing cyclic attractors but rather can be, in part, attributed to the intrinsic chaoticity of the system. So although frustration seems to further increase the instability of the system in a similar way to IIN (changing erratically the composition of the double-unit), its effect in the CML is less remarkable than in the IIN due to the genuine unstable nature of this network inherent to the chaotic dynamics of the units.

4. FRUSTRATED CHAOS IN HOPFIELD NETWORKS

In its original conception, symmetric and without self-connection ($w_{ij} = w_{ji}$ and $w_{ii} = 0$), HN dynamics relaxes to fixed points. These fixed points are minima of an energy function which decreases as the network evolves in time. Frustration was first discovered and discussed by Toulouse (1977) in the context of spin glasses in which unit settles in one or the other state so as to decrease a similar energy function. Since spin glasses and HN share the same energy function, some physicists like Amit (1989) or Sherrington (1990) have tried to rely on statistical physics results obtained in the field of spin glasses to better characterize the capacities of HN. In a frustrated network, it is easy to see that there is no configuration which collectively drives the energy to a global minimum. All couples of units are unable to simultaneously settle in their state/anti-state pairing and then the network is driven into one among several intermediary configurations with higher energy. Together frustration raises the minimum energy and increases the degeneracy of the ground state. When HN are used as a mechanism for associative memory, it is interesting that there be many available fixed points namely an energy function with a lot of equivalent minima, a situation typically arising in frustrated networks. This is one of the few cases where frustration is considered to be beneficial to the network.

More interesting for understanding the un-stabilizing effect of frustration is the study of the same HN but now allowing for asymmetric connectivity (then loosing the proof of convergence to fixed-point attractors) and taken in its continuous form. Atiya and Baldi (1989) have done a deep analysis on how the neurons behave when they are interconnected in a loop or a ring and confirmed a preliminary investigation of Hirsch (1987) where it was shown that a necessary condition for the HN to oscillate is indeed to exhibit frustration in its connectivity. Very naturally a question comes to mind. Besides the oscillatory behaviour resulting from frustrating a HN with fixed points, is frustrated chaos a possible regime in an asymmetric HN ? We believe the answer to be positive and also that such a regime was already presented in a paper by Lewis and Glass (1992) although the authors did not make any explicit connections with the frustration phenomenon and did not propose any description of this regime as a composition of brief repelling cycles. The network they presented in their paper will be the starting point of this study and it will be proposed that chaos in this network might indeed result from some form frustrated connectivity, although not as easy to pinpoint as in the IIN and the CML .

The continuous version of the Hopfield Network is given by:

$$\frac{da_i}{dt} = -\frac{a_i}{\tau} + f(\varepsilon \sum_{j=1}^{n} w_{ij} a_j) - \beta \qquad \text{n is the number of neurons} \qquad (5)$$

f(x) is the hyperbolic tangent function. The following values have been taken for the parameters: τ=2.5, ε=10 and β=0.5 which makes the network behaves in the chaotic regime. The time unit is given in second. The connectivity matrix w_{ij} is exactly the one discussed in the paper by Lewis and Glass (1992) : $\begin{bmatrix} 0 & -1 & 0 & 0 & -1 & -1 \\ 0 & 0 & 0 & -1 & -1 & -1 \\ -1 & -1 & 0 & 0 & -1 & 0 \\ -1 & -1 & -1 & 0 & 0 & 0 \\ -1 & -1 & 0 & -1 & 0 & 0 \\ 0 & -1 & -1 & -1 & 0 & 0 \end{bmatrix}$. All six neurons are connected in an homogeneous way by inhibitory synapses (-1) to three of their neighbours. Although the presence of odd loops as generator of instability is simple to detect a priori, which key structural feature of this connectivity matrix is responsible for chaos deserves more study and is still the object of investigations.

Again, no parametric bifurcation analysis is presented here since the emphasis lies on the structural sensitivity of the network with respect to its connectivity rather than on the sensitivity with respect to parametric change. It is just worth saying that a careful tuning of the parameters has been done so as to obtain the dynamical regime which allows an easy observation and characterisation of the chaotic regime. Fig.10 shows a two dimensional representation of the chaotic attractor where $a_4(t)$ is plotted against $a_3(t)$. The selection of neurons 3 and 4 has been done for sake of clarity and of visual representation. The calculation of the Lyapunov exponents gives $\lambda_1 = 0.14$ for the largest exponent and a negative sum for the six exponents, two facts testifying for a chaotic regime. In fig.11, 12 and 13 you can observe the same plotting but now for three non-frustrated matrices: one in which the connection 5-->2 has been suppressed $\begin{bmatrix} 0 & -1 & 0 & 0 & -1 & -1 \\ 0 & 0 & 0 & -1 & -1 & -1 \\ -1 & -1 & 0 & 0 & -1 & 0 \\ -1 & -1 & -1 & 0 & 0 & 0 \\ -1 & 0 & 0 & -1 & 0 & 0 \\ 0 & -1 & -1 & -1 & 0 & 0 \end{bmatrix}$, a second one in which the connection 1-->5 has been suppressed $\begin{bmatrix} 0 & -1 & 0 & 0 & 0 & -1 \\ 0 & 0 & 0 & -1 & -1 & -1 \\ -1 & -1 & 0 & 0 & -1 & 0 \\ -1 & -1 & -1 & 0 & 0 & 0 \\ -1 & -1 & 0 & -1 & 0 & 0 \\ 0 & -1 & -1 & -1 & 0 & 0 \end{bmatrix}$ and the last one in which the connection 2-->4 has been suppressed $\begin{bmatrix} 0 & -1 & 0 & 0 & -1 & -1 \\ 0 & 0 & 0 & 0 & -1 & -1 \\ -1 & -1 & 0 & 0 & -1 & 0 \\ -1 & -1 & -1 & 0 & 0 & 0 \\ -1 & -1 & 0 & -1 & 0 & 0 \\ 0 & -1 & -1 & -1 & 0 & 0 \end{bmatrix}$. When carefully observing the fig.10, it is easy to observe the intermittent attraction exerted by the cycles presented in fig.11, 12 and 13. At least, one can clearly see the first cyclic attractor (seen in fig.11) standing out against the chaotic one. So the classical characterisation of chaos as a random itinerancy around brief orbits clearly applies here again. However the additional original fact is that in our case these background oscillations are the ones obtained by "non-frustrating" the network.

< INSERT FIGURE 10>

< INSERT FIGURE 11>

<INSERT FIGURE 12>

<INSERT FIGURE 13>

This chaos in small Hopfield Network can again be seen as a recurrent alternating between possible orbits obtained by opening here and there the connectivity matrix. One great weakness remains in this analysis of frustration in HN: The impossibility (in contrast with the classical characterisation of frustration in (Toulouse, 1997; Hiernaux, 1977; Amit, 1989; Sherrington, 1990; Marcus and Westervelt, 1987; Marcus et al., 1991; Bersini and Calenbuhr, 1995; Daido, 1992; Omata and Yamaguchi, 1988; Thomas, 1991) to anticipate the appearance of chaos due to a certain connectivity pattern and accordingly to clearly identify what is responsible in the matrix for this further source of instability (besides the presence of odd inhibitory loops which is known to produce oscillations).

Again, symbolic dynamic analysis is a precious tool to characterize this chaotic regime. Here, the 3-4 neuron phase space is discretised in four regions by just dividing the variable $a_3(t)$ into four intervals, each labeled by a letter: ‘a’, ‘g’, ‘e’,’d’, like indicated in fig.14.

<INSERT FIGURE 14>

The dynamics generates words in the following way: As soon as one of the four intervals is reached, i.e. when the frontier between two intervals is crossed, the letter associated with the subsequent interval is added at the word. So for instance the dynamics plotted in fig.11, and departing from the extreme right position, repeatedly writes the word: “degage”. This oscillatory regime will in fact be symbolized by the word: “degage”. The dynamics plotted in fig.12 repeatedly writes the two words “de” and “degagage” subsequently, while the two words “degage” and “degegage” written subsequently characterize the dynamics plotted in fig.13.

When running the chaotic attractor for a huge number of time steps, only 6 words turn out to be possible which, with their associated frequency, are: 1: “degage” (90%), 2: “de” (3%), 3: “dege” (2.5%), 4: “degagegagage” (1.6%), 5: “degagage” (1.6%), 6: “degagegage” (1.3%). For instance the 165 first appearances of these six words (numbered from 1 to 6) is the following (1 5 1 is thus equivalent to: “degagedegagagedegage”).

1 5 1 1 1 1 1 1 1 1 1 1 1 1 1 5 1 1 1 1 1 1 1 1 1 1 1 1 6 1 1 3 1 1 1 1 1 1 1 1 1 3 2 1 1 1
1 3 2 1 1 3 2 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 3 1 1 4 1 1 5 1 1 6 1 1 1 1 3 1 1 4 1
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 4 1 1 1 1 1 1 1 2 1 1 1
1 1 1 1 1 1 1 1 1 1 1 1 1 5 1 1 1 1 1 1 1 1 1 1 2 1 1

So “degage” (associated with number 1), which characterizes the non-frustrated cyclic attractor shown in figure 11 and 13, is by far the most frequent word of the chaotic attractor. It remains the most salient regularity of the chaotic attractor together with some parasitic cycles (2,3,4,5,6) which un-stabilize it and which are due to the presence of the other cycles (in their totality or in pieces) associated with other non-frustrated connectivity matrices. The average period of a word can be easily estimated by computing the time needed between two occurrences of “d”. In the experiments, we found that this average period was approximately 10 sec.

A further procedure helping to reveal the periods of local cyclic stability is to plot the largest Lyapunov exponent time-local value as a function of time. The time-local value of a Lyapunov exponent $\lambda(n)$ is restrictively computed over a limited amount of time steps, say T: $\lambda(n) = \frac{1}{T}\sum_{t=n}^{t=n+T}\|e(t+1)\|$ and plotted as a function of n (e(t+1) is the expansion of the first normalized vector given by the GSR procedure (Wolf et al., 1985)). The classical Lyapunov exponents are obtained for T being the full period and n=1. In fig.15, $\lambda(n)$ is plotted as a function of n for n varying between 100 and 995 by successive steps of T=5 sec (179 points are then plotted). There is an irregular mixing of negative and positive values which could be roughly assimilated to the intermittence of cycles and departure from these cycles.

<INSERT FIGURE 15>

Lastly, the autocorrelation coefficient r_k has been calculated for the first neuron activity and for k varying from 1 to n sec with n = 100 sec for the matrix without the connection 5-->2 and n=200 sec for the frustrated matrix:

$$r_k = \frac{1}{n-k}\sum_{t=1}^{n-k}(a_1(t)-\bar{a}_1(t))(a_1(t+k)-\bar{a}_1(t))$$

r as a function of k is plotted for both cases in figures 16 and 17. Again, one can see how the autocorrelation coefficient of the chaotic regime (fig.17) presents some damping oscillation with a period of approximately 10 sec, nearly the same period of oscillation as given by the non-frustrated network (which is slightly longer). The damping results from the lowering of correlation in time and the overcoming of unpredictability.

<INSERT FIGURE 16>

<INSERT FIGURE 17>

5. CONCLUSIONS: THE BIOLOGICAL GOODNESS OF BEING FRUSTRATED

It has been shown in (Calenbuhr et al., 1995) how, when coupled to an auto-antigen, the frustrated chaotic attractor degenerates into one of the three periodic regimes and how the network realizes then a form of tolerant response to this auto-antigen. The presence of the auto-antigen stops the frustration by making the concentration of the clone with which it presents affinity to vanish. This is a very simple illustration of a particular idiotypic network showing tolerance towards auto-antigen without the need for ad hoc mechanisms that prevent an immune response. Moreover the resulting two-clone oscillatory network, when having one of its clone connected with an auto-ag (like done before), will see its connected clone to grow exponentially in a way which reminds the classical immune reaction against an external antigen. This two stages phenomenon obtained by two successive antigenic encounters: first tolerance with a three-clone network and then immune reaction with the two-clone network resulting from the first interaction, can be seen as a low scale qualitative replica of the two consecutive lives of the immune system: tolerant in its embryonary state and defensive in the adult state.

An interesting observation was that not all initial conditions of the three-clone frustrated network lead to the “tolerant” periodic regime. We found that about 1/4 of the initial conditions gives rise to unstability when reacting to the auto-antigen perturbation. We have tried to characterize the initial conditions leading to either one of the two behaviours and have found none. This result is a nice confirmation of the fractal nature of the basins of attraction of the cyclic attractors (Ott, 1993) and of the fact that the frontiers being impossible to trace, when and how the frontiers are crossed turn out to be unpredictable.

The tolerance phenomenon presents also interesting similarities with the control of chaos since it is by perturbing the dynamics that the system is trapped into one of the oscillatory attractors that it was recurrently visiting. However a fundamental difference lies in the fact that the control is here achieved by a parametric perturbation, and the dynamics can be trapped only into one of the three oscillatory attractors that are recurrently visited, not into one of the infinite oscillatory modes characterizing more classical form of chaos. Apart from positively answering to a fundamental question in immunology: can a dynamic idiotypic network which grows in the relatively stable somatic molecular environment develop a natural tolerance to endogenous components?, this way of stabilizing the dynamics by external interaction reflects a key and appealing property of frustrated biological networks.

Frustrated networks, when de-stabilized by the presence of odd negative loops, wanders continuously among different stable configuration, and it is the external interaction which makes the network to settle into one of these stable regimes. Let's characterize any dynamical regime by different degree of complexity: for instance 1 for fixed point, 2 for oscillations, 3 for chaos. A frustrated network is following a regime of degree n which visits recurrently all possible regimes of degree n-1 until this wavering is stopped by being externally perturbed and stabilized into a regime of degree n-1. This new regime is the one which gives sense or label the external perturbation. In the field of neurophysiology Skarda and Freeman (1987) have shown how a neural net can exploit chaos for the generation of an enormous repertoire of attractors. It is the encounter with an external stimulus, like an odor, that will turn the chaotic regime into an oscillatory one.

The fact that frustration has been detected in the great majority of physical and biological networks studied so far: spin glass, genetic, neural, oscillatory and immune, whose mathematical description can be quite different, is pleading for the understanding of frustration as dependent just upon the structure of connectivity. Such a generic phenomenon should not be restrictively construed as an insignificant artifact of our mathematical and computer modeling but rather as a real biological effect, playing yes or not a benefic role (if not a natural way to un-frustrate the network must exist), that further investigation will have for goal to better characterize.

Acknowledgments: The authors want to thanks V. Detours for his precious computational works and interactions, Prof. Nicolis for his help while doing the symbolic Markovian analysis and Prof. Kaneko for his help in analysing the frustration effect in his coupled map lattice.

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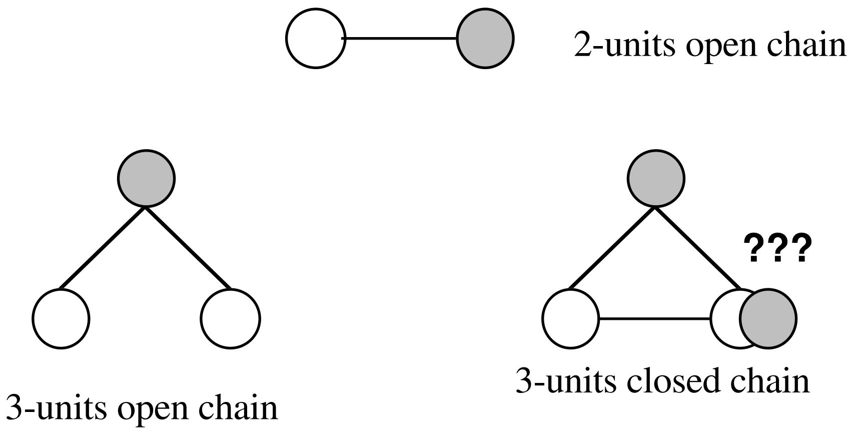


Fig.1. The frustration phenomenon

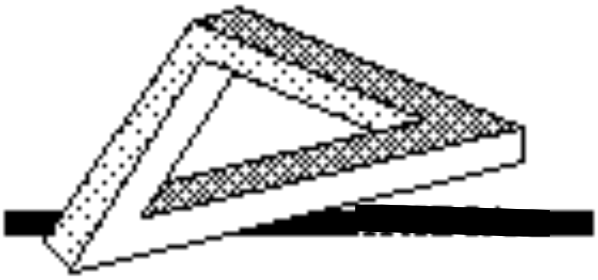
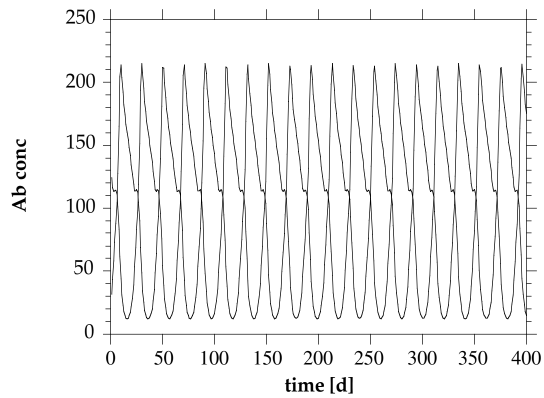
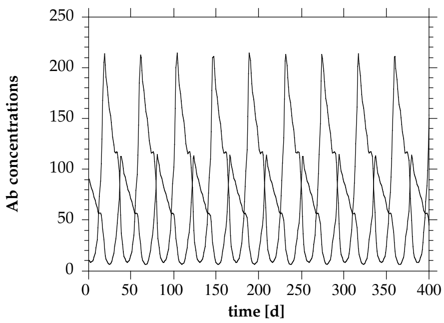
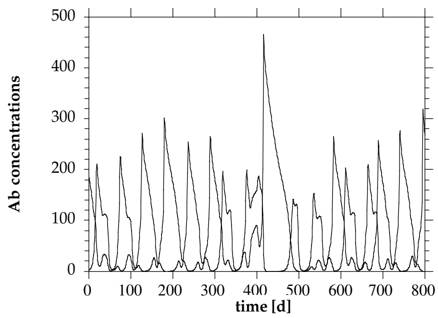


Fig.2: A Moebius triangle is a frustrated figure



2-clone case $\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}$





3-clone open chain $\begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix}$

3-clone closed chain $\begin{bmatrix} 0 & 1 & 1 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \end{bmatrix}$

Fig.3: Time series of the 2 and 3-clone cases, respectively. In all three cases, the concentrations of the antibody of the first and second clone are displayed.

Fig.4: Plotting the concentration of antibody 2 vs antibody 1 for the non-frustrated and the frustrated 3-clone IIN.

Fig.5: Power Spectrum of the 3-clone closed chain system

Fig. 6: First Return Maps of the two of the three antibodies concentration for the 3-clone closed chain case.

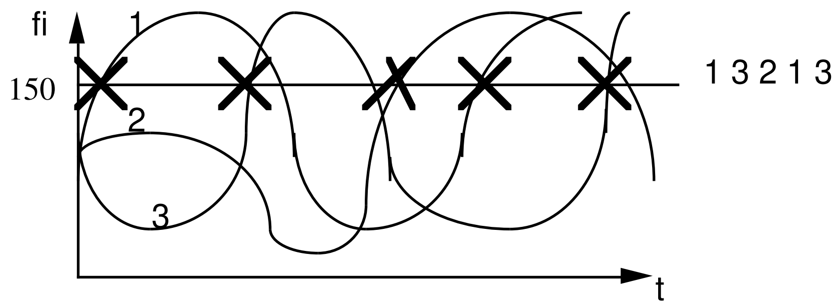


Figure 7: The generation of a “three-digit” symbolic string from the dynamics

Fig.8 Plotting the time dynamics of unit 1 and 2 of a 3-unit non frustrated and frustrated CML. The change in the composition of the double-unit is easy to see in the middle of the second figure.

Fig. 9 Plotting of unit 2 vs 1 for the non frustrated and frustrated CML. The diffusion in the space reveals chaos in both cases.

Figure 10: Plotting the chaotic attractor given by frustrating the connectivity of an Hopfield network. The activation of neuron 4 is plotted against the activation of neuron 3.

Figure 11: Plotting the oscillatory attractor given by suppressing connection 5-->2 and thus non frustrating the connectivity. The dynamics is projected onto the plane a_3-a_4.

Figure 12: Figure 3: Plotting the oscillatory attractor given by suppressing connection 1-->5 and thus non frustrating the connectivity in a second way. The dynamics is projected onto the plane a_3-a_4.

Figure 13: Plotting the oscillatory attractor given by suppressing connection 2-->4 and thus non frustrating the connectivity in a third way. The dynamics is projected onto the plane a_3-$a_{4.}$

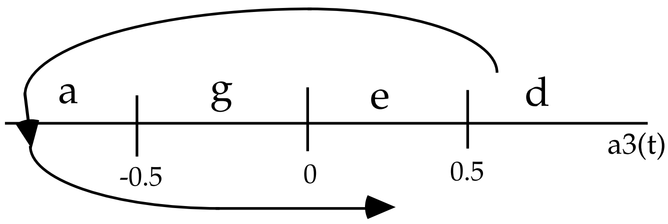


Figure 14: How are the words generated by the HN dynamics. Four letters labelize the four intervals on the variable $a_3(t)$. Each time $a_3(t)$ reaches a new interval the letter symbolizing this interval is added at the word.

Figure 15: Plotting the time-local Lyapunov exponent computed every 5 second for a total period of 900 sec.

Figure 16: Plotting the autocorrelation coefficient as a function of the time interval (from 1 to 100 sec.) for the non-frustrated network given by suppressing connection 1-->5.

Figure 17: Plotting the autocorrelation coefficient as a function of the time interval (from 1 to 200 sec.) for the frustrated matrix.