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Hierarchical Functional Organization of Formal Biological Systems: A Dynamical Approach. II. The Concept of Non-Symmetry Leads to a Criterion of Evolution Deduced from an Optimum Principle of the (O-FBS) Sub-System

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Hierarchical functional organization of formal biological systems: a dynamical approach.
II. The concept of non-symmetry leads to a criterion of evolution deduced from an optimum principle of the (O-FBS) sub-system

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CONTENTS

SUMMARY

In paper I a theory of functional organization in terms of functional interactions was proposed for a formal biological system (FBS). A functional interaction was defined as the product emitted by a structural unit, i.e. an assembly of molecules, cells, tissues or organs, which acts on another. We have shown that a self-association hypothesis could be an explanation for the source of these functional interactions because it is consistent with increased stability of the system after association. The construction of the set of interactions provides the topology of the biological system, called (O-FBS), in

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contrast to the (D-FBS) which describes the dynamics of the processes associated with the functional interactions. In this paper, an optimum principle is established, due to the non-symmetry of functional interactions, which could explain the stability of an FBS, and a criterion of evolution for the hierarchical topological organization of a FBS during development is deduced from that principle. The combinatorics of the (O-FBS) leads to the topological stability of the related graph. It is shown that this problem can be expressed as the re-distribution of sources and sinks, when one of them is suppressed, given the constraint of the invariance of the physiological function. Such an optimum principle could be called a 'principle of increase in functional order by hierarchy'.

The first step is the formulation of a 'potential' for the functional organization, which describes the ability of the system to combine functional interactions, such that the principle of vital coherence (paper I) is satisfied. This function measures the number of potential functional interactions. The second step is to discover the maximum of this function. Biological systems in such a state of maximum organization are shown to satisfy particular dynamics, which can be experimentally verified: either the number of sinks decreases, or this number increases, in a monotonic way. The class of systems considered here is assumed to satisfy such an extremum hypothesis. The third step is a study of the variation of the degree of organization (paper I), i.e. the number of structural units when the biological system is growing. We establish an optimum principle for a new function called 'orgatropy'. By adding a criterion of specialization to the system we show the emergence of a level of organization with a re-organization of the system. A 'hierarchization operator' is defined, which leads to the fourth step of this theory, i.e. the conditions of the variation in time of the (O-FBS) sub-system, as described by a 'functional order' mathematical function. It is shown that this function is a Lyapounov function, and drives the system towards a stable state with maximum specialization. Two consequences of the theory are studied: (i) the monotonic phases which are observed during development of the nervous system, and (ii) the similarities and differences observed between physical systems and biological systems.

NOTATIONS AND SYMBOLS

$g_k(n)$	number of synapses for the k-th target-neuron, $k = 1,n$
k	Boltzmann constant
n	number of units with a specific property
$(n^l_\alpha)_{\alpha=1,\mu^l}$	distribution of functional links between structural units at this level: defines the functional organization
$n_{\bar{P}_1 P_2}$	number of units that synthesize P_2 and not P_1
$n_1^{(0)}$	number of sinks for the product P_1 in initial state at time $t^{(0)}$
o^l	number of organizations at level l
r,r_0	space coordinates
u,u_i,u_j	structural units
$u_1(P_1,P_2,P_3,P_4, \ldots)$	units that supply $P_1,P_2,P_3,P_4, \ldots$ (number $N_1^{(0)}$ in initial state)
u^*	modified structural unit having a missing product
$u_2 \equiv (u_1,u_1^*),u_{k+1} \equiv (u_k,u_1^*)$	associated structural units
$y_M = \Pi_{\max}(x_M)$	value of potential in the state of maximal organization
$D(x) = \Pi_{\max} - \Pi(x)$	Lyapounov function for Π
D_s	domain in the s-space
$E(x^l_\alpha) = n^l_\alpha$	integer part of the real x^l_α
$E^{MP}_\alpha \equiv S_\alpha$	set of substructures: channels, receptors, . . . : the synapse
$E^{AP} = \{E^{EM}_\alpha;\ \forall\alpha\}$	set of structures which produces the action potential: the neuron
$E^{NN} = \{E^{AP}_i;\ \forall i\}$	the real neural network localized in the r-space
F	hierarchical system
$F\colon\ v \rightarrow x_M \rightarrow y_M = F(v) = \Pi_{\max}\ o\ h(v)$	orgatropy
$F^l(l = 1, \ldots, L)$	elementary physiological function: defines the level of organization (L^l)
F_{kj}	number of elementary transformations per time unit from a class E_j to a class E_k
F_{ej}	number of elementary transformations per time unit towards the environment
$\boldsymbol{G}$	graph of the functional organization
H	Boltzmann quantity of information
S	entropy
(L^l)	level of organization of rank l
L	number of levels of organization
$\boldsymbol{M}$	matrix of the functional organization
N	occupation number of the classes
$N^{(\cdot)}_\alpha$	number of units specialized in the production of P_α in a given state $(\cdot)$, e.g. initial or final
N^β_α	total number of units which synthesise α- and β-products
(N,a)	representation in terms of occupation numbers
$P_\alpha,\ 1 \leqslant \alpha \leqslant \mu$	products in a structural unit
$P_{\alpha,i} \equiv P_{\alpha,u_i}$	denotes an α-product synthesized in the i-unit u_i
P_1,P_2	products
$S^{(l)}$	biological sub-system at level l
S_i	substrate
T_0	time coordinate
T^l	timescale at level l
U_j	population of elements u_j, each element containing j units
$X \equiv [mRNA]$	
$X_M \equiv (x_M,x_M, \ldots, x_M) \equiv (x_1,x_2, \ldots, x_\mu)_M$	equilibrium point
δ	hierarchization operator

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Φ,ϕ,ψ transformations that describe the functional interaction: $P_2^* = \Phi(P_1) = \phi \; o \; \psi(P_1)$

Φ_1 postsynaptic potential

$\mu_{12}(t)$ functional interaction between two elements s_1 and s_2 localized in D_s.

v^l degree of functional organization

$v^{(f)} = n_1^{(f)} + n_2^{(f)}$ degree when the specialization of the l-level exists at final time $t^{(f)}$ (corresponds to a partition into two subsets of $n_1^{(f)}$ and $n_2^{(f)}$ units)

$\Omega(t) = -\sum_{l=1}^{L} F^{\,l}(v^l)$ functional order

π density-connectivity of synapses between neurons

(ψ,ρ) representation

ψ_{ij}^{α} functional interaction (α) from the i- to the j-unit

ρ geometrical parameter of the biological system

ρ density of neurons

$\Pi^l(n)$ potential of functional organization at level l for n of the v units

${}^{(0)}\Pi^l$ potential of functional organization for the l-level at initial time t_0

${}^{(f)}\Pi^l = \Pi^{l+1}$ the same for the l-level before reorganization (or the $l+1$-level after reorganization) at final time t_f

Π_{ω}^l potential of organization after a total hierarchization when the number of products is odd, i.e. after complete specialization

1. INTRODUCTION: VARIATIONAL PRINCIPLES IN BIOLOGY

A theory of functional organization in terms of functional interactions was proposed for a formal biological system (FBS) in the previous paper of this series (Chauvet 1993*c*), referred to below as paper I. A functional interaction, identified in the theory to an elementary physiological function, was defined as the action of a product emitted by one structural unit on another. The emitted product $P_{\alpha,1}$ synthesized by the source u_1 is transferred towards a sink u_2. This process is described by the relation: $P_{\alpha,2} = \psi_{12}^{\alpha}(P_{\alpha,1})$. For example, a molecule emitted by a specific cell acts on another cell within which it induces a series of transformations. The FBS concept was introduced to provide a mathematically defined biological system with specific properties as similar as possible to those of a real biological system. An FBS is characterized by two such properties: (i) it is an 'equipotent system', i.e. all the potentialities of the genome are identical at each level of organization; and (ii) it is a 'mutational system' (see paper I), in which the structural units undergo independent, modifications. The construction of the set of functional interactions, constituting the topology of the biological system, is based on a very simple – although non-trivial – hypothesis, called the self-association hypothesis. According to this hypothesis, an interaction between two structural units becomes necessary when the elementary function of one of them is destroyed, i.e. when a source becomes a sink. Indeed, each elementary function can be potentially executed by a structural unit for its own survival. Thus, if such a function is lost, for example due to the occurrence of micromutations, the survival condition of the structural unit (the cell for instance) implies that the missing product be made available by another unit synthesizing the product. The topological system (O-FBS) composed of such functional interactions represents the functional organization of the FBS. The (O-FBS) is constructed according to what we have called the principle of vital coherence (paper I).

The hypothesis of self-association was shown to be valid, at least in the case of an FBS with two fundamental properties of living organisms: metabolism and self-reproduction. For a specific example, we demonstrated that self-association increases the domain of stability of the dynamic system (D-FBS) describing the physiological function, represented by the hierarchical system of functional interactions. The (D-FBS) is associated with the (O-FBS) defined by the mathematical graph representing the set of functional interactions. The property of the self-association that increases the domain of stability may then be formulated by saying that the increase in the complexity of the (O-FBS) by self-association is a natural tendency of the biological system since it accompanies an increase in the domain of stability of the corresponding (D-FBS). Thus, there exists a natural tendency for a biological system to move towards greater complexity during development as soon as the conditions for self-association are satisfied, for example after the occurrence of micromutations or under the influence of a genetic program.

An integrated description of physiological phenomena from the cell level to the organ level must include a unique formalized definition of the biological subsystem within a mathematical framework. Such a description will have to be able to deal simultaneously with several levels of organization. Indeed, the nuclear and cytoplasmic subsystems of the cell and, for example, the renal or respiratory subsystems of living organisms can all be considered as hierarchical systems based on the same organizational principles (Chauvet 1987, 1990). At the higher levels of functional organization, we have the intuitive impression of an increase in complexity, which may be thought of as an increase in the number of state variables of the biological system. However, in reality the hierarchy of the system leads to a decrease in the number of state variables.

In the conceptual framework proposed here, we shall see that because of the relationship between the topology and the dynamics of a biological system, there is a simultaneous increase in the complexity of the (O-FBS) and the (D-FBS). The hypothesis of self-association will be used to express functional complexity in terms of combinations of functional interactions represented by oriented diagraphs.

The measurement of the complexity of a system poses a fascinating challenge in all branches of science and has stimulated much research. For example, Ferdinand (1974) has used the concept of 'default entropy' to evaluate the complexity of computer circuitry, and Walter (1980, 1983) has defined a family of indices of complexity linked to the stability of compartmental systems. In the case of biological functional organization, the advantage of our method stems from the double description: topological and dynamical. The former describes the existence of functional interactions, whereas the latter describes the spatiotemporal changes of the processes associated with these interactions. Consequently, the stability of the biological system will correspond to that of the two systems when the number of structural units varies.

In this variational approach, a fundamental theoretical question arises concerning the existence of an optimum principle, similar to optimum principles known in the physical sciences, capable of explaining the stability of a formal biological system. Such a principle could be used as a criterion for the evolution of hierarchical biological systems and would provide a model for the comparison of biological and physical systems. We shall therefore address this important question. The topological stability of the graph of the system (O-FBS) will be expressed as the redistribution of the edges between the vertices of the graph, i.e. as the redistribution of the sources and sinks when one of these is destroyed, taking into account the constraint of the invariance of the physiological function. This constraint, expressed in terms of the principle of vital coherence, implies that the functional interactions reorganize themselves by self-association in such a way that the collective function subsists after the reorganization. We shall demonstrate that only one hypothesis, experimentally verifiable, is sufficient for the basis of this theory.

2. THE POTENTIAL OF FUNCTIONAL ORGANIZATION

(*a*) *The nature of the concept: combinatorial approach and non-symmetry*

If an FBS is considered to be an equipotent system, i.e. made up of structural units that can have the same elementary physiological functions, then the self-association hypothesis originates in the functional organization of these structural units (paper I), and subsequently in a hierarchical system. As mentioned above, all the cells of a given organism have the same potentialities of expression at the lowest gene level of organization. As we shall see, this property can be used for the construction of the FBS corresponding to the hierarchical system. The (O-FBS) consists in functional interactions, i.e. structural units and elementary functions, the topology of which is the functional organization. More precisely, the functional organization at level l is defined by the distribution $(n_\alpha^{(l)})_{\alpha=1,\mu^{(l)}}$ of functional links between structural units at this level. This distribution will be called a state of organization. According to the definitions given in paper I, $n_\alpha^{(l)}$ is also the number of zeros in the row α of the matrix M, i.e. the number of sinks for the function P_α of the system.

The FBS in the observed state of organization, because of the property of idempotence, presents other non-observed, potential states of organization. These states exist as potentialities in the system, but are not expressed. For example, the passage of organisms through particular stages during morphogenesis and the capacity of regeneration in certain species show that such potential states of organization can be observed during the life of the system.

Let (S) be a set of ν structural units all having the same potentialities. According to the self-association hypothesis, each unit is either a source or a sink. If a source could not become a sink it would die following an alteration in the function. Suppose that n of the ν units do not yield the product necessary for their survival. These n units will therefore have to be coupled to the other $(\nu - n)$ units. A number of possibilities exists for the associations that create the topology of an (O-FBS). I propose a function $\Pi(n)$, called the potential of functional organization, representing the reservoir of possibilities during the lifetime of the system. This mathematical function is determined if the following properties are verified: (i) Π gives a measure of the number of potential functional interactions; (ii) Π leads, under some conditions, to a hierarchy of the system; (iii) the hierarchy found is such that the value of Π^l, calculated for a level l, decreases from this level l to the next higher $(l+1)$; and (iv) the value of Π, calculated for the total hierarchical system, increases, whereas a re-organization of the system, as defined below, implies a decrease in this value.

These four properties can be seen to represent general facts about biological systems. However, the problem of the evolution of the functional organization is difficult to solve. Indeed, if a function such as Π admittedly describes a certain biological reality, further questions immediately arise. Among all the possible organizations available to the system during its evolution, which particular one was chosen? And why?

(*b*) *Definition and formulation*

Definition VI: potential of functional organization

The potential, Π^l at level l is the logarithm of the number o^l of all functional organizations that are available (and possible) for the observed state of organization, at its *i*th-level. It is assumed that all structural units have identical potentialities.

Let o^l be the number of organizations available for the observed state, i.e. a sequence $(n_\alpha^l), \alpha = 1, \mu^l$, where n_α^l is the number of sinks for the P_α-function at level l:

$$o^l = \prod_{\alpha=1}^{\mu^l} (\nu^l - n_\alpha^l)^{n_\alpha^l}, \tag{1}$$

because n_α^l units can be coupled to the $(\nu^l - n_\alpha^l)$ units which have the P_α-function, and all organizations can be associated to one another such that $1 \leqslant \alpha \leqslant \mu^l$. The number of structural units at level l is ν^l, and is called the degree of organization of the system at this level because it is the number of classes of structural equivalence (see paper I). Then:

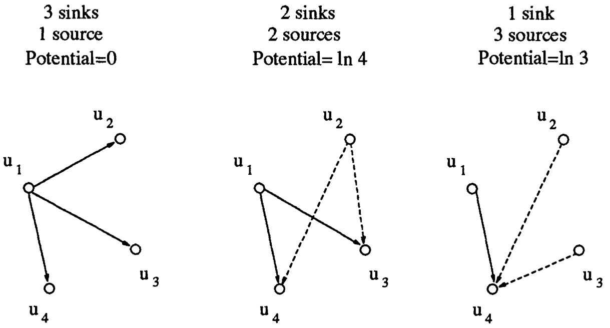

Figure 1. Combinatoric representation of the functional organization as relations between sources and sinks. In this example, with four structural units and one product, there exist three values of the potential of organization when the number of sinks equals 3,2,1. The condition is that a source cannot be a sink.

$$\Pi^l = \ln o^l = \sum_{\alpha=1}^{\mu^l} n_\alpha^l \ln(\nu^l - n_\alpha^l),$$

$$\Pi = \sum_{l=1}^{L} \ln o^l = \sum_{l=1}^{L} \sum_{\alpha=1}^{\mu^l} n_\alpha^l \ln(\nu^l - n_\alpha^l), \qquad (2)$$

where L is the number of levels and μ^l is the number of products at level l. A simplified form would be:

$$\Pi = \sum_{\text{levels}} \sum_{\text{products}} [\text{sinks}] \ln [\text{sources}].$$

Note that $\nu^l - n_\alpha^l > 0$ and $\Pi = 0$, if $n_\alpha^l = 0$ or $\nu^l - n_\alpha^l = 1$, i.e. if there exists no sink or only one source (for an example, see figure 1). These two eventualities are the simplest; all the others are more complex and correspond to combinations of interactions (Chauvet 1987). Thus, Π could be interpreted to represent functional complexity. However, as we shall see, the concept of potential can be used as the basis for the development of a variational theory.

3. CRITERION OF MAXIMALITY FOR THE POTENTIAL OR ORGANIZATION: A CLASS OF BIOLOGICAL SYSTEMS

(*a*) *States of maximum organization*

Can the Π-function describe the dynamics of an (O-FBS)? A positive answer is supported by the existence of a particular organization (n_M) for which $\Pi(n_M)$ is the maximum value (figure 2). It is easy to deduce the following properties from definition VI:

Property I

The potential of organization Π increases with both the degree of organization and the number of levels for a given distribution (n_α^l), $\alpha = 1, \mu^l$.

Property II

For a given l-level and a given ν^l-degree of organization, there exists a maximum for the potential of organization obtained for the value (n_M) of the organization. This particular value $\Pi_{\max}(n_M)$ is called the maximal potential or organization and describes a compromise between the complete interaction and the complete independence of the units at this level.

Proof: let $n_\alpha^l = E(x_\alpha^l)$ be the integer part of the real x_α^l. Then, Π^l is now the real function: $x \rightarrow \Pi^l(x)$ defined in $\mathbb{R}^1$. As mentioned in the introduction, the system is Darwinian and characterized by random suppressions or appearances of an individual product P_α. Mathematically, this property corresponds to independent variations $\mathrm{d}x_\alpha$ of x_α that occur in a given unit. Then, the maximum of Π (which is not a bound maximum) is obtained for $(x_\alpha)_{\alpha=1,\mu^l}$, which verifies the equation:

$$\mathrm{d}\Pi = \sum_{\alpha=1}^{\mu} \mathrm{d}\Pi_\alpha = \sum_{\alpha=1}^{\mu} \left(\ln(\nu - x_\alpha) - \frac{x_\alpha}{\nu - x_\alpha} \right) \mathrm{d}x_\alpha = 0,$$

where $\Pi_\alpha = x_\alpha \ln(\nu - x_\alpha)$ is the potential corresponding to product P_α, and where the superscript l has been suppressed for clarity. Therefore, $\forall \alpha \in [\![1,\mu]\!]$ a necessary condition for extremum is:

$$\ln(\nu - x_\alpha) - \frac{x_\alpha}{\nu - x_\alpha} = 0. \qquad (4)$$

It is possible to show that (i) $\Pi(x)$ has really a maximum at one point in $[0,\nu-1]^\mu$; and (ii) this maximum is unique (Appendix 1).

All structural units involved in the generation of a physiological function are supposed to have identical elementary physiological functions. This is the case in a non-differentiated tissue, in which all cells have the same individual potentialities, and which is being transformed into a differentiated tissue, i.e. one in which some cells achieve individual products for all the others. We could say that the graph G and the matrix M come into being when the 'functional isotropy' has disappeared. The two limit cases correspond to 'functional isotropy': (1) when $n_\alpha = 0$, and all units are independent; and (2) when $n_\alpha = \nu - 1$, and only one unit is specialized for the elementary function P_α. Then, a possible interpretation of Π could be the maximum of functional anisotropy associated with potential organizations.

(*b*) *Extremum hypothesis: a class of biological systems*

Two important properties can be deduced from the definition of $\Pi(x)$.

(i) *The organizational state is an attractor*

Property III

The state of maximal organization (called the organizational state) for the maximal potential $y_M = \Pi(x_M)$ is an attractor for the dynamics of the organization which tends to x_M, either by decreasing or by increasing values of x when the time t tends towards t_M.

Proof: $D(x) = \Pi_{\max} - \Pi(x)$, where $\Pi_{\max}$ is the state of maximal organization, is a Lyapounov function when $x(t)$, considered to be a dynamical system, tends towards x_M either by decreasing or by increasing values, according to the initial value of x, i.e.:

$$\forall \alpha \in [1,\mu] \qquad \forall x_\alpha \qquad D(x_\alpha) > 0.$$

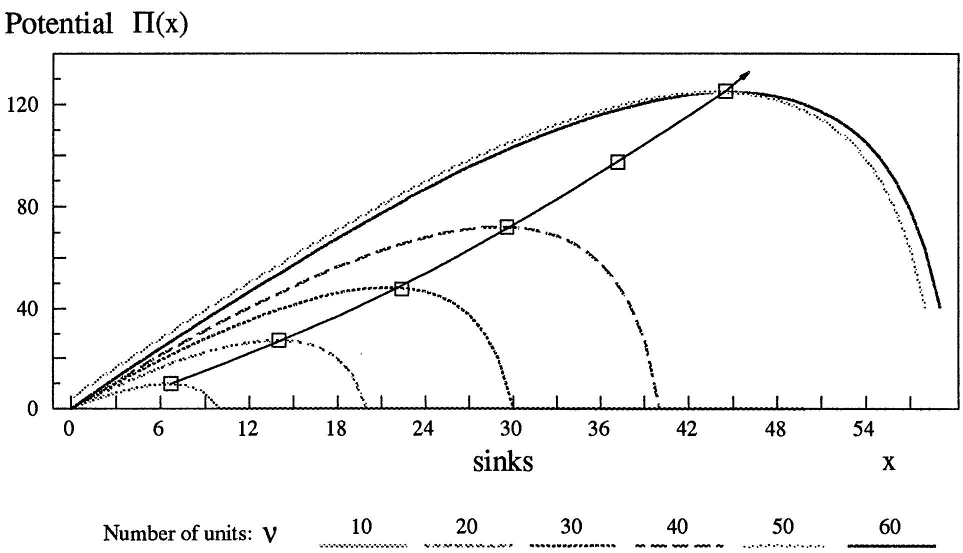

Figure 2. Potential of functional organisation for six values of the degree, from 10 to 60. The maximum of the potential determines a particular organization that is assumed to define the biological system.

The time derivative of $D(x(t))$ is negative or null:

$$\frac{\mathrm{d}D}{\mathrm{d}t} = \sum_{\alpha} \frac{\partial D}{\partial x_\alpha} \frac{\mathrm{d}x_\alpha}{\mathrm{d}t},$$

if the two following derivatives:

$$\partial D/\partial x_\alpha, \qquad \mathrm{d}x_\alpha/\mathrm{d}t, \tag{5}$$

have opposite signs (Appendix 2). Then the dynamical system which describes the time evolution of the graph:

$$\mathrm{d}x_\alpha/\mathrm{d}t = f_\alpha(x_1,x_2, \ldots, x_\mu), \tag{6}$$

has an equilibrium point at $X_M \equiv (x_M, x_M, \ldots, x_M) \equiv (x_1,x_2, \ldots, x_\mu)_M$ which is reached at a time t_M according to increased values when $x < X_M$, and decreased when $x > X_M$. In the latter case, $\partial D/\partial x_\alpha$ is positive ($x > X_M$) and the time derivative of x_α must be negative (figure 3). Similarly, in the first case ($x < X_M$), the partial derivative $\partial D/\partial x_\alpha$ is negative and the time derivative of x_α must be positive.

(ii) *Consequence: extremum hypothesis for the time variation of the number of sinks*

There are two possibilities for the functional organization of the biological system for which the potential of organization is given by the function $\Pi(x)$: before t_M, the number of sinks is either decreasing or increasing towards a stable limit. Such a monotone property of the variation of the number of sinks is important for the characterization of the potential of organization. An interpretation of this result in the second case could be the special role given to the sources of a system for having a maximal redundance among the structural units: the biological (Darwinian) system would evolve in time so that the number of sites of production (the sources) remains maximum.

Extremum hypothesis

A biological system evolves from initial conditions such that the number of sinks either decreases or increases, i.e. corresponds to a time monotonic function, and therefore reaches a state where the potential of organization is maximum. This extremum hypothesis defines a class of formal biological systems.

The validity of the proposed theory, which is finally based on this extremum hypothesis can be experimentally tested. The definition of functional interactions makes it possible to identify sources and sinks, and to verify the decreasing monotonic property of the number of sinks, even if the explicit dynamics of the system is unknown. Another possibility would be to check the validity of the consequences of the theory developed below.

4. CRITERION OF EVOLUTION FOR THE FUNCTIONAL ORGANIZATION: ORGATROPY

(*a*) *The concept of 'orgatropy'*

In the preceding section, the influence of the variation of the number of sinks on the functional organization was studied by means of the potential of organization. In this section, we shall explore the effect of a variation of the number of structural units in the system, i.e. the effect of the degree of organization. Some interesting results can be deduced from such variations corresponding to the development of the biological system. For example, when the degree of organization increases, the topology of the system is transformed such that the constraint of maximum potential is satisfied. We shall see that the evolution of the system is governed by a function called 'orgatropy', deduced from the function Π.

Property IV: the concept of orgatropy

If the degree of organization ν^l changes with a variation in the number of structural units in the level l without re-organization of the system, then the

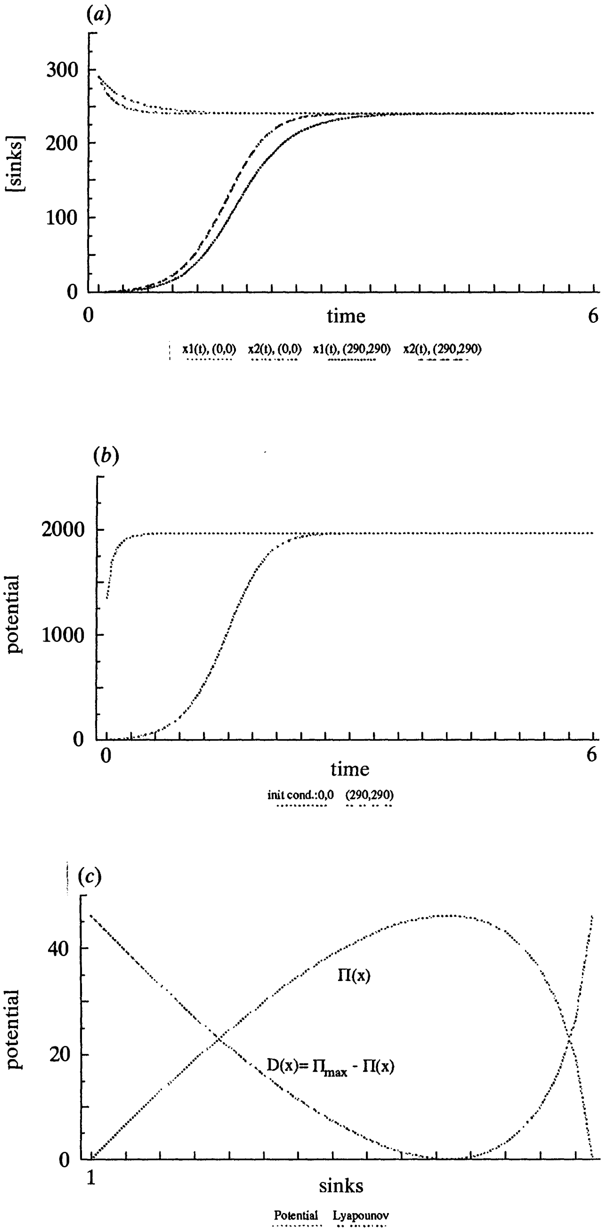

Figure 3. This set of three figures illustrates the fundamental general property III of the existence of an attractor for an organization having a maximal potential. Here is represented a specific case with two state variables and a degree that equals 300. (*a*) The dynamics of the organization $(x_1(t), x_2(t))$, i.e. the number of sinks for two products P_1 and P_2, tend asymptotically towards $x_M=160$ either by decreasing values from initial conditions (0,0), or by increasing values from initial conditions (290, 290). (*b*) Corresponding variation in time of the potential $\Pi(x_1(t),\ x_2(t))=x_1 \ln(\nu-x_1)+x_2\ln(\nu-x_2)$ for the dynamics shown in (*a*). (*c*) Potential and related Lyapounov function of the dynamics shown in (*a*) and (*b*), with degree $\nu=30$.

system with maximum potential satisfies the criterion of evolution for the function F called orgatropy:

$$\mathrm{d}F^{l}(\nu^{\lambda}) \geqslant 0, \tag{7}$$

and defined from the following functions h and $\Pi_{\max}$ as:

$$F: \nu \rightarrow x_M \rightarrow y_M = F(\nu) = \Pi_{\max}\ o\ h(\nu).$$

This function is of importance with regard to the evolution of the system (O-FBS) and has been called orgatropy because of its similarity in form to physical entropy, as discussed below: the variation in time of $\Pi(n^{l}_{M})$ for level l is given by the function F when the degree of organization at that level varies without a re-organization of the system.

Proof: the maximum of Π is given by equation (4):

$$\mathrm{d}\Pi(x_M) = 0 \Leftrightarrow x_M = (\nu - x_M)\ln(\nu - x_M). \tag{8}$$

Let h be the implicit function of $\nu: \nu \rightarrow x_M = h(\nu)$. Then the equation of the maxima is obtained by eliminating ν between $\Pi(x) = x\ln(\nu - x)$ at x_M and $\mathrm{d}\Pi(x_M) = 0$:

$$y_M = \Pi_{\max}(x_M) = x_M^2/(\nu - x_M).$$

Then:

$$y_M = 2x_M \ln x_M - x_M \ln y_M. \tag{9}$$

For the function $F(\nu) = \Pi_{\max}\ o\ h(\nu)$, as defined above, it is easy to show that F is the product of two increasing functions, h and $\Pi_{\max}$. Indeed, by differentiating their definitional equation, one has

$$\frac{\mathrm{d}y_M}{\mathrm{d}x_M} = \frac{2 + \ln(x_M^2/y_M)}{1 + (x_M/y_M)}, \tag{10}$$

and:

$$\frac{\mathrm{d}x_M}{\mathrm{d}\nu} = \frac{1 + \ln(\nu - x_M)}{2 + \ln(\nu - x_M)} > 0. \tag{11}$$

Because

$$\frac{x_M^2}{y_M} = \nu - x_M > 1, \qquad \frac{x_M}{y_M} > 0,$$

the first ratio (10) is positive. Thus, $\Pi_{\max}$ and h increase, and therefore the product F also increases. Finally, $F(\nu)$ is obtained from the solution of:

$$x_M^2 + x_M y_M - \nu y_M = 0,$$

which is moved in $y_M = \Pi_{\max}(x_M)$.

(*b*) *Does orgatropy provide a criterion of evolution for the* (O-FBS)*?*

When the system grows by an increase in the number $\nu(t)$ of structural units, the concentration of sources and sinks varies such that the potential of organization remains maximum. But the quality of structural units is conserved, i.e. a source remains a source, and a sink remains a sink. In this case, the system (O-FBS) evolves in time without re-organization. We have shown that orgatropy cannot decrease, and thus gives a direction for its time evolution. The biological system evolves during development such that orgatropy, which represents the most developed combination of potentialities, increases.

chical system. A major problem is to determine if some

However, re-organizations are observed during the developmental process. Such re-organizations may be formally described as a sequence of specializations (paper I). Functional interactions are created during development, i.e. sources and sinks result in a hierar- principle governs this evolution. The orgatropy function does not include the process of specialization and therefore cannot describe the evolution of the system as a hierarchical system. It describes only a part of this evolution, i.e. the fact that functional interactions are added to the system without re-organization, therefore without the emergence of a hierarchy. But orgatropy includes the non-symmetry which is the main property of the functional interaction. This result is important in the framework of the theory, because of its self-coherence, and shows a fundamental distinction with physical entropy $S = \rho \ln \rho$ that describes the symmetrical structural interactions (see below).

5. CRITERION OF SPECIALIZATION AND RE-ORGANIZATION OF THE (O-FBS)

(*a*) *Criterion of specialization*

(i) *The concept of specialization*

The mathematical definition of specialization and the emergence of levels of organization in a hierarchical system raises a major difficulty. If the concept of functional interaction is accepted, then we can assign the following meaning to the notion of specialization. Let us assume that the l-level contains n_1 sinks for the product P_1, and n_2 sinks for the product P_2 such that $n_1 + n_2 < \nu$ (figure 4). Thus, at level l, some structural units synthesize a product P_1, some synthesize P_2, some synthesize both, and some synthesize other products different from P_1 and P_2, i.e.:

$$\nu = n_{P_1P_2} + n_{\overline{P_1}P_2} + n_{P_1\overline{P_2}} + n_{\overline{P_1P_2}}.$$

In this equation, $n_{\overline{P_1}P_2}$ for example, is the number of units that synthesize P_2 and not P_1. Therefore:

$$n_1 = n_{\overline{P_1}P_2} + n_{\overline{P_1P_2}}, \qquad n_2 = n_{P_1\overline{P_2}} + n_{\overline{P_1P_2}}.$$

If $n_1 + n_2 < \nu$ then: $n_{P_1P_2} \neq 0$, i.e. some units synthesize P_1 and P_2. Thus: $n_{P_1P_2} > n_{\overline{P_1P_2}}$.

Therefore, we define specialization as follows:

Definition

Given, at initial time $t^{(0)}, n_1^{(0)}$ sinks for the product P_1, and $n_2^{(0)}$ sinks for the product P_2, such that $\nu^{(0)} > n_1^{(0)} + n_2^{(0)}$, the transformation at this l-level, called specialization of the l-level at final time $t^{(f)}$, corresponds to a partition into two subsets of $n_1^{(f)}$ and $n_2^{(f)}$ units such that:

$$\nu^{(f)} = n_1^{(f)} + n_2^{(f)}. \qquad (12)$$

(ii) *The relation between specialization and hierarchization*

Thus, according to the definition of a structural unit (definition I, paper I), the subset constitutes a class of equivalence, and therefore a new structural unit: the transformation from initial time $t^{(0)}$ to final time $t^{(f)}$ corresponds to the emergence of a level of organization defined by new structural units that are specialized in the dynamics of $\{P_1,P_2\}$. This transformation of the 'quality' of units, which implies a different number of these units with a given quality, will be denoted by the specific operator δ. When, at time $t^{(0)}, n_1^{(0)}$ sinks for the product P_1, and $n_2^{(0)}$ sinks for the product P_2 constitute a partition of $\nu^{(0)}$ at $t^{(0)}$, we have the following property:

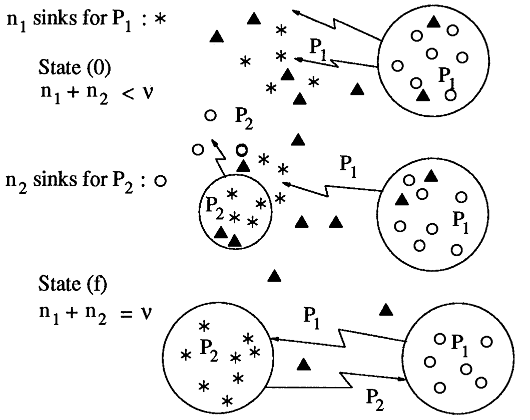

Figure 4. An interpretation of the mechanism of specialization with two products. From the top to the bottom, successive self-associations lead to two sets of structural units that produce only P_1 or P_2. At the beginning of the process, in the state denoted as (0), there are n_1 sinks for P_1, and n_2 other sinks such that: $n_1 + n_2 < \nu$. In the final state (f) there are only two sets, one producing P_1 (on the right), the other producing P_2 (on the left), and therefore: $n_1 + n_2 = \nu$, which is the condition of specialization.

Property V: hierarchization operator

Let l be a level of organization with $\nu^{(0)}$ structural units whose $n_1^{(0)}$ and $n_2^{(0)}$ are sinks for the products P_1 and P_2 respectively. A necessary and sufficient condition for the re-organization of the system through emergence of a higher level of organization is the maximization of Π^l:

$$\mathrm{d}\Pi^l(n_1^{(0)}, n_2^{(0)}) = 0, \qquad (13)$$

where $n_1^{(0)}$ and $n_2^{(0)}$ are two sets of structural units such that $\nu^{(0)} \neq n_1^{(0)} + n_2^{(0)}$, specialized in the production of P_2 and P_1 respectively. Then:

$$\delta \nu^l = \nu^{(f)} - \nu^{(0)} < 0, \qquad \delta F^l \leqslant 0, \qquad (14)$$

and the system, which reaches its maximum is stabilized for P_1 and P_2.

Note that if $\mathrm{d}\nu^l > 0$ without re-organization, then $\nu^{(f)} - \nu^{(0)} < 0$ after re-organization. That transformation in the hierarchical system is denoted by the operator $\delta : \delta \nu^l < 0$. With the same notation, $\delta F^l \leqslant 0$ whereas $\mathrm{d}F^l > 0$.

Proof: the condition of maximality of Π is:

$$\partial \Pi / \partial x_1 = \partial \Pi / \partial x_2 = 0. \qquad (15)$$

In the initial state (0), there are $n_1^{(0)}$ sinks and $n_2^{(0)}$ sources in the l-level of organization, such that: $\nu^{(0)} \neq n_1^{(0)} + n_2^{(0)}$. In the final state (f), the partition of the system is expressed by:

$$\nu^{(f)} = n_1^{(f)} + n_2^{(f)}, \qquad \nu^{(f)} \neq \nu^{(0)}. \qquad (16)$$

Conditions (4) give two relations in x_1 and x_2:

$$\ln(\nu - x_1) - x_1/(\nu - x_1) = 0 \Rightarrow \ln x_2 = x_1/x_2,$$
$$\ln(\nu - x_2) - x_2/(\nu - x_2) = 0 \Rightarrow \ln x_1 = x_2/x_1, \qquad (17)$$

which determine $x_1^{(f)}$ and $x_2^{(f)}$, and then $\nu^{(f)}$. The vector $(x_1^{(f)},x_2^{(f)}) = (e,e)$ is the only solution of the system (17):

$$x_1 = x_2 \ln x_2,$$

$$x_2 = x_1 \ln x_1. \qquad (18)$$

A mathematical difficulty exists for the solution in integer numbers. In Appendix 3, we show that the partition of the system with a maximum potential can also be obtained for the vectors (3,3) and (4,4). An interpretation of this strange property will be given below. Let us assume now that these three solutions are possible, and take the solution (2,2) as a representative solution in the following. Then:

$$(n_1^{(f)},n_2^{(f)}) = (2,2), \qquad (19)$$

is the integer solution of this problem. Inversely, if e is a solution of (17), then Π is maximal. Thus, we see that if we have a partition of $\nu^{(f)}$ units into $x_1^{(f)}$ sinks for P_1 and $x_2^{(f)}$ sinks for P_2, then the potential Π will be maximal if $x_1^{(f)} = x_2^{(f)} = e$.

Finally, $\mathrm{d}F = 0$, because $\mathrm{d}\Pi(x)/\mathrm{d}x = 0$ for $x = e$, and $\Pi_{\max}(e) = e$. The transformation from $\nu^{(0)}$ to $\nu^{(f)} < \nu^{(0)}$, which corresponds to an increase of units $\nu(t_f) > \nu(t_0)$ without re-organization is such that $\mathrm{d}F(\nu) \geqslant 0$: the criterion of evolution $F(\nu(t_f)) \geqslant F(\nu(t_0))$ is verified, and emergence of a level of organization represented by operator δ is described in terms of the orgatropy function by the relation: $\delta F(\nu) = F(\nu^{(f)}) - F(\nu^{(0)}) \leqslant 0$ that is therefore verified with $e = F(\nu^{(f)})$. For this reason, δ will be called the 'hierarchization operator'.

(*b*) *Consequence: mathematical expressions of specialization and emergence of a level of organization*

When the l-level of organization contains exactly $\nu = N$ structural units whose n_1 receive P_1 (or equivalently, $N_1 = N - n_1$ emit P_2), and n_2 receive $P_2 (N_2 = N - n_2$ emit $P_1)$, then the constraint:

$$\nu^{(f)} = n_1^{(f)} + n_2^{(f)}, \qquad (20)$$

implies the creation of a higher $(l+1)$-level, so that N_1 structural units synthesize P_2, and N_2 synthesize P_1. From definition I (see paper I), a structural equivalence class results from the specialization of units, and a higher level is obtained (figure 5). From property III, this system passes from one stable extremum of the organization to another when the degre of organization varies. So, in one state of organization, one has a mathematical expression of specialization as:

$$N_1(t;P_1) + N_2(t;P_2) = N_1^2 = \text{constant}.$$

Or:

$$\mathrm{d}N_1^{2,l}(t) = 0, \qquad (21)$$

that describes the time invariance of the partition at level l for products P_1 and P_2.

Both conditions: Π maximal and partition of ν, lead to a reduction of the number of structural units, and correlatively to the creation of a level for the corresponding hierarchical system:

$$n_1^{(f)} = 2 \ll n_1^{(0)} \qquad n_2^{(f)} = 2 \ll n_2^{(0)}. \qquad (22)$$

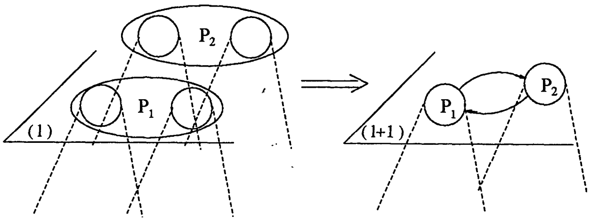

Figure 5. Emergence of a level of organization. Assuming that the conditions of specialization have occurred, as in figure 4, then we see that two new structural units have been created at the upper level, because they are respectively specialized in the production of P_1 and P_2. On the left, a similar figure to figure 4; on the right, the new level of organization.

These two new sets of units collectively execute the elementary physiological functions P_2 and P_1 respectively. The variation of the potential of organization from the initial state (0) to the final state (f) is expressed by:

$$^{(0)}\Pi^l = n_1^{(0)} \ln n_2^{(0)} + n_2^{(0)} \ln n_1^{(0)},$$

$$^{(f)}\Pi^l = n_1^{(f)} \ln x_2^{(f)} + n_2^{(f)} \ln x_1^{(f)} = 4. \qquad (23)$$

Then:

$$^{(0)}\Pi^l > {}^{(f)}\Pi^l = \Pi^{l+1}. \qquad (24)$$

This relation corresponds to the required property (iii) of Π in § 2*a*. Expression (24) mathematically describes the emergence of a level of organization.

(*c*) *Functional order*

In section 4, a function $F(\nu)$ was used to describe the evolution of an FBS without re-organization. Here, a similar function is found to describe the evolution of the FBS when re-organization (with specialization) is assumed. It is shown that a function $\Omega(t)$, called the functional order, describes the evolution of the hierarchical system.

Definition

The functional order of a biological hierarchical system is defined by the state function:

$$\Omega(t) = -\sum_{l=1}^{L} F^l(\nu^l). \qquad (25)$$

Theorem: on the time evolution of an (O-FBS)

Let a biological system be defined by the extremum hypothesis:

$$\Pi(n_M^l)_{l=1,L} \text{ maximal} \Leftrightarrow \forall\alpha = 1,\mu^l$$

$$\begin{aligned} &(\mathrm{d}n_\alpha^l(t) < 0 \quad \text{if} \quad n_\alpha^l > n_M^l),\\ \text{or}\quad &(\mathrm{d}n_\alpha^l(t) = 0 \quad \text{if} \quad n_\alpha^l = n_M),\\ \text{or}\quad &(\mathrm{d}n_\alpha^l(t) > 0 \quad \text{if} \quad n_\alpha^l < n_M), \end{aligned} \qquad (26)$$

for all $l = 1,L$. If its degree of organization, ν^l, is modified such that the criterion of specialization is satisfied for products P_α and P_β:

$$\mathrm{d}N_\alpha^\beta(t) = 0, \tag{27}$$

then the self-organization of the system is such that:

1. At most two structural equivalence classes are created, each being specialized in the production of a given product, according to a bi-unitary process (by association of two units):

$$\delta\nu^l < 0. \tag{28}$$

2. Its functional order increases and corresponds to the emergence of one level of organization:

$$\delta\Omega \geqslant 0, \tag{29}$$

and simultaneously its orgatropy decreases:

$$\delta F \leqslant 0.$$

3. The potential of organization Π decreases:

$${}^{(0)}\Pi^l \rightarrow \Pi^{l+1} = {}^{(\int)}\Pi^l < {}^{(0)}\Pi^l. \tag{30}$$

4. At the limit, in the state of maximum specialization, Π is minimum and its value is:

$$\Pi^{l+p} = 2\mu^l, \tag{31}$$

with $p = \mu/2$ if μ^l is even, and:

$$\Pi^{l+p} = 2(\mu^l - 1) + \Pi^l_\omega, \tag{32}$$

with $p = (\mu^l - 1)/2$ if μ^l is odd, where μ^l is the number of products in the l-level before the complete specialization of the units, and p is the step of the last product synthesized.

Demonstration

1. Property V (the criterion of specialization) can be generalized as follows. The question is: in a system with ν^l structural units that exchange their products, is it possible to obtain a partition of ν^l according to the numbers $(n_\alpha^l)_{\alpha=1,\mu^l}$? In other words, can the number of units $N_\alpha = N_\alpha^\beta - n_\alpha$ evolve towards the number of units $N_\alpha^{(\int)}$ which are specialized in the production of P_α, i.e. which emit only the product P_α consumed by all the other units? The extremum condition (26) leads to a system that is similar to (17):

$$n_\alpha = S_\alpha \ln S_\alpha \qquad \forall\alpha = 1,\mu^l,$$

and:

$$S_\alpha = \sum_{\beta=1}^{\mu} n_\beta \qquad \beta \neq \alpha,$$

whose solution in $\mathbb{R}^\mu$ is:

$$x_\alpha = (1/(\mu - 1)) \exp 1/(\mu - 1)\,,$$

for all α. In $\mathbb{N}$, $n_\alpha = 0$ when $\mu \geqslant 3$. Therefore, the partition applies only to a maximum of two sets of units.

2. The functional order is defined by (25), and its time derivative is:

$$\frac{\mathrm{d}\Omega}{\mathrm{d}t} = -\sum_{l=1}^{L} \frac{\partial F^l}{\partial \nu^l}\frac{\delta\nu^l}{\partial t} \geqslant 0,$$

due to the signs of $\mathrm{d}F/\mathrm{d}\nu \geqslant 0$ (property IV), and $\delta\nu < 0$ (property V for two given products at this level).

3. The potential of organization in the initial state (0) is:

$${}^{(0)}\Pi^l = \sum_{\alpha=1}^{\mu^l} (\nu^l - N_\alpha^l) \ln N_\alpha^l\,. \tag{33}$$

The condition of specialization (27) implies:

$$N_\alpha(t;P_\alpha) + N_\beta(t;P_\beta) = N_\alpha^\beta = K, \tag{34}$$

where K is a constant. It describes the invariance of the partition at this level and indicates whether a variation occurs in the topology of the system. Therefore, with $\alpha = 1$ and $\beta = 2$, following the property V, the outcome is:

$${}^{(0)}\Pi^l = N_1^{(0)} \ln N_2^{(0)} + N_2^{(0)} \ln N_1^{(0)} + \sum_{\alpha=3}^{\mu^l} \Pi^l_\alpha\,, \tag{35}$$

and:

$$\begin{aligned} N_1 &= N_2 \ln N_2, \\ N_2 &= N_1 \ln N_1, \\ N_1^{(\int)} &= N_2^{(\int)} = 2. \end{aligned}$$

So the re-organization of the l-level leads to:

$${}^{(\int)}\Pi^l = 2 + 2 + \sum_{\alpha=3}^{\mu^l} \Pi^l_\alpha < {}^{(0)}\Pi^l, \tag{36}$$

assuming that Π^{l+1} is defined by:

$$\Pi^{l+1} = {}^{(\int)}\Pi^l. \tag{37}$$

4. This condition of specialization can be repeated for two elementary functions P_α and P_β, $\alpha,\beta = 3$ to μ^l if μ^l is even, and $\alpha,\beta = 3$ to $\mu^l - 1$ if μ^l is odd. Then, the decomposition of this expression is obtained $p = \mu^l/2$ times, if μ^l is even, and $p = (\mu^l - 1)/2$ if μ^l is odd.

(*d*) *Evolution of an (O-FBS) during development: discussion*

Two biological properties are characteristic of the FBS studied here: (i) identical potentialities for all structural units (equipotent system) at each level, and (ii) variations within a given unit for a given product (Darwinian mutational system or genetic program). It is important to know whether these biological properties lead to the interpretation of other biological properties, and whether they provide the means of evolving into a more complex biological system, closer to a real biological system. The criterion for the evolution of functional organization can lead to some formalized properties of biological systems that will have to be experimentally confirmed.

For example, let us consider a (formal) tissue having the following organization: $N_1^{(0)}$ units $u_1(P_1,P_2,P_3,P_4,\ldots)$ which supply $P_1,P_2,P_3,P_4,\ldots$. With the same notation, $N_2^{(0)}$ units $u_2(P_1,P_2,P_3,P_4,\ldots)$, $N_3^{(0)}$ units $u_3(P_1,P_2,P_3,P_4,\ldots),\ldots$ supply $P_1,P_2,P_3,P_4,\ldots$. According to the above theorem, the l-level will evolve towards a new organization $(N_1^{(\int)},N_2^{(\int)},N_3^{(0)},N_4^{(0)},\ldots)$ that can be described by the sequence:

$$2{*}u_1(P_1,P_3,P_4,\ldots),\quad 2{*}u_2(P_2,P_3,P_4,\ldots),\quad N_3^{(0)}{*}u_3(P_3,P_4,\ldots),\quad N_4^{(0)}{*}u_4(P_3,P_4,\ldots),\ldots$$

So, we can say that, in the final state (f), the two units $u_1(P_1,P_3,P_4,\ldots)$ are two structural equivalence classes that contain all units supplying P_1, which is considered in state (0) before the re-organization of the entire system. They constitute the highest level of organization of the hierarchical system, which is specialized in the production of P_1. The same result is obtained for $u_2(P_2,P_3,P_4,\ldots)$. Therefore, two parallel hierarchical systems, coupled by both functional interactions P_1 and P_2, appear in the final state (f) (figure 5).

In the previous section, we have shown that a system with a maximum potential can increase its specialization by achieving a partition into two new structural units. The analysis with real numbers, which gives a unique solution (e,e) leads to three possibilities with integer numbers: (2,2), (3,3) and (4,4). It is interesting to look for some physiological functions having such a number of structural units. At the highest level of functional organization, most of the physiological functions are realized by two structural units, e.g. eyes, lungs, and kidneys, but only one function, calcium control, involves four structural units: the parathyroids.

6. APPLICATION TO THE NERVOUS SYSTEM

(*a*) *Controlling and controlled systems*

It is possible to elicit at least two kinds of interaction in a physiological system composed of structural units (definition I, paper I): (i) the organical links are the functional interactions between, and within, the levels of organization of the (O-FBS) (see definition II, paper I). The collective behavior of such interactions, at a given level, is a collective function called a physiological function. The levels are arranged in a hierarchical system that together can be identified as one organ (or an organit) of an organism, (ii) the control links need another hierarchical system, called the controlling system, whose physiological functions act upon defined sites (levels of organization) of the controlled system. Finally, there exists a constitutive coupling due to the internal dynamics of each system: the dynamics at one level will be shown (paper III) to act as a parameter upon the next higher level. Thus, an extrinsic control achieved by specific systems, such as the nervous or hormonal systems, is added to the intrinsic one. In the nervous system, a neuron or a group of neurons acts on another and modifies its activity.

(*b*) *Levels of organization in the nervous system*

(i) *Derivation from the definitions*

With the general concepts introduced in the foregoing section, it is possible to identify two levels of organization: the set of neurons and the set of structures in one neuron. But, with groups of neurons and intracellular structures, at least five levels may exist in the central nervous system. Specifically, in a given area of the cell, (i) membrane structures like synapses, extra- and intra-synaptic channels and receptors, and (ii) internal neuronal cytoplasmic structures, are associated in a collective function which determines the soma membrane potential, the modification of which can give rise to an action potential. Let $E_{s_\alpha}^{MP} \equiv s_\alpha$ be this set of substructures. Then s_α, $\alpha = 1$, N is one element of the set E^{AP} that produces the action potential. That is to say, E^{AP} is the set of structural units $s_1,s_2,\ldots,s_\alpha,\ldots$ which participate in the emission of an action potential. The set E^{MP} constitutes one level of organization, and E^{AP} is another level of a hierarchical functional system (figure 6). Therefore, dynamical equations apply to these interactions from one element s_1 to another s_2 localized in the space of synapses, the s-space denoted D_s. Since s_α contains extrasynaptic elements, such as voltage-dependent channels or cytoplasmic structures, we shall call each element in E^{AP} a 'synapson'.

Let $\mu_{12}(t)$ be the functional interaction between two such elements s_1 and s_2 localized in D_s. With these notations, $\mu_{12}(t)$ will describe the ability of a synapse (synapse 1) to conduct the signal from the presynaptic to the postsynaptic neuron, but it also represents the action from one synapse s_1 to another s_2 by diffusion of the mediator in the extracellular medium, or via the membrane or the cytoplasm (cytoskeleton), or because of electrotonic conduction. At this point it is not useful to go into further details, but it is important to note that the abstract representation must contain all the physiological elements that participate in the propagation of the signal. The transport of the signal between two synapsons s_1 and s_2 can be specifically described according to the equation:

$$\Phi_2(s_2) = \mu_{12}(\Phi_1;s_1), \tag{38}$$

where Φ_1 is the postsynaptic potential that results from a sequence of phenomena such as transmitter release in the synaptic cleft, binding with postsynaptic receptors, and ion channel activation. The postsynaptic

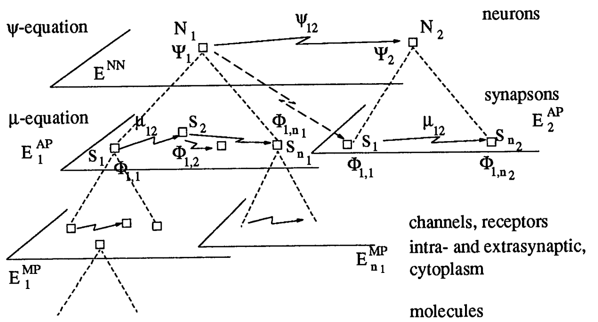

Figure 6. Functional organization in the nervous system with, at least, three levels of organization. A neuron N_i is considered to be composed of 'synapsons' s_j, $j=1$, n_i at the lower level. Each synapson is composed of structural units channels, receptors, etc. Functional interactions are represented by ψ_{12}, μ_{12}, etc. Levels are denoted by E^{NN}, E_1^{AP}, E_1^{MP}.

potential Φ_2 results from: (i) non-local interaction due to, among other causes, the electrotonic conduction; (ii) local transformation localized in s_2 due to internal biochemical processes, and which is, for this reason, called a source. The equation that describes the time-evolution of the μ_{12}'s is:

$$\mathrm{d}\mu/\mathrm{d}t = f_{\mu}(\mu;\pi), \tag{39}$$

where π represents the geometrical factors that determine the connectivity and the number of synapsons. Finally, the synaptic level of organization $E^{AP} \equiv \{s_{\alpha}, \forall\alpha\}$ is represented by extrasynaptic and synaptic structures s_{α} with a functional interaction between the structures, and a local transformation within the structures.

(ii) *Interpretation based on the general schema of self-association (paper I)*

We have shown in paper I (equation 12) that the diagram:

$$\begin{tikzcd} P_1 \arrow[rr, "\Phi"] \arrow[dr, "\psi"'] & & P_2^* \\ & P_1^* \arrow[ur, "\phi"'] & \end{tikzcd} \tag{40}$$

represents a sequence Φ of a non-local interaction ψ (left part) between two units u and u^*, and local transformations ϕ (right part) in u^*. This elementary diagram has been generalized into an abstract composite diagram (paper I, schema 15):

$$\begin{tikzcd} P_1^* \arrow[r, "\alpha_1"] \arrow[d, shift left] & P_2^* \arrow[r, "\alpha_2"] \arrow[d, shift left] & P_3^* \arrow[r, "\alpha_3"] \arrow[d, shift left] & P_4^* \arrow[r, "\alpha_4"] \arrow[d, shift left] & \ldots \\ P_1 \arrow[r, "\alpha_1"'] \arrow[u, shift left, "g_1"] & P_2 \arrow[r, "\alpha_2"'] \arrow[u, shift left, "g_2"] & P_3 \arrow[r, "\alpha_3"'] \arrow[u, shift left, "g_3"] & P_4 \arrow[r, "\alpha_4"'] \arrow[u, shift left, "g_4"] & \ldots \end{tikzcd} . \tag{41}$$

Such schemes result from the general description of the theory. In the following, we will describe how they can be interpreted for the two present levels of organization of the nervous tissue.

The set $E_1^{AP} \equiv \{s_{\alpha}^1, \alpha = 1, n_1\}$ of n_1 synapsons s_{α}^1 constitutes the 1-neuron. The collective behavior of E_1^{AP} is to produce an action potential Ψ_1 that acts upon another set $E_2^{AP} \equiv \{s_{\alpha}^2, \alpha = 1, n_2\}$ of n_2 synapsons, i.e. a 2-neuron set, that produces an action potential Ψ_2 (figure 6). Therefore, the set of neurons E^{NN}, which is a real neural network localized in a space denoted the r-space, constitutes a third level of organization. In other words, a structural unit of the neural network is composed of the structural units that are represented by one set of synapsons (the neuron), with functional interactions between them due to their connectivity. These interactions couple the two levels of organization, because one neuron is connected to other neurons via their synaptic connections, i.e. the units of the second level directly connect (regarding their topology and not their possible distance) the units of the first level. Because the end-product in relations (41) can be interpreted as the membrane potential, the non-local and non-symmetric transport function $g \equiv \psi$ as the transport of the action potential, and the local transformations at the lower level as the non-symmetric interactions between synapses, diagram (40) can be represented:

$$\begin{tikzcd} \Psi_1 \arrow[rr, "\Phi"] \arrow[dr, "\mu_{12}"'] & & \Psi_2 \\ & \Phi_{\alpha} \arrow[ur, "\Gamma_{\psi}"'] & \end{tikzcd} , \tag{40$'$}$$

and, by using the diagram (41) extended to two levels of organization (thus with a different meaning for the lines), we can obtain at least for the two first steps:

$$\begin{tikzcd} \Psi_1 \arrow[r] & \Psi_2 \\ (\Phi_{\alpha})_1 \arrow[r, "\mu_{12}^{1,2}"'] \arrow[u, "\Gamma_1"] & (\Phi_{\alpha})_2 \arrow[u, "\Gamma_2"'] \end{tikzcd} . \tag{41$'$}$$

This diagram shows the two levels of organization with their respective functional interactions μ and ψ. In this diagram, the two subscripts 1 and 2 at the lower level correspond to each of the neurons of the upper level: This is included in the notation of the functional interaction $\mu_{12}^{i}, i = 1,2$. The local transformations in each i-neuron ($i = 1,2$) are represented by Γ_i. Two consequences appear from this abstract representation: (i) because each neuron is at a different location in physical space, the interaction is a field variable and Γ_i is the source of the field (Chauvet 1993*a*,*b*). We have the same consequence for the synapses. Moreover, as will be shown in more detail in paper III, interactions are non-local and non-symmetric; and (ii) the abstract diagram (41) is very general, and valid for many systems, because the fundamental concepts of non-locality and non-symmetry, and the functional hierarchy thereof, are included. The self-association hypothesis on which the present formulation is based, leads to an hierarchical interpretation of the nervous system. In the specific example described in paper I, a micromutation was the source of the association between two structural units, one is 'normal' and the other is 'pathological' or 'modified'. The related physiological process is non-symmetrical because the global result of the transport is positive from u to u^*, even in the case of pure diffusion. Any kind of transformation can lead to such a schema, particularly a structural transformation in the unit which involves a functional modification. For example, in the case of the nervous tissue, a neuron u^* is different from a neuron u because of a difference of synaptic structure, e.g. due to the connectivity. It is known that an isolated neuron cannot survive. We may therefore say that, for its survival, each neuron has to associate with at least another. The association between two neurons corresponds to the diagram (40′) and the collective function of emitting an action potential to act on the second neuron corresponds to the diagram (41′). An important question is to know whether there is an increase of the domain of stability after association (see paper III). This question is related to the dynamics of the system, which can be expressed according to the diagram (40′) by $\Psi_2 = \psi_{12}(\Psi_1)$ or:

$$\Psi_2 = F[(\Phi_{\alpha}^{1,2})_1, (\Phi_{\alpha}^{1,2})_2; \mu_{12}, \Gamma_2]. \tag{42}$$

This equation is obviously more complicated than the preceding because of the couplings between the two levels of organization. Finally, the dynamics of the functional interaction ψ_{12} are governed by:

$$\mathrm{d}\psi_{12}/\mathrm{d}t = f(\psi_{12};\mu_{12}^{1,2},\rho,\pi), \tag{42'}$$

where ρ is the density of neurons, and π is the density-connectivity of synapses between neurons. This equation yields $\mu_{12}^{1,2}$ as a parameter: $\mu_{12}^{1,2}$, which is a variable at the first level satisfying equation (39), constitutes a parameter for the second level. This parameter, which concerns the (D-FBS), will be studied in paper III.

(*c*) ***Extremum hypothesis***

The potential of functional organization can be calculated from equation (1) as follows. The link between two neurons is, in fact, the link between one neuron, the source, and several sinks, the synapses in the neuron target. Therefore, the two levels of organization previously described have to be considered for the determination of the potential of functional organization. The 'product' can be identified as the electrical potential transmitted between the two neurons, including axon and dendrites which are the support of these potentials. For example, we can consider the simple monosynaptic pathway represented in figure 7, where two layers of pre- and postsynaptic neurons at r and r_0 respectively are separated by a given number of synapses at s. Formally, each neuron target at r_0 is coupled with a source at r through the synapses sinks.

Under the conditions of the above theory, we study the growth of such a nervous monosynaptic tissue when the number of sinks varies in the system that is constituted of ν neurons. Let n be the number of neuron targets, $N = \nu - n$ the number of neuron sources, because a sink cannot be a source for the same product, i.e. a transformation exists in the source, and, therefore, because of the following constraint: number of neuron sources + number of neuron targets = total number of neurons. Let $g_k(n)$ be the number of synapses for the kth target-neuron, $k = 1,n$. Then, the number of potential associations is:

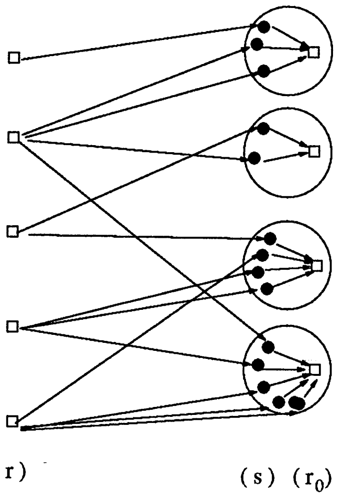

Figure 7. A monosynaptic pathway in the nervous system represented as the two sets of sources and sinks in the general theory. Neurons at r_0 contain synapses s originating from neurons at r. The calculation of the potential of organization has to take into account this specific organization.

$$o = \prod_{k=1}^{n} (C_N^1 + C_N^2 + \ldots + C_N^{g_k}), \tag{43}$$

and, from definition VI, the potential of organization is:

$$\Pi = \sum_{k=1}^{n} \ln(C_N^1 + C_N^2 + \ldots + C_N^{g_k}), \tag{44}$$

which is a generalization of equation (3). In paper III, a more precise expression will be given as a function of the spatial location of neurons and synapses. It is possible to show that Π satisfies property II, i.e. the existence of a maximum for the curve $\Pi(n)$. Such a function can be expressed by means of a function of repartition, and exact results for the potential of organization can be deduced. In the particular case where $g \ll N$ with g_k large enough, for example, $g_k \simeq 100$, $N \simeq 10\,000$. Then the sum in (44) is equivalent to the term with largest degree in g_k:

$$o = \prod (N^{g_k}/g_k!), \tag{45}$$

and:

$$\Pi(n) = \left(\sum_{k=1}^{n} g_k\right) \ln N - \sum_{k=1}^{n} \ln(g_k!). \tag{46}$$

By applying the Sterling formula: $g_k! \simeq g_k \ln g_k - g_k$, g_k large, we have:

$$\Pi(n) = \sum_{k=1}^{n} g_k \left(1 + \ln \frac{\nu - n}{g_k}\right). \tag{47}$$

The variational approach can be applied to the nervous system by varying the number $\nu - n$ and n of pre- and post synaptic neurons. In this case, the number g_k of synapses is obviously variable: $g_k \equiv g_k(n)$. The calculation of the differential of Π gives:

$$\mathrm{d}\Pi(n) = \sum_k \left(\frac{\mathrm{d}g_k}{\mathrm{d}n} \ln \frac{\nu - n}{g_k} - \frac{g_k}{\nu - n}\right) \mathrm{d}n + g_n(n) \left(1 + \ln \frac{\nu - n}{g_n}\right). \tag{48}$$

As shown in figure 8, the sum of n functions

$$g_k(n) \left(1 + \ln \frac{\nu - n}{g_k(n)}\right)$$

that have one and only one maximum also has this property. A sufficient condition of existence of a maximum is that curve $1/X$ cuts the curve $\ln X$ where $X = (\nu - n)/g_k$, i.e. function $g_k(n)$ describes an increase in the total number of synapses with the number of

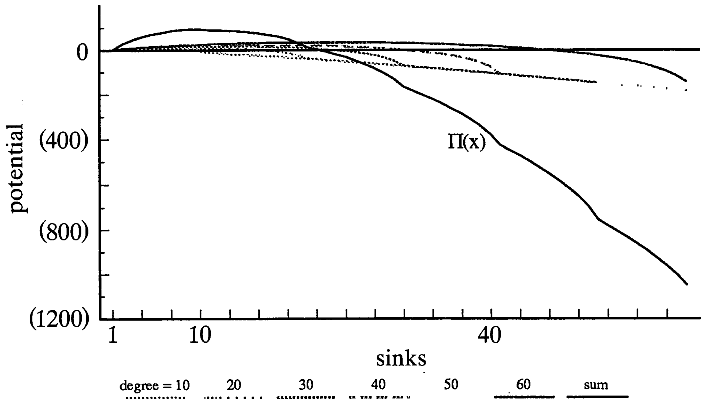

Figure 8. Potential of functional organization for the monosynaptic pathway represented in figure 7. The fundamental property is again obtained: there is a maximum for each term of the sum, and thus for the potential $\Pi(x)$.

neurons. Because this property can be accepted in absence of re-organization:

$$\frac{\partial g}{\partial n} > 0, \qquad \mathrm{d}n > 0,$$

we can assume that the monosynaptic pathway satisfies property II of the general theory. Is this system an element of the class of biological systems that satisfy the extremum hypothesis? In other words, according to property III, do these systems lead to monotonic dynamics of the number of sinks? It is known (see, for example, Hopkins & Brown (1984)) that, after a period which corresponds to proliferation and settling at their final destination, during which the number of neurons rises to a maximum, extensive death eliminates at least half of the total number of neurons. Neuronal death is a major event in neuronal development. In the proposed theory, the initial time of the dynamics of the sinks corresponds to the time where a given functional process starts. This theory predicts the existence of two different functional processes. The first concerns the proliferation by cell division (ν increases, $\mathrm{d}F(\nu) > 0$), from initial time to a maximum, then a second process (different from a physiological point of view) that concerns the organization of synaptic connections with a decrease in the number n of neuron targets. Simultaneously, a re-organization of synaptic connections is observed such that the number of synapses decreases ($\delta g < 0, \delta F(\nu) \leqslant 0$). Are these predictions verified? It is known that there exists an elimination of multiple innervation in the submandibular ganglion of the rat which corresponds to what we have called 'specialization' (figure 9). Thus, the consequences of the present theory agree with experimental observations, including the polysynaptic pathway. All of these arguments agree to assume that the potential of functional organization remains maximum during development. Of course, it will be necessary to enter into more details, e.g. to find out the dynamics of the sinks, and to use the exact conditions of derivation for equation (47), but the preliminary results obtained here give the bases of a variational approach. In paper III, it will be shown the effect of dynamics on the variation of the number of sinks, i.e. the coupling between a physiological function such as learning (the process) and the functional organization (the synaptic specialization).

7. CONSEQUENCES AND CONCLUSION: BIOLOGICAL AND PHYSICAL SYSTEMS

(*a*) *(Structural) entropy and (functional) orgatropy*

For a molecular gas described by a velocity distribution function $f(v)$, Boltzmann (1872) defined the quantity H:

$$H = \iiint f(v) \ln f(v) \mathrm{d}v,$$

such that $\mathrm{d}H \leqslant 0$. Later, Boltzmann (1877) identified the quantity H with the entropy S:

$$S = -k H.$$

Therefore: $\mathrm{d}S \geqslant 0$. In that expression, k is the Boltzmann constant. This definition is statistical in character, because it is based on the statistical mechanical description of a molecular gas. More generally, a statistical mechanical definition of S, valid for an arbitrary system obeying the laws of classical mechanics in canonical form versus phase variables (p,q), is:

$$S = -k \iint f(p,q) \ln f(p,q) \mathrm{d}p \mathrm{d}q.$$

Then Gibbs (1902), with his formulation in terms of

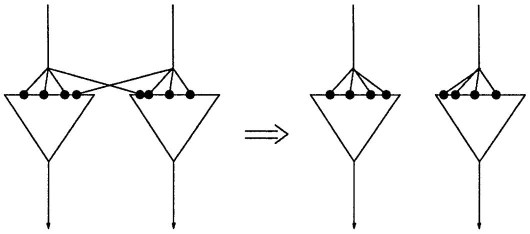

Figure 9. Mechanism of specialization in the nervous system during development. The synaptic connections between two neurons are suppressed. This fact corresponds to the property of 'specialization', and verifies the prediction of the present theory, at least for the nervous system.

Table 1. *Comparison between physical systems and biological systems*

	function	derivative	
structural organization (in physical isolated systems and biological systems)	thermodynamical entropy	S	$\mathrm{d}S \geqslant 0$
	neguentropy	$N = -S$	$\mathrm{d}N \leqslant 0$
	Lyapounov function	$P = d_i S \quad P \geqslant 0$	$\mathrm{d}P \leqslant 0$
functional organization (in biological systems only)	orgatropy	F	$\mathrm{d}F(v) > 0 \quad \delta F(v) \leqslant 0$
	functional order	$\Omega = -F$	$\delta\Omega \geqslant 0$
	Lyapounov function	$\Omega < 0$	$\delta\Omega \geqslant 0$

statistical ensembles, conceived entropy as an ensemble property. This definition of entropy provides a link between information and entropy. Our definition of orgatropy F is of a different nature:

1. $F(v)$ describes the maximum potential of organization $\Pi_{\max}$ for a non-statistical ensemble.
2. The definition of Π elicits a property of non-symmetry expressing the fact that a source is not equivalent to a sink. This property appears as basic: in physics, interaction is a force which couples two elements (action and reaction imply interaction); in biology, the functional interaction describes a non-symmetrical effect of one element on another. So, distinctive roles are attributed to the source and the sink.
3. The definition of Π needs an equipotence principle for each level of organization. In contrast, a physical system is intrinsically supposed to apply to an equilibrium state, and therefore satisfies a principle of energy equipartition.
4. Orgatropy is a global concept regarding sources and sinks.

A physical system is defined by the large number of states in the phase space through which it can pass. Thus, a definition of the equilibrium state is the condition of greatest probability with present constraints. A biological system is defined, in part, by its functional topology. The related organizational system, represented by (O-FBS), is not statistical in character, although the dynamic system (D-FBS) has this property. One important problem will be the effect of a perturbation of the (D-FBS) related to geometry on the (O-FBS), i.e. the influence of a structural perturbation on the functional organization.

(*b*) *What is the essential consequence of the optimum principle?*

What is the major result of the theorem on the evolution of the (O-FBS)? The criterion (7) and the extremum hypothesis (26) imply an increase in the complexity at the l-level. At the same time, the system decreases this complexity by means of a re-organization which, in turn, increases the number of levels. Assuming the proposed definitions, it is possible to conclude that an organism, i.e. a system that possesses both the basic qualities of being equipotent and mutational, evolves according to the principles of a decrease in orgatropy and an increase in functional order.

This consequence of the optimum principle provides a definition for living systems, by making a clear distinction between biological and physical systems (table 1). The evolution of a physical system is characterized by an increase in the thermodynamical entropy, i.e. by an increase in the molecular disorder (second principle of thermodynamics). Regarding its structure, i.e. its physical, molecular structure, a biological system obviously satisfies the second principle, which states that the production of entropy $P = d_i S$ is a Lyapounov function. In contrast, the functional organization, which is the critical feature of a biological system, evolves with a decrease in orgatropy and an increase in functional order.

In summary, a living system is characterized by two complementary sets of mathematical laws: the first set governs the physical structure with an optimum principle concerning thermodynamical entropy (Prigogine's criterion of evolution: Prigogine 1947; Glansdorff & Prigogine 1971), including living organisms (Prigogine *et al.* 1972); whereas the second set governs the organization of physiological functions with an optimum principle concerning the potential of organization. A law concerning the functional order results from this second optimum principle. The state functions, and their criterion of evolution, for both structural organization and functional organization are summarized in table 1.

(*c*) *What is the meaning of the optimum principle?*

Our theory of functional organization is based on the extremum hypothesis: a biological system evolves such that its potential of organization remains maximum. A sufficient condition of this extemum hypothesis is the monotonic trend of the dynamics of the sinks towards an asymptotical limit. Even without the complete knowledge of the dynamics, such a property can be experimentally observed and constitutes an argument if it is observed for a specific biological system, as we have seen in the case of the nervous system. Therefore, the problem in biological terms is to find out if such behaviour can be observed during development, and, in particular, if during embryogenesis, an organism has an optimum number of sources which emit chemical products, signals, or execute any kind of elementary function, necessary for the maintenance of life.

Probably a living system has to have an optimum number of sources, i.e. defined as implying Π maximum, at least at the beginning of life, before some adjustments are achieved by intrinsic and/or extrinsic controls. Then, it could be said that the number of sinks as a function of time evolves toward a minimum. For example, we know of the occurrence of spontaneous neuronal death during neuroembryogenesis and of the regression of the number of nerve endings. As we have shown, the latter process presumably corresponds to 'learning' or adaptation to specific circumstances. At this point, experimentation will have to be done on a living system to determine whether the number of sinks evolves, monotonically, towards a minimum or a maximum during its development.

This formulation of a biological system was made in terms of functional interactions in the representation (ψ,ρ). There is a great difference with the representation (N,a) (see paper I), where N (generally a large number) is the occupation number of a functional equivalence class, and a is the rate constant between classes. Statistical methods can be employed: Kerner (1957, 1972) and Cowan (1968) have transposed statistical mechanics to population models. Demetrius (1983, 1984) has extended and found a variational principle for evolutionary models, and Auger (1986) has given the conditions for the emergence of a hierarchy in such systems. All of these methods apply to structural organizations.

In contrast, this theory concerns functional organization. It shows that the observed organization, from among all those that would be possible and lead to the correct couplings, is the one that implies an increase in the functional order. This is an optimum constraint for the physiological mechanisms of an individual system subject to micromutations. Another constraint is given by external, i.e. environmental pressure, which causes the micromutations in the population of such interactive systems. In paper I, some results were presented regarding the influence of defined parameters on the dynamics of the system (D-FBS). Now, the problem is to know whether this second constraint at the level of the population leads to the selection of the organization that has in fact been chosen during the course of the species evolution. This problem could be formalized as follows: does there exist a similar optimum principle, unifying physiological mechanisms and behavior for the population of biological systems, that could describe the evolution of functional organization during development at the highest level of organization? If the answer is positive, then the highest level of organization in the species population would be ecological, because the 'biological system' to be considered is the environment (included all organisms) and the given organism. In this case, the set of biological systems in its environment, with the functional interactions between them describing their ethological behaviour, would be one and only one biological system.

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APPENDIX 1. MAXIMUM OF THE FUNCTION POTENTIAL Π

1. Let us show that $\Pi(x)$ has a maximum at one point in $[0,\nu-1]^\mu$: $\Pi(x) = \Pi(x_1, \ldots, x_2)$ is an application from $[0,\nu-1]^\mu$ to $\mathbb{R}$, with $\nu \geqslant 2 \in \mathbb{N}$, $\mu \geqslant 1 \in \mathbb{N}$ and defined by:

$$\Pi(x) = \sum_{\alpha=1}^{\mu} x_\alpha \ln(\nu - x_\alpha).$$

For all $x_\alpha \in [\nu-1]$:

$$\partial\Pi/\partial x_\alpha = \ln(\nu - x_\alpha) - x_\alpha/(\nu - x_\alpha).$$

Then Π has continuous first partial derivatives. If Π has a local extremum at one point $x^0 = (x^0_1, \ldots, x^0_\mu)$, then the gradient will be zero at x^0:

$$\forall\alpha\in[\![1,\mu]\!] \quad \left(\frac{\partial \Pi}{\partial x_\alpha}\right)_{x^0} = \ln(\nu - x^0_\alpha) - \frac{x^0_\alpha}{\nu - x^0_\alpha} = 0.$$

There is a unique point $x\in]0,\nu - 1[$ such that:

$$f(x) = \ln(\nu - x) - x/(\nu - x) = 0,$$

because: $f(0) = \ln\nu > 0$, $f(\nu - 1) = 1 - \nu < 0$, $f'(x) = (x - 2\nu)/(\nu - x)^2 < 0$, so that the function f is continuous, monotonously decreasing in $[0,\nu - 1]$, with $f(0) > 0$, $f(\nu - 1) < 0$. Therefore $\Pi(x)$ has a unique stationary point $(x_M, \ldots, x_M)$.

2. This equilibrium point is a maximum: $\Pi(x)$ has continuous partial second derivatives $\forall\alpha,\beta\in[\![1,\mu]\!]$:

$$\frac{\partial^2\Pi}{\partial x^2_\alpha} = \frac{x_\alpha - 2\nu}{(\nu - x_\alpha)^2} < 0, \qquad \frac{\partial^2\Pi}{\partial x_\alpha \partial x_\beta} = 0 \qquad \forall\alpha \neq \beta.$$

The point $(x_M, \ldots, x_M)$ will be a maximum if the second differential $d^2\Pi$ at this point is a positive definite quadratic form. According to the criterium of Sylvester, the quadratic form:

$$\mathrm{d}^2\Pi = \frac{1}{2}\sum_{\alpha,\beta=1}^{\mu} \frac{\partial^2\Pi}{\partial x_\alpha \partial x_\beta}\mathrm{d}x_\alpha \mathrm{d}x_\beta,$$

is definite positive if the 'descending' determinants have alternate signs: $\delta_1 < 0, \delta_2 > 0, \delta_3 < 0 \ldots$, with:

$$\delta_1 = \frac{\partial^2\Pi}{\partial x^2_1} \ldots \delta_\mu = \begin{pmatrix} \dfrac{\partial^2\Pi}{\partial x^2_1} & \cdots & \dfrac{\partial^2\Pi}{\partial x_1 \partial x_\mu} \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \dfrac{\partial^2\Pi}{\partial x_\mu \partial x_1} & \cdots & \dfrac{\partial^2\Pi}{\partial x^2_\mu} \end{pmatrix}.$$

Of course this property is verified.

APPENDIX 2. STABILITY IN THE SENSE OF LYAPOUNOV

Because $\Pi(x)$ has a unique maximum $\Pi_{\max}$ at $(x_M, \ldots, x_M)$, the function $D(x) = \Pi_{\max} - \Pi(x)$ verifies: $D(x) \equiv D(x_1, \ldots, x_\mu) > 0$ $\forall x \neq (x_M, \ldots, x_M)$, $D(x_M, \ldots, x_M) = 0$.

The stability in the sense of Lyapounov can be enonced as follows:

If a dynamical system:

$$\mathrm{d}x_\alpha/\mathrm{d}t = f_\alpha(x_1, \ldots, x_\mu) \qquad \forall\alpha\in[\![1,\mu]\!],$$

is such that:

$$f_\alpha(x_M, \ldots, x_M) = 0, \quad \frac{\mathrm{d}D}{\mathrm{d}t} = \sum_{\alpha=1}^{\mu} \frac{\partial D}{\partial x_\alpha}\frac{\mathrm{d}x_\alpha}{\mathrm{d}t}$$
$$= \sum_{\alpha=1}^{\mu} \frac{\partial D}{\partial x_\alpha} f_\alpha(x_1, \ldots, x_\mu) \leqslant 0,$$

i.e. the total derivative along the phase trajectories is negative or null, then $(x_M, \ldots, x_M)$ is a stable equilibrium point in the sense of Lyapounov (see, for example, Zubov (1964)). If inside an arbitrary small neighborhood of $(x_M, \ldots, x_M)$ one has:

$$\mathrm{d}D/\mathrm{d}t \leqslant -\beta < 0,$$

where β is an arbitrary constant, then the equilibrium point is asymptotically stable. Figure 3 is an example of this property of stability.

APPENDIX 3. MAXIMALITY OF THE POTENTIAL FOR INTEGERS NUMBERS

For a partition of ν units into two sets, we have shown that, in $\mathbb{R}$, the potential is maximum if the number of units in each set equals e. In $\mathbb{N}$, this property is not verified for small numbers:

$\nu=2$		$\nu=3$		$\nu=4$		$\nu=5$		$\nu=6$		$\nu=8$		$\nu=10$	
n	Π	n	Π	n	Π	n	Π	n	Π	n	Π	n	Π
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	**1**	**ln2**	1	ln3	1	ln4	1	ln5	1	ln7	1	ln9
		2	0	**2**	**ln4**	**2**	**ln9**	2	ln16	2	ln36	2	ln64
				3	0	3	ln8	**3**	**ln27**	3	ln125	3	ln343
						4	0	4	ln16	**4**	**ln256**	4	ln1296
								5	0	5	ln243	5	ln3125
										6	ln64	**6**	**ln4096**
										7	0	7	ln2187
												8	ln256
												9	0

The bold numbers indicate the maximum of the potential: it is clear that this maximum is obtained for three sets of partition (except for odd ν numbers), (2,2), (3,3) and (4,4).