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Hierarchical Functional Organization of Formal Biological Systems: A Dynamical Approach. III. The Concept of Non-Locality Leads to a Field Theory Describing the Dynamics at Each Level of Organization of the (D-FBS) Sub-System

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Hierarchical functional organization of formal biological systems: a dynamical approach. III. The concept of non-locality leads to a field theory describing the dynamics at each level of organization of the (D-FBS) sub-system

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CONTENTS

SUMMARY

In paper I, the construction of the graph of interactions, called (O-FBS), was deduced from the 'self-association hypothesis'. In paper II, a criterion of evolution during development for the (O-FBS), which represents the topology of the biological system, was deduced from an optimum principle leading to specific dynamics. Experimental verification of the proposed extremum hypothesis is possible because precise knowledge of the dynamics is not necessary; only knowledge of the monotonic variation of the number of sinks is required for given initial conditions. Essentially, the properties of the (O-FBS) are based on the concept of non-symmetry of functional interactions, as shown by the 'orgatropy' function (paper II). In this paper, a field theory is proposed to describe the (D-FBS), i.e. the physiological processes expressed by functional interactions: (i) physiological processes are conceived as the transport of a field

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variable submitted to the action of a field operator; (ii) because of hierarchy, this field theory is based on the concept of non-locality, and includes a non-local and non-symmetric interaction operator; (iii) the geometry of the structure contributes to the dynamics via the densities of structural units; and (iv) because a physiological process evolves on a particular timescale, it is possible to classify the levels of organization according to distinct timescales, and, therefore, to obtain a 'decoupling' of dynamics at each level. Thus, a property of structurality for a biological system is proposed, which is based on the finiteness of the velocity of the interaction, thus, with distinct values of timescales for the construction of the hierarchy of the system. Three axioms are introduced to define the fields associated with the topology of the system: (i) the existence of the fields; (ii) the decoupling of the dynamics; and (iii) the ability of activation-inhibition. This formulation leads to a self-coherent definition of auto-organization: an FBS is self-organized if it goes from one stable state for the (D-FBS) to another under the influence of certain modifications of its topology, i.e. a modification of the (O-FBS). It is shown that properties deduced with this formalism give the relationship between topology and geometry in an FBS, and particularly, the geometrical re-distribution of units. In the framework of this field theory, a statistical distribution function of the states of the field is introduced, which shows that the collective behavior of the population of units is not a simple summation of the individual elements, and gives a solution to the problem of the passage from one level to another. Two examples are given: a justification of the self-association hypothesis in the case of field variables, and a method to determine the 2-level neural field equations. Finally, the concepts of complexity and autonomy are discussed, and we show that the autonomy of a biological system increases with the potential of organization. The proposed principle of functional order from hierarchy, which describes the natural trend towards time decoupling of the physiological function, leads, in that sense, towards a simplification of the dynamics.

NOTATIONS AND SYMBOLS

A,B 'propagators', attenuation functions of potentials along the membrane

$AJ(r^{(l)})$ amount of product that leaves the element of volume at $r^{(l)}$ through area A

$D(x,y,z)$ diffusion 'constant'

D_r r-space of units

$D_l(r_0^{(l)})$ subspace of units $u^{(l)}$ that are connected to the given unit $u_0^{(l)}$ at level l

$D_s(r,r_0)$ space of synapses at $s(r,r_0)$ in the r-neurons connected with the r_0-neurons

$D_R(r_0)$ combination of subspaces $D_s(r,r_0)$ when r varies

D^r and D^s diffusion coefficients in the r-space and in the s-space

$D_{l-1}(r_i^{(l)},r_0^{(l)})$, $i = 1$, $N^{(l)}$ set of units at level $l-1$ which corresponds to the i-unit $u_i^{(l)}$ at level l

$F(r^{(l)})\mathrm{d}r^{(l)}$ amount of product that leaves the element of volume along the distance $\mathrm{d}r^{(l)}$ in the space of units $u^{(l)}$

$\boldsymbol{H}$ field operator applying to the field vector ψ for functional interactions.

$H_I^{\psi}(r)\mathrm{d}r$ non-local interaction operator included in the operator $\boldsymbol{H}$

$H_I^{\psi}(r^{(l)})\mathrm{d}r^{(l)}$ non-local quantity of product that leaves the element of volume along the distance $\mathrm{d}^r(r^{(l)})$ in the physical space

$H_I^{+,-}$ activator-inhibitor non-local interaction operator for the ψ^+ and ψ^- field equations

$Ifield(r,t)$ intracellular field potential

$K(\psi^+,\psi^-)$ rate constant of the reaction $u_1 + u_1^* \rightarrow u_2$

K_{11} rate constant of the reaction $\rho^1 + \rho^{1*} \rightarrow \rho^2$

$N_{k'}$ number of units in the K' groups $E_{k'}$, $k' = 1$, K'

$N_{\alpha k'}$ number of sources for the product P_α

N^l total number of units $u^l(s;r_0)$ in space $D_l(r;r_0)$ at level l located in r_0

N_j^l jth term in N^l corresponding to non-associated units u^l and to other units that are associated in order to create the higher levels $(l+1)$, $(l+2)$, . . .

P_e environmental substance

P_α^{l-1} physiological α-products that are the fields ψ^{l-1} at level $l-1$

$Q(t)$ fraction of units that change their state

$Q_{i\rightarrow e}$ intra–extracellular factor transformation

$Q_{syn\rightarrow e}$ synaptic–extracellular factor transformation

$\boldsymbol{R}$ field operator applying to the field vector density ρ

$\{T^l\}$ timescale at level l

$U(s,t,s',t';\Phi,\delta\Phi)$ potential kernel function

V volume in the physical or cartesian space

$V^{(l,l-1)}(r^{(l)};\psi)$ potential function or kernel function

$V[r_l,t(r_l),r_k,t'(r_k);\Gamma(\psi_k)]$ potential interaction between the current point $r_l \equiv r_0$ and any other point r_k in the network at time t'

$V^{syn}(r,t)$ average of the distribution of postsynaptic potentials

V_E extracellular field potential

V_E^{fir} extracellular field potential due to firing

$V_E^{syn}(r,t)$ extracellular field potential due to synapses activity

$X(r^{(l)})$ domain in the real physical space corresponding to $D_{l-1}(r_i^{(l)},r_0^{(l)})$, $i = 1$, $N^{(l)}$

$X(r_0,T_0)$, instantaneous local somatic activity

$\mathrm{d}^{r^{(l)}}(r^{(l)})$ distance extent at a lower level of organization at $r^{(l)}$

$f^l(\psi^0,\psi^1,\ldots,\psi^l)$ distribution function of the states variables from the 0-level to the l-level

r,r_0 space coordinates

(r,t), (r_0,t_0) space–time coordinates

$r^{(l)}$ units in the $u^{(l)}$ space

$r^{(l)} \equiv s$, $r^{(l)'} \equiv s'$; $r_0^{(l+1)} \equiv r_0$; $r^{(l+1)} \equiv r$, $r^{(l+1)'} \equiv r'$

simplified notations for coordinates in spaces of units

$r \equiv r^{(2)}$, $q \equiv r^{(3)}$, $q_0 \equiv r_0^{(3)}$ simplified notations for the location of neurons and groups of neurons

u_1 structural unit

u_1^* modified structural unit

$u^{(l)}$ space of units at level l (where the coordinates of the unit in this space are $r^{(l)}$)

v_ψ velocity of the interaction

x_r location of a structural unit at r in physical space

α^l source term for the density field equation

μ global non-local synaptic efficacy

$\mu^2(u,t^3)$ efficacy of neurons at level 2

$\phi(\rho^1,\rho^2)$ relation between densities deduced from the local condition of constant organization

π density-connectivity function

$\pi(r^{(l+1)},r^{(l)};r_0^{(l+1)})$ density of units in $r^{(l)}$, in a group localized at $r_0^{(l+1)}$ and connected to other groups localized at $r^{(l)}$

$\pi(s,r;r_0)$ density-connectivity of synapses defined in a space $D_s(r,r_0)$ at $s(r,r_0)$ in the r_0-neurons connected with the r-neurons

ψ_{env} parameter which depends on the environment

$\psi_k \equiv \psi(r_k)$, $t_k \equiv t(r_k)$

ψ_{st}^2 stable steady-state solution of the field equation at level 2

$\psi(r,t)$ space–time functional interaction value = field variable

$\psi_i^k(r,t)$ internal field variables at levels $k \neq l$

$\psi_e^k(r,t)$ internal field variable for the k-level, external variable for other levels $l \neq k$

$(\psi^+,\psi^-)^l$ 2-component activator–inhibitor field vector

$\psi(r_0,T_0)$ local soma membrane potential field variable at the neuronal level with a timescale {T}

$\psi^3(q,t^3)$ activity of the groups u^3 of neurons

$\rho^3(q)$ density of the groups u^3 of neurons

$\rho(r_0)$ distribution of units at point r_0 in the r-space of units

ρ^1, ρ^2 variation in time of the densities of units u_1 and $u_2 \equiv (u_1,u_1^*)$

$\rho^{(l)}(r^{(l)})$ density in an element of space $\mathrm{d}r^{(l)}$

$\rho(r)$ density of neurons at r defined in the space $D_R(r_0)$

$\rho(r)$ density of groups

$\xi(s,t;\langle X\rangle)$ presynaptic efficacy

$\eta(s,t;\langle X\rangle)$ postsynaptic efficacy

Δf_{ext}^l variation in time of the distribution function

$\Delta f_{\psi^i}^l$ state transition of the distribution function after a transformation

$\Phi_0(s,T)$ postsynaptic local membrane potential field variable at the synaptic level with the timescale {T}

$\Gamma(r_0,t_0)$ source term in the field equation

$\Gamma_\psi(r_0,T_0)$ source term of the field at the neurons level

$\Gamma_\mu(s,t)$ source term of the field at the synapses level

$\bar{A}_x^{r^{(l)}}$ non-local operator

$\Pi_\alpha^{l,l+1}$ potential of organization for the α-product, for the two levels and for the whole system

1. INTRODUCTION: GEOMETRY AND TOPOLOGY IN BIOLOGY SYSTEMS

In the two first papers, a theory of functional organization of formal biological systems (FBS) was proposed on the basis of a self-association hypothesis (Chauvet 1993*c*; referred to hereafter as paper I). The combination of functional interactions due to this hypothesis leads to the topology of the biological system as a hierarchical system represented by an oriented graph and called the (O-FBS). An optimum principle for the time evolution of the (O-FBS) was deduced from a state function called the potential of organization (Chauvet 1993*d*; referred to hereafter as paper II). In this paper, the dynamical processes associated with the functional interactions are shown to satisfy a non-local field equation. The fundamental reason for this specific representation is the functional hierarchy of the physiological processes. These processes occur in spaces called 'spaces of units' that are distinct from the physical space where structural units are located.

Functional interactions considered in this theory constitute the basis of biological systems. They have a very different meaning from physical interactions. A physical structure results from the combination of physical interactions, i.e. the gravitational, electromagnetic and nuclear forces acting between particles at different levels of description. A force acting on a particle implies the quantum or classical movement of the particle. The equilibrium state of a many-particle isolated system corresponds to an optimum principle in thermodynamics implying a null variation of entropy for reversible processes, and a positive variation for non-reversible processes such as those found in biology. It is clear that the structure of a system, such as an assembly of particles, is governed by the second law of thermodynamics which specifies the arrow of time. From a mechanical viewpoint, the movement of conservative systems satisfies the Hamilton principle, which is also an optimum principle.

Although a biological system is made up of physical structures, molecules and assemblies of molecules, another kind of interaction characteristic of physiological systems is considered here, i.e. the action of one structural unit on another. A structural unit, the 'source', which may be a gene, a cell, a group of cells, or an organ, or any group of such structures, emits a 'product' which may be a molecule, a potential, or some parameter, that operates on another structural unit, the 'sink'. Physical interactions maintain a set of particles in a given state of energy. Functional interactions bring a product from one unit to another, induce a transformation leading to the emission of another product, which then acts upon another unit, and so on. Thus, functional interactions correspond to various products emitted by the sources and act at a distance, creating non-local effects in the sinks. Of course, the local interaction between the product and the receptive structural unit has a molecular physical character. The functional interaction is defined by three elements: the source u_i at r and the sink u_j at r_0, the transport of the 'α-product' $P_{\alpha,i}$ synthesized in r, and the induced transformation in the sink. The 'α-

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

product' is denoted as $\psi^{\alpha}_{i,j}$ between r and r_0 (paper I). $P_{\alpha,j}$ is the product synthesized in r_0 corresponding to $P_{\alpha,i}$. $P'_{\alpha,j}$ is the transformed value of $P_{\alpha,j}$ in r_0. With these definitions, $P_{\alpha,j}$ or $P'_{\alpha,j}$ are identified as elementary physiological functions. Thus, the elementary physiological function is described as a mathematical function, from r to r_0:

$$P_{\alpha,j}(r_0) = \psi^{\alpha}_{ij}(P_{\alpha,i};\, r), \tag{1}$$

or with the transformed value:

$$P'_{\alpha,j}(r_0) = \Phi^{\alpha}_{ij}(P_{\alpha,i};r) = \phi^{\alpha}_{j}(r_0)\, o\, \psi^{\alpha}_{ij}(P_{\alpha,i};r), \tag{2}$$

where ϕ^{α}_{j} represents the transformation induced in r_0. In a certain sense, the functional organization described in terms of these interactions is superposed on the structural physical organization, and leads to a mathematical definition of what could really be a physiological function. If F^l represents the product, i.e. the collective behaviour at the l-level, $l = 1,2, \ldots, L$, then the physiological function F is the collective behavior of the L levels of organization that constitute the hierarchical system:

$$F = f(F^1, F^2, \ldots, F^L). \tag{3}$$

In paper I, the construction of the graph of interactions, called (O-FBS), was deduced from the 'self-association hypothesis' stating that in a system in which all the units have the same potentialities, any unit that does not synthesize the product it needs, either dies, or for its survival, must receive this function from another structural unit that possesses the function. Evidence for this hypothesis is the increase of the domain of stability after self-association. This property was proved in paper I for a metabolic auto-replicative system with two levels of organization. In the present paper, an extension will be proposed for diffusive metabolic auto-replicative systems.

In paper II, a criterion of evolution for the (O-FBS), which represents the topology of the biological system, was proposed and deduced from an optimum principle leading to specific dynamics. The precise knowledge of the dynamics is not necessary, but only the sense of variation of the number of sinks: the number of sinks either decreases or increases monotonically according to initial conditions. Essentially, the properties of the (O-FBS) are based on the property of non-symmetry of functional interactions, as shown by the 'orgatropy' function.

The present paper gives the properties of the (D-FBS), the dynamical system for state variables ψ^{α}_{ij}. A field theory for a hierarchical system is proposed to describe the (D-FBS), which is based on the concept of non-locality. Properties deduced with this formalism give the relationship between topology and geometry in an FBS. The general structure of the field equation is discussed, and a discrete derivation is proposed. Two examples are considered: a space–time model of metabolic and self-replicative structural units, which is an extension of the model proposed in paper I in support of the self-association hypothesis, and the determination of the neural field equations in a system with two levels of organization. A solution to the problem of the determination of the relation between population and elements is presented in terms of field variables.

2. THE NATURE OF A POSSIBLE FIELD THEORY IN BIOLOGY

(a) *Geometry and finiteness of the velocity of interaction*

The physiological processes expressed by functional interactions related to the geometry of the structure can be conceived as the transport of a field variable submitted to the action of a field operator. Let $\psi(r,t)$ be the field variable defined in the r-space, and let H be the field operator which depends on ψ and on successive derivatives $\psi^{(n)}$ with respect to time and space coordinates. The field equation, as an extension of equations (1–3), can be written in a general form as follows:

$$H(\psi,\psi^{(n)},n = 1,2, \ldots)\psi(r,t) = \Gamma(r,t), \tag{4}$$

where Γ is the source term. In this equation, H describes the propagation of the field variable ψ from r to r_0, the local transformation in r_0 is represented by $\Gamma(r_0,t_0)$ (figure 1). Because the operator acts from one point of space to another, it must take into account the distance between these two points, and therefore must include an interaction operator. More generally, the influence of the location of points, i.e. the role of geometry, on the dynamical processes, can be studied with a field theory. The dynamical processes that express the behaviour of the related functional interactions continuously occur in space and time with a finite velocity. Therefore, what is observed at point (r_0,t_0) results from what was emitted at point (r,t) where $t_0 = t + (\|r - r_0\|)/v_\psi$ and v_ψ is the velocity of the interaction.

The first property giving specific consequences to biological systems is the finitude of velocity of functional interactions. We can see why the finite value of the velocity v_ψ of the transport of the interaction, which is the transport of molecules, potentials, cur-

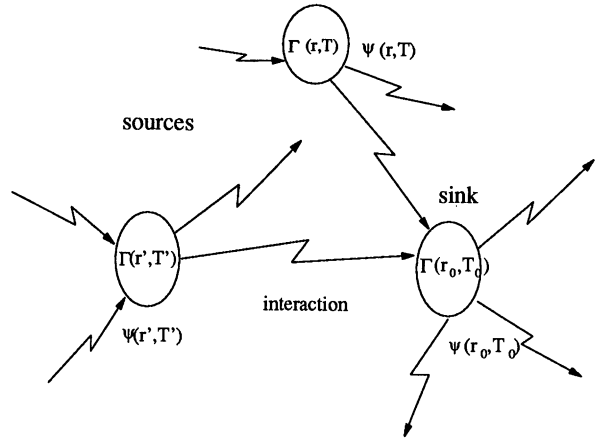


Figure 1. Sources and field variables. A field operator H acts on the field variable and carries it from point r in the space of units to point r_0. Sources are denoted Γ.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

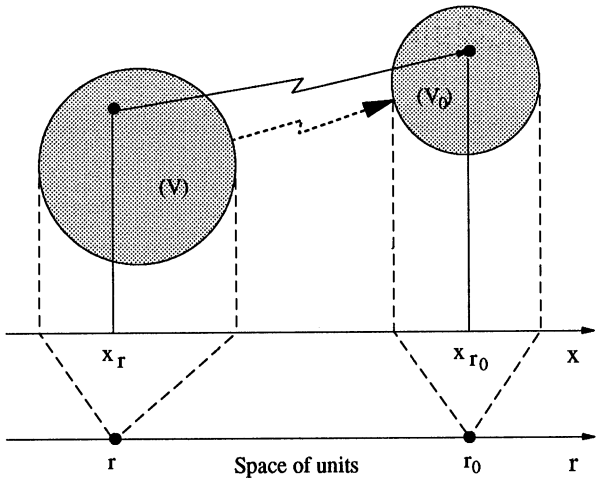


Figure 2. Non-locality: a functional interaction exists from volume (V) to volume (V_0) in the physical cartesian space, represented here by axis (x). However, because of the functional hierarchy of the system, it is formulated in terms of fields in the space of structural units from r to r_0 represented by axis (r).

rents, or parameter effects depending on the elementary physiological function, has an important consequence on the behavior of the biological system, e.g. the delay in the response between units at different times of their production. These effects are included directly in the field interaction operator. Fields are therefore useful for the description of the propagation of field variables between distant units. However, it is difficult to determine the specific operator that describes the physiological phenomena.

(*b*) *Non-locality derives from hierarchical organization*

The second and the more important property of the hierarchical biological system is 'non-locality' (Chauvet 1993*a*). This concept was introduced for a description of the physiological mechanisms in a hierarchical system. Figure 2 gives an intuitive description of non-locality. Because of the functional hierarchy, the abstract 'structural unit' element occupies a certain volume V in the physical or cartesian space. The action of this unit on another with volume V_0 is an interaction between volumes and not between points in the sense of the field theory. Thus, we have:

Property VI: existence of non-locality

The following invariance of the functional interaction ψ in a hierarchical system,

$$\psi : V \nearrow \searrow V_0 \;\Leftrightarrow\; \psi : r \nearrow \searrow r_0,$$

expressed in the physical space $\mathbb{R}^3$ and in the space of units D_r, where the symbol $\nearrow\searrow$ denotes a volume-to-volume application in the physical space, implies non-locality.

In the physical space, the location of a structural unit at r is denoted as x_r (figure 2) and the location of units at the lower level will be x_s. Because the structural unit is not reducible to a point from where the interaction originates, it is difficult to locate x_r and x_s. This fundamental incertitude raises conceptual and technical difficulties in the use of a field theory in biology. We have chosen to represent the biological structure in 'spaces of units', i.e. r-space and s-space with the above notations, which are the abstract spaces where the functional process occurs. For example, let us recall the field description of nervous processes. Since the space of synapses is structurally included in the space of neurons, and since two timescales are functionally attached to these spaces, a hierarchical functional system is defined from the two field variables: soma membrane potential and synaptic efficacy. The field variable 'soma membrane potential' evolves from r to $r + \mathrm{d}r$ in the continuous r-space, i.e. between two infinitesimally close neurons, considered to be points. But, the structural unit 'neuron' is not reducible to a point because other different structural units ('synapses') exist on the neuron.

The general presentation of this property has been made elsewhere (Chauvet 1993*a*). Without restricting generality, two successive levels of organization can be considered. The first level $l-1$ consists of sinks that receive the product emitted by sources at the second level l. In a system with $N+1$ levels of organization, subscript l ranges from $l=0$ to $l=N$, where 0 represents the 'fundamental level', e.g. the molecular level. Units belong to a space, denoted as $u^{(l)}$-space at level l, where the coordinates of the unit in this space are $r^{(l)}$, and the density in an element of space $\mathrm{d}r^{(l)}$ is $\rho^{(l)}(r^{(l)})$. This continuous density function can be deduced from Dirac functions at each point of the cartesian space. There exists a specific subspace of units $u^{(l)}$ that are connected to the given unit $u_0^{(l)}$. This subspace at level l is denoted $D_l(r_0^{(l)})$. We consider now the units at lower level $l-1$ that are *in* the unit $u_0^{(l)}$ and are connected with another i-unit at level l. Such a set of units at level $l-1$, which corresponds to the i-unit $u_i^{(l)}$ at level l is denoted $D_{l-1}(r_i^{(l)},r_0^{(l)})$, $i = 1, N^{(l)}$ (figure 3). The related domain in the real physical space is $X(r^{(l)})$. Therefore, if $N^{(l)}$ i-units are connected

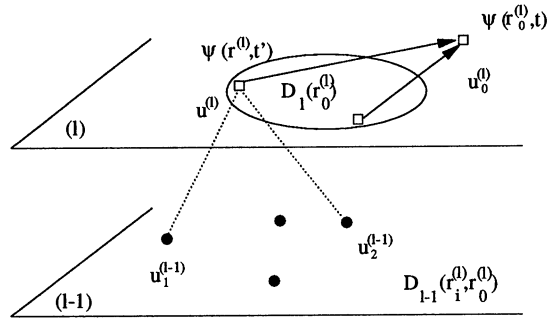


Figure 3. Notations used in the text. The subspace of units $u^{(l)}$ that are connected to the given unit $u_0^{(l)}$ at level l is denoted $D_l(r_0^{(l)})$. The units at lower level $l-1$ that are in the unit $u_0^{(l)}$ and are connected with another i-unit at level l constitute the set $D_{l-1}(r_i^{(l)},r_0^{(l)})$, $i = 1, N^{(l)}$.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

to $u_0^{(l)}$, the functional relationship between the two considered levels l and $l-1$ is:

$$D_l(r_0^{(l)}) = \bigcup_{i=1}^{N^{(l)}} D_{l-1}(r_i^{(l)}, r_0^{(l)}). \quad (6)$$

Such a relation gives an expression of non-locality because a unit at $r^{(l)}$ extends over a distance $\mathrm{d}^{r^{(l)}}(r^{(l)})$ at a lower level of organization, the physiological mechanisms at $r^{(l)}$ depend on mechanisms that evolve 'in' that point, i.e. along the line $\mathrm{d}^{r^{(l)}}(r^{(l)})$. This new function represents the size of units at $r^{(l)}$, and is defined as follows:

$$\forall r \in D_r \rightarrow \mathrm{d}^r(r) \in X(r) \subset \mathbb{R}^3, \quad (7)$$

where superscript (l) has been suppressed for clarity. When there is no ambiguity, superscript (l) is suppressed in r, r_0, etc. Because the functional interaction ψ occurs in r at the level of one structural unit, i.e. is emitted at $x_r - \mathrm{d}^r$ and propagated from this point to x_r with the velocity v_ψ, a non-local interaction operator $H_I^\psi(r)\mathrm{d}r$ has to be included in the operator H (equation 4).

(c) *Consequences: timescale and spacescale*

The principle of construction of the hierarchical functional organization is based on the existence of functional interactions between structural units. The collective behavior of a subset of these structural units constitutes the physiological function and defines a level of organization. Because a physiological function evolves on a particular timescale, i.e. its dynamics are such that we see real variations in a certain interval that can be considered as a unit of time, it is possible to identify the level of organization by the timescale of the process. An important consequence of the principle of construction is the ability of classifying the levels of organization according to the timescales of the physiological functions. Therefore, in this representation, the differences in timescales of the dynamics at different levels of organization lead to a 'decoupling' of dynamics at each level. This ability of decoupling allows the study of the dynamics of large systems to be based on those of its subsystems. The transformation of the large nonlinear dynamical system by decoupling is similar to the linear decomposition of a matrix into submatrices, where the non-diagonal elements correspond to the coupling between subsystems, each subsystem having its own timescale. For example, specific properties of the cerebellar cortex regarding learning and memory of space–time trajectories are due to the hierarchical organization (Chapeau-Blondeau & Chauvet 1991). An interesting property characterizes the fundamental distinction between functional organization and structural organization: there is no direct relation between the rank of the level in the functional hierarchical system, the rank of the level in the hierarchical structural system, and the timescale at each functional level.

For example, in nervous tissue there are two timescales for the state variables: synaptic efficacy and activity. Synaptic efficacy changes on a long timescale (several seconds to hours), and is the collective behaviour of 'synapsons', complex structure including not only synapses but also extrasynaptic and cytoplasmic structures (paper II), i.e. the solution in a one neuron s-space–t-time of the dynamical system that describes their elementary mechanisms. Similarly, activity occurs on a short timescale (ms), and is the collective behaviour of neurons, i.e. the solution in a one network r-space–T-time of the dynamical system that describes their elementary mechanisms. It is clear that timescale for synapses is larger than timescale for neurons, although synapses are included in neurons.

Due to the finite value of the interaction velocity, the spacescale is different for each level of organization, and gives another feature of this type of hierarchical system. In the case of the nervous system, because potential is propagated with a finite velocity, synaptic efficacy and activity have different velocities. Thus, the two corresponding 'physiological functional spaces' have different spacescales that lead to non-locality as shown above. Therefore the finiteness of the velocity of functional interactions with a different value at each level determines the non-locality, because the expression (7) imposes the delay $\mathrm{d}^r(r)/v_\psi$ for the transport of functional interaction ψ. This fact leads to dynamics with different characteristics at each level. All the specific concepts introduced above, including the property of non-symmetry of functional interactions, can be summarized as follows:

Property VII: structurality of a biological system

A biological system is characterized by the finiteness of the velocity of interactions and therefore by the dynamics that occur on a specific timescale, and which constitute the collective behaviour of sources and sinks. The distinct values of timescales allow the construction of the hierarchy of the system. In such a hierarchical system, the interaction operator is non-local and non-symmetric. There is no relation between the ranks of levels of organization and timescales.

(d) *Relation between the geometry and the topology of an FBS*

Property VII gives the relation between the topology of the biological system (O-FBS), described as a hierarchical set of non-symmetric functional interactions, and the dynamics of the associated processes (D-FBS) that occur on a specific timescale. The two basic concepts of functional organization, non-symmetry and non-locality, are implicitly included in the formulation: In paper II, a criterion of change in Π, the potential of organization, and a sufficient condition for the dynamics of the number of sinks was obtained. The continuous representation considered in the present approach implies that the number of sinks is represented as a density per unit volume. In the r-space of units, the distribution of units is $\rho(r_0)$ at point r_0 and the field variable ψ is propagated from r to r_0. Thus, the topology of the FBS in the continuous representation is described by the variation in time of the density function $\rho(r,t)$. In the present theory we do not need the explicit formulation of the dynamics of the density but only the sense of the monotonic

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

variation. The knowledge of this function $\rho(r,t)$ and of its variation in time satisfying the optimum principle (paper II), associated with the dynamics of the processes of functional interactions, gives the relation between the two systems (O-FBS) and (D-FBS). The geometry and the topology of the system are thus included in the dynamics of the processes. This aspect of the theory will be studied in more detail in § 4. There are two consequences to this formulation: (i) the monotonic variation of the densities of structural units; and (ii) the existence of a non-local and non-symmetric interaction operator in the dynamics.

$$\boldsymbol{H}\Psi = \Gamma \qquad \text{with} \qquad \boldsymbol{H} = \begin{pmatrix} H^+ & 0 \\ 0 & H^- \end{pmatrix} \qquad \Psi = \begin{pmatrix} \psi^+ \\ \psi^- \end{pmatrix} \qquad \Gamma = \begin{pmatrix} \Gamma^+ \\ \Gamma^- \end{pmatrix}.$$

3. A MULTIPLE FIELD THEORY OF FUNCTIONAL ORGANIZATION

(a) *Axiomatic presentation: definition of the fields*

Three axioms may be introduced to define the fields associated with the topology of the system. The field equation at level l, and in timescale $\{T^l\}$, can be written, following (4).

Axiom I: existence of the fields

At each l-level, an excitatory field $\psi^l(r,t)$ describes the time evolution of the system (D-FBS):

$$H^l[\psi,\psi^{(n)},n = 1,2,\ldots]\psi^l(r,t) = \Gamma^l(r,t), \quad t\in\{T^l\}. \tag{8}$$

The solution of this field equation is called a dynamical state in organization described by graph (G).

In an N-level system, adjacent levels $k = 1, \ldots l-1, l+1, \ldots, N$ are coupled to the l-level by external variables, or parameters, that are internal variables $\psi^k_l(r,t)$ at levels $k \neq l$.

Axiom II: decoupling of the dynamics

For each l-level, a timescale $\{T^l\}$ characterizes the dynamics of the functional process supported by the structural units. This parameter allows the construction of the hierarchical system, and implies a temporal decoupling of the levels according to their dynamics, i.e. their collective behaviour.

This axiom provides a method for the construction of the hierarchical system. Let $\psi^k_e(r,t)$ be the variable for the k-level, which constitutes an external variable for the other levels $l \neq k$. This variable can be: either (i) a steady-state solution of the field equation at the k-level for a timescale $\{T^k\}$:

$$H^k[\psi^k(r,t)]\,\psi^k(r,t) = \Gamma^k(r,t), \qquad t\in\{T^k\}, \tag{9}$$

ψ^k_e is a steady-state, i.e. a solution of this equation when $\mathrm{d}\psi^k_e/\mathrm{d}t = 0$; or (ii) a parameter of this equation when the process at level k evolves slowly relatively to the process at level l. This property can be expressed by:

$$t^k = g(t^l), \quad \mathrm{d}g/\mathrm{d}t^l \approx 0, \quad t^k\in\{T^k\}, \quad t^l\in\{T^l\}. \tag{10}$$

Finally, the field equations can be written:

$$H^l\psi^l(r,t) = \Gamma^l[r,t;\psi_e(r,t')]$$
$$\mathrm{d}t'/\mathrm{d}t \approx 0 \qquad t\in\{T^l\} \qquad t'\in\{T^k\}. \tag{11}$$

Axiom III: activation-inhibition

In the most frequent cases, the excitation field is activator-inhibitor at a given level. Then ψ^l is a 2-component vector denoted $(\psi^+,\psi^-)^l$ that verifies the field equation:

For example, abstract activating and inhibitory components of activity can be defined in a nervous system (Chauvet 1990).

(b) *Field and functional organization*

The existence of the two systems (O-FBS) and (D-FBS) leads to a definition of the self-organization of an FBS that takes into account their relationship:

Definition VIII: self-organization

An FBS is self-organized if it goes from one stable state for the (D-FBS) to another under the influence of certain modifications of its topology, i.e. a modification of the (O-FBS).

With a 2-level system, the field equations are:

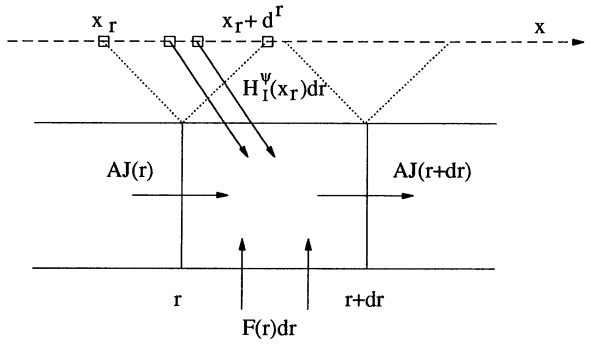
$$H^2\psi^2(r,t^2) = \Gamma_2(r,t^2;\psi_{env}) \qquad t^2\in\{T^2\}, \tag{12.1}$$
$$H^1\psi^1(r,t^1) = \Gamma_1(r,t^1;\psi^2_{st}) \qquad t^1\in\{T^1\}, \tag{12.2}$$
$$\{T^1\} \ll \{T^2\} \qquad \mathrm{d}\psi^2_{st}/\mathrm{d}t^1 \approx 0, \tag{12.3}$$

where ψ_{env} is a parameter which depends on the environment. ψ^2_{st} is the stable steady-state solution of (12.1), the field equation at level 2, which is the slow, or external, variable, for the 1-level, because of the difference of timescales:

$$\mathrm{d}\psi^2_{st}/\mathrm{d}t^1 \approx 0 \qquad t^1\in\{T^1\} \tag{13}$$

ψ^1 is the internal variable for the first level. Thus it is possible to say that the parameter ψ^2_{st}, solution of equation (12.1), drives the evolution of the subsystem at level 1 (Haken 1978). The solution (ψ^1,ψ^2) depends intrinsically on ψ^2 and extrinsically on ψ_{env} whose value is determined by the environment. After constraints upon the FBS in the steady-state $(\psi^1,\psi^2)_{st}$, the subsystems of the FBS evolve as follows:

1. For the (D-FBS): a fluctuation of the environment $\delta\psi_{env}$, or an internal fluctuation that modifies ψ^1_{st}, leads the (D-FBS) system from $(\psi^1,\psi^2)_{st}$ to $(\psi^1,\psi^2)_{st} + \delta(\psi^1,\psi^2)$ according to dynamics which could be given either by the bifurcation theory (Iooss & Joseph 1980), or by the catastrophe theory (Thom 1972) for a uniform field.
2. For the (O-FBS): a modification of the organization changes the structure of the dynamical system, and



$$AJ(r) + F(r)dr + H_I^{\psi}(x_r)dr = AJ(r+dr)$$

Figure 4. Explanation of the balance equation with the non-local term $H_I^{\psi}(x_r)dr$ which represents all the inputs ψ from the sub-levels, i.e. the transport of the field variable in the physical space from x_r to $x_r + d^r$. Other local inputs are: (i) $AJ(r)$ at r through cross-section A, where J is the flow per unit area; and (ii) $F(r)dr$ along the distance dr.

then its steady-state: the topology of the attractors is modified and the (D-FBS) system goes instantaneously from one steady state to another, with the possible corresponding instabilities.

(c) *Structure of the field equation: non-local operator*

The determination of H is not easy because it contains all orders of time and space derivatives, and integral operators. When the geometry of space or some symmetry considerations impose $H(\psi)$ as invariant with regards to rotations and translations, then:

$$H \equiv \partial/\partial t - D\nabla^2 - H_I, \tag{14}$$

where ∇^2 is a diffusion term and H_I is the interacting non-local operator.

The formulation of H_I can be deduced from the balance equation (figure 4):

$$AJ(r^{(l)}) + F(r^{(l)})dr^{(l)} + \bar{A}_x^{r^{(l)}}\psi(r^{(l)},T^l)dr^{(l)} = AJ(r^{(l)} + dr^{(l)}),$$

where $J(r^{(l)})$ is the flow through the area A of an element of volume $dr^{(l)}$ in the space of units $u^{(l)}$. This equation describes the conservation of matter associated with the 'transport' of the product corresponding to the functional interaction $\psi^{(l)}(r^{(l)}(x),T^l)$ in an element of volume $dr \equiv dr^{(l)}$ (Chauvet 1993*a*). The amount of product that leaves this element of volume $AJ(r^{(l)} + dr^{(l)})$ is equal to the one that enters into the same volume $dr^{(l)}$, and is the sum of three contributions: (i) $AJ(r^{(l)})$ at $r^{(l)}$ through area A; (ii) $F(r^{(l)})dr^{(l)}$ along the distance $dr^{(l)}$ in the space of units $u^{(l)}$; and (iii) the non-local quantity $H_I^{\psi}(r^{(l)})dr^{(l)}$ along the distance $d^r(r^{(l)})$ in the physical space. This non-local term is denoted:

$$H_I^{\psi}(r^{(l)})dr^{(l)} = \bar{A}_x^{r^{(l)}}\psi^{(l)}(r^{(l)}(x),T^l)dr^{(l)}. \tag{15}$$

A general expression of the non-local interaction operator can be derived as follows (figure 4). At level l, the unit $u_0^{(l)}$, located at $r_0^{(l)}$, receives the product from units $u^{(l)}$ located at $r^{(l)}$. All the physiological transformations from one unit to another are supposed to be represented by a specific mathematical function, called a potential function $V^{(l,l-1)}(r^{(l)},r_0^{(l)};\psi)$, or a kernel function, which expresses the action at $r_0^{(l)}$ of units located at $r^{(l)}$, i.e. the action at time t of what was emitted at time $t' = t - (\|r^{(l)} - r_0^{(l)}\|)/v^{(l)} = t - (d^r(r_0^{(l)}))/v^{(l)}$, where $d^r(r_0^{(l)})$ is known from the geometry of the system. The two following features can be observed: (i) the product emitted by $u^{(l)}$ acts on units at the lower level, i.e. on $u^{(l-1)}$, the density of which is $\rho^{(l-1)}(r^{(l-1)})$ in the $u^{(l-1)}$-space; (ii) all the units $u^{(l)}$ at $r^{(l)}$, with density $\rho^{(l)}$, contribute in an additive manner to the global action on the given unit $u_0^{(l)}$. The sum of these non-local effects are described by the operator derived from (14) and (15):

$$\bar{A}_x^{r^{(l)}} \equiv \int_{D_l(r_0^{(l)})} \rho^{(l)}(r^{(l)}) \int_{D_{l-1}(r^{(l)},r_0^{(l)})} \rho^{(l-1)}(r^{(l-1)})\, V^{(l,l-1)}(r^{(l)},r^{(l-1)})\, dr^{(l-1)}dr^{(l)}.$$

Therefore, the field equation includes the term:

$$\bar{A}_x^{r^{(l)}}\psi^{(l)}(r^{(l)},t;\psi^{(l-1)}) = \int_{D_l(r_0^{(l)})} \rho^{(l)}(r^{(l)}) \int_{D_{l-1}(r^{(l)},r_0^{(l)})} \rho^{(l-1)}(r^{(l-1)})\, V^{(l,l-1)}[r^{(l)},r^{(l-1)},\psi^{(l)}(r^{(l)},t),\psi^{(l-1)}(r^{(l-1)},t')]\, dr^{(l-1)}dr^{(l)}, \tag{16}$$

where $t' = t - (\|r^{(l)} - r_0^{(l)}\|)/v^{(l)} = t - d^r(r_0^{(l)})/v^{(l)}$ results from non-locality. The determination of the potential function V depends on the specific case studied, e.g. the propagation of nervous activity in the neural network, or the synaptic activity in the neuron (Chauvet 1993*b*).

A physical interpretation of the potential function created in space by the sources is the following: a 'product' (that is the field variable) in the potential is submitted to this potential. For example, the active sites of a membrane, which are the sinks for a product P_α, create a virtual potential in space for the chemical substance P_α emitted by cells. All other substances able to react with P_α and placed in this potential will react according to a specific law of the system, represented by the operator V. Therefore, the role of V is to transmit the field ψ over a distance, e.g. from (r,t) to (r_0,t_0).

(d) *Structure of the field equation: second differential operator*

The second order differential operator exists in various fields of mathematical physics (Courant & Hilbert 1953, 1962) and mathematical biology (Murray 1977): the temperature diffusion equation in thermodynamics related to brownian motion by Einstein's formula $D = \omega RT$ where D is the diffusion

coefficient, R the perfect gas constant, and T the temperature; the Laplace equation $\nabla^2\psi = 0$ for electrostatic fields; and more generally, the Poisson equation $\nabla^2\psi = -\rho(x,y,z)/\epsilon_0$ for the potential ψ created by the density of charges $\rho(x,y,z)$ at a point (x,y,z). In quantum mechanics, the time-dependent Schrodinger equation has the same form, except for the presence of the complex number i, which is imposed by the boundary conditions:

$$i\hbar\frac{\partial\psi}{\partial t} = -\frac{\hbar^2}{2m}\nabla^2\psi + V(r)\psi, \tag{17}$$

where m is the mass, ψ the field variable, V the potential and $\hbar$ a constant related to the Planck constant. All these equations show several common features:

1. They are local, i.e. they describe a process at a point, which depends only on mechanisms localized at this point in an infinitesimal part of the space. As a consequence, the summation of many local and partial processes gives the global, observed process in all space. For example, the energy function (hamiltonian H) in a lattice, the structure of which is similar to a biological membrane, satisfies the equation, at each point l,l' of the lattice, for momentum p_l and displacement u_l:

$$H = \frac{1}{2m}\sum p_l^* p_l + \frac{1}{2}\sum_l\sum_{l'} u_l^* G_{l-l'} u_{l'}, \tag{18}$$

where the potential $G_{l-l'}$ describes the interaction between the two points l and l' of the lattice. This is a non-local interaction operator. In the quantum field theory, such an expression of the potential, introduced in the Lagrangian, would lead to many complications.
2. They show a space symmetry, i.e. an isotropic propagation, because the term $\nabla^2\psi$ implies the same evolution ψ with (x,y,z) positive or negative. In contrast, the Naviers–Stokes equation is non-symmetric:

$$\frac{\eta}{\rho}\nabla^2 v = \frac{\partial v}{\partial t} + v\frac{\partial v}{\partial x} + \frac{1}{\rho}\frac{\partial p}{\partial x}, \tag{19}$$

where v is the velocity of a volume element of matter with specific mass ρ and viscosity η, and where p is the pressure that applies to this element. The two last terms make this equation very different from the others, and come from Newton's local law which implies a global non-symmetric movement of the given volume, described by $v\partial v/\partial x$ due to the local force gradient. Here too, the second order differential operator describes the diffusion, symmetric effect, in the moving volume element. The property of symmetry appears also in the numerical form of ∇^2. If x_i and x_{i+1} are two consecutive points such that: $x_{i+1} = x_i + \nabla x$, then a second order development gives the derivatives:

$$\dot{\psi} = (\psi_{i+1} - \psi_{i-1})/2\Delta x,$$
$$\ddot{\psi} = (\psi_{i+1} + \psi_{i-1} - 2\psi_i)/(\Delta x)^2. \tag{20}$$

The second order derivative is obviously symmetrical with respect to Δx.

3. They are physically defined in an homogeneous space the homogeneity of which can be broken with the diffusion 'constant' $D(x,y,z)$ or the potential $V(x,y,z)$ depends on a space-function.

(e) *Derivation of the discrete case from excitation fields*

When a large number of structural units is considered, e.g. in the nervous system, continuous spaces of units with density $\rho(r)$ can be used (with, to simplify, $r \equiv r^{(l)}$ at level l, in the following). We have seen in paper II that this result is correct at the lower levels of the functional organization, but, at higher levels, the number of units decreases. However, the formal field equation:

$$H\psi = \Gamma, \tag{21}$$

is always valid with H being a non-differential operator that acts from (r,t) to (r_0,t_0), and $\Gamma(r,t)$ the source term at point r. It is possible to transform a continuous mathematical system into a discrete one, i.e. a partial derivative equation into a differential equation as follows.

Let us assume that structural units are distributed at v points r_k which are at a distant such that continuous approximation is not valid. The interaction term can be written:

$$H_I\psi(r_0,t_0) = \sum_k V[r_0,t_0,r_k,t_k;\ \Gamma(\psi_k)]\ \psi(r_k,t_k), \tag{22}$$

where $\psi_k \equiv \psi(r_k)$, $t_k \equiv t(r_k)$. If U_k denotes the potential at r_k, i.e. the interaction between the field at r_0 and the source at r_k we have:

$$H_I\psi(r_0,t_0) = \sum_k U_k(r_0,t_0,t_k)\psi(r_k,t_k). \tag{23}$$

The process at current time t can be only considered to be located in structural units, such that the interaction between the current point $r_l \equiv r_0$ and any other point r_k in the network at time t', is described with the potential $V[r_l,t(r_l),r_k,t'(r_k);\ \Gamma(\psi_k)]$. Therefore:

$$H_I\psi(r_l,t) = \sum_k U_k(r_l,t,t')\psi(r_k,t') = \sum_{k\neq l} F'_{kl}(t,\psi_k(t')),$$
$$= \sum_{k\neq l} F_{kl}(\psi_k), \tag{24}$$

where, in the last equation, the delay has been suppressed, i.e. $t = t'$. This expression can be included in the general field equation to provide the classical reaction-diffusion equation:

$$\partial\psi_l/\partial t = D\nabla^2\psi_l + \sum_{k\neq l} F_{kl}(\psi_k) + \Gamma_l(\psi_l). \tag{25}$$

Finally, when the distance between units is large with respect to the length of diffusion, the differential equation is:

$$\mathrm{d}\psi_l/\mathrm{d}t = \sum_{k\neq l} F_{kl}(\psi_k) + \Gamma_l(\psi_l) \qquad l = 1,2,\ldots,v. \tag{26}$$

So, it is always possible to eliminate the geometry from the system, so as to keep only its topology. Such an example is given by the passage from biological

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

neural networks to formal neural networks, when the density is replaced by a Dirac distribution.

4. EVOLUTION OF A FUNCTIONAL ORGANIZATION BY COUPLING OF THE GEOMETRY AND THE TOPOLOGY IN AN FBS

(*a*) *Potential of functional organization and geometry*

Functional organization is measured by the function Π (equation (3), paper II):

$$\Pi = \sum_{\text{levels}} [\text{sinks}] \ln [\text{sources}]. \tag{27}$$

In a continuous representation, sink and source concentrations are given by their densities, respectively, $\rho_0(r)$ and $\rho(r)$ at a point r in the space of units, at the level l of organization. The total number of structural units is $v = \int(\rho(r) + \rho_0(r))\mathrm{d}r$. Because $n = \int\rho_0(r)\mathrm{d}r$ sinks in a volume $\int\mathrm{d}r$ must be associated in some way with the $(v - \int\rho_0(r)\mathrm{d}r)$ other units that are sources, the potential of organization (see paper II) is:

$$\Pi^l = n \ln(v - n), \qquad n = \int(\rho_0(r)\mathrm{d}r, \qquad v = \int(\rho_0(r) + \rho(r))\mathrm{d}r, \tag{28}$$

for a level of organization l. This will be called the intra-level potential.

Let us consider now the inter-level potential. Discrete groups of units are distributed in the space of units and connected by functional interactions. The calculation can be made in discrete space and extended to continuous space by tending to the limit. Let there be $N_{k'}$ units in the K' groups $E_{k'}$, $k' = 1,K'$, and $N_{\alpha k'}$ sources for the product P_α (figure 5). The topology of the FBS is defined by the graph that specifies the connections between the $N_{\alpha k'}$ sources in the group $E_{k'}$, and the $N_k - N_{\alpha k}$ sinks in the group E_k. Then, it is possible to generalize equation (28) to the case of inter-level links: the number of potential functional organizations between level $l + 1$ with $N_{\alpha k'}$ sources and level l with $N_k - N_{\alpha k}$ sinks in the group E_k, depends, first on the number of units in the group, and second, on the number of groups, i.e. the number of units at level $(l + 1)$. The mathematical expression is:

$$\Pi_\alpha^{l,l+1}(k) = \sum_{k'=1}^{K'} (\ln N_{\alpha k'})\ (N_k - N_{\alpha k}). \tag{30}$$

This calculation gives the potential of organization between levels l and $(l + 1)$.

Now, in the continuous space, let $\rho(r)$ be the density of groups, and $\pi(r^{(l+1)}, r^{(l)}; r_0^{(l+1)})$ the density of units in $r^{(l)}$, in a group localized at $r_0^{(l+1)}$ and connected to other groups localized at $r^{(l)}$. Equation (30) gives:

$$\Pi_\alpha(r_0^{(l+1)}) = \int_{D_R} \ln[\rho(r^{(l+1)})] \int_{D(r^{l+1}, r0^{(l+1)})} \pi(r^{(l)}, r^{(l+1)}; r_0^{(l+1)})\mathrm{d}r^{(l)}\mathrm{d}r^{(l+1)}, \tag{31.1}$$

and $\Pi_\alpha^{l,l+1}$ for the whole system is obtained with an integration for $r_0^{(l+1)}$ in space D_R:

$$\Pi_\alpha^{l,l+1} = \int_{D_R} \Pi_\alpha(r_0^{(l+1)})\ \mathrm{d}r_0^{(l+1)}.$$

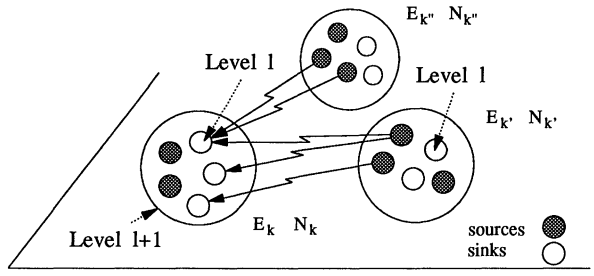


Figure 5. Inter-level potential of organization between groups of units. Every sink in the group E_k is connected with a source in the groups $E_{k'}$, $E_{k''}$, for all $k' \neq k''$.

The potential of organization for the two levels l and $l + 1$ is the sum of equations (28) and (31):

$$\Pi_\alpha = \sum_{l=0}^{N} \Pi_\alpha^{l,l+1}. \tag{31.3}$$

Therefore, three space functions determine the topology of the system in a continuous hierarchical space: (i) $v(r)$ is the total number of $(l + 1)$-units at $r^{(l+1)}$; (ii) $\pi(r^{(l)}, r^{(l+1)}; r_0^{(l+1)})$ is the density of l-units at $r^{(l)}$, in the group localized at $r_0^{(l+1)}$, i.e. a $(l + 1)$-unit at $r_0^{(l+1)}$, and connected to other groups at $r^{(l+1)}$. π will be called the density-connectivity function. (iii) $\rho(r)$ is the density of groups at r, i.e. the density of $(l + 1)$-units at r. It is clear that the potential of organization of this 2-level-FBS integrates both topology and geometry: (i) when functions π,v,ρ depend on time, the optimum principle shown in paper II could give a response to the problem of the time-evolution for an (O-FBS); (ii) a similar optimum principle for a (D-FBS) i.e. a principle that implies the 'movement' of the biological system, could be investigated. The consequences of an optimum time control hypothesis on the evolution of an FBS will be presented elsewhere. Specifically, a non-hamiltonian dynamics deduced from this hypothesis could lead to an interpretation of aging in biological systems (Chauvet 1990).

(*b*) *Dynamics of functional organization by coupling topology and geometry*

In paper I, a simple evolutionary model was presented as an illustration of a 2-level dynamical functional organization. This Eigen–Goodwin system was a paradigm for the study of the dynamics of functional interactions in a 3-level biological system. When continuous spaces are considered, such a paradigm can still be used where ψ and ρ are two space and time field-functions. Before studying numerically the specific case of the Eigen–Goodwin model, it is

useful to prove a general property of such hierarchical systems, which could be observed in real biological systems.

Let $\boldsymbol{R}$ be the field operator applying to the field vector density ρ, as $\boldsymbol{H}$ is the operator that applies to the field vector ψ for functional interactions. Due to the self-association hypothesis, a unit at level $l-1$ is associated with a modified unit, denoted with a '*' superscript, at the same level, to obtain units at the higher level l, according to the schema:

$$u^{(l-1)} + u^{*(l-1)} \rightarrow u^{l}. \tag{32}$$

More generally, units at the $(l-1)$-level of organization are connected, following this schema (32) from a functional point of view, with units of the l-level of organization according to the density-connectivity function $\pi^{l-1,l}$. The consequence is a $\pi^{l-1,l}$-operator dependence that can be formally written as:

$$\begin{aligned} &\boldsymbol{H}^{l}(\psi^{l},\rho^{l})\ \psi^{l} = \Gamma^{l}(\psi^{l},\psi^{l-1}) && t^{l}\in\{T^{l}\},\\ &\boldsymbol{R}^{l}(\psi^{l-1},\rho^{l-1})\ \rho^{l} = \alpha^{l}(\rho^{l-1},\rho^{l}) && t^{l'}\in\{T^{l'}\}, \end{aligned} \tag{33}$$

where $\{T\}$ and $\{T'\}$ are the time scales in the space of interactions and in the space of densities, and α^{l} is the source term for the densities at level l. The first equation describes the dependence of the field at level l on the field at level l, on the geometry at level l, and on the field at level $l-1$ via the source term. The second equation describes the dependence of the concentration of units at level l on the concentration of units at level $l-1$ according to (32), and on the field at level $l-1$. This dependence is due to the fact that the rate of association in (32) depends on the interaction ψ^{l-1}, the 'product', that is transported along the distance in the cartesian space. With inter-level links, the schema (32) of self-association represents units at a level l connected with adjacent levels $l-1$ and $l+1$ according to densities-connectivities $\pi^{l-1,l}$ and $\pi^{l,l+1}$ respectively. Therefore, equations (33) can be generalized at level l into:

$$\begin{aligned} &\boldsymbol{H}^{l}(\psi^{l},\pi^{l-1,l},\pi^{l,l+1})\ \psi^{l} = \Gamma^{l}(\psi^{l},\psi^{l-1}) && t^{l}\in\{T^{l}\},\\ &\boldsymbol{R}^{l}(\psi^{l-1},\psi^{l},\psi^{l+1},\pi^{l-1,l},\pi^{l,l+1})\pi^{l,l+1} = \alpha^{l}(\pi^{l-1,l},\pi^{l,l+1}) && t^{l'}\in\{T^{l'}\} \quad l=1,\ldots,N-1. \end{aligned} \tag{34.1}$$

Two limit cases are obtained for $l=0$ and $l=N$ if an $(N+1)$-level system is considered:

$$\begin{aligned} &\boldsymbol{H}^{0}(\psi^{0},\rho^{0},\pi^{01})\ \psi^{0} = \Gamma^{0}(\psi^{0}) && t^{0}\in\{T^{0}\},\\ &\boldsymbol{R}^{0}(\psi^{0},\psi^{1},\pi^{01},\rho^{0})\ \pi^{01} = \alpha^{0}(\pi^{01}) && t^{0\prime}\in\{T^{0\prime}\}, \end{aligned} \tag{34.2}$$

$$\begin{aligned} &\boldsymbol{H}^{n}(\psi^{n},\pi^{n-1,n},\rho^{n})\ \psi^{n} = \Gamma^{n}(\psi^{n},\psi^{n-1}) && t^{n}\in\{T^{n}\},\\ &\boldsymbol{R}^{n}(\psi^{n-1},\psi^{n},\pi^{n-1,n},\rho^{n})\ \rho^{n} = \alpha^{n}(\pi^{n-1,n},\rho^{n}) && t^{n\prime}\in\{T^{n\prime}\}. \end{aligned} \tag{34.3}$$

The general formal system (34) allows us to derive the property of re-distribution of units among the different levels of the FBS. One unit at $r^{(l)}$ is composed of sources whose density is $\rho(r^{(l-1)})$, connected with sinks whose density is $\rho(r_0^{(l-1)})$. Density-connectivity $\pi^{l,l+1}(r^{(l)},r^{(l+1)},t^{l};\ r_0^{(l+1)})$ now is a function which represents the variation in time of the number of units $u^{l}(r)$ in r connected with units $u^{l-1}(s;r_0)$ in r_0 because they are solutions of equations (34): $\boldsymbol{R}\ \rho = \alpha$. For clarity, the coordinates in spaces of units will be denoted

$$r^{(l)} \equiv s, r^{(l)'} \equiv s'; r_0^{(l+1)} \equiv r_0; r^{(l+1)} \equiv r, r^{(l+1)'} \equiv r'.$$

Let N^{l} be the total number of units $u^{l}(s;r_0)$ in space $D_l(r;r_0)$ at level l located in r_0 where the timescale is $\{T\}$. They are connected with units in a space D_{l+1} at higher level $l+1$. In the most general case, this number is the sum of several terms that correspond to non-associated units u^{l} (they are hierarchical systems whose highest level is l), and to other units that are associated in order to create the higher levels $(l+1)$, $(l+2)$, ... The first term is:

$$N_1^{l} = \int_{D_l(r;r_0)} \rho^{l}(s,t^{l})\ \mathrm{d}s\mathrm{d}r. \tag{35}$$

The second term corresponds to $\rho^{l+1}(r)$ units u^{l} in volume $\mathrm{d}r$, connected with $\pi^{l,l+1}(s,r,t^{l};r_0)$ units $u^{l}(s;r_0)$ at $(s;r_0)$:

$$N_2^{l} = \int_{D_{i+1}} \int_{D_l(r,r_0)} \pi^{l,l+1}(s,r,t^{l};r_0)\ \rho^{l+1}(s,t^{l+1})\ \mathrm{d}s\mathrm{d}r,$$

where $D_{l+1} \equiv D_r$. The following terms would have the same form:

$$N_3^{l} = \int_{D_{i+2}} \int_{D_{i+1}} \int_{D_l(r,r_0)} \pi^{l,l+1}(s,r,t^{l};r_0)\ \pi^{l+1,l+2}(r,q,t^{l+1};q_0)\ \rho^{l+2}(q,t^{l+2})\ \mathrm{d}s\mathrm{d}r\mathrm{d}q, \tag{36}$$

where $D_{l+2} \equiv D_q$. Finally, N^{l} is obtained as the sum:

$$N^{l}(t^{l},t^{l+1},t^{l+2},\ldots;r_0,q_0,\ldots) = N_1^{l}(t^{l}) + N_2^{l}(t^{l+1};r_0) + N_3^{l}(t^{l+2};q_0) + \ldots \tag{37}.$$

Equations (34) and (37) show that a geometrical re-distribution of units follows a variation in time of density-connectivities when a global condition of conservation as (37) is imposed on the system. The potential of functional organization $\Pi^{l,l+2}$ can be written as in (31.3) for two levels of organization, but the time dependence of density-connectivities provides Π as a function of time. Thus, we have:

Property VIII: geometrical re-distribution of units

A biological system whose dynamics is described at each level by functional interactions and densities: (i) has a time-dependent potential of organization $\Pi(t)$ in the timescale of the last level; and (ii) changes its topology at a given level because of the geometrical re-distribution of units after the variation in time of density-connectivities.

This property describes the relation between the two systems (O-FBS) and (D-FBS).

5. STATISTICAL APPROACH BASED ON THE FIELD THEORY

Is the collective behavior of the population of units a simple summation of the individual elements? Results obtained in statistical physics have given a negative answer since the work of Boltzmann (1877) and Gibbs (1902). In this section, a solution to the problem is given for the present description of the functional organization. We show that the hierarchical construction of the functional system, with each level describing the collective behavior in a distinct time scale, leads to a possible determination of the statistical distribution of the states of the field.

At each level of the functional organization exists a state variable, the field variable, decoupled in time. Therefore, it is possible to introduce a distribution function of the states variables $f^l(\psi^0,\psi^1, \ldots, \psi^l)$ from the 0-level to the l-level. Such a function gives the proportion of structural units that are in the state determined by the field. It depends on specific parameters of the system, which describe the influence of the units on the population of these units. The statistical distribution function can be obtained as the solution of a certain equation that describes the balance of units submitted to various influences, e.g. elementary physiological mechanisms.

Two classes of mechanisms are assumed:

1. An external influence on the system, e.g. an excitation from another system in the biological system, or a stimulation, which changes the proportion of units in a given state. Because each unit has an equal probability of passing from one state to another, this process is similar to the change of states in a compartment: the corresponding variation in time Δf^l_{ext} of the distribution function is in direct relation with the number of units at the present time. Let $Q(t)$ be the coefficient that expresses the fraction of units that change their state. Then:

$$\Delta f^l_{ext} = \left(\frac{\partial f^l}{\partial t}\right)_{ext} \Delta t = Q(t) f^l \Delta t. \tag{38}$$

2. An internal transformation corresponding to the elementary mechanisms described by the field variable: a state transition $\Delta f^l_{\psi^i}$ occurs as soon as there exists a transformation in the biological system, particularly when a stimulation is applied to the system. The formulation of this term depends on the mechanisms that make the field variables evolve, i.e. on the field equations themselves:

$$\Delta f^l_{\psi^i} = \left(\frac{\partial f^l}{\partial t}\right)_{\psi^i} \Delta t. \tag{39}$$

The effect of all the state transitions can be assumed as additive, because each field equation represents a process on a different timescale. Therefore:

Property IX: Statistical equation of field states

The action of the fields on the population of structural units is described by a statistical distribution function of the states $f^l(\psi^0,\psi^1, \ldots, \psi^l)$ which is a solution of the equation:

$$\frac{\partial f^l}{\partial t} = Q(t) f^l + \sum_{i=0}^{l} \left(\frac{\partial f^l}{\partial t}\right)_{\Delta\psi^i}, \tag{40}$$

where $Q(t)$ is a rate constant, positive for an 'attractive' population, negative for a 'repulsive' population. Specific parameters are included in the terms

$$\Delta f^l_{\psi^i} = \left(\frac{\partial f^l}{\partial t}\right)_{\Delta\psi^i} \Delta t$$

that describe the state transitions.

In the present case of a biological system, the temporal hierarchy that corresponds to the construction of the physiological functions provides a means to make the contributions non-dependent. For each specific biological system, the time partial derivatives $(\partial f^l/\partial t)_{\Delta\psi^i}$ include new parameters that describe the population effects under the action of the fields.

6. TWO EXAMPLES: SELF-ASSOCIATION HYPOTHESIS AND NEURAL FIELD EQUATIONS

(a) *Role of geometry on the self-association hypothesis*

In paper I, it was shown that an increase of the domain of stability could be a natural cause of self-association between structural units, and therefore, a cause for the creation of functional interactions and hierarchy. It is important to know whether this property still exists when the role of geometry is taken into account, i.e. when processes are described by field equations. Because we have not yet identified the class of dynamical systems that satisfy this property, the basic processes studied in paper I, i.e. metabolism and replication, are considered here (figure 6). At initial time $t = t_0$, a micromutation occurs in a structural

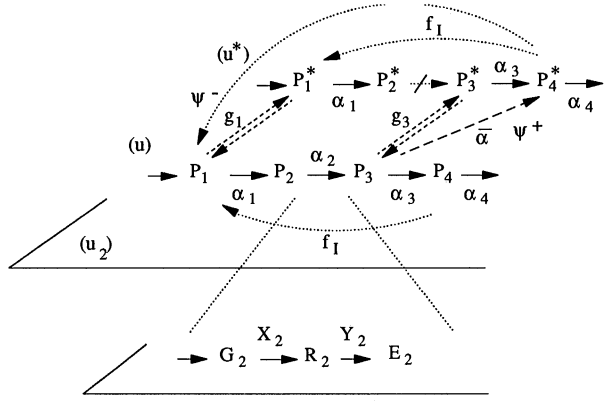


Figure 6. Self-association between two units. A pathological unit, u^*, has created a functional interaction with u. The product P_3 is assumed to act on P_4^* at a distance, and therefore is identified to the field variable ψ^+ with rate constant $\bar{\alpha}$. The negative feed-back from product P_4^* acts on the first enzyme E_0 in the biochemical pathway (see figure 8*a*, paper I). The similar interaction from the pathological unit u^* on u allows identification of the inhibitor field variable ψ^-. The set (u,u^*) constitutes a new unit u_2 at the higher level.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

unit u_1, producing a modified structural unit u_1^*. According to the principle of vital coherence, the maintenance of the physiological function, called 'product', needs an association of this unit with another that has the missing product. In mathematical terms, this means a coupling between the dynamical system that describes the metabolism in u_1 and the modified dynamical system for u_1^*. In this problem, two levels of organization are considered: metabolism inside a unit, and replication of units. With the present formalism, we can say that a unit u_1^* satisfies the principle of vital coherence if it is placed in the field of excitation of u_1-units (Chauvet 1990).

Let us consider the metabolic level. Without space influence, metabolic regulation is described by the dynamical system (equations (19), paper I):

$$\begin{aligned}
\mathrm{d}P_1/\mathrm{d}t &= -\alpha_1 P_1 + f_{I,4}(P_4;\tilde{\omega},\kappa,\alpha_0) + f_{I,4}(P_4^*;\tilde{\omega},\kappa,\alpha_0),\\
\mathrm{d}P_2/\mathrm{d}t &= -\alpha_2 P_2 + \alpha_1 P_1,\\
\mathrm{d}P_3/\mathrm{d}t &= -(\alpha_3 + \bar{\alpha})P_3 + \alpha_2 P_2,\\
\mathrm{d}P_4/\mathrm{d}t &= -\alpha_4 P_4 + \alpha_3 P_3,\\
\mathrm{d}P_4^*/\mathrm{d}t &= -\alpha_4 P_4^* + \bar{\alpha} P_3, \qquad (41)
\end{aligned}$$

where $\bar{\alpha}$ is a positive constant included in the transport mechanism and described by a function Φ as explained in paper 1, and simply describes the contribution of product $P_3 \in u_1$ to the production of $P_4^* \in u_1^*$; the parameter $\tilde{\omega}$ is the stoechiometry of the allosteric reaction: $f_{I,4}(P_4;\tilde{\omega},\kappa,\alpha_0) = \alpha_0/(1 + \kappa P_2^{\tilde{\omega}})$. According to figure 6, with space influence, P_3 is identified to ψ^+ because it activates the synthesis of P_4^* at a distance, and P_4^* can be identified to ψ^-. We assumed in this model that P_1,P_2,P_3 are substances that act locally, i.e. inside a unit. In matrix form, the dynamical system is written:

$$\boldsymbol{H}(\Psi)\Psi = \Gamma, \qquad (42)$$

where

$$\Psi = \begin{pmatrix} \psi^+ \\ \psi^- \\ P_1 \\ P_2 \\ P_4 \end{pmatrix} \qquad \Gamma = \begin{pmatrix} -(\alpha_3 + \bar{\alpha})\psi^+ + \alpha_2 P_2 \\ -\alpha_4\psi^- + \bar{\alpha}\psi^+ \\ -\alpha_1 P_1 + f_{I,4}(P_4;\tilde{\omega},\kappa,\alpha_0) + f_{I,4}(P_4^*;\tilde{\omega},\kappa,\alpha_0) \\ -\alpha_2 P_2 + \alpha_1 P_1 \\ -\alpha_4 P_4 + \alpha_3\psi^+ \end{pmatrix}. \qquad (43)$$

The non-local operators $H_I^{+,-}$ that describe the non-locality property VII are included in the field equations for ψ^+ and ψ^-. The partial derivative equations (42) describe metabolism in unit u_2 where a functional interaction has been created. The stability of a simpler system where a non-local operator is assumed to be absent, i.e. the space extension of a unit is considered to be a point, has been studied recently by Machbub *et al.* (1991) with numerical methods. Such a system is an extension of (41) with diffusion terms. The numerical resolution is based on a variational method studied by Burger & Machbub (1991). A threshold of concentration is chosen which determines when the unit dies. Given this threshold, it is possible to verify the relation between the distance of the units and the ability of self-association (figure 7),

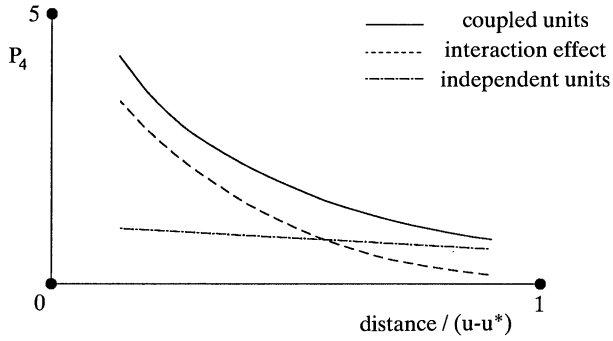


Figure 7. Solution of equations (43) giving the concentration of P_4 versus distance between units: (i) when units are coupled (solid line); and (ii) when units are independent (dot–dashed line). The interaction effect is obtained as the difference (dotted line). The concentration of product P_2 is the largest when units are coupled, and decreases when distance increases.

and thus obtain a measurement of the coupling between units.

At the level of populations of units u_1 and $u_2 \equiv (u_1, u_1^*)$, the variation in time of the densities ρ^1 and ρ^2 is supposed to satisfy the dynamics proposed by Eigen (1971) with a condition of constant overall organization. However, the model has to be transformed as follows to take into account the first level of organization: (i) to simplify the formulation, it is assumed that there does not exist for ρ^1 a potential created by the distribution ρ^2, in which u_1 would be immersed. Therefore:

$$\partial\rho^1/\partial t = D_1\nabla^2\rho^1 + \Gamma_1(\rho^1,\rho^2). \qquad (44.1)$$

(ii) As verified previously, the intensity of coupling depends on space distance, because u_1^* must be in the excitation field of u_1 to survive. Therefore, the densities evolve in time following the variation in time of the coupling that is deduced from the dynamics of the field (ψ^+,ψ^-). A consequence of the dynamics of processes is the existence of the dynamics of organization. Specifically, three mechanisms originate in the time variation of ρ^2: (i) free diffusion of u_2-units; (ii) self-replication and local competition between species which generate the source term $\Gamma_2(\rho^1,\rho^2)$; and (iii) creation by coupling according to the reaction:

$$u_1 + u_1^* \rightarrow u_2, \qquad (45)$$

located in:

$$(r,t) \qquad (r',t') \qquad (r,t),$$

or:

$$(r',t') \qquad (r,t) \qquad (r,t),$$

with a rate constant $K(\psi^+,\psi^-)$. Therefore, the ρ^2-equation is:

$$\frac{\partial \rho^2}{\partial t} = D_2 \nabla^2 \rho^2 + \Gamma_2(\rho^1,\rho^2) + H_I^2[\psi^+,\psi^-,\rho^1,\rho^{1^*}]\ \rho^1(r,t), \quad (44.2)$$

where the interaction operator H_I^2 is:

$$H_I^2[\psi^+,\psi^-,\rho^1,\rho^{1^*}] = \int_{(D)} K(\psi^+,\psi^-)\, f(\|r - r'\|)\ [\rho^{1^*}(r)\rho^1(r',t') + \rho^{1*}(r')\rho^1(r,t)]\ \mathrm{d}r', \quad (46)$$

with the condition of global organization when the number of modified units is small relatively to the other units:

$$\int_{(D)} [\rho^1(r,t) + 2\rho^2(r,t)]\ \mathrm{d}r = \text{constant}, \quad (47)$$

which is similar to the condition $u_1(t) + 2u_2(t) =$ constant imposed on the non-space model (paper I). We have studied a simpler case (Machbub *et al.* 1992), which is deduced from the non-space model:

$$\partial\rho^1/\partial t = D_1 \nabla^2 \rho^1 + a_1\rho^1 - (1/c)\phi(\rho^1,\rho^2)\ \rho^1,$$
$$\partial\rho^2/\partial t = D_2 \nabla^2 \rho^2 + a_2\rho^2 - (1/c)\phi(\rho^1,\rho^2)\ \rho^2 + K_{11}\rho^1\rho^{1*},$$
$$c = \rho^1 + 2\rho^2, \quad (44.3)$$

with the relation $\phi(\rho^1,\rho^2) = (a_1 + 2K_{11}\rho^{1*})\rho^1 + 2a_2\rho^2$ deduced from the local condition of constant organization. Machbub *et al.* (1992) have shown that diffusion can stabilize the null equilibrium state of the locally unstable kinetic model. The non-null equilibrium state can be studied with the same method: with diffusion, the domain of stability of this equilibrium state in phase space (K_{11},ρ^{1*}) is shown to be increased. Therefore, the field equations for structural units u_2 at the second level have a larger domain of stability than the field equation at level 1. Self-association is a natural trend of this particular biological system. Equations (44) can be written in matrix form:

$$\boldsymbol{R}\ \rho = \alpha$$

that, with equation (42), are a particular case of equations (34). The condition of a constant number of units (37) is equivalent to (47) for the simple connectivity $2u_1 \rightarrow u_2$.

(*b*) *A field theory for the nervous system*

The previous sections have shown at least four fundamental properties for a functional interaction which lead to a field theory (Chauvet 1993*b*): (i) non-instantaneity, i.e. its transport with a finite velocity; (ii) non-locality because of the possible distance between sources and sinks considered at different levels of organization; (iii) non-symmetry between sources and sinks; and (iv) non-homogeneity of the medium. Non-locality and non-symmetry are included in the local dynamical equation of one neuron, by means of a non-local and non-symmetric term which describes the unidirectional action of this neuron at a distance. In this section, a method to determine 2-level neural field equations is offered (Chauvet 1988, 1993*b*). First attempts for a 1-level field theory have been proposed by Beurle (1956) and Griffith (1963, 1965).

(i) *A general definition of synaptic efficacy*

A general definition of synaptic efficacy μ, which takes into account local and non-local effects, and both levels of organization, is a function of quantities for the presynaptic neuron in r' and for the postsynaptic neuron in r_0: at the neuronal level with a timescale $\{T\}$, $X(r_0,T_0)$, instantaneous local somatic activity, and $\psi(r_0,T_0)$, local soma membrane potential; at the synaptic level with the timescale $\{T\}$, $\Phi_0(s,T)$, postsynaptic local membrane potential. Therefore, the passage from one level of organization (synapses) to the other (neurons) with ψ and μ as local somatic depolarization and synaptic efficacy respectively, implies the measure of the ψ- and μ-fields in two different spaces whose points are denoted by (r,T) and (s,t), respectively (figure 8).

(ii) *Local effects at the level of synapses*

Local effects at the neuron level include pre- and postsynaptic biochemical mechanisms, from which the local synaptic efficacy has to be deduced. Presynaptic mechanisms are included in the presynaptic efficacy $\xi(s,t;\langle X\rangle)$ and described following Magleby & Zengel (1982). Postsynaptic mechanisms are included in the postsynaptic efficacy $\eta(s,t;\langle X\rangle)$. They are described by a simple two-state kinetic model for describing the transmitter-receptor binding, and are defined as a conductivity that is in the number of non-modified (but modifiable) channels, the number of activated receptors, and the number of modified channels. By using the well-known cable equation (Hodgkin & Huxley 1952):

$$\partial\Phi_0(s,T)/\partial T = D_0 \nabla_s^2 \Phi_0(s,T) - k_0\Phi_0(s,T), \quad (48)$$

postsynaptic potential (PSP) changes are described by two local mechanisms: (i) local free diffusion of ions represented by the first term, which depends on the conditions of extracellular space, e.g. extracellular

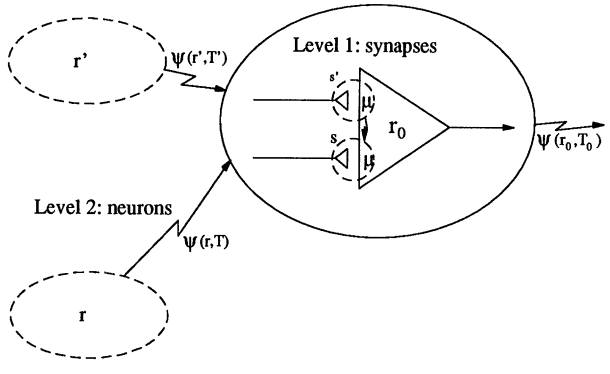


Figure 8. Two levels of organization in the nervous system: at the level of neurons (level 2), the field variable is the soma membrane potential ψ at point (r,T), and at the level of synapses (level 1), the field variable is synaptic efficacy μ at (s,t) in the neuron at r_0.

potentials; and (ii) a local spontaneous loss or gain represented by the second term to describe the homosynaptic effects. Because of the non-existence of an interaction operator, the non-symmetry and the non-locality are not included in this equation.

(iii) *Non-local effects at the level of synapses: μ-field equation*

Non-local effects for a given synapse result from the influence of electrical phenomena that occur at a distance. The interaction operator describes this influence, and is obtained by taking into account non-local potentials that depend on membrane receptors and neurotransmitters: the PSP of the r_0-neuron in s, which is connected with neurons in r, results from other synapses localized in s' on the same dendritic tree, due to the activation of neurons in r' (figure 9). As shown in section 4, geometry and topology, which are included in the model, lead to these heterosynaptic effects, and are described by two anatomical functions: (i) the density-connectivity $\pi(s,r;r_0)$ of synapses defined in a space $D_s(r,r_0)$ at $s(r,r_0)$ in the r_0-neurons connected with the r-neurons; (ii) the density of neurons $\rho(r)$ at r defined in the space $D_R(r_0)$ which is the combination of subspaces $D_s(r,r_0)$ when r varies. A potential kernel function $U(s,t,s',t'; \Phi,\delta\Phi)$ leads to an equation for the global non-local synaptic efficacy μ depending on long-term variables:

$$\partial\mu/\partial t = D\nabla_s^2\mu + H_I^{\mu}(\mu) + \Gamma_{\mu}. \tag{49}$$

The first term corresponds to a local spatial variation and is directly deduced from equation (48).

The second term expresses the long-term spatio-temporal summation of all local and non-local effects that lead from $\psi(r',T')$ to $\Phi(s,t)$ via $\Phi(s't')$ (figure 10). The local dependence of μ_0 on the molecular kinetics is assumed to be a multiplicative interaction of local pre- and postsynaptic efficacies ξ and η. This assumption corresponds to the natural composition of ξ and η considered as mathematical applications: $\mu_0(s,t) = \langle\xi(s,t)\eta(s,t)\rangle$. The simplest manner to deduce this interaction is to suppose that it results from the long-term variation of chemical substances, neurotransmitters and neuromodulators, the dynamics of which change on a longer timescale. This long-term change determines the variation of activated receptors and thus the variation of long-term pre- and postsynaptic efficacies assumed to be the time-average of the

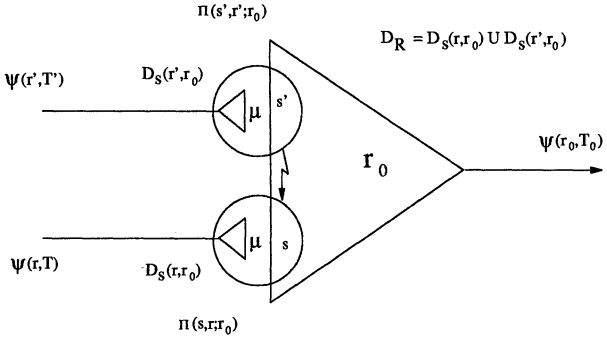


Figure 9. Definition of the spaces of units, synapses and neurons, in nervous tissue. Notations are similar to the ones presented in figure 3, where $l \equiv R$, $l-1 \equiv s$. Thus: $D_l(r_0^{(l)}) \equiv D_R(r_0)$ and $D_{l-1}(r_i^{(l)};(r_0^{(l)}) = D_s(r_i,r_0)$.

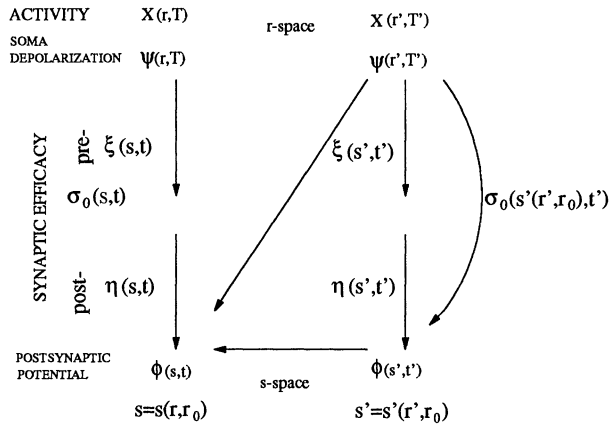


Figure 10. Non-locality at the level of synapses, expressed as a composition of applications in the space of units: The transformation $\sigma_0(s,t)$ is the local synaptic efficacy that transforms soma membrane potential $\psi(r,T)$ into $\phi(s,t)$ where $s = s(r,r_0)$ is the location of synapses in the neuron at r_0 connected with neurons at r. The non-local transformation σ acts from neurons at r' on synapses at s via the synapses at s', i.e. is the product of σ_0 at $s'(r',r_0)$ and the non-local, hetero-synaptic transformation from s' to s.

current synaptic efficacies. These variations are included in the potential kernel function U_{μ} so that pre- or postsynaptic efficacies act as parameters. The local dynamics could be obtained from the description of the molecular kinetics. A particular form, that leads to Hebbian associative equations of learning, is a multiplicative interaction of average pre- and postsynaptic activities for a simplified description of the complex internal dynamics:

$$\xi = a\langle X(r,T)\rangle(t), \quad \eta = b\langle X(r_0,T_0)\rangle(t). \tag{50}$$

The third term corresponds to the source and expresses, e.g. the local dynamics with coefficient $m(t)$ inside the synapse:

$$\Gamma_{\mu} = m(t)\,\mu(s,t). \tag{51}$$

(iv) *Non-local effects at the neuron level: ψ-field equation*

Non-local effects for a given neuron result from the influence of other neurons of the network that are localized at a distance. They imply that the neural activity must be a solution of a field equation at the level of the network. The mathematical potential function describes the effect of divergent or convergent neurons from or to a (r_0,T_0)-point: postsynaptic soma depolarization $\psi(r_0,T_0)$ results from the presynaptic neurons $\psi(r,T)$ that are modified according to the values $\mu(s,t)$ of synaptic efficacy. The synaptic space $\{s(r,t)\}$ is in the neural space $\{(r,T)\}$, and this correspondence is expressed by the density-connectivity function $\pi(s,r;r_0)$. The source term $\Gamma_{\psi}(r_0,T_0)$, assumed to be in direct relation with ψ with a coefficient $p(T)$, describes the local generation of a neuron soma depolarization:

$$\Gamma_{\psi} = p(T)\,\psi(r_0,T_0). \tag{52}$$

(v) *Neural field equations*

The μ-field equation and the ψ-field equation are deduced from equation (49):

$$\frac{\partial\mu(s,t)}{\partial t} = \nabla_s(D^s\nabla_s\mu(s,t)) + \int_{D_R(r_0)}\rho(r')\int_{D_s(r',r_0)}\mu_0(s',t')\pi(s',r';r_0)A(s,s')\mathrm{d}s'\mathrm{d}r' + \Gamma_\mu(s,t), \quad (53.1)$$

$$\frac{\partial\psi(r_0,T_0)}{\partial t} = \nabla_r(D^r\nabla_r\psi(r_0,T_0)) + \int_{D_R(r_0)}\rho(r)\psi(r,T)\int_{D_s(r,r_0)}\mu(s,t)\pi(s,r;r_0)B(r_0,T_0,r,T)\mathrm{d}s\mathrm{d}r + \Gamma_\psi(r_0,T_0), \quad (53.2)$$

$$s \equiv s(r_0), \qquad D_R(r_0) = \bigcup_{r'} D_s(r',r_0).$$

$D_R(r_0)$ is the combination of subspaces $D_s(r,r_0)$, i.e. the space of synapses in neurons that are localized in r_0 and correspond to neurons in r. A, B are attenuation functions of potentials along the membrane between two points. Equations (53) constitute the neural 2-level field equations for the activity of neural tissue. Their coupling is imposed by μ and the neural tissue is characterized by two geometrical functions: the density of neurons ρ and the density-connectivity of synapses π. They imply non-linearities that appear via the source terms. The relation between instantaneous local somatic activity, in timescale {T}, and soma depolarization (generally considered as a non-linear sigmoïd function (Kishimoto & Amari 1979)) is deduced from the solution for the field equations (53.1) and (53.2) that include local and non-local effects from multiplicative interaction, from pre- and postsynaptic efficacy dynamics, and from the space functions π and A. Learning rules can be either imposed on the network (Hebb 1949; Kohonen 1978; Hopfield 1982, 1984) or derived from the dynamics of the pre- and postsynaptic efficacies.

The physiological interpretation is as follows. The local effects, which are described by the diffusion terms (the first term in the field equations (53.1) and (53.2)), correspond to transport across the 'external' medium, i.e. the cytoplasm for synaptic efficacy, and the extracellular space for soma depolarization. They are included in the diffusion coefficients D^r and D^s, respectively. The non-local effects, due to the hierarchy of the system, which are described by the interaction terms (the second term in the field equations (53.1) and (53.2)), correspond to the propagation 'inside' the medium, i.e. the membrane for synaptic efficacy, and the neuron for soma depolarization. What we see in the continuous space at each level of organization is the combination of these two types of transport, diffusion and propagation. Thus, the proposed 2-level field theory gives the value of the intracellular field potential *Ifield*(r,t) for given initial conditions, e.g. stimulation at the presynaptic level. The extracellular field potential can be derived from the intracellular one $Q_{i\to e}$ *Ifield*(r,t) for all elements dr in the space of neurons, and constitutes the cell activity contribution.

(vi) *Statistical distribution function of the states of the fields (property IX)*

The second contribution is the statistical 'activity' of synapses even when the postsynaptic cell is not active, and which can be determined by chosing a distribution function of synaptic states $f(t)$ because of the large number of synapses per cell. As shown in § 5, the time variation of $f(t)$ is the sum of: (i) the fraction $Q(t)$ (equation 38) of synapses that modify their state under the influence of stimulus intensity; (ii) the modification (equation 39) of the internal state of the cell and the corresponding synaptic states, as a consequence of soma depolarization, e.g. firing (feedback from the action potential to the emitting cell); and (iii) any long-term variation in synaptic efficacy. Then, from equation (40):

$$\left(\frac{\partial f}{\partial t}\right) = \left(\frac{\partial f}{\partial t}\right)_{ext} + \left(\frac{\partial f}{\partial t}\right)_{\psi} + \left(\frac{\partial f}{\partial t}\right)_{\mu}. \quad (54)$$

The state of a synapse is defined by the field variables considered in this problem. In the general case, the previous equation can be re-written:

$$\mathrm{d}f = Q(t)\,f(t)\mathrm{d}t + \mathrm{d}f_\psi + \mathrm{d}f_\mu, \quad (55)$$

and has a solution that provides the distribution of postsynaptic potentials, then the average $V^{syn}(r,t)$, and finally the extracellular potential $Q_{syn\to e}\ V^{syn}$ for all element dr in the space of neurons.

(vii) *Extracellular field potential*

For a stimulating intensity I, let $E(I)$ the space of stimulated neurons that includes a certain number of activated neurons, depending on the previous determination. Therefore, the extracellular field potential is the sum of two contributions:

$$V_E(t;I) = V_E^{fir}(t;I) + V_E^{syn}(t;I), \quad (56)$$

where:

$$V_E^{fir}(t;I) = \int_{E(I)} Q_{i\to e}(r)\,Ifield(r,t)\rho_0(r)\mathrm{d}r \qquad V_E^{syn}(t;I) = \int_{E(I)} Q_{syn\to e}(r)\,V^{syn}(r,t)\rho_0(r)\mathrm{d}r, \quad (57)$$

where ρ_0 is the density of postsynaptic neurons. Coefficients $Q_{syn\to e}(r)$ and $Q_{i\to e}(r)$ describe the interactions between the neuron and the extracellular space (Costalat *et al.* 1991, 1993). With this model deduced from the theory, it has been possible to give a mathematical interpretation of the waveform recorded in a monosynaptic pathway (figure 11), specifically, the dentate gyrus in hippocampus (Chauvet & Berger 1990, 1993, submitted). The parameters introduced in the model to describe the sources of the processes can be testable, and lead to specific experiments.

(viii) *Geometrical re-distribution of neurons (property VIII)*

As shown in paper II, the topology of the neural system changes such that the potential of organization remains maximum. The dynamics of the system varies according to equations (53) where the density ρ is

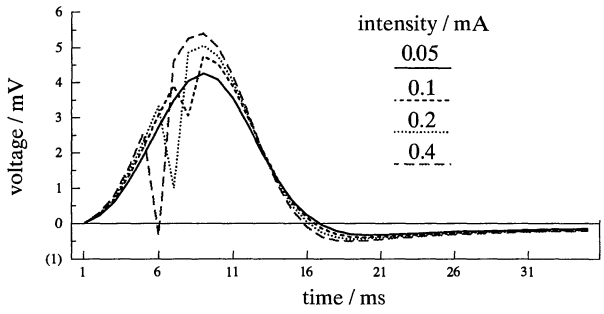


Figure 11. Extracellular field potential waveform interpreted with the present field theory. The curve is obtained from numerical simulations of equations (57) for four values of stimulating intensity (Chauvet & Berger 1990). The waveform is obtained as the superposition of the synaptic activity described by the distribution function of the synaptic states, and the population spike due to the action potential of active neurons.

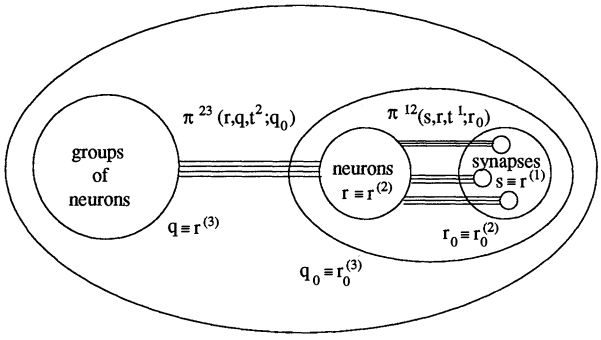


Figure 12. Notations for a system with four levels in the nervous tissue. The location of units at each level is: $s \equiv r^{(1)}$, $r \equiv r^{(2)}$, $q \equiv r^{(3)}$, $q_0 \equiv r_0^{(3)}$ for synapses, neurons, and groups of neurons. The density-connectivity between each level is $\pi^{12}(s,r,t^1;r_0)$ and $\pi^{23}(r,q,t^2;q_0)$ respectively. Notations are the same as in figures 3 and 9.

replaced by density-connectivity from one level to another. The dynamics of densities-connectivities are given by:

$$\mathrm{d}\pi^{l,l+1}/\mathrm{d}t^l = R_l^l[\psi^{l+1}(r,t^{l+1}),\pi^{l,l+1}(t^l)]\pi^{l,l+1}(t^l). \quad (58)$$

At least two levels could be considered in the functional organization of the nervous system, a group of neurons with a specific function, and an assembly of these groups of neurons, in addition to neurons with neuronal activity, and synapses with synaptic efficacy. Since the field equation in this N-level field theory has the same form at each level, we can introduce an 'efficacy' for one neuron and an 'activity' for a group of neurons. Simplified notations are used (figure 12) to describe units and field variables at each level: neurons at $r \equiv r^{(2)}$, groups of neurons at $q \equiv r^{(3)}$, $q_0 \equiv r_0^{(3)}$. Therefore, in this neural system with 4 levels, the field equation at the highest level, deduced from equations (53), is:

$$\frac{\partial\psi^3(q_0,t_0^3)}{\partial t_0^3} = \nabla_q(D^q\nabla_q)\psi^3(q_0,t_0^3) + \int_{D_4(q_0)} \rho^3(q,t^3;q_0)\psi^3(q,t^3) \int_{D_3(q,q_0)} \mu^2(r,t^2)\pi^{23}(r,q,t^2;q_0)B(q_0,t_0^3,q,t^3)\mathrm{d}r\mathrm{d}q + \Gamma_\psi^3(q_0,t_0^3), \quad (59)$$

where $\psi^3(q,t^3)$ is the activity of the groups u^3 of neurons. The density is $\rho^3(q)$, and neuron efficacy at level 2 is $\mu^2(u,t^3)$. The dynamics at the highest level is:

$$\rho^3(q,t^3;q_0) = f(q,q_0), \quad (60)$$

since a plausible assumption is a given constant space function for the density of groups of neurons. Property VIII thus leads to a law of evolution by selection for functional interactive groups of units. This was partly suggested by Edelman (1981) who showed the ability of competition for the selection of neural groups in the cerebral cortex. The result obtained here is a mathematical expression of the reciprocal influences between the topology and the geometry of functional interactions.

7. DISCUSSION: FUNCTIONAL ORGANIZATION, COMPLEXITY AND AUTONOMY: A PRINCIPLE OF ORDER FROM HIERARCHY

The present theory of functional organization offers some definitions for the terms 'complexity' and 'autonomy' that are used to specify some 'obvious' properties of biological systems. For example, we may wonder if amoeba can be considered less autonomous than mammals in terms of functional interactions. Many definitions have been given from a mathematical (Ferdinand 1974; Cornacchio 1977) or biological (Walter 1980, 1983; Demetrius 1983, 1984) point of view. This theory constitutes a possible approach to a description of functional organization.

As shown in paper I, the functional organization is described by matrix $\boldsymbol{M}$ and graph (G), and the dynamics of the system by equation (4). In this equation, $\Gamma^l(r,t)$ represents the local transformations in structural units at level l. Then Γ^l is a function of the excitation field ψ^{l-1} at level $l-1$, i.e. a function of some variables P_α^{l-1} that are the physiological products at this level. Because of the coupling of dynamics for each level, although organized and simplified according to different timescales, the field equation is more and more complex as the number of levels and the potential of organization given by equation (27) increase. But complexity decreases with hierarchical re-organization of the system, so that the functional order of the system increases. Mathematically, this topological property is deduced from the principle of vital coherence. If geometry is added to the system, then a phenomenon of re-distribution of units among groups is obtained. As shown above in nervous system, such mechanisms are observed during development and aging.

When structural units are independent, each unit supports the same dynamical processes, and a physiological collective process between them would not result. Therefore, a higher level of organization for such units does not exist. Functional independence cannot appear in the case of a hierarchical system built according to definition I of a physiological

function (see paper I). This result leads to a definition of an autonomous physiological system versus environment. Therefore, we can deduce the following property: the autonomy of a biological system increases with the potential of organization in a multiple field hierarchical system.

It is possible to prove this property as follows. Let P_e be the environmental substance that disappears from the environment, and is 'absorbed' by the system. The interdependence between the biological system and the environment is supposed to be represented by this substance whose concentration is the state variable at level 1 and is the parameter ψ_{env} at level 2 in the dynamical system (12). There are two eventualities for the functional organization, after an event that stops the synthesis of P_e.

1. P_e was synthesized at this 1-level. Although the eventuality of synthesis of P_e is rare, because of the generally accepted economy principle of living organisms (only the non-degradable elements are taken in from the environment), the (O-FBS) which satisfies the optimum principle for the orgatropy function (see paper II):

$$\mathrm{d}F(v) \geqslant 0, \tag{61}$$

can change: (i) with the creation of a new coupling that leads to an organization (n_e) for this product P_e: a new positive term is added to the potential of organization; and (ii) with a re-organization of this 1-level such that there is an association with a unit that synthesizes $P_e \equiv \psi_{env}$. Thus the degree of organization v, and subsequently the potential of organization Π are increased.

2. P_e was not synthesized at any level of organization. Then, either the system dies or a new dynamical process is created. Let N be this new level of organization. Therefore ψ^N, the vector that contains ψ_{env}, becomes a parameter at level 2:

$$H^N\psi^N = \Gamma^N$$
$$H^2\psi^2 = \Gamma^2(r,t;\psi^N). \tag{62}$$

Thus the number of levels of organization increases, and subsequently, the potential of organization Π.

A much more difficult problem is the real origin of the increase of Π. Is it an increase of autonomy which implies an increase of Π due to the optimum principle, or the inverse, i.e. an internal re-organization of the (O-FBS) after fluctuations near the bifurcation points of the (D-FBS), which implies the evolution of the system towards a different stable steady-state corresponding to the synthesis of the vital product? In the latter case, a new physiological function is created, and an increase of autonomy is observed. Probably, only precise knowledge of the functional organization and the associated dynamics could give an answer to this question. If we accept that the general functioning of a biological system is conceived as the dynamics of a set of functional interactions hierarchically organized, and described by activator-inhibitor fields at each level of organization with their own timescale, then the present theory suggests that the transformations, for instance from amoeba to mammals, correspond to an 'over-organization', i.e. an increase of functional order. Several principles have been postulated to explain biological organization: e.g. the principle of order from noise introduced by Von Foerster (1960), and developed by Yockey (1958) and Atlan (1972) in the framework of the theory of information, which describes the increase of information submitted to random fluctuations. However, this principle, which can be considered as a functional principle, is not expressed in terms of physiological functions, because of its generality. According to the principle of order from order described by Schrödinger (1944), an organism 'feeds upon negative entropy, attracting, as it were, a stream of negative entropy upon itself, to compensate the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level'. It is now known that non-linearities of the system can lead to non-equilibrium steady states of the dynamics (Prigogine 1972; Nicolis & Prigogine 1977). Such instabilities from one steady state to another, far from thermodynamical equilibrium, can be caused by small fluctuations. Like the Schrödinger principle, this principle of order from fluctuations describes the variation of the physical structure, i.e. an assembly of chemical structures such as molecules. In contrast, the principle of functional order from hierarchy proposed here describes the natural trend towards time in the decoupling of the physiological function, and, in that sense, towards a simplification of the dynamics, i.e. an order of the system, expressed in terms of the hierarchical functional organization. Specifically, the variation of the physiological function, conceived as a collective process resulting from the combinatorics of functional interactions, is due to variations of the topology of the system composed of structural units. This functional order, based on the concept of the non-symmetry of functional interactions, is related to the non-locality of the dynamics, and can be considered as the formalized expression of some ideas already conceived by physicists as Brillouin (1951): 'an entire organism is an organized system, and it is the long distance coupling which contributes to the value of this organization'.

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