Mesophysical Anticipatory Cell Behavior - Enroute to Quantum and Classical Nanobiology

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Abstract
Recent experiments showed that genomes in their evolutionary changes follow real *molecular strategies* leading to biological evolution through mutations that are not *small*, *rare* and *random* as is taught by Darwinian theory. This *mesoscopic anticipatory behavior* is here interpreted as evolutionary *classical/quantum chaos* mesoscopic information processing and through the coupling of electronic and mechanical degrees of freedom giving rise to the ***syntax ⇔ semantics ⇔ pragmatics*** *closed loop* as a *dissipative evolutionary* chain capable of overcoming logic self-reference paradoxes *just through dissipation*, and embodying the notion of biological information as inseparable from biological intelligence. A Quantum Field Theory of bio-mesoscopic subcellular structures as *"extended objects"* is proposed, so as to link micro- and mesophysical subcellular processes to the *vacuum structure* and fluctuations.

Keywords: nanobiology, anticipatory behavior, chaos, quantum fields, information

1 Introduction

A growing and fascinating wealth of experimental data, much of it presented at a recent meeting of the New York Academy of Sciences (Caporale, 1999), stress that genomes and their evolutionary changes must be considered in Theoretical Biology in a new light with respect to the current Darwinian concept that genetic change, and hence the evolution of new species stems from *small, random mutations in individual genes*. The notion of DNA's capacity to *slightly blunder* making it possible the earliest biota to evolve up to present upper rank living beings should now give way to the concept of *real molecular strategies* leading to biomolecular and biological evolution through mutations which are *not that small, rare and random*, involving both *mechanical* and *chemical* changes that result in the evolution of new *structure-function* relationships. Thus, cells look like engineering at a certain extent their own genomes, the latter being organs possibly capable of starting their own renovation by themselves *if necessary*. Accordingly, the nanobiologist should think of cells and genomes as objects of Nature that feature a *mesoscopic, i.e. nanoscale, anticipatory behavior*. This extremely intriguing aspect of matter contradicts the notion of biological evolution synthesized by the physician Lewis Thomas (Goldsmith and Owen, 1992) with the comment *"The capacity to blunder slightly is the real marvel of DNA. Without this special attribute, we would still be anaerobic bacteria and there would be no music"*. The new view would

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imply that *"chance favors the **prepared** genome"* (Caporale, 1999a). This is the real marvel indeed, and the new exciting challenge to Theoretical Biology for the next years to come.

It's a problem of Nanobiology, the newborn science (1992-93) whose objective is to understand the ultimate *physical* roots of life and biological intelligence, to give its contribution by trying and explaining the possibility of such ***anticipatory behavior*** as *mechanistically* arising from the *hard-to-determine* nanoscale quantum and classical interactions within cells, their genomes, and among subcellular structures. The recent findings mentioned add to the very cutting and subtle concept formulated some years ago by Lynn Margulis (1981) in one of the many attempts, ineffectual as yet, of theoretical biologists at characterizing life definitely, even though phenomenologically: *"Living matter is matter that chooses"*. The active role of living matter in evolution is a strong point in the famous Monod's essay (1970): the so-called *"environmental pressure"* too often is misleadingly thought of as a kind of force that *actively* shapes living matter pushing it to evolve; on the contrary, it is the living being that *"chooses"* (sic) e.g. to get out of waters and to conquer the earthly environment through adaptation. Living matter would thus *decide* its becoming. Anyway, life, its origin and evolution, and biological intelligence as well, keep at present their character of vague expressions and fundamentally elusive notions from the physical standpoint. Tackling the problem of life on physical grounds means tackling jointly the problem of biological intelligence: in both cases, the nanobiologist's hope to give these concepts a physical meaning would mainly rely on a reconceptualization of the notion of information and of the exploitability of formal tools — *logic*, mainly the set-theoretic logic, and *platonistic* (Gödelian) *mathematics* as opposed to the *constructivist* (Aristotelian) *conception* of mathematics (Bishop, 1967), boiled down into the *"infinitum actu non datur"* (no infinite in act) Stagirites' concept (Bekker, 1961) — in investigating the physics of *origin, evolution* and *self-reproduction* of living matter. A new, *evolutionary approach* to logic would mainly rely on constructive mathematics for an understanding of how matter *does choose*: i.e., of those deeply rooted properties by which matter passed *spontaneously* from the less than 200 bits of the primeval Earth's environmental information (3.5 - 4 x 10^9 years ago) to the information content of about 10^8 bits of the human genome, a succession of steps from what we *call "chemical information"* up to *"biological information"*, i.e. from molecules to mind.

My attitude in tackling the problems coming from the new experimental results stems from the warnings given by the famous mathematician Stan Ulam of the Los Alamos National Laboratory to a biophysicist and to a scientist devoted to studies in artificial intelligence: *"Do not ask what physics can do for biology; ask what biology can do for physics"* (reported by Frauenfelder, 1987) and *"Your Cartesian idea of a device in the brain that does the registering is based on the misleading analogy between vision and photography. Cameras always register objects, but human perception is always the perception of **functional roles**. The two processes could not be more different. ... When you perceive intelligently, ..., you always perceive a **function**, never an object in the set-theoretic or physical sense"* (reported by Rota, 1986). Accordingly, on this occasion of doing physics by putting on biological glasses, I am trying and doing physics ***from*** biology, not ***for*** biology. And, with p and q as the momenta and positions in phase space as usual, recalling that *"physics is where the action is,* or *minding your p's and q's"* (Hilborn, 1994) the approach to interpret the anticipatory behavior will mainly rely on the interplay of quantum and classical chaos at the mesoscopic level. This way might lead down to the roots of the living, and perhaps to reconsider and deepen the suggestive hypothesis put forward and deeply discussed by Michael Conrad (1997) that the underlying physics of the Universe could conceivably possess features that capture the essence of life processes. Such hypothesis would explain why in spite of more than fifty years of efforts to understand the origin of life, of a huge amount of geological, geochemical and chemical data collected about primeval Earth, and of much biochemical and molecular biological insight attained since the time of the earliest experiments carried out by Stanley Miller and Harold Urey in 1952 (Fox and Dose, 1972), we are not able to explain how life began and to synthesize even the simplest cell or virus. Briefly summarizing that hypothesis, as to the possibility of fabrication of living systems the question is: would a collection of particles, brought together *deliberately* and whose positions and momenta (the q's and p's) correspond exactly to those of particles in a cell, *result in a living cell*? According to Conrad's *"fluctuon"* theory (Conrad, 1997) that tries by this way to overcome the gap between Quantum Physics (a linear theory) and General Relativity (a nonlinear theory) what might be lacking would be the consistency of quantum vacuum density with the particles distribution. The organization should be consistent with the vacuum structure, otherwise *"it would be ripped apart by the inexorable evolution to a self-consistent state"* (Conrad, 1997). Should this be the case for the stage of *preparation* of our particle ensemble, we would perhaps be hopeless in trying and engineering the synthesis of living matter, even through an advanced nanotechnology and nanobiology. Anyway, Conrad's attempts show that doing physics from biology might even result in a deeper understanding of fundamental physics.

2 Biological Evolution as a Problem of Dynamics in Phase Space

To use our p's and q's correctly both in the quantum and the classical case to try and describe biological evolution in phase space, the introduction of some concepts as well as some rethinking and reshaping of a number of current notions is in order.

2.1 What Does It Mean "Computing"?

Biophysical numbers arising in calculations concerning an evolutionary problem can be much larger than astronomical and cosmological numbers. This, and other observations that can be drawn from *nanoscale physics* and from *algorithmic information theory* as applied to the environmental time series impinging on an observing system — i.e., a protobiota, an eukaryotic cell and even human brain — set a number of problems as to the formulation of ***realistic*** theories about the outside world: its very laws and the nature of its relationships with a living system.

2.1.1 Bremermann's Limit of Information Processing Rate

Let us consider the number of phase space configurations that a DNA/RNA made up of 10^9 nucleotides could explore in its evolution by just random walk mutations during the whole Earth's lifetime mentioned above. The estimated replication rate of nucleic acids is 1 s^{-1}, so that the configurations would amount to about 10^{60}. Indeed, this is just a very small fraction of the total number T of all the possible arrangements:

$$T = 4^{10^{9}} = \text{about } 10^{6\,x\,10^{8}} \qquad (1)$$

The expression of T belongs to the kind of computations known in mathematical complexity theory as not soluble in polynomial time or as "intractable", meaning that they could be solved in theory but, in practice, a computation time equal to the age of the Universe would not suffice even to write out the result. From the quantum theory of matter it can be stated (Bremermann, 1962) that no data processing system, whether artificial or living, can process serially more than $2\,x\,10^{47}$ bits s^{-1} g^{-1}. Nothing made up of atoms and electrons can go beyond that rate. Further refinements of the theory (Deutsch, 1982) based on quantum states degeneracy and concerning states of matter not involved in practical or living systems have slightly increased this rate. Thus, even invoking parallel computation with tons of computing system and centuries of time, the estimated total amount processed would be about 10^{80} bits, and T would be a number enormously larger than the value attainable according to Bremermann's bound on information processing rate. Taking the whole Universe as a computer working at such limiting rate, the bits processed up to now would be

$$2\,x\,2^{47}\,x\,(\text{age of the Universe})\,x\,(\text{mass of the Universe}) = 2\,x\,2^{47}\,x\,10^{17}\,\text{s}\,x\,10^{57}\,\text{g} =$$
$$= (\text{just about})\ 10^{122}\ \text{bits}$$

Let us consider two more cases of evolutionary interest: the estimated number of genes in a human somatic cell is between 10^4 and $4\,x\,10^4$; each gene corresponds to about 10^5 nucleotide bridges, which can be of four kinds, so that each one corresponds to 2 bits. Thus for the human genome we have

$$\text{total number of bits} = 4\,x\,10^4\,x\,10^5\,x\,2 = 8\,x\,10^9 = \text{about } 10^{10}\ \text{bits} \qquad (2)$$

If $F(x_1, ..., x_n)$ with x's taking the values = and 1, is a function whose numerical value measures the genotype fitness, F can take up to $N = 2^n$ values:

1) taking into account all nucleotide bridges, it would be $N = 2^{10^{10}}$ values

2) taking into account genes only, it would be $N = 2^{10,000}$ = about $10^{3,000}$

and in both cases non-polynomial time computations are obtained.

Again, working on some estimates concerning the number of neurons in human brain and their state change rate and including the cytoskeleton, the brain computing power would be

$$\text{(number of neurons)}\ x\ \text{(neuron state change rate)}\ x\ \text{(number of microtubules)}\ x\ \text{(microtubules state change rate)} = (40 \text{ x } 10^{9})\ x\ (10^{2}\ s^{-1})\ x\ (10^{14})\ x\ (10^{9}\ s^{-1}) =$$

$$= 40\ x\ 10^{34} \text{ bits } s^{-1} \qquad (3)$$

This power is much lower than Bremermann's limit, the latter looking like restricting inanimate as well as living matter, knowledge and science. Should our theories be so structured that this limit would become an integral part of them?

2.1.2 *To Land or Not to Land*: A Lesson in Information Processing Comes from Flight Controllers

In spite of Bremermann's limit, as a matter of fact inanimate matter evolved, *by means of nanoscale physical processes*, up to the human brain, and the latter can be shown to be able to compute well beyond that limit. Flight controllers offer a very lucid proof of that. A plausible assumption for a flight control tower can consider 20 people who control the arrival of say 1,000 planes per day. *To land or not to land*: that is their problem. Flight controllers and their devices *designed and built by humans* make up a system, whose input is 1,000 requests per day, the output being the answers "yes" or "not", i.e., an amount of $2^{1,000}$ binary inputs with a total number of possible answers or, in Planck's terminology, complexions of

$$2^{2^{1,000}} \qquad (4)$$

which corresponds to a Shannon information of

$$\log_2(2^{2^{1,000}}) = 2^{1,000} = 10^{131} \text{ bits} \qquad (5)$$

i.e. 179 orders of magnitude larger than that processed by the whole Universe as a *perfect*, though serial computer. It is true that computers have been used in obtaining the output as above, but they have acted just as formal automatic, preprogrammed systems which have helped the flight controllers realize a *machine mediated* ***human computation.*** Two moments are to be distinguished to build a ***physical***, be it quantum or classical, notion or, less generally, a ***thermodynamic-level*** notion of "computation": *programming*, prepared by a *human being* from the computer outside and introduced into the same through setting forth a sequence of instructions coded in some symbols which will be accepted *passively* by the machine, *whose software according to the current paradigm in computer science is hardware-independent*, and *execution*. As a whole, the information processing in the flight controllers' case has been *actually* carried out as biological information processing. The symbols introduced in the computer and their logical interplay during operation *represent* something to the operator that has nothing to do with their physical implementation on the computer hardware, to which they are just values of voltages at some logic gates that set the hardware's state in its own phase space. The set of *logical states* written on the computer hardware does not correspond to microscopically accessible states of the hardware as a *physical system*, whose state is identifiable just by the (macroscopic) free energy of the logical gates themselves (cf. **Section 3** for the case of a nanoscale computer).

The two features mentioned just above —*passive acceptance*, *introduction from the outside* — have a deep logic and physical (thermodynamical, just in case of *local equilibrium*) meaning as regards *self-organization, cognition* and the *quantum/classical dynamics* of a set of interconnected ***evolutionary*** hierarchical subsystems like that making up a living system, *as processes pictured in the form of computations in phase space* as will appear partly from what follows immediately and partly from **Section 3**, whose results would also concern any perspective, *actually evolutionary* artificial automaton. This is a much sought after goal at present (Higuchi, Iwata and Liu, 1996) though through macroscopic physics. As shown (Santoli, 2000) any embodiment of that idea would necessarily involve nanoscale-structured components and devices as the ultimate macroscopic system: action, i.e. *signal processing plus mechanical motion*, should arise on the molecular level and move therefrom to reach up to the automaton effectors. And that is not out of merely structural reasons, but out of the basicly necessary *structure - function* evolutionary solidarity which is the very root of such computing process that arises *within thermal noise* and from the inseparably intertwined chain ***syntax*** $\Leftrightarrow$ ***semantics*** $\Leftrightarrow$ ***pragmatics*** *shaped* through evolutionary self-organization and cognition and transmitted by self-reproduction, as shown in **Section 3**.

2.1.3 Looking for the Bases of *Ultimate Computing*

2.1.3.1 Simulation, Anticipatory Behavior and the Sequential Machine

Information processing **(IP)** in the form of *simulation through compression* of the stimuli impinging on a living system from the outside can be invoked to explain its **IP** capabilities. *Compression* is to be understood as computation and transmission throughout the hierarchical levels of the system not by a *one-to-one mapping* as occurs in telecomunication, in which Shannonian information applies to a flow **f** of p's and q's in phase space going on according to Liouville's theorem

$$\nabla \bullet \mathbf{f} = 0 \tag{6}$$

i.e. an *isentropic* flow of an *incompressible* fluid that changes shape but keeps constant in volume: a "message" to be reproduced at the receiving end exactly as it was at the transmission end. Again in terms of p's and q's, what is compressed is the number of degrees of freedom, the result being an *"abstraction"* as *"formation of collective properties"*, which corresponds to a non-isentropic flow: $\nabla \bullet \mathbf{f} < 0$, entropy being rejected into the environment. Statistical physics equations describing systems at the *hydrodynamic level* are just compressions exerted by our mind of an enormous number of degrees of freedom into the much smaller number corresponding to the description at that level. Navier - Stokes's equation of hydrodynamics is a concrete example. This view embodies physically the notion of intelligence formulated by Steinbuch (1963) ("in an *internal model* of the *external world* the thinking being puts to test the influence of the external world like in an experiment and then reacts in an optimal way") as well as Rosen's notion of *"anticipatory system"* (Rosen, 1985) as a system that contains a predictive model of itself and/or of its environment that allows it to compute its present state as a function of the model's predictions belonging to a later time. Such capability to anticipate, i.e. *"to realise beforehand"* (Rosen, 1985), that has been embodied in the mathematics of *"incursion"* and *"hyperincursion"* (Dubois, 1997) is taken by Rosen to be the basic feature that differentiates living systems from inanimate matter. The notion of modeling the environment (and any other system in the same, possibly even as a similar *"opponent"* system) through formation of collective properties at a given level of description embraces the very elementary biota, as well as any upper rank biosystems like the human brain, and any interlevel interactions in the hierarchical chain making up the biosystem. Finality of anticipatory systems shows implicitly embedded in any mathematical models of laws of Nature (Dubois, 2000) and is related to Maupertuis's least action principle in Newtonian mechanics and quantum relativistic physics. This is suggestive of further reflection, mainly in connection with the problems outlined in Subsection 2.1.3.2 and their discussion in **Section 3**.

Let us see now what would happen in trying and simulating through a deterministic finite state logical machine the behavior of a "compressive machine", i.e., by assuming the same to behave as a fully causal system. If N observations are made, there are 2^N possible sequences of the same. Let us suppose for simplicity that all sequences are equiprobable, with probability 2^{-N} and let S designate the number of states for an automaton modeling the system. The maximum number M of models possibly obtained by an *optimal modeler* so able as to always choose machines featuring the minimal number of states, will be

$$M = S\,x\,2^S > 2^N \tag{7}$$

this number including also models with less than S states. If

$$M(R) = \int_1^R (dM(R)/dR)dR = \textit{probability of models with states from } R{=}1 \textit{ to } R \qquad (8);$$

for R as a discrete variable, and with $\sum$ as the sum from R = 1 to R = S -1,

$$M(R) = [1/(S - 1)]\,x\,\Sigma\,(\Delta M(R)/\Delta R)R \tag{9}$$

$$(\Delta M(R)/\Delta R) = 2^R + R\,x\,2^{R-1} = R\,x\,2^R - (R - 1)2^{R-1} \tag{10}$$

$$M(R) > [1/(S - 1)]\,x\,\Sigma R\,x\,[R\,x\,2^R - (R - 1)2^{R-1}] \tag{11}$$

and, with μ_S as the average number of state S, $\mu_S\,x\,2^S > M(R)$, so that

$$\mu_S\,x\,2^S > (S - 1)^{-1}\,x\,\Sigma R\,x\,[R\,x\,2^R - (R - 1)2^{R-1}] \tag{12}$$

and

$$\mu_S > \{[(S - 1)\,x\,2^S]^{-1}\}x\,(1/2)\,\Sigma(R^2\,x\,2^R + R\,x\,2^R) \tag{13a}$$

or

$$\mu_S > S - 2 + 2/(S - 1) - 2/[(S - 1)\,x\,2^{S-1}] > S - 2 \tag{13b}$$

and from (6) we have $S + \log_2 S > N$, so that as $S < N$, it is $S > N - \log_2 N$, and

$$\mu_S > S - 2 > N - \log_2 N \text{ so that}$$

(*expected number of states of the model/number of observations*)$=1- [(\log_2 N+2)/N]$ (14)

which goes to unity as $N \rightarrow \infty$ and means that *going on simulating a stochastic behavior by a deterministic finite state automaton leads to an increasingly complex description of the observed system.* Even the smartest parallel logical computer will never be smarter than a vinegar fly, and the earliest biota would have been hopeless in attempting evolution through a *one-to-one mapping* machinery. But there are some problems with an *extralogical* compressive machine also, as shown in the following.

2.1.3.2 The Compressive Machine – *How Far Can the Environment Be Compressed for Simulation?*

Let us apply Chaitin's notion of algorithmic complexity (Chaitin, 1987) to the time series impinging from the environment (the *observed system*) on any living system (the *observing system*), be it a cell or the human perception system. Picturing such external stimuli as binary strings of length N, the number Σ of the a priori equiprobable sequences compressible to any number K of bits and the *percentage* α of compressible sequences would respectively be

$$\Sigma = 2^1 + 2^2 + \ldots + 2^{N-K-1} = 2^{N-K} - 2 \tag{15}$$

$$\alpha = \Sigma / 2^N = \text{about } 2^{-K} \tag{16}$$

α is a fraction that decreases very rapidly with K; e.g. for $K = 10$, just one series out of one thousand is compressed up to ten bits. Stated otherwise, the number of series (the impinging stimuli) that can give rise to an algorithm of length $N - K$ that, when fed into a finite state machine, would yield the full series of length N is extremely low. This means that *the observing compressive machine (the cell or the human mind as the "anticipatory systems") can simulate an extremely small number of natural phenomena, independent of the mechanistic tools* employed, e.g. those investigated in **Section 3**. ***Most signals keep undetected***. It will be shown (Section **3.2**) that while this sets two basic problems, it also stresses a fascinating fundamental aspect of the living. A way out of such drawbacks will be supplied just by those very tools.

2.1.3.3 Physical Reality and Its Levels of Description; or *Why Did Nanophysics Come Later Than Macro- and Microphysics?*

Any physical system is made up of three hierarchical levels: the particle level, that is characterized by the strong nuclear force F_1; the atomic level, characterized by strong electromagnetic interactions F_2; and the molecular level, where London-van der Waals weak interactions F_3 hold the *dominant* sway. If we reconsider our equations describing a system, we can realize that we always assume an *"almost decomposability criterion"*, based on the fact that *relaxation times* characterizing three such worlds are practically inversely proportional to the *interaction strengths*; i.e., as $F_2 \approx 10^{-6} F_1$; $F_3 \approx R^{-5} F_2$ with R as distance between interacting atoms, one full *"cycle"* at level 2 means about 10^6 cycles at level 1 and about 10^{-10} - 10^{-4} cycles on level three: dynamical processes go on increasingly slower from level 1 to level 3. This means e.g. that atoms can be studied without taking into account (i.e., separately from) what happens with energetic interactions at the nucleon level, which are describable as a *boundary condition* (an average value) and what happens at the macroscopic level, that can be taken as a *constant*.

As to the coupling on the nanoscale level (i.e. the molecular level) of degrees of freedom in living systems, that gives rise to macroscopic behavior, this decomposability principle cannot be assumed, and it will be much harder to describe the system: inter- and intralevel hierarchical dynamics go on as a functionally *"compartmentalized"* dynamical system *closely connected* through feedforward - feedback loops, working on comparable values of *relaxation times*. This will be perhaps the main source of difficulty e.g. in trying and solving the problem of connection between the level of language (an upper rank code) and the level of its hardware or of a lower-rank cognitive software: stated otherwise, in finding out how a combinatorial *symbolic dynamics* mediated by strings of interdependent symbols (the language) emerges from a dynamics mediated by energetic interactions (the hardware, i.e., the cerebral tissue governed by classical electromagnetism and by quantum mechanics). And this is why nanoscale physics came well after macro- and microphysics: we as the observing system work and transform on the same time scales (relaxation times) as the observed system. Moreover, on the mesoscopic level there is a rich and hard-to-identify interplay between the classical and the quantum world which is of the essence to understand evolutionary computation and anticipatory properties.

3 Envisageable Classical/Quantum Nanoscale Evolutionary Computing: Identifying Tools for Anticipatory Behavior

Subcellular structures span sizes in the range from the lower to the upper end of the mesoscopic level, i.e. from a few to some hundred nanometres, so that classical and quantum physics coexist. *Action* and *meaning* arise on that level, where *molecular* mechanical motions and electronic degrees of freedom couple into a *structure - function* solidarity and move up to the macroscopic level: mechanical deformations and other kinds of motion just stem from bending of polymer chains, spiralisations, formation of ternary or quaternary structures, motion of ribosomes and enzymes, deformation of membranes, mitochondries etc., while electrons and e.m. waves transfer through atoms, macromolecules, excited states. *Coded interactions*, or interactions depending on *frequency and/or space arrangements* as distinguished from just *energy strength* interactions or *parametric interactions* stem from such mechanical, electronic and field dynamics and form an organised system (as opposed to an unstructured ideal gas) capable of responding to other coded interactions and even of *controlling parametric* *processes* up to isolating the system from the environment (*parametric isolation*) to a certain extent: otherwise, e.g. in case of strong coupling, the environment as a heat bath would deadly work as an immediate *energy* and *information sink*. This view extends the notion of code and will allow such complex dynamics, that contributes to anticipatory behavior, to be interpreted. The simplest example of this view is Planck's equation

$$E = h\nu \tag{17}$$

(parametric part) = (coded part)

The environment is of the essence in this whole process which, involving in any case *mechanical nonequilibrium*, is not amenable to treatments employing thermodynamic entropy that is a *state* (i.e. equilibrium) function. And in nanoscale studies, *even in case of equilibrium*, the way a heat bath is coupled to the system must be taken into account as such way can affect the system's *detailed dynamics* in phase space strongly (cf. **3.1**). Macroscopic reaction-diffusion systems as occurring in cells under conditions of no mechanical actions *may* be described through thermodynamic entropy in case of local equilibrium conditions (Prigogine and Nicolis, 1981) but here we are trying and setting forth physical criteria for *mesoscopic systems of molecular nature* (biomacromolecular, super- and supramolecular structures) and more particularly for *electron and charge transfer processes accompanying (mechanical) conformational changes*. Information as a process arising from convolution of internal dynamics of the living system with time series from the environment cannot be described as negentropy, and the concept of "information flow" as well as its feature of incompressible-fluid flow, variable just in shape, must be left to telecommunication engineering.

Explaining the **IP** compressive biological machinery implies the changing of many ideas of ours as to the notion of information and its relationships to entropy. The following is a detailed deepening of the more general concepts formulated previously (Santoli, 1999) according to which *Shannonian information*, which is just syntactic, *one-to-one logical mapping information*, taken uncritically as *negentropy*, and *set theoretic logic* are real stumbling blocks for a physical theory of life and intelligent behavior, e.g. for explaining the experimentally observed anticipatory cell behavior and for a physical understanding of the vague, *anthropomorphism - minded* notion of *"intelligence"*. Cells, complex tissues and even the earliest biota show to be not only compressive machines processing *environmental* and *intra-hierarchical* information *extralogically* and *non-algorithmically*, but they are also its own interpreters in the simulation of their environment and in anticipatory behavior, and the only recognizers of that information as a ***Syntax* ⇔ *Semantics* ⇔ *Pragmatics*** inseparable wholeness (*individuality*) resulting from the *coupling of electronic and mechanical degrees of freedom* in *macrobiomolecules*: in particular, in the DNA component moieties characterized by highly nonlinear interactions, e.g. in movements of large pieces of DNA like those of its transposable elements (the observed *stretching* of mobile DNA in maize) (Caporale, 1999) or in protein conformational changes, like *Amoeba proteus* ambulatory and phagocytosis *motilities* briefly outlined below, or in protein motions clearly not of thermal origin but linked to a *functional meaning*. Coupling of nuclear and electronic motions, and resonance electroconformational coupling of membrane receptors and enzymes realize respectively the hierarchical *intramolecular* and the *intracellular*, *organ-to-organ*, and even *organism-to-organism* communication, this last occurring in humans at the brain level through the upper-rank *coded interactions* we call *"language"*, whose *"machine-level language"* would sound to the level of our consciousness just like mere *noise* indeed, not signals, in a *transmembrane electric field.*

In higher animals the functions of perception, judging and acting are attributed to a nervous system and to the presence of a brain. But e.g. the unicellular organism *Amoeba proteus* (Kobatake, Ueda and Matsumoto, 1989) although primitive, has sensors to detect the nature, position and size of the prey organism; in its protoplasm, there are very complex chemical networks which make possible the **IP** that leads ultimately to an organized and integrated cell behavior: when a ciliate comes close to it, the amoeba senses the prey, and unless it senses an alarm signal, it tries to catch the prey by extending its pseudopodia, finally incorporating the prey and digesting it. *Phase waves*, responding to external stimuli, in a population of coupled chemical oscillators as opposed to electrical processes are the bases of the *Amoeba*'s **IP** system and of its tactic behavior, the chemical oscillators generating *new patterns of behavior* in said population on receiving outside signals from receptors. This should dispel what might be dubbed the *"microsize-and-central nervous system"* syndrome fallacy which would usually attribute sensing, judgement and decision to higher animals only.

Further to the results of Section 2.1.3.2, an investigation of the envisageable quantum/classical physics embodying such evolutionary behavior will show that not just the claimed realizability of the "dream of *downloading* human consciousness" (Hameroff, 1989), but even that of downloading *Drosophila melanogaster*'s (the vinegar fly) intelligence would fade into the collection of a huge, congealed set of *abstract (meaningless) information*. Surely enough, as dull, colorless and unevocative a reading as a telephone directory.

3.1 Syntax ⇔ Semantics ⇔ Pragmatics Unity from the Coupling of Nanoscale Electronic and Mechanical Degrees of Freedom

We can define as a *purely mechanical phenomenon* one that can be described in phase space just in terms of atomic (i.e. nuclear) positions and motions, without reference to electronic properties other than their effect on the *potential energy surface* (**PES**). **IP** in biological systems is realized by motion in multiple well potentials of such **PES**. Encoding, motion and possibly erasure of information *on the nanoscale* correspond to molecular events — translations, torsions, internal vibrations — on **PES**s accompanied by a dynamics strongly depending on the environment, usually pictured as a quantum or classical heat bath coupled at various extents with the system. *Compression* of potential wells, *transitions* among time-dependent wells, *expansion*, and *symmetrical* and *asymmetrical well merging* can be described by well known thermodynamic state functions (Gibbs free energy, entropy) just if *relaxation to equilibrium* occurs at a rate much faster than the rate of such "reactive" occurrences, at least as a *local equilibrium* condition in the **PES** "hilly" landscape. Dissipation in all such mechanisms except in well merging is *velocity dependent*, meaning that at slow rate the process might be isentropic (in the language of what follows, it might consist in a Hamiltonian, *integrable* or *nonintegrable*, flow): *"well merging"* means erasure of information and is dissipative even in slow processes (this is the very ultimate reason that exorcises Maxwell's Demon, the earliest invented nanomechanical device: he cannot have an infinite-size memory to avoid the need for erasures, and the 2nd Principle is on safe *in the long term*). Thus, equilibrium *well merging* can be described as an increase in entropy and a loss of *physical information*, but *on the nanoscale this does not imply that information is always a monotonic function of entropy*, mainly in biomacromolecular events, in which nonequilibrium transitions may occur in time intervals of 20 fs, i.e. ***non-ergodically***.

3.1.1 Sketching a Theory of Quantum/Classical Information Processes in Biomesoscopic Structures

Ordinarily, descriptions of kinetics of charge transfer processes, e.g. electron transfer in molecules (Kramers, 1940; Naeh, Klosek, Matkowsky and Schuss, 1990) rely on Langevin-type equations for a Brownian particle in the **PES** landscape, coupled with a classical heat bath, while recent attempts (Pohlmann and Tributsch, 1992) invoke semiclassical kinetic models in stimulated cooperative phenomena for efficient energy conversion and catalysis. But indeed, on the mesoscopic level of biomacro-, super- and supramolecular structures both the interplay of chaos and quantum coherence, and the dominance of either one can supply a host of coded interactions among mechanical and electronic degrees of freedom, mainly because we are dealing with *open quantum systems* (dissipation is essential for life) and/or with a *driven* nonlinear quantum or classical system. The latter condition comes from the intimate hierarchical structure of the living, and from the fact that even its ultimate boundary — the environment — acts not as a *passive* heat bath, but as an *active* reservoir. More concretely, e.g. proteins of a cell membrane are adapt to receive and decode even very weak electromagnetic signals, so oscillations of protein conformers can be induced, and if a ligand is present its binding energy can be spent to drive an endergonic reaction. And a membrane-embedded enzyme, coupled to a free energy source, can catalyze a reaction away from its equilibrium position. Anyway, even in case of quite a close coupling with a heat bath, the equilibration process of nuclear and electronic modal excitations will occur via anharmonic interactions, due to the nonequilibrium nanoscale event, together with interaction with the heat bath. As discussed in the following (*equation 24*) the fast nuclear (i.e. mechanical) motion will embody a *detailed* (non-statistical) determining physical event that shows how it can be misleading to suppose that information is always a monotonic function of entropy.

Accordingly, the following archetypal case of a double-well potential system with time-dependent Hamiltonian (the driving action) and quartic double well potential can illustrate the concept of *active* (driving) reservoir, as it features a *classical chaotic dynamics* and *quantum coherent tunneling*:

$$H(q,p;t) = p^2/2m + V_0(q) + qS\sin(\omega t + \varphi) \tag{18}$$

$$V_0(q) = - m\omega_0^2\, q^2/4 + m^2\omega_0^4\, q^4/64E_B \tag{19}$$

with m = mass of the particle, ω_0 =classical frequency at the bottom of each well, E_B = barrier height, S and ω as the amplitude and angular frequency of the *driving force*. While the undriven double well Hamiltonian is fully integrable (no chaos), the harmonically driven quartic double well increases the dimension of space space to three and the smooth separatrix between the undriven wells becomes a highly complex chaotic layer in classical phase space acting as a dynamical barrier of complicated effects as to the motion between the two wells. Quantum mechanically, the transition from chaotic to regular states is continuous, i.e. there are states of an intermediate character, with an interplay between *chaotic diffusion* and *coherent tunneling*, that are under the *control of the amplitude S of the driving action*. We can speak of chaos-assisted tunneling. Through S the chaotic layer can be spread at the expense of the regular region, so that some tori are destroyed, and the initially small splittings d

$$d \propto \exp(-S_t)2\pi/h \tag{20}$$

of the associated states gradually widen until reaching the mean level separation of states in the chaotic layer, where a level repulsion interaction prevails.

This rich molecular mesoscopic dynamical repertoire, that would supply a host of coded interactions, can also be found in the case of the long-chain informational molecules of nucleic acids (DNA, RNA) considered as *extended objects* (i.e., made up of a large number of identical or similar elements), where chaotic diffusion, wave packet spreading and Anderson localization, e.g. in the case of a perturbation introducing disorder, add to the general features of quantum chaos. A case of interest for the long-chain polymer molecular world as an extended object is that of a planar rotor driven by sharp torque pulses whose strength depends in a nonlinear way on the angular position of the rotor. Indeed, as the Hamiltonian is

$$H(l,\theta;t) = l^2/2 + k\cos\theta\, \Sigma_{n=-\infty}^{n=+\infty}\, \delta(t - n\tau) \tag{21}$$

with $-\pi \leq \theta < \pi$ as the angle, and $l = 0, \pm1, \pm2, \ldots$ as the canonically conjugate angular momentum measured in units of $h/2\pi$, the classical phase space has the topology of a cylinder, so that the rotor represents an extended object *with respect to angular momentum* (not to its spatial coordinate θ). While the classical chaotic map shows a diffusive increase of the angular momentum and lasts forever, the quantum wavepacket merely fluctuates around a time-independent mean shape that decays exponentially in space from the site where it has been prepared (Casati and Ford, 1983).

Going now from (approximately) Hamiltonian flows, valid for *slow motion* through cols on the **PES,** to more realistic pictures contemplating dissipative motions, coherence effects like tunneling and localization degrade, while other important information processing chaotic elements come about (Santoli, 1995) like *strange attractors*, *fractal basin boundaries and their complex topologies*, *intermittency*. It is essential for understanding the **IP** and interlevel relationships in the hierarchical dynamical living system to observe that:

a) quantum coherence effects are suppressed by a heat bath if

$$t_{\mathrm{decoherence}} << t_{\mathrm{coherence}} \qquad (22)$$

b) the effect of a *noisy driving action* mimics the effect of a heat bath just on a short time scale, being non equivalent to a heat bath on long time scales (Gisin and Percival, 1992)

c) counterintuitive though it may be, at equilibrium, *how* (e.g., through vibration of bonds, absorption or emission of thermal radiation, or impact of molecules etc.) *any system* is coupled to a heat bath can affect its *detailed* (i.e., nonstatistical) dynamics, like the smoothness or irregularity of its trajectory in phase space, the decay time for oscillations of unusual amplitude, etc., *but not the statistical distribution of dynamical quantities*; this is simply because the coupling does not alter the **PES** and hence the Boltzmann distribution. Under nonequilibrium conditions, in the case of anharmonic oscillators moving on the **PES** and *with dissipation*, their complex dynamics can result even in self-organization

d) in the mentioned case of dissipation depending on velocity, if dissipation is proportional to speed through a coefficient γ reflecting the fluctuation-dissipation theorem, a contraction of phase space in the p direction occurs that adds to a possible contraction by the chaotic flow but is not compensated by an expansion in other directions; the time scale

$$t_{\mathrm{relaxation}} = 1 \qquad (23)$$

can be larger than the other time scales and is the crossover to irreversible evolution.

An important result comes about and adds to the **IP** capabilities realizable through Hamiltonian flows: dissipation on the *mesoscopic level* in such macro- and supra-molecular systems, just as on the *bulk level* in chemical reaction kinetics (i.e. in *reaction - diffusion* processes) can result in self-organization; in this case, of multicharge (e.g. multielectron) transfer processes. Considering that the associated nuclear motion in a conformational change is so fast as to exclude the application of adiabatic Born-Oppenheimer's principle, and that the openness of the quantum system means the possibility of action of radiation from an *active* "environmental compartment" making part of the living itself or outside it (cf. the mentioned membrane actions) the complete general Hamiltonian would be

$$H = (T_q)_e+(T_q)_n+V(q_e,q_n) + \text{terms representing radiation field and its interaction with electrons} \qquad (24)$$

with the T'*s* as the electron and nucleus kinetic energies and V as the potential energy of the configuration. Solution of this general, model-independent equation would give the detailed dynamics of the coupling of multielectron transfer and nuclear mechanical degrees of freedom leading to a *conformational energy-* or *phononic energy-activated self-organized transition state*, embodying a structure - function wholeness, *the shape of the probability distribution inside the potential well(s) involved being very far from equilibrium.*

Mesoscopic classical/quantum chaos, and *quantum coherence* can account for so-called *"functionally important motions"* and their built-in evolutionary properties in proteins and nucleic acids of biological tissues, so dispelling the Cartesian mind-body dichotomy both on the macroscopic and the microscopic level. Much more might come about from a deeper understanding of the links between the two worlds, e.g. along the lines proposed below.

3.1.2 Further Physics *from* Subcellular Supramolecular Structures?

Let us extend the notion previously mentioned of *"extended object"*, defining it as a classically behaving object in a *quantum ordered state*, e.g., a manifestation of condensation of bosons associated with a quantum collective mode. This might orig-inate e.g. from a boson condensation that would make N in the quantum number hN carried by the bosons themselves so large that the ratio

$$(\textit{quantum fluctuations})/hN = h\Delta N/hN = \Delta N/N \qquad (25)$$

would become so small that the system behaves classically. This can occur in biomacromolecules and large supramolecular structures made up of repeated units (e.g. the cytoskeleton, the microtubules etc.) of subcellular *organelles*, in which highly nonlinear local (vibronic) and global (phononic) oscillations and conformational motions can interact and couple with charge transfer processes. Solitons, e.g., as localized wave solutions of a classical nonlinear equation have been theoretically shown possible in microtubules (Sataric, Zakula and Tuszynski, 1992) and other subcellular structures. But if just the displacements of molecules are treated as fields (phonons), the soliton and other classical localized manifestations can be described phenomenologically only; a full microscopic approach to describe them as extended objects and to set forth their relationships to fundamental physics would entail the quantization of the many interacting molecules through quantum field theory (**QFT**). Through the **QFT** techniques, a general, model-independent approach would start from a Lagrangian for the the system of one kind of molecules represented by a quantized, self-interacting field (Heisenberg field) $\psi(x)$

$$L[\psi(x)]=i\psi^{\dagger}(x)\partial\psi(x)/\partial t-(1/2M)\nabla\psi^{\dagger}(x)\bullet\nabla\psi(x)-(1/2)\int d^3y\, \psi^{\dagger}(x)\psi^{\dagger}(y)V(x-y)\psi(y)\psi(x) \qquad (26)$$

where V(x-y) is the potential between two molecules, M is the mass of a molecule and the time coordinates of x and y are taken to be equal. Extension can be made to a system with many kinds of molecule fields and with an electron field. The corresponding Heisenberg equation and the condition for the Lagrangian to satisfy the translational invariance for a repeated-module structure are respectively

$$i\psi(x)\partial\psi(x)/\partial t = -\,(1/2M)\nabla^2\psi\,(x) + \int d^3y\, \psi^{\dagger}(y)V(x-y)\psi(y)\psi(x) \qquad (27)$$

$$\int d^4x\, L[\psi(\mathbf{x}, t)]= \int d^4x\, L[\psi(\mathbf{x} + \alpha, t)] \qquad (28)$$

with α as an arbitrary vector. Similarly to the successful description of elementary particles and quark confinement in high-energy physics as extended objects with a variety of topological singularities, including solitons, the classically behaving macroscopic objects occurring in the *mesoscopic* dynamics of subcellular structures would be described within the framework of a quantum microscopic theory. And solitons, already theoretically discussed as possible occurrences in DNA chains (Schempp, 1993) might be the key to decode a lesson, if any, hidden in subcellular structures: i.e., the fact that they include *mono-*, *bi-* and *three-dimensional* structures as separate, interacting units. Would such 3D-structures be a confirmation of the existence of the much sought after 3D-solitons? Anyway, this approach would link biological micro- and mesophysical processes to the vacuum structure and its fluctuations.

3.2 Logic, the Paradigm of Measurement and Internal Models

Anticipatory behavior through formation of internal models has been very recently clearly identified experimentally (Imimazu et al., 2000) and the use of internal models for distinguishing gravity from linear acceleration, against Einstein's equivalence principle stating that all *linear* accelerometers must measure both linear acceleration and gravity, has been assessed (Merfeld et al., 1999). All that involves compression of an enormous number of degrees of freedom through the central nervous system and the muscular fibrils into the six-coordinate state space of our macroscopic consciousness, through the dissipative chaotic information processes dispelling the self-reference paradoxes of abstract logic (that corresponds, in the language of p's and q's, to unphysical isentropic flows in phase space; Turing's machine and its halting problem correspond physically to the flow of an ideal, purely Hamiltonian gas (Santoli, 1999, 1995), and making up the physical bases of evolutionary, *"structurally"* intelligent systems, of category formation (e.g., through basins of attraction and the fractal separatrices in dissipative chaotic flows, or the dynamic separatrices in coexisting chaotic/quantum flows), learning etc. (Santoli, 1999) together with quantum coherence processes as symmetries (Marcer, 1995) that would thus embody Aristotle's "formal cause" (Dubois, 1997). Both processes and their interplay on the mesoscopic level introduce semantics in the *paradigm of measurement* that implies openness of both the observed and the observing system, and put thus that paradigm in a more convincing relationship with constructivistic mathematics than with abstract logic and the Platonistic interpretation of mathematics, both of which might "exist" just in closed (i.e. isolated) systems, that would **always** be Hamiltonian: but in measurements, information on the system is conveyed by a "prepared probe" to a large number of degrees of freedom which are of "secondary" character with respect to what is to be measured, and are distributed over different relaxation times, so that the system's fundamental (quantum) dynamics is made nonunitary. No observation might be made by a closed system: *"existence"* as a scientific concept implies openness and dissipation. A *source* and a *sink* of *energy*, both far from thermodynamic equilibrium distribution (i.e., acting also as *information* source and sink) are required. *"Per se"* existence is to be left to investigations of philosophers.

It is worth thus elucidating the notions of *sink* and *source*: both terms mean essentially a change of *knowledge*, but by sink it is to be meant the exertion of a constraining action performed by the dynamic flow on *knowledge*, so that information is *revealed* if our question is a *prospective* one (a value constrained in a smaller interval corresponds to increase in information) or is *lost* (dissipated in the thermodynamic sense) in case of the *retrospective* question (a value within a larger interval is a decrease in information), and thus the sink is a source of negentropy if the flow is a thermo-dynamic one. By source it is to be meant a *creation action* exerted through expansion, i.e. an action that is a loss of information from the *prospective* standpoint (uncertainties in a starting range increase in an expanded interval) but is an information increase according to a *retrospective* standpoint (uncertainties decrease within a smaller interval). These are features of strange attractors that make them powerful mechanistic devices as suitable components of *smart*, *evolutionary* and *strategy-devising* systems (explaining the new biological findings, Caporale 1999) generating information or increase in entropy along some degrees of freedom and compressing flows so as to generate negentropy along other directions. *On the average*, the flow increases entropy, because at least on the macroscopic level any *new knowledge* is accompanied by production of entropy. Let us calculate now the time t_f for the attractor to become dis-connected from the initial conditions so that *it would start generating new information* as a result of its own flow evolving in phase space, instead of revealing information just through removal of uncertainties in the initial conditions. The following symbols will be used:

$<I>$ = information change as change of knowledge per iteration of an orbit in phase space
$\lambda(a)$ = Lyapunov exponent for the value a of a control parameter
$P(x)$ = asymptotic probability distribution of an orbit at the same value of a
$F(x)$ = a nonlinear difference equation
$P_1(x)$ = initial probability density (i.e. $P_n(x)$ = values of $P_1(x)$ on successive iterations

So,

t_f = [entropy as a priori uncertainty about the initial point according to

$$P_1(x)]/[\text{information production rate as bits s}^{-1}] \equiv \tag{29}$$

$$S/<dI/dt> = \int P_I(x) \log_2[P_1(x)/P(x)]dx \,/\, \int[P(x)/t(x)] \log_2[\,|dF(x)/dx|\,] \tag{30}$$

because

$$<I> \equiv \lambda(a) = \int P(x) \log_2 |[dF(x, a)/dx]| \, dx \tag{31}$$

Moreover,

$$I = \log_2 |dF(x, a)/dx| \text{ bits per iteration} \tag{32}$$

According to the mesoscopic interpretation developed above concerning the strategic anticipatory behavior observed in addition to Darwinian evolutionary mechanisms (Caporale, 1999), it is to be observed that the *charge-transfer* processes discussed above involving both electronic and mechanical (nuclear) degrees of freedom as the bases of the ***syntactic* ⇔ *semantic* ⇔ *pragmatic*** behavior, being processes occurring throughout the nanoscale cellular *"circuitry"* would surely violate the so-called *central paradigm* of theoretical computer science consisting in the independence of computer conceptions from their realization. Problems arise in connection with the notion of *"programmable matter"*. Indeed, in computation systems we have to distinguish the dynamics of the computation process from the basic physics involved. The basic, or *"low-level"* computation dynamics of cell circuitry would be based on, and strongly affected by, a *"low-level"* physics working on London – van der Waals forces of the form F ~ $(distance)^{-7}$ resulting from the interactions between *instan-taneous dipole moments*, i.e. between mesoscopic nonlinear coupled oscillators whose eigenfrequencies would depend also on the degree of coupling: i.e., the coupling constants of a computing model could not be chosen at will. Such *"compressive"* molecular computers inside a cell, that make it *anticipatory* and *strategic*, would be extremely efficient as to the *"special purposes"* of cells themselves. They would work as a kind of *"intuitive machines"* for the development of *their own* self-organization and kind of cognition, thus creating from their own existence different worlds.

But two problems arise for such machines from the result in Section 2.1.3.2, i.e., from the extremely large number of externally impinging time series that keep uncompressed (undetected, or just *random*) by any evolutionary system:

1) why has the system basins of attraction, i.e., categories of its software, that correspond to some of those independent outside stimuli? 2) in the case of human brain, why such software, if coming from a genuinely random evolutionary process, can simulate the very laws of Nature that would have just triggered its formation?

Three observations can counteract these conundrums and lead to the conlusion:

1) the facts that evolutionary systems are autopoietic as portions of their environment of origination, that they keep physically connected to their environment, even on the microscopic quantum level, and that their energetic/symbolic processes come from convolution with environmental stimuli and keep memory, both on the classical and the quantum level, of the environment actions (on the nanoscale the p's and q's of the system keep memory for some time even of a passive thermal bath); their physics and logic - a kind of dynamic construct - are deeply different from von Neumann's self-reproducing machines, that escape Richard self-reference paradox because their reproduction program is supplied to them from the outside (it is not autopoietic; they are not ***structurally*** *intelligent systems) (Santoli, 1995);*

2) much more than developing information through convolution with external stimuli, the evolutionary system through its classical/quantum chaos mathematical tools generates information as an emergent property from its own inside in its anticipatory activity so as to become independent of initial conditions: it becomes self-organized and cognitive, providing for its own internal descriptions and control through creation of new symbolic activities (the simulation, or anticipatory behavior). Moreover, through Berry's geometric phase notion (Shapere and Wilczek, 1989) in Quantum Physics it is shown that the system history record involves regions not visited by the system during its evolution;

3) the results of compression are "scientific laws", i.e., images of the "laws of Nature", and are built up by the same observer's activity. Thus, an elementary particle would represent a ***compressed description*** *of a number of phenomena that are the very bases which gave rise through their interactions to evolution up to the same mind that now describes its existence. Within abstract logic, the elementary particle notion would be an absolutely unacceptable concept indeed, due to Gödel's incompleteness theorem, as this scientific concept would represent the lowest (and not allowable!) level in the hierarchy of symbolic levels making up the scientific laws.*

4 Conclusion

The theoretical framework devised above can supply a physical interpretation of the whole chain of the intra-connected levels, from the micro- to the macroscopic levels, of the *biological evolutionary hierarchy* of the *symbolic/energetic dynamics* rooted in the *mesoscopic structure - function solidarity* of the living being.

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