1° Congresso Brasileiro de Redes Neurais

Escola Federal de Engenharia de Itajubá
Itajubá, 24 a 27 de outubro de 1994

Defining Cognition: Adaption by the Unstable Search for Coherent Conservation

Sérgio U. Dani[1,2] and
Gerhard F. Walter[2]

Abstract

Knowledge in the cognitive sciences is becoming more and more holistic, as opposed to fragmentary, in order to be real. An encompassing definition of cognition is then necessary. Evidence is reviewed here which allows to the conclusion that cognition stands for an adaptive ability to environmental changes, operating through non-linear search for coherent conservation of complex organismal features.

Cognitive science has witnessed a great advancement which has much to do with its multidisciplinary character. As a new branch of science, however, it still deserves the aims of classification. More specifically, a generally accepted lexicon is desirable in order to avoid misconceptions or misunderstandings, to enable easy information exchange and also as a guide to address experimental approaches.

For the sake of achieving these aims, it is worthwhile to make use of different tools from distinct sciences - including those that are usually maintained apart from each other. Chagas (1990) pointed out that a particular science can only be regarded as autonomous just in those respects in which less progress has been achieved. The reason for that, according to Chagas' view, has to do with the realization that knowledge is becoming more and more holistic, as opposed to fragmentary, in order to be real.

To date, some definitions of cognition or cognitive systems, such as "a device to organize knowledge" (Berrios 1984), "the use or handling of knowledge" (Gregory 1987) or "the overall function" of all "mental abilities" (Glass, Holyoak & Santa 1979), remain scientifically unsatisfying. Further definitions, despite being more elaborated, are either too particular or ambiguous (compare with Costall 1984, Goldberg 1989).

A definition should be as much encompassing as possible in order to appropriately reflect a phenomenon in its distinct manifestations. As a statement, it is a law if it satisfies the following criteria: (a) it is general in the sense that it contains a universal quantifier; (b) it is general in the sense that it does not mention particular individuals, times or places; (c) it has empirical content; (d) it is well-confirmed, and (e) it is well-

---

1 Departamento de Neurobiologia, Instituto de Biofísica Carlos Chagas Filho, UFRJ, Rio de Janeiro, RJ, Brazil

2 Institut für Neuropathologie der Medizinischen Hochschule Hannover, 30625 Hannover, Germany (correspondence address)

entrenched (i.e. it belongs to a theory) (Van der Steen & Kamminga 1991).

The evidence reviewed here allows for an encompassing definition for cognition, from an evolutionary, biophysical and molecular point of view. The definition fulfils the above criteria, and is based on some basic concepts: conservation, evolution, thermodynamics, natural selection and some concepts of the chaos-theory, which are highlighted next.

Conservation and evolution

Conservation is a major attribute of living systems. Here we define this feature as follows:

Throughout a process of change or transformation, conservation is the dynamic matching of innovative features to preexisting ones

It has been suggested elsewhere that replication - a copying process achieved by a special network of interrelationships of components and component-producing processes that produce the same network as the one which has produced them - characterizes the living organization (Maturana & Varela 1980, Csányi & Kampis 1985). This replicative ability (referred to as *autopoiesis*), nevertheless, could not account for evolution of living systems, if only preexisting features were to be maintained. This would be preservation, in the sense of immutability.

Conversely, innovations alone are not capable of inducing evolution if they can not be incorporated to preexisting features (compare with Monod 1985), in such a way that "a small change (...) be accompanied by many simultaneous compensating changes elsewhere" (Marr 1976) or by a "precise readjustment of all other components of the system" (Ashby 1960; see also Macnair 1991).

The ultimate basis of conservation in living organisms lies on the remarkable physico-chemical features of at least three elements: carbon (C), nitrogen (N) and hydrogen (H). The covalent bounds between these elements make it possible reproducible chemical combinations to occur along with the physical properties elicited by the resulting molecular systems. These include the hability to allow for transformations or innovations. These mechanisms sometimes involve the displacement of so extremely small particles that they can be operated analogously to the probability fields of quantum physics, as described by Margenau (1984), but also in accordance to deterministic chaos, as proposed by Crutchfield *et al.* (1986) (compare with Feigenbaum 1978, Prigogine & Stengers 1984, Elskens & Prigogine 1986, Ko 1991). As a result, conservation can be viewed as a "generator of variety" (Simon 1969, Changeux & Dehaene 1989), starting from the molecular level.

Purely mathematical reasoning shows that relatively simple systems can develop quite complex behavior even after slight perturbations, if non-linear interactions are involved (Van der Steen & Kamminga 1991, May 1976). This phenomenon is regarded as important for empirical research since it is exhibited by certain physical and chemical systems. Relatively simple instances of such systems have been long recognized: protobiotic coacerbation of lipoprotein membranes maintained by weak intermolecular attractive forces of the van der Waals type. This system is instructive because it leads us to the considerations about the fundamental relationships between conservation and life at its very beginning.

More complex systems involve associations between peptides and nucleotide sequencies that are capable of self replication, modulation and modification, the most readily recognized example of which is desoxiribonucleic acid synthesis, recombination, transcription and repair. Recently, it has been possible to synthesize very simple self-replicating molecules that are also capable of "successful mutation" (Amato 1992, Hong *et al.* 1992). This evidence constitutes a strong experimental support for the molecular theory of evolution and for the definition of conservation.

However, not only complex molecular (Turing 1952, Britten & Davidson 1969, Strehler *et al.* 1971, Tonegawa 1983), but also microscopic and macroscopic living systems undergo combinations and reciprocal modulation, which are attributable to conservative mechanisms. The successful association of an *akaryotic* (Forterre 1992) system like a mitochondrion with a *synkaryotic* (*ibidem*) cell, the epigenesis of neural networks (Changeux, Courrège & Danchin 1973) or the phenomenon of ecological successions are instructive examples. In summary, conservation accounts for evolution and for the occurrence of complexity in living systems.

Thermodynamics and conservation

The realization that living organisms obey to the laws of physics can help us understand ourselves, as antecipated by Goethe:

"Wär' nicht das Auge sonnenhaft, die Sonne könnt' es nie erblicken"

Living organisms are open systems. They change mass and energy with the environment. As energy must be conserved throughout transformations (First Law of Thermodynamics, attributed to H. von Helmholtz), an energy inflow to such a system can produce new combinations or alter preexisting ones. This capacity to perform "useful" work has been related to free-energy changes within the system. J.W. Gibbs defined such variations in the free energy function, G, as:

$$\blacktriangle G = H - \blacktriangle T S \quad \text{[Eq. 1]}$$

where H is the enthalpy; T, temperature and S, entropy. In a steady-state, the variation of S ($\blacktriangle S$) equals zero, so that a positive $\blacktriangle S$ is balanced by a negative $\blacktriangle S$, and the system feeds on *negentropy* from the surroundings (see Welch 1991). It results that living organisms build up and maintain low-entropic states at the expenses of a net increase in the entropy of the universe.

Nevertheless, free energy tends to increase within a system, i.e., entropy (or chaos) tends to increase internally (Second Law of Thermodynamics). The maintenance of the corresponding changes that can be either vital (e.g. nutrition, photosynthesis) or deleterious (e.g. letal mutations after ionizing radiations) renders the putative conservative forces consistent with the First Law of Thermodynamics.

Similarly, the assumption that the quite complex living systems that we know are just the sustainable portion of the total number of complex living systems that already existed (compare with Stanley 1987) renders conservation compatible with the Second Law of Thermodynamics as well: individual organisms can disappear, by means of extinction or evolution, thanks to their conservative features that maintain not only novel sustainable combinations, but also the highly entropic, unsustainable ones.

Natural selection, environment, and cognition

Whereas conservation agrees well with the first and second laws of thermodynamics, it alone does not suffice as to determine whether particular innovations are to be sustainable or not. It is the dynamic relationships established within the "inner" and "outer" environments of the living system that account for this (compare with Mayr 1963, Jerne 1967, Simon 1969, Monod 1970, Changeux & Danchin 1976, Purves & Lichtman 1980, Lumsden & Wilson 1981, Heidmann, Heidmann & Changeux 1984, Changeux & Dehaene 1989). The role played by these relationships in cutting out the "less fitted" living forms or combinations has been classically described as natural selection in the Darwin-Wallace theory of the evolution of species (Darwin 1859).

Although natural selection is not necessarily intrinsic to individual organisms, living systems can survive novel genetic and epigenetic acquisitions as a result of a somewhat random production of new sustainable patterns for the aforementioned dynamic relationships (compare with Fodor & Pylyshyn 1988), by selection-adaptive forces. This mechanism seems to operate through the matching between entropy-derived combinations and preexisting features (conservation), in an innovative, though coherent manner. A "compensatory", "buffer" or "reset" effect results, by which conservative mechanisms could no more threaten the sustainability (survival) of the system, at least within a given environmental condition and time.

This feature or "natural probability" is, in fact, the determinant of what has been frequently called cognition. In other words, cognition should be understood as the intrinsic adaptive ability of living systems to environmental changes. As a non-linear function, cognition would operate in molecular, micro- and macroscopic levels, by continuously "resetting" such systems within coherent limits. These limits are made up by the interaction between intrinsic "behavior norms" and multiple environmental factors, eliciting a given number of possible phenotypes. The situation is analogous to the principle of the "attractors" of chaos theory (more detailed descriptions of attractors can be found in Hénon 1976, and Gleick 1987). Summarising our definition:

Cognition is the intrinsic adaption of the system by the unstable search for coherent conservation in respect to the environment

Relationships between intrinsic factors to environmental factors have attracted attention of foremost researchers, and there is work in which "the species-typical environment is regarded as being an equal partner to the genotype" (Morton 1992). French physiologist Claude Bernard (1878) talked about a "perpetual communication of the anatomical element with the medium surrounding it, (...) a continuous relationship of exchange, (...) the continuous mutation of the particles which constitute the living being,(...) [the trait] which ought and could (by itself) suffice to characterize life, (...) the most constant and universal of its manifestations (...)". Young (1964) sustained that "the organism is (or contains) a representation of its environment". Changeux & Dehaene (1989) stated that "the achievement of such adequacy (fitness) with the environment (or with a given cognitive state) would then become the basic criterion for selection".

In the neurophysiology the matching between a *percept* [("in which the correlation of firing among the component neurons is directly determined by the interaction with the outside world and ceases when the stimulation has stopped")] and a *pre-representation* [("analogous to the Darwinian variations")] has been referred to as resonance and its unmatching as dissonance (Changeux 1983, Toulouse, Dehaene & Changeux 1986). In the chaos theory, "the existence and location of attractors is not set in stone but is a function of the environment - though not a linear one" (Firth 1991).

Validation

The above definition of cognition can be tested and validated in a variety of settings. Though it is not the aim of this paper to explore all possibilities, some general exemplification should be of interest.

Ecosystems

Ecosystems are a setting for validation in the macro-scale. In 1838 Grisebach (1814-1879) proposed the modern concept that plants and animals occur in integrated communities. The work of Clements (1874-1945) then consolidated the concept of *biotic unity* of ecosystems, which allows for considerations involving cognition in such systems.

Intrinsic adaptive ability of ecosystems to environmental changes are sometimes referred to as *homeostasis*, a term proposed by Claude Bernard to account for the constancy of the *milieu interne*. A deforestation, for instance, can elicit a dynamic *ecological succession* within a given *biom*. Empirically, this succession operates analogously to the search for coherent conservation. Depending upon the grade of the destruction ("entropy"), it will lead or not to the reconstitution of the ecosystem's original complements and patterns of biodiversity, starting from atypical ones (compare with Gough & Marrs 1990, Overpeck, Bartlein & Webb III 1991).

This dichotomical pattern of non-linear "decision making" has been referred to as analogous to the geometry of fractals and attractors, thus definitely linking cognition with chaos theory

(Feigenbaum 1978, Mandelbrot 1982, Prigogine & Stengers 1984, Elskens & Prigogine 1986, Goldberger, Rigney & West 1990) (Figure 1-a).

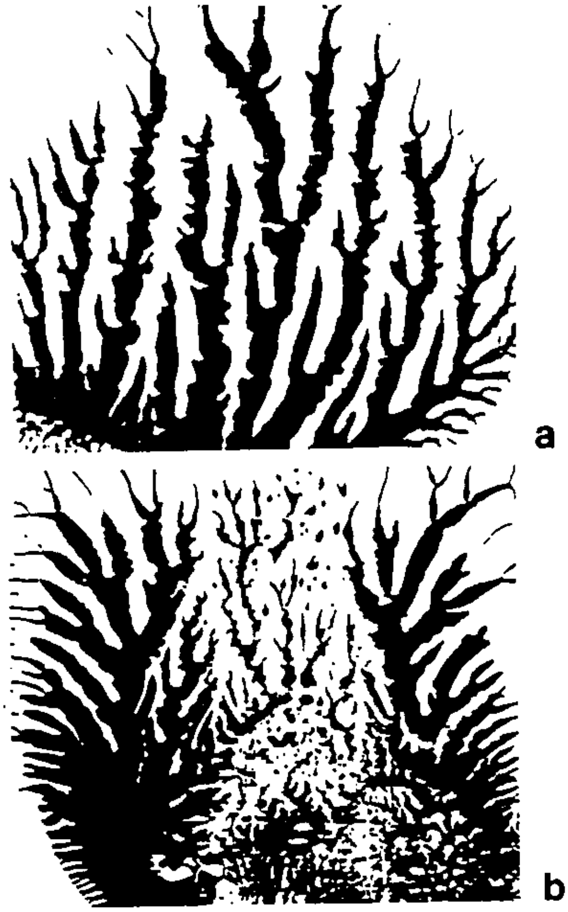

Figure 1. *Fractals can be easily obtained by splitting apart two clean glass slides joined by a drop of ink (a). A break in expected patterns is observed in the center of (b), which corresponds to a track that had been previously covered with a thin layer of fat, resembling the interplay of a "strange attractor".*

Immune systems

A given infectious agent is capable of eliciting a cascade of humoral and cellular events in the synkaryotic host organism, namely the immunological response of the host's immune system. The ability of the immune system in differentially dealing with the "self" and the "non-self" can be regarded as cognitive (compare with Jerne 1967).

At the molecular level, it has been suggested that a bacterial population may switch recognition sequences of its "type I" gene restriction-modification systems by single recombination events and thus being able to maintain an akaryotic analogue of the immune system of variable specificity (Gubler *et al.* 1992).

Alternatively, both somatic recombination and mutation may contribute greatly to an increase in the diversity of antibody synthesized by a single organism (Tonegawa 1983).

Systems of enzymes

Allosteric properties of enzymes have been referred to as "cognitive" (Monod 1970, see also Monod 1966a, Monod 1966b, Schmitt 1967).

Nervous systems

In no other instance, the concept of cognition has been so deeply employed as in the study of the CNS. Therefore, we would like to discuss this setting to some depth.

Nervous systems are syncytium-like neuron and glia systems, and neurons are highly differentiated cells. The process of differentiation is fully impregnated by cognition. It implies that a primitive cell type undergoes a progression of changes that results in changing capacity to perform activities that the cell was previously uncapable of performing (Hayflick 1991).

Neuronal function correlates directly with its structure (Jackson 1932, Chomsky 1979, Changeux 1983b, Babb & Brown 1986, Benes & Bird 1987, Eccles 1990). During development, the neuroarchitecture is achieved by cell proliferation and migration, followed by neurite outgrowth, and finally synaptogenesis (see Lund 1978, Purves & Lichtman 1980, Purves & Lichtman 1985, Chagas, Linden & Lent 1987). In the adult organism, the neuroarchitecture may change adaptively and undergo remodeling, with formation of new synapses and breaking or modification of old ones. All these phenomena should be regarded as cognitive ones, in the inner and outer environmental aspects. As pointed out by Changeux & Dehaene (1989), "the formation of brain architectures is not independent of cognitive processes but, rather, is deeply impregnated by them, starting from the early stages of postnatal development".

Neuronal plasticity, modulation and transmission have been the major morphofunctional basis for observable cognitive processes in the CNS (compare with Von der Malsburg 1987, Alkon *et al.* 1991). Assessment of cognitive function has been possible through field observations, tests of psychometric intelligence, clinical neuropsychologic tests and laboratory tests (Meyer *et al.* 1988, Colsher & Wallace 1991, Chen 1991). Consequently, the main functions attributed to cognitive processes in the CNS to date are those related to acquisition, storage and retrieval of visuo-spatial, auditory, tactile, kinesthetic, gustatory and olfactory information.

In the human species, the direct assessment of these informations has become possible thanks to our highly developed symbolic representations, such as language and speech. It is noteworthy that language, as a "manner of living", has been "conserved reproductively" in the form of an ontogenetic phenotype (Maturana 1989). Interesting demonstrations of the relationships between genom and language in humans can be found in DeFries *et al.* (1976) and Pennington & Smith (1983).

Mental function

It has been ventured that mental function is based on the ability to keep ideas - units of information, specific representations - distinctly and apart, so that attempts to achieve novel solutions could be made by rearranging the data until the final arrangement corresponds to the desired goal (Kinsbourne 1981).

According to Glassman (1974), creative problem solving consists fundamentally of the activation of global structures derived from past experience and a selection process based on feedback resulting from the interaction of these internal structures with each other or with the environment. The activation of the structures may result from associative (Hebb 1949) and spontaneous arousal processes. Also in this latter instance one can suppose that a basal "noise" corresponding to the oscillation of the system within the fields or boundaries defined by an attractor or set of attractors (generating the rest potential, for instance) can be shifted to an unstable state, influenced by the interplay of another attractor (generating an action potential, in the given instance; compare with Freeman 1988).

The event-related potential (ERP)

The major source of information concerning the neurophysiology of cognitive processes in humans is the scalp-recorded event-related potential (ERP) (John and Schwartz 1978). ERP's can, by habituation and long-term potentiation - an ubiquitous phenomenon of the cerebral cortex (Creutzfeldt 1990, Singer 1990a) - imprint new circuitry patterns in the brain.

Changeux & Dehaene (1989) commented that self-reinforcing circuits may be built at the level of neuronal receptors (Changeux & Heidmann 1987, Crick 1984, Lisman 1985), gene receptors (Britten & Davidson 1969, Monod & Jacob 1961), and at the level of the synapse, on the basis of a sequence of chemical reactions (Changeux, Klarsfeld & Heidmann 1987, see also Petit 1988).

The hypotheses that the CNS produces coherent patterns of linear or cyclic sequences of activity (Grillner 1975, Stent *et al.* 1978, Getting 1981), that neuronal connections are selected according to functional criteria and stabilized if they convey temporally coherent activity (Changeux *et al.* 1973, Dehaene, Changeux & Nadal 1987, Singer 1990b) and that oscillatory responses of neurons can synchronize across spatially separate columns if elicited by stimuli sharing coherent features (Gray *et al.* 1989) have been put forward.

Brains and computational machines

The comparison between information processing in brains and information processing by contemporary computational machines also offers a setting for the validation of our definition of cognition.

Comparative studies have led to "a picture in which disanalogies are more fundamental than analogies" (Conrad 1989). One of the most significant conclusions derived may be the statement that current computational machines are not capable of cognition just because they are not endowed with the capacity of adaption to environmental changes, in other words, probably because of the lack of coherent conservative processes.

This paradigm is well illustrated by the statement: "brains know what they do, while computers do what they know".

Cognitive impairments

Once cognition relies upon conservative mechanisms, and conservation obeys to the first and second laws of thermodynamics, it follows that cognition is subject to the effects of energy and mass conservation throughout transformations. It is also subject to entropy increase in underlying conservative processes (instances from the medical practice are given by Fukui *et al.* 1991, and Halberg *et al.* 1991).

A cognitive impairment would then take place when conservation overwhelms the system with such an amount of changes that the probability that they could be met to preexisting acquisitions in a sustainable, balanced or coherent manner would decrease critically. When this critical threshold has been achieved, the organism would undergo cognitive dysfunction ("incoherence", "dissonance"), the severity of which correlating to an increase in disease, death or extinction probabilities (compare with some theoretical reasoning by Mézard, Nadal & Toulouse 1986, Nadal *et al.* 1986).

These deviations from stability to irreversibility, in the chaos theory, are possible when there is a "continuous injection of enough energy to drive the system to a high enough excitation that non-linearity becomes appreciable" (Firth 1991).

The encompassing definition of cognition should be of some utility also in the controversial assessment and classification of cognitive impairments, especially in gerontology and pathology. Discrepancy between field and laboratory findings and also weak inter-rater reliability are frequent and contribute to hinder a comprising understanding of these issues (see Avorn 1983). Nevertheless, the assumption that cognition operates through the search for coherent conservation until a given limit, at which entropy reaches a critical point and cognitive impairment supervenes, seems to be a rationale for further studies.

Brain pathology is a quite instructive standpoint. Neuronal populations display varying sensibility to different environmental changes such as hypoxia, vitamin B-deficiency or, much interestingly for our discussion, to the incidence of microscopic aging lesions in the cerebral cortex, e.g., neuritic plaques and neurofibrillary tangles (Ball 1978, Brun & Englund 1981, Braak & Braak 1985, Braak, Braak & Kalus 1989, Dani 1994a). The realization that these aging changes are rather focal dysfunctions affecting susceptible neuronal populations (Tomlinson, Blessed & Roth 1968, Brun & Englund 1981, Gibson 1983, Rafalowska *et al.* 1988) seems to be consistent with the notion of cognitive impairment: they can be regarded as the result of incoherent conservative processes, a dissonant, chaotic deviation ("alienation") of susceptible neurons from expected patterns (Figure 1-b).

Aging

A relatively great amount of evidence of aging at the molecular level has been gathered recently (see, for instance, Strehler *et al.* 1971, Hayflick 1991, Robert 1991, Rose 1991, Macieira-Coelho 1991). Kyriazis (1991) proposed an application of chaos theory for the description of proteolysis, the failure of which could reflect in an increased rate of accumulation of abnormal protein, which has been related to the generation of neuritic plaques and neurofibrillary tangles in the aging brain: when abnormal protein (AP) concentrations rise, there would be an increased synthesis of heat-shock proteins, for example, ubiquitin (Ub). Ubiquitin in turn, would bind covalently to the abnormal protein (compare with Mori, Kondo & Ihara 1987, Harrison & Mullan 1991, Goedert, Spilantini & Crowther 1991) with the help of a number of enzymes. Some of the steps involved would be energy-dependent. Following this, the polyubiquitinated protein (PUbp) would be degraded by energy-dependent proteases (e.g., unfoldase, isopeptidase, etc.), and the concentration of the abnormal proteins would fall again [It is interesting to remark the similarity of such model with predator-prey models in ecology, "one of the pathbreakers in the study of chaos" (Firth 1991, see also May 1976)]. The initial steps for a mathematical description of this operation would be in the form of the equation:

$$x = G(s)\, f(x) \quad \text{[Eq. 2]},$$

where x is the normalised concentration of the intracellular PUbP, f(x) is the dependence of AP on PUbP in normalised coordinates and G(s) depicts the sequence of intermediate biochemical steps between synthesis of ubiquitin and the onset of the decrease in the concentration of abnormal proteins.

The enhanced incidence of neuritic plaques and neurofibrillary tangles in the human cerebral cortex has been correlated to the severity of cognitive impairment (dementia) as assessed clinically by psychometric tests (Tomlinson *et al.* 1968, Blessed, Tomlinson & Roth 1968, Tomlinson, Blessed & Roth 1970, Wilcock & Esiri 1982, Zubenko *et al.* 1991). Severely demented patients (Alzheimer's disease) usually die within 5-10 years after diagnose of first clinical signs of the disease. It seems that, thanks probably to a feedforward effect (see Rosen 1978), an imbalance between incoherent and coherent conservation operates in the definition of the future cognitive state of the organism; ultimately, in its adaptive ability to environmental changes (compare with Elskens & Prigogine 1986, Freeman 1988, Dani 1994b).

Conclusion

Cognition, defined as the adaption ability of living systems to environmental changes, operates through the unstable search for coherent conservation and is instrumental for life. The term "unstable" refers to dynamic and chaotic features of the search for adaption and accounts also for environmental influences on the destiny of a given cognitive process.

In the words of Firth (1991), "non-linearity is necessary for, and is fundamental to, chaos, but it can also endow stability. Non-linear systems can seek out and maintain essentially the same optimum state in response to a wide variety of external conditions: it is precisely this feature that gives us individuality and continuity".

References

Alkon DL, Amaral DG, Bear MF, Black J, Carew TJ, Cohen NJ, Disterhoft JF, Eichenbaum H, Golski S, Gorman LK, Lynch G, McNaughton BL, Mishkin M, Moyer Jr JR, Olds JL, Olton DS, Otto T, Squire LR, Staubli U, Thompson LT & Wible C (1991) Learning and memory. *Brain Research Reviews*, 16, 193-220.

Amato I (1992) Capturing chemical evolution in a Jar. A system of self-replicating molecules can now spin off a faster-multiplying "mutant" form. *Science*, 255, 800.

Ashby WR (1960) *Design for a Brain*. New York: Wiley.

Avorn J (1983) Biomedical and social determinants of cognitive impairment in the elderly. *Journal of the American Geriatrics Society*, 31, 137-143.

Babb TL & Brown WJ (1986) Neuronal, dendritic, and vascular profiles of human temporal lobe epilepsy correlated with cellular physiology in vivo. *Advances in Neurology*, 44, 949-966.

Ball MJ (1978) Topographic distribution of neurofibrillary tangles and granulovacuolar degeneration in hippocampal cortex of aging and demented patients. A quantitative study. *Acta Neuropathologica* , 42, 73-80.

Benes FM & Bird ED (1987) An analysis of the arrangement of neurons in the cingulate cortex of schizophrenic patients. *Archives of General Psychiatry*, 44, 608-616.

Bernard C (1878) *Leçons sur les Phénomènes de la Vie Communs aux Animaux et aux Végétaux* (Translated by HE Hoff, R Guilleman & L

Guillemin, Springfield, IL: Charles C Thomas Publisher, 1974), as cited by GR Welch (1991)

Berrios GE (1984) Descriptive psychopathology: conceptual and historical aspects. *Psychological Medicine*, 14, 303-313.

Blessed G, Tomlinson BE & Roth M (1968) The association between quantitative measurements of dementia and of senile changes in the cerebral grey matter of elderly subjects. *British Journal of Psychiatry*, 114, 797-811.

Braak H & Braak E (1985) On areas of transition between entorhinal allocortex and temporal isocortex in the human brain. Normal morphology and lamina-specific pathology in Alzheimer's disease. *Acta Neuropathologica*, 68, 325-332

Braak H, Braak E & Kalus P (1989) Alzheimer's disease: areal and laminar pathology in the occipital isocortex. *Acta Neuropathologica*, 77, 494-506.

Britten RJ & Davidson EH (1969) Gene regulation for higher cells: a theory. *Science*, 165, 349-357

Brun A & Englund E (1981) Regional pattern of degeneration in Alzheimer's disease: neuronal loss and histopathological grading. *Histopathology*, 5, 549-564.

Chagas C, Linden R & Lent R (1987) *Developmental Neurobiology of Mammals*. Vatican: Pontificial Academy of Sciences.

Chagas C (1990) Introduçao ao Curso de Pós-Graduaçao em Ciências Biológicas, Area de Concentraçao em Biofísica. "Catálogo das Disciplinas". Rio de Janeiro: Coordenaçao de Pós-Graduaçao do IBCCF, Universidade Federal do Rio de Janeiro.

Changeux JP, Courrège P & Danchin A (1973) A theory of the epigenesis of neural networks by selective stabilization of synapses. *Proceedings of the National Academy of Sciences of the USA*, 70, 2974-2978.

Changeux JP & Danchin A (1976) Selective stabilization of developing synapses as a mechanism for the specification of neuronal networks. *Nature*, 264, 705-712

Changeux JP (1983) *L'Homme Neuronal*. (Paris: Fayard. English translation by L Garey, *Neuronal Man*. New York: Pantheon Books (1985)

Changeux JP, Klarsfeld A & Heidmann T (1987) The acetylcholine receptor and molecular models for short and long term learning. In Changeux JP & Konishi M (Eds.) *The Cellular and Molecular Bases of Learning*. Chichester: Wiley.

Changeux JP & Heidmann T (1987) Allosteric receptors and molecular models of learning. In Edelman G, Gall WE & Cowan WM (Eds.), *Synaptic Function*. New York: Wiley.

Changeux JP & Dehaene S (1989) Neuronal models of cognitive functions. *Cognition*, 33, 63-109.

Chen ACN (1991) Cognitive neuropsychophysiology of thought imagery versus imagination imagery. *International Journal of Neuroscience*, 60, 65-77.

Chomsky N (1979) Le débat entre Jean Piaget et Noam Chomsky. In *Théories du Langage - Théories de l'Apprentissage*. Piattelli-Palmarini M (Ed.) Paris: Le Seuil.

Colsher PL & Wallace RB (1991) Epidemiologic considerations in studies of cognitive function in the elderly: methodology and nondementing acquired dysfunction. *Epidemiologic Reviews*, 13, 1-27.

Conrad M (1989) The brain-machine disanalogy. *Biosystems*, 22, 197-213.

Costall AP (1984) Are theories of perception necessary ? A review of Gibson's the ecological approach to visual perception. *Journal of Experimental Analysis of Behavior*, 41, 109-115

Creutzfeldt OD (1990) Neuronal responses in human and monkey temporal lobe during memory tasks: compartmentalization of memory functions. In *Vision, Memory, and the Temporal Lobe*. New York: Elsevier.

Crick F (1984) Memory and molecular turnover. *Nature*, 312, 101

Crutchfield JP, Farmer JD, Packard NH & Shaw R (1986) Chaos. *Scientific American*, 255. 38-49.

Csányi V & Kampis G (1985) Autogenesis: the evolution of replicative systems. *Journal of Theoretical Biology*, 114, 303-321

Dani SU (1994a) Spatial patterns of plaques and tangles in Alzheimer's disease. Dementia 5:53.

Dani SU (1994b) Larger neuronal size overwhelms maintenance capacity with aging. Medical Hypotheses 42:208-210.

Darwin C (1859) *On the Origin of Species*. London: Murray.

DeFries JC, Vandenberg SG & McClean GE (1976) Genetics of specific cognitive abilities. *Annual Reviews in Genetics*, 10, 179-207.

Dehaene S, Changeux JP & Nadal JP (1987) Neural networks that learn temporal sequences by selection. *Proceedings of the National Academy of Sciences of the USA*, 84, 2727-2731.

Eccles Sir J (1990) A unitary hypothesis of mind-brain interaction in the cerebral cortex. *Proceedings of the Royal Society of London. B* 240, 433-451.

Elskens Y & Prigogine I (1986) From instability to irreversibility. *Proceedings of the National Academy of Sciences of the USA*, 83, 5756.

Feigenbaum MJ (1978) Quantitative universality for a class of nonlinear transformations. *Journal of Statistical Physics*, 19, 25 -52.

Firth WJ (1991) Chaos - predicting the unpredictable. *British Medical Journal*, 303, 1565-1568.

Fodor J & Pylyshyn Z (1988) Connectionism and cognitive architecture: a critical analysis. *Cognition* 28, 3-71 .

Forterre P (1992) Neutral Terms. *Nature*, 355, 305.

Freeman WJ (1988) Strange attractors that govern mammalian brain dynamics shown by trajectories of electroencephalographic (EEG) potential. *Transactions on Circuits and Systems*, 35, 781.

Fukui Y, Hoshino K, Hayasaka I, Inouye M & Kameyama Y (1991) Developmental disturbance of rat cerebral cortex following prenatal low-dose gamma-irradiation: a quantitative study. *Experimental Neurology*, 112, 292-298.

Getting PA (1981) Mechanism of pattern generation underlying swimming in *Tritonia*. I. Neuronal network formed by monosynaptic connections. *Journal of Neurophysiology*, 46, 65-79.

Gibson PH (1983) Form and distribution of senile plaques seen in silver-impregnated sections in the brains of intellectually normal elderly people and people with Alzheimer-type dementia. *Neuropathology and Applied Neurobiology*, 9, 379-389.

Glass AL, Holyoak KJ & Santa JL (1979) *Cognition*. Reading, MA: Addison-Wesley.

Glassman RB (1974) Selection processes in living systems: role in cognitive construction and recovery from brain damage. *Behavioral Science*, 19, 149-165.

Gleick J (1987) *Chaos: Making a New Science*. New York: Viking.

Goedert M, Spilantini MG, & Crowther RA (1991) Tau proteins and neurofibrillary degeneration. *Brain Pathology*, 1, 279-286.

Goldberg E (1989) Gradiental approach to neocortical functional organization. *Journal of Clinical and Experimental Neurophysiology*, 11, 489-517.

Goldberger AL, Rigney DR & West BJ (1990) Chaos and fractals in human physiology. *Scientific American*, 262, 35-41.

Gough MW & Marrs RH (1990) A comparison of soil fertility between semi-natural and agricultural plant communities: implications for the creation of species-rich grassland on abandoned agricultural land. *Biological Conservation*, 51, 83-96

Gray CM, König P, Engel AK & Singer W (1989) Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature*, 338, 334-337.

Gregory RL (1987) *The Oxford Companion to the Mind*. Oxford, England: Oxford University Press.

Grillner S (1975) Locomotion in vertebrates. Central mechanisms and reflex interaction. *Physiological Review*, 55, 247-304.

Gubler M, Braguglia D, Meyer J, Piekarowicz A & Bickle T (1992) Recombination of constant and variable modules alters DNA sequence recognition by type IC restriction-modification enzymes. *The EMBO Journal*, 11, 233-240.

Halberg FE, Kramer JH, Moore IM, Wara WM, Matthay KK & Ablin AR (1991) Prophylatic cranial irradiation dose effects on late cognitive function in children treated for acute lymphoblastic leukemia. *International Journal of Radiation Oncology in Biology and Physics*, 22, 13-16.

Harrison PJ & Mullan MJ (1991) Alzheimer's disease: the significance of a ß-amyloid precursor protein gene mutation. *Current Opinion in Neurology and Neurosurgery*, 4, 908-913.

Hayflick L (1991) Aging under glass. *Mutation Research*, 256, 79-80.

Hebb DO (1949) *Organization of Behavior*. New York: Wiley.

Heidmann A, Heidmann T & Changeux JP (1984) Stabilisation sélective de représentations neuronales par résonance entre "pré-représentations" spontanées du réseau cérébral et "percepts" évoqués par interaction avec le monde extérieur. *Comptes Rendues Académie de Sciences, Paris (série 3)*, 229, 839-844.

Hénon M (1976) A two-dimensional mapping with a strange attractor. *Communications in Mathematical Physics*, 130, 69-77.

Hong J-I, Feng Q, Rotello V & Rebek Jr. J (1992) Competition, cooperation, and mutation: improving a synthetic replicator by light irradiation. *Science*, 255, 848.

Jackson H (1932) In Taylor J (Ed.). *Selected Papers (Vol.2)*. London: Hodder & Stoughton.

Jerne N (1967) Antibodies and learning: selection versus instruction. In *The Neurosciences*, Quarton G., Melnechuck T & Schmitt FO (Eds.). New York: Rockfeller University Press.

John ER & Schwartz EL (1978) The neurophysiology of information processing and cognition. *Annual Reviews in Psychology*, 29, 1-29.

Kinsbourne M (1981) Cognitive deficit and the unity of brain organization: Goldstein's perspective updated. *Journal of Communication Disorders*, 14, 181-194 .

Ko MSH (1991) A stochastic model for gene induction. *Journal of Theoretical Biology*, 153, 181-194.

Kyriazis M (1991) Applications of chaos theory to the molecular biology of aging. *Experimental Gerontology*, 26, 569-572.

Lisman JE (1985) A mechanism for memory storage insensitive to molecular turnover: a bistable autophosphorylating kinase. *Proceedings of the National Academy of Sciences of the USA*, 82, 3055-3057.

Lumsden C & Wilson EO (1981) *Genes, Mind and Culture: the Coevolutionary Process*. Cambridge, MA: Harvard University Press.

Lund RD (1978) *Development and Plasticity of the Brain*. New York: Oxford University Press.

Macieira-Coelho A (1991) Dérégulation du flux d'information dans l'organisme âgé. *Comptes Rendues de Société de Biologie*, 185, 110-120 .

Macnair MR (1991) Why the evolution of resistance to anthropogenic toxins normally involves major gene changes: the limits to natural selection. *Genetica* 84, 213-219 .

Mandelbrot BB (1982) *The Fractal Geometry of Nature*. New York: Freeman.

Margenau H (1984) *The Miracle of Existence*. Woodbridge, Connecticut: Ox Bow Press.; cited by Eccles, Sir J. (1990).

Marr D (1976) *Philosophical Transactions of the Royal Society of London, B*, 275, 483-519, quoted in Shallice, 1981.

Maturana H (1989) Lenguaje y realidad: el origen de lo humano. *Archivos de Biologia y Medicina Experimentales*, 22, 77-81.

Maturana HR & Varela FJ (1980) *Autopoiesis and Cognition, Boston Studies in the Philosophy of Sciences*, 42. Boston: D.Reidel.

May RM (1976) Simple mathematical models with very complicated dynamics. *Nature*, 261,459-67.

Mayr E (1963) *Animal Species and Evolution*. Cambridge, MA: Harvard University Press.

Mézard M, Nadal JP & Toulouse G (1986) Solvable models of working memories. *Journal de Physique (Paris)* 47, 1457-1462.

Meyer DE, Osman AM, Irwin DE & Yantis S (1988) Modern mental chronometry. *Biological Psychology*, 26, 3-67.

Monod J (1966a) From enzymatic adaption to allosteric transitions. *Science*, 154, 475-483.

Monod J (1966b) On the mechanism of molecular interactions in the control of cellular metabolism. *The Upjohn Lecture of The Endocrine Society USA*, 78, 412-425.

Monod J (1970) *Le Hasard et la Nécessité*. Paris: Le Seuil.

Monod J & Jacob F (1961) General conclusions: teleonomic mechanisms in cellular metabolism, growth and differentiation. *Cold Spring Harbor Symposium for Quantitative Biology*, 26, 389-401.

Monod JL (1974) Sobre a Teoria Molecular da Evoluçāo. In Rom Harré (Ed.), *Problems of Scientifical Revolution. Progress and Obstacles to Progress in the Sciences* (Portuguese translation by L Hegenberg & OS da Mota). Belo Horizonte: Itatiaia.

Mori H, Kondo J & Ihara Y (1987) Ubiquitin is a component of paired helical filaments in Alzheimer's disease. *Science*, 235, 1641-1644.

Morton J (1992) Between brain and culture. Origins of the Modern Mind: Three Stages in the Evolution of Culture and Cognition, by Donald M, Harvard University Press:1991. *Nature*, 355, 31.

Nadal JP, Toulouse G, Changeux JP & Dehaene S (1986) Networks of formal neurons and memory palimpsests. *Europhysics Letters* 1, 532-542.

Overpeck JT, Bartlein PJ & Webb III T (1991) Potential magnitude of future vegetation change in eastern North America: comparisons with the past. *Science*, 254, 692-695.

Pennington BE & Smith SD (1983) Genetic influences on learning disabilities and speech and language disorders. *Child Development*, 54, 369-387.

Petit TL (1988) The neurobiology of learning and memory: elucidation of the mechanisms of cognitive dysfunction. *Neurotoxicology*, 9,413-428.

Prigogine I & Stengers I (1984) *Order out of Chaos: Man's New Dialogue with Nature*. Toronto:Bantam.

Purves D & Lichtman JW (1980) Elimination of synapses in the developing nervous system. *Science*, 210, 153-157.

Purves D & Lichtman JW (1985) *Principles of Neural Development*. Sunderland, Sinauer.

Rafalowska J, Barcikowska M, Wen GY & Wisniewsky HM (1988) Laminar distribution of neuritic plaques in normal aging, Alzheimer's disease and Down's syndrome. *Acta Neuropathologica*, 77, 21-25.

Robert L (1991) Mécanismes cellulaires et moléculaires du vieillessement: une revue. *Comptes Rendues de Société de Biologie*, 185, 97-109.

Rose MR (1991) *Evolutionary Biology of Aging* New York: Oxford University Press.

Rosen R (1978) Feedforwards and global system failure: a general mechanism for senescence. *Journal of Theoretical Biology*, 74, 579-590.

Schmitt FO (1967) Makromolekulare Datenverarbeitung im Zentralnervensystem. *Klinische Wochenschrift*, 45, 863-868 .

Shallice T (1981) Neurological impairment of cognitive processes. *British Medical Bulletin* 37, 187-192.

Simon HA (1969) *The Sciences of the Artificial* Cambridge, MA: MIT Press.

Singer W (1990a) Ontogenetic self-organization and learning. In Mc Gaugh JL, Weinberger NM & Lynch G (Eds.) *Brain Organization and Memory: Cells, Systems and Circuits*. New York: Oxford University Press.

Singer W (1990b) Search for coherence: a basic principle of cortical self-organization. *Concepts in Neuroscience*, 1, 1-26 .

Stanley S (1987) *Extinction*. New York: Freeman.

Stent GS, Kristan WB, Friesen WO, Ort CA, Poon M & Calabrese RL (1978) Neuronal generation of the leech swimming movement. *Science*, 200, 1348-1356.

Strehler B, Hirsch G, Gusseck D, Johnson R & Bick M (1971) Codon-restriction theory of aging and development. *Journal of Theoretical Biology*, 33, 429-474.

Tomlinson BE, Blessed S & Roth M (1968) Observations on the brains of non-demented old people. *Journal of the Neurological Sciences*, 7, 331-356.

Tomlinson BE, Blessed S & Roth M (1970) Observations on the brains of demented old people. *Journal of the Neurological Sciences*, 11, 205-242.

Tonegawa S (1983) Somatic generation of antibody diversity. *Nature*, 302, 575-581.

Toulouse G, Dehaene S & Changeux JP (1986) Spin glass model of learning by selection. *Proceedings of the National Academy of Sciences of the USA*, 83, 1695-1698.

Turing AM (1952) The chemical basis of morphogenesis. *Philosophycal Transactions of the Royal Society of London*, 237, 37-72

Van der Steen WJ & Kamminga H (1991) Laws and natural history in biology. *British Journal of the Philosophy of Science*, 42, 445-467 .

Von der Malsburg C (1987) Synaptic plasticity as basis of brain organization. In JP Changeux & M Konishi (Eds.) *The Neural and Molecular Bases of Learning*. Chichester: Wiley.

Welch GR (1991) Thermodynamics and living systems: problems and paradigms. *Journal of Nutrition*, 121, 1902-1906 .

Wilcock GK & Esiri MM (1982) Plaques, tangles and dementia. A quantitative study. *Journal of the Neurological Sciences*, 56, 343-356.

Young JZ (1964) *A Model of the Brain*. Oxford: Claredon Press.

Zubenko GS, Moossy J, Martinez J, Rao G, Claassen D, Rosen J & Kopp U (1991) Neuropathologic and neurochemical correlates of psychosis in primary dementia. *Archives of Neurology*, 48, 619-624.

Acknowledgements

Work supported by CAPES (Brazil). Eugênia Vale Marques, M.Sc., kindly collaborated with one reference. Valuable comments on the manuscript by Professor JEH Pittella are kindly acknowledged.

Correspondence should be sent to:

Sérgio U. Dani, MD
Institut für Neuropathologie der MHH
Konstanty-Gutschow-Str. 8
30625 Hannover
Germany
Fax: (0049-511) 532 4550
E-mail: dani@dhvmhh1.bitnet
or dani@mhrz.mh-hannover.de