

# GENES, DEVELOPMENT AND SEMIOSIS

By

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## FORMALIZATION AND REALIZATION

Capacity for prediction has always been a highly estimated value in science but biology has not fared well in this respect. Only rarely has it been possible to formalize the description of a living system to an extent such that its future fate could be deduced in more than the most general way. Recently however even physics has encountered non-predictability in cases of non-linear dynamic systems where initial conditions cannot - in principle - be measured with sufficient precision. Since living systems are necessarily far-from equilibrium systems characterized by complex non-linear dynamics, the non-predictability of such systems should no longer surprise us.

But opinions differ as to whether this unpredictability is rooted solely in epistemological problems or whether it reflects a deeper reality pertaining to our universe. This question concerns the ontological status of chance. If chance is interpreted as *uncertainty*, as has been the case in most of modern science (Hacking 1990), i.e. as a lack of knowledge about true causative agencies, then chaos dynamics remains inside the secure deterministic vision of classical physics. If however chance is seen as reflecting a real indeterminacy of the world, as has been suggested by among others Karl Popper (Popper 1990) then initial conditions are indeterminate in principle and chaos dynamics becomes an explanatory tool for our understanding of irreversibility and history. Such a view fits well into modern interpretations of the second law of thermodynamics (Salthe 1993; Swenson and Turvey 1991; Ulanowicz 1997).

We believe there are strong reasons to adopt the conception of chance as expressing a real indeterminacy inherent to our world, and one major route of reasoning which has led us to this view is a growing understanding of the "inverted" temporal relation between formalizations and realizations in evolutionary systems. Science, in the spirit of engineering, has tended to believe that digital blueprints always came before and specified the construction of real systems. Outstanding examples are the belief that DNA originated before cells, that accumulation of new genetic material (mutations) was the essence of speciations and evolution, that cognition is based on the manipulation of symbolic objects, that human language is pure syntax insulated from meaning, perception and emotion and ultimately coded for

in the genes, or that efficient robots could be constructed through advance programming.

It now seems more and more likely that evolutionary systems in general work the other way around. Formal aspects of the systems do not specify them beforehand but on the contrary have to be established in the very process of their evolution. Thus the view of RNA as the "magic molecule" behind the origin of life has been severely criticized by among others Stuart Kauffman who showed that the formation of a complex autocatalytically closed chemical system was not only a possible but also a likely precursor for life (Kauffman 1995; Kauffman 1993). Others have emphasized the importance of membranes for the origin of life (Hoffmeyer 1998b; Morowitz 1992; Weber 1998; Weber, Depew et al. 1989). The view of speciation as founded upon a gradual accumulation of genetic novelties is presumably still held by a majority of biologist, but it has become strongly challenged from many corners. At least a more pluralistic understanding seems to penetrate evolutionary biology in these years, allowing the organismic level a bigger share of the evolutionary agency (Depew and Weber 1995). And developmental system theory claims parity between genes and other organismal or environmental factors which collectively influences the future of the species (Griffiths and Gray 1994; Oyama 1985)(further references in (Sterelny and Griffiths 1999)).

In cognitive science we can see that the "symbolic paradigm" is now challenged by a "dynamic approach" (Van Gelder and Port 1995), and the Chomskyan idea of language as inherent to our computational brains is strongly opposed by a growing understanding of the "embodied nature" of natural language. See e.g. (Lakoff and Johnson 1999) for a recent summary. Michael Polanyi should be credited as an early proponent of this view which lay in fact implicit in his ideas of "tacit knowledge" more than 40 years ago (Polanyi 1958). The American neurobiologist Terrence Deacon who has dealt thoroughly with the evolution of the human brain claimed that even human children have no inborn mastering of symbolic reference but have to learn it by growing up in a linguistic culture (Deacon 1997). His surprising thesis is that language and brain have co-evolved in the human lineage, but that language did most of the evolving by adapting its syntactic structure to the nature of children's guessings. Finally let me refer to the very persuasive work on robotics that confirms this general trend towards "embodiment". Bottom-up programming through "situated emergence" rather than top-down programming apparently holds the key to the construction of efficient autonomous agents (Clark 1997; Hendriks-Jansen 1996).

In sum there seems to be a convergence of new insights from different areas that points to a new conception of formalizations: *Apparently real systems do not have formal origins; formalizations become possible only after realizations, never before.* Thus the need for deterministic causation fades away and it becomes a more plausible

to see irreversible time as a real phenomenon. Something just happens in evolutionary systems that no formula could have predicted and this strongly supports the conception of chance fluctuations as an ontologically real aspect of our universe. The combination of chance fluctuations and chaos dynamics can be seen as responsible for the making of history in the true sense of this word as a unique and unpredictable series of temporal events at a macro-scale.

But it should be noticed just as soon that while the combined effect of chance and chaos dynamics is what makes history possible, it does not at all *explain* history. Chaos dynamics may legitimize the conception of living systems as creative agents, but it does not tell us how creativity actually works in these systems. This is where the concept of *semiosis* (signification or sign-processes) becomes a useful tool for our descriptions. If strict determinism is given up we are left with a more open causative universe where cohesiveness and self-organization is assured through *semiotic emergence*<sup>1</sup> (Hoffmeyer 1997) consistent with the second law of thermodynamics (see below).

#### SEMIOSIS AND INFORMATION IN LIVING SYSTEMS

That even molecular biology could not escape a communicative or informational dimension lay implicit already in Francis Crick's postulate of the central dogma. As everybody knows this dogma stipulated that something, termed information, could only be passed on in one direction, that is from DNA to RNA to protein, and never in the other direction. Crick certainly saw no parity here which is due of course to the narrow focus of his statement<sup>2</sup>.

But what about this entity, information, which so elegantly got transported away from master (DNA) to pupil (protein)? What was the nature of information? We shall not exhaust the reader's patience by entering the endless discussions on the proper understanding of this term but we dare say that 1) no agreement has been reached or is even in sight, and 2) for the practicing biologist the central dogma always meant simply that "instructions" were passed on from DNA to protein. In the absence of any rigid definition of the term information the instructional conception of this word imperceptibly slid into the matrix of tacit metaphors nourishing the minds of modern biologists.

The adoption of an instructional understanding of the "something" transmitted from DNA to protein is no innocent move however. It immediately raises questions about how we should understand the relation between senders and receivers of this

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<sup>1</sup> The emergence through situated semiotic activity of patterns of activity whose high-level structure cannot be reduced to specific sequences of low-level activity

<sup>2</sup> Parity in the sense of a two-way flow of information requires the introduction of longer timescales (lifecycles) and more complex level of organism-environment interaction.

"information": are they supposed to be connected through a causal relation? A yes to this question would seem to violate Norbert Wiener's famous statement that "Information is information, not substance or energy. No materialism that fails to admit this can survive today" (Wiener 1962). The concept of a passage between molecules of something, which is neither substance nor energy, feels foreign to materialistic science.

In a somewhat different way this peculiar aspect of living systems was touched upon by John von Neumann (von Neumann 1966). Von Neumann claimed that replication in real existing cells (as opposed to cellular automata) requires not only dynamical fabrication, i. e. active enzymatic rate control of synthesis, but also non-dynamical<sup>3</sup> ("quiescent") constraints, i. e. genetic memory description. How such functional organization could arise was to him "a miracle of the first magnitude" says Howard Pattee (Pattee 2000).

Howard Pattee has further developed this "complementarity" between "dynamic and linguistic modes of complex systems" (Pattee 1973; Pattee 1977). Living systems are inherently engaged in what Pattee calls measuring processes, i.e., processes whereby the living system observes its environment, and this creates an epistemological problem: "We must define an *epistemic cut* separating the world from the organism or observer" (Pattee 1997) (*italics mine*). The concept of semantic information requires the separation of the knower and the known. Pattee underlines that he is not suggesting a Cartesian dualism here but only a "descriptive dualism", for although a measuring process depends on choices which cannot be derived from laws, such choices are seen by Pattee as functions coded in DNA and ultimately generated by natural selection.

Measurement and observer are epistemic concepts and as such they presuppose at least an organization that can construct the measuring device and use the results for its survival. Subcellular entities such as enzymes are not sufficiently sophisticated as to be accounted for as measuring devices: "To qualify as a measuring device it must have a function, and the most primitive concept of function implies improving fitness of an organism. Thus, observation and measurement require an organization that (1) constructs the measuring device and (2) uses the results of the measurements for survival. This requirement I have called the *semantic closure* principle (Pattee 1982). This provides an objective criterion for distinguishing measurements and observations from other physical interactions. Only organizations with this semantic closure property should be called observers. The cell is the simplest natural case of an observing system" (Pattee 1996).

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<sup>3</sup> i.e., time independent

A major difficulty with this "epistemic cut position" is that it makes it very difficult to see how life could ever have evolved at all. How did physical constraints become semiotic controls? (Hoffmeyer 2001a)

I think the central dogma is to blame for the whole epistemological misery. The essential idea of "something" which is passed on from DNA to protein is a misunderstanding and a false reification for that. Nothing is passed on, I suggest. In stead *the cell interprets the DNA as a set of instructions*.

Remark that this understanding not only gets rid of the mysterious "something/information" package but it also immediately changes "the burden of agency" from the passive, hermetically closed DNA-molecule to the very active biochemical machinery of the cell. Obviously the cell is the "doer", not the DNA.

But of course the problem is: what do we mean by cellular interpretation? Answering this question brings us to the core of the new field of *biosemiotics* which will be presented in the next session, but a preliminary answer might refer to the formation of an interpretant in the form of the specific activity of that complex of finely regulated and membrane associated enzymatic reactions which collectively are known as transcription and translation. While these processes *per se* remain firmly inside Pattee's "dynamic mode" their historically appropriated functional organization reflects the semiotic dynamics of the organism-environment interface (Hoffmeyer 1998b). The regulated transcriptional and translational enzyme systems are tuned to the semiotic history of the organism. Accordingly we have suggested that the "epistemic cut" may be transcended through the application of the semiotic distinction between different sign categories, i.e. iconic, indexical and symbolic signs (Hoffmeyer 2000b).

## BIOSEMIOTICS

According to biosemiotics, all processes that take place in animate nature, at whatever level, from the single cell to the ecosystem, should be analyzed and conceptualized in terms of their character as sign processes (Hoffmeyer 1998a). Biosemiotics does not contradict well-established physical and chemical laws; it simply claims that life processes are part of - and are organized in obedience to - a semiotic dynamic. Biosemiotics, however, is still in a state of vagueness, and a diversity of interests and viewpoints have come to express themselves under its umbrella, as witnessed by the collection of articles edited by Sebeok and Umiker-Sebeok (Sebeok and Umiker-Sebeok 1992) and in a recent special issue of *Semiotica* devoted to biosemiotics (Hoffmeyer and Emmeche 1999; Sebeok 1999).

As linguistic animals human beings are inescapably suspended from early childhood in a world of signification. But linguistic signification is just one very peculiar and highly developed form for signification. Although traditionally much of

semiotics, following the paths laid out by Swiss linguist Ferdinand de Saussure in the beginning of 20<sup>th</sup> century, has been exclusively concerned with the sign processes of language, modern semiotics has widened its scope to embrace the much broader understanding of semiosis originally suggested by the American scientist and philosopher Charles Sanders Peirce (1839-1914).

The existence of signification as a dimension of the human condition challenges biological theory to find out what may be the roots for this phenomenon in pre-human nature. This challenge has been met often enough by a reductive strategy in which semiotic processes are identified as signals unambiguously releasing well-defined effects. While such a strategy may help in reassuring deep-rooted beliefs in the omnipotence of traditional explanatory strategies of science it does so only at the cost of leaving our subjective experience of what it feels like to be conscious behind as an illusion. Worse yet, it leaves us with a mind-body dualism, which from an intellectual point of view at least, cannot decently be believed. As pointed out by the philosopher John Searle the experience of being a 1. person singular cannot possibly be explained through 3. person discourse (Searle 1992) or to state it a little pointed: An "I" cannot be derived from "it"s, no matter how complicated patterns of "it"s one constructs.

Biosemiotics can be seen as an alternative to this approach, namely to accept that signification in the true sense of this word did not suddenly appear with the human creature but that it has a natural history of its own, beginning with modest unpersonalized forms of signification such as the kind of natural preferences we use to call natural laws, such as e.g. the preference of massive bodies for approaching each other. This was the route to understanding of our existence as sentient beings in the universe suggested more than a century ago by Peirce.

Peirce was strongly opposed to the "necessitarians" of his time. In 1891 he wrote:

“Uniformities are precisely the kind of fact that need to be accounted for. That a pitched coin should sometimes turn up heads and sometimes tails calls for no particular explanation; but if it shows heads every time, we wish to know how this result has been brought about. Law is *par excellence* the thing which wants a reason. Now the only possible way of accounting for the laws of nature and the uniformity in general is to suppose them results of evolution. This supposes them not to be absolute, not to be obeyed precisely. It makes an element of indeterminacy, spontaneity, or absolute chance in

nature” (CP 6.12-13)<sup>4</sup>.

Thus according to Peirce natural laws cannot explain evolution since they are themselves a product of evolution. And behind our evolving universe we find in his vision one fundamental principle or law, which he sometimes called *nature's tendency to take habits*: As this terminology suggests he saw human mind and its associative or generalizing power as just one peculiar instantiation of a much broader principle pertaining to our universe as such.

Peirce's "cosmogonic philosophy" appears strangely well-suited to cope with many challenges of modern science (Christiansen 1999), but there is no reason for a biosemiotic understanding of life to commit itself to a strict dependence on this particular metaphysical system. The idea of nature's tendency to take habits however is central to biosemiotics. As Peirce himself observed, a habit is the most general form of an interpretant, since the formation of a habit implies that an event will (nearly) always provoke the same response, so that therefore the response is not just accidental but must be related to the event. Habit formation thus is the core of *semiosis* (sign-process). *Biosemiotics holds, that semiosis is a fundamental aspect of our universe, a principle which however only manifests itself in its genuine triadic form through the birth of life.*

Many scientists may think that these ontological commitments puts biosemiotics far apart from decent natural science. And yet, recent interpretations of the second law of thermodynamics seem very close to the assumptions of biosemiotics. Thus according to the *maximum entropy production* principle suggested by Rod Swenson (Swenson 1989), thermodynamic fields will behave in such a fashion as to get to the final state - minimize the field potential or maximize the entropy - *at the fastest possible rate* given the constraints. This implies that “progressive evolutionary ordering entails the production of increasingly higher ordered states.” The point is this: Every time an ordered state is produced in some system, implying a lowering of the entropy at that location, there must be produced even more entropy at other locations in the world in order to obey the thermodynamic dictate to always increase the total entropy in the universe. For this reason it appears that the best way to produce entropy as fast as possible should be by producing order as fast as possible. Or in the words of Swenson and Turvey:

“The world is in the order production business, including the business of producing living things and their perception and action capacities,

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<sup>4</sup> References to the work of Peirce is given as CP (i.e. Collected Papers of Charles S. Peirce (Peirce 1931-35)), followed by volume number and paragraph number.

*because order produces entropy faster than disorder.*' (Swenson and Turvey 1991, 345) my italics).

Now, as Swenson and Turvey goes to great detail in showing, "perception and action cycles", which are of course key processes in the semiotic dynamic of living systems, are even more instrumental than physical systems in furthering the entropy production:

"Living things with the capacity to perceive how and where they are moving, and with the coordinate capacity to move in ways that allow them to perceive more and to perceive better, expand the patches of the planet in which energy degradation can take place. In the terms introduced above, they expand the Earth's dissipative space. Thus the purpose of living things are differentiations or productions, literally higher order symmetry states, of the environment itself towards its own ends"(Swenson and Turvey 1991).

Biosemiotics suggests that our universe has an built-in tendency (originating in the 2. law of thermodynamics) to produce organized systems possessing increasingly more *semiotic freedom* in the sense that the semiotic aspect of the system's activity becomes more and more autonomous relative to its material basis (Hoffmeyer 1992; Hoffmeyer 1996). The semiotic dimension of a system is always grounded in the organization of its constituent material components, and cannot exist without this grounding, but evolution has tended to create more and more sophisticated semiotic interactions which were less and less constrained by the laws of the material world from which they were ultimately derived.

It seems obvious to this author that science must somehow come to terms with the necessity of "understanding our universe in such a way that it is not absurd to claim that this universe has itself produced us", to quote Ilya Prigogine and Isabelle Stengers (Prigogine and Stengers 1984). Accepting the Peircean idea that semiosis as a general aspect of our universe, or in his own words, that nature has a tendency to take habits, seems like a modest step to take in order to produce a description of the world which do not preclude our own existence as real persons, as "I's", in it.

#### SIGN ACTION

"Every reasoner" Peirce said "has some general idea of what good reasoning is. This constitutes a theory of logic" (CP 2.186), and since "all thought [is] being performed by means of signs, logic may be regarded as the science of the general laws of signs"

(CP 1.191). This is how Peirce comes to his conception of the sign as a *triadic* unit, i.e. as an undecomposable unity of three interdependent relations. Peirce thought that traditional logic being based on two-factor, *dyadic*, relations is too limited. Bound as this logic is to the single dimension of the linear chain, it cannot be made to branch out. He believed that logical processes ought rather to be regarded as a multi-dimensional network. Such a network can be arrived at by combining three-factor relations, triads or *signs*. So the sign in Peirce's understanding is a logical node. The following quote catches the essence:

"I define a Sign as an thing which is so determined by something else, called its Object, and so determines an effect upon a person, which effect I call its Interpretant, that the latter is thereby mediately determined by the former. My insertion of "upon a person" is a sop to Cerberus, because I despair of making my own broader conception understood. [...]" (Peirce 1908).

Although Peirce derived his concept of the sign from his understanding of logic, he didn't think of signs (or logic) as bound to the mental sphere of humankind, rather - as already noticed - he saw human mind as a particularly highly elaborated instantiation of nature's general tendency to take habits, or as he sometimes called this "the law of mind". Putting the word "person" into his definition thus was "a sop to Cerberus", a limitation of its true reach which he conceded in order to not turn people against the general idea. As a proponent of a biosemiotic understanding I am obviously not here in a position to throw the same sop to Cerberus whatever much it might still be needed. In stead I endorse the Brazilian Peirce scholar Lucia Santaella's interpretation of the Peircean sign that: "Since the three elements, sign, object, and interpretant, by themselves, or better, by their existential nature, may belong to various orders of reality as single objects, general classes, fictions, mental representations, physical impulses, human actions, organic activities, or natural laws, what constitutes the sign relation in its logical form is the particular way in which this triad is bound together" (Santaella-Braga 1999).

For illustration let us consider the human Y-chromosome. Analyzed in an overall process view this chromosome may be seen as a sign for maleness. Growing human embryos encountering the Y-chromosome in their genomic setup normally "knows" what to do about it, namely constructing a biologically male baby. Graphically we can depict this as a Peircean triadic sign process (a in figure 1) in which the Y-chromosome occupies the position of the primary sign, maleness stands in the position of the object, and the embryonic reading of the chromosome is the interpretant (b in figure 1). Looked upon in more detail what happens is that around the 7th week certain embryonic cells called epithelial sex cord cells for unknown reasons begin to express a gene (termed tdf) located at the Y-chromosome. This results in the production of a so-called testis-determining factor (TDF) (Gilbert 2000).

From there on, apparently, the male sex determination process is taken care of by these transformed cells.

What we see is that the organism acquires its male determination through a series of steps whereby semiotically competent cells "reads the messages" made available to them in part from their internal genetic make-up, and in part from the external biochemical context set by a multitude of cues (molecular signs) derived from neighboring cells or from other embryonic tissues. These contextual cues are received at specific receptors located in the plasma membrane. Stanley Salthe has used the term *system of interpretance* to indicate the integrated character of this web of often poorly understood interpretative mechanisms involved in even the most simple cases (Salthe 1993).

Put figure 1 about here

Even though all these processes may sooner or later be fully characterized at the biochemical level, this will not by itself exhaust our need for explanation. For obviously we are not dealing here with a haphazard mixture of biochemical processes but with a delicately organized system of processes. What we really want to know is the logic of the organization of these biochemical processes, and this logic has to do with their developmental function.

In figure 1 c-e, is shown three chained semiotic steps in the matrix of male sex determination. First an unknown biochemical event, perhaps the activation of a specific inducer, refers the epithelial sex cord cells to the tdf-gene (the object) by way of the binding of a transcription complex to the gene. Here the binding process occupies the position of an interpretant to the signal (c). This activates the tdf-gene to guide the formation of a new interpretant in the form of tdf-gene expression whereby testis-determining-factor (TDF) is produced (d). With increasing concentrations of TDF a level is reached such that further steps of embryonic processes are released in the chain of male sex determining semiosis (e). In each step the interpretant becomes a sign in yet a new semiotic triad.

Basically the triadic nature of this functional logic derives from the fact that the expression of the tdf-gene is undertaken only because some unknown signal provokes the cellular machinery to relate to the tdf-genes in a way which represents the historical relation of the unknown signal to those same tdf-genes. The sign points out a historically created relational logic of the macromolecular events. History is of essence in the semiotic analysis.

It should be noticed that semiosis as described here is actually sign *action* (Deely 1990). In science we are used to talking about actions in a dyadic sense of the word, as dynamical interaction or (coercive) "brute force" relating cause and effect. Action in this sense is also always involved as a central element in the actions of signs

(while reading this for instance numerous neural actions are performed in your brain, or so we hope) but the particular effect of sign action is the pointing out of an interpretant, i.e. signs do not just act, they point out actions which are related to something else (the object) in ways which is inherent to the system of interpretance. The Peircean sign in other words unites the formal and the functional aspects of action, it is both *logical node*, i.e. a triadic relation, and *material process*, i.e. semiosis. And for this reason the Peircean sign cannot be decomposed into three dyads. The positions in the triad are not logically equivalent since the interpretant is related both to the sign and to the object but in such a way that the relation to the object is grounded in the sign's relation to that same object<sup>5</sup>.

Biosemiotics insist on a view of process in which agency cannot be left out of analysis. Without denying the physical and chemical nature of biological processes biosemiotics claim that these processes when occurring in living systems are always organized into functional systems with an agential<sup>6</sup> character and that neither development nor evolution can be adequately accounted for as long as this aspect is not integrated in the conceptual structure of our explanations.

The developmental process depends on the proper function of a highly tuned set of semiotic checkpoints, i.e. cellular bifurcations controlled by recognition processes whereby tissues and organs communicate in time and space. The reduction of such semiotic checkpoints to dyadic relations of cause and effect not only complicates matters unnecessarily (since the organizational logic is triadic, not dyadic) but it also tends to blind us to the contextual character of the recognition processes. How cells respond to given signals often does not depend on the signal itself and neither on the cell, but on cellular history as well as the whole communicational setting into which the signal becomes situated. The proper level of description therefore is the triadic level of sign processes rather than the dyadic level of cause and effect.

#### THE EXTENDED MEMBRANE

The semiotics of DNA is inherently tied to the semiotics of the organism-environment interface. The surface of an organism (or an embryo) is the locus where it meets its environment and through which passes the cues which must be correctly interpreted in order to enjoy life and survive. I deliberately put in this "enjoy life" expression because I want to stress that, apart from highly peculiar human animals, survival does

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<sup>5</sup> The interpretant belongs to Peirce's category of Thirdness, whereas the sign is Firstness, and the object Secondness.

<sup>6</sup> i.e. systems exhibiting *agency* in the sense that the activities of the systems are tied to internal settings reflecting history of survival. The origin of agency was analyzed in (Hoffmeyer 1998b).

not normally enter the perceptual (or cognitive) universe of organisms, their *umwelts*<sup>7</sup>. Organisms may feel fear, they may flee, they may search for food, but they never try to survive, that's just the eventual outcome of their behavior. In other words "survival" is a descriptive category in evolutionary theory, and should never be ascribed to actual behavior, whether genetic or organismic.

For the organism the environment is that "reality" which it senses through the respective receptors situated at its surface and which it projects out into the world around it. The environment in other words is a kind of virtual reality or model of the world. As biologists we can try to unravel the characteristics of this virtual reality and eventually to understand its evolutionary role as a tool for survival. As such the virtual reality, the *umwelt*, has itself become molded by the evolutionary process tuning it to the motoric means of the organism as well as to its physiological and morphological needs (Hoffmeyer 2001b).

If we move inside the surface of a multicellular organism we run into new surfaces enveloping tissues, organs or single cells. Here again we meet virtual worlds constructed by the macromolecular machinery of the cells in order to cope with cellular environments. The cell membranes act as interfaces through which signs from the outsides are converted to cascading processes on the insides. Moreover in animals specialized cells from the immune system are relentlessly patrolling the body fluids thereby assuring the amazing swarm semiotic organization of bodies which may often consist of thousands of billions of cells. Located in the cell membranes of each of these cells are millions of specific receptor molecules ready to grasp whatever molecular sign might travel their way and prepare the cell on its changing situations in the "milieu interieur" of the body.

Should we move yet another step in through the cell membrane we immediately run into new membranes belonging to cellular organelles like mitochondria, chloroplasts, lysosomes, endoplasmic reticulum, golgi apparatus etc. The endoplasmic reticulum is composed of one continuous membrane, which ramifies through most of the cell. More significant in our context is that the space enclosed by the endoplasmic reticulum, as well as that enclosed by the Golgi apparatus, lysosomes, and transport vesicles, is topologically the same as the extracellular space (Barrit 1996). To these structural elements can be added the multitude of filaments forming the cytoskeleton, microtubules, intermediate filaments and actin filaments. It has been suggested that an even finer network of filaments, the microtrabecular lattice, penetrates the residual space between the intracellular membranes. A consequence of this is, that the

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<sup>7</sup> The term *umwelt* was introduced by the German biologist Jakob von Uexküll to denote the fundamentally subjective character of the animal's own perceptual world [Uexküll, 1982 [1940] #112]

topological ordering of biochemical processes becomes of key importance for understanding cellular activity.

Cellular membranes never form *de novo* by self-assembly of their constituents; they always grow, in an essentially homomorphic fashion, by accretion, that is, by the insertion of additional constituents into pre-existing membranes. The corresponding patterns are transmitted from generation to generation by way of the cytoplasm (e.g. of egg cells) which contains samples of the different kinds of cytomembranes found in the organism (de Duve 1991).

The ordinary textbook talk of DNA as governing cellular or even organismic behavior is therefore rather misleading. In fact if any entity should be thought of as a governor of cellular activity this should certainly be the membrane. DNA contains the recipes for constructing the one-dimensional amino acid chains, which form the backbones of enzymes, and among them the enzymes needed for catalyzing the formation of the constituents of lipid bilayers and assembling them. But whether these recipes are actually 'read' and executed by cellular effectors depends on membrane bound activity.

All major activities of cells are topologically connected to membranes. In the prokaryotes (bacteria) the plasma membrane (the active membrane inside the cell wall) is itself in charge of molecular and ionic transport, biosynthetic translocations (of proteins, glycosides etc.), assembly of lipids, communication (via receptors), electron transport and coupled phosphorylation, photoreduction photophosphorylation, and anchoring of the chromosome (replication) (de Duve 1991). In eukaryotic cells these tasks has been taken over by specific subcellular membrane structures of mitochondria, chloroplasts, the nuclear envelope, the Golgi apparatus, ribosomes, lysosomes etc. Many - if not all - of these membranes are themselves descendants from once free living prokaryotic membranes which perhaps a billion years ago became integrated into that co-operative or symbiotic complex of prokaryotic membranes which is the eukaryotic cell.

Membranes also are the primary organizers of multi-cellular life. The topological specifications necessary for growth and development of a multi-cellular organism cannot be derived from the DNA for the good reason that the DNA cannot 'know' where in the organism it is located. Such 'knowledge' has to be furnished through the communicative surfaces of the cells. Morphogenesis is mostly a result of local cell-cell interactions in which signaling molecules from one cell affect neighboring cells. Animal cells, for instance, are constantly exploring their environments by means of little cytoplasmic feelers called filopodia (filamentous feet) that extend out from the cell. These cytoplasmic extensions that drive cell movement and exploration are expressions of the dynamic activity of the cytoskeleton with its microfilaments and microtubules that are constantly forming and collapsing

(polymerizing and depolymerizing), contracting and expanding under the action of calcium and stress' writes Brian Goodwin(Goodwin 1995):36).

But not only are membranes involved in all the organized activities of the life sphere, the membrane can actually be seen as the principal locus for life itself (Hoffmeyer 1998b; Hoffmeyer 2000b)<sup>8</sup>. It's the membrane that creates the potential inside-outside asymmetry from which the organism-environment asymmetry must have grown out. The origin of life is by necessity also the origin of the environment, and lack of concern for this aspect of the origin problem has seriously hampered much theorizing on prebiotic evolution. Somehow the world became divided into organism and environment, and the formation of a closed membrane must have been part of this process. Here the membrane not only assures the necessary topological closure, but more significantly it takes on the role of an interface facilitating a flow of messages between its interior and exterior domains.

Considered from the point of view of the membrane prebiotic evolution is essentially a process of "interiorisation" (Hoffmeyer 2000b). Prebiotic membranes colonized the interior space and thereby scaffolded themselves through the formation of a multitude of autocatalytic metabolic loops and finally of replicative molecules mapping constituents of the internal autocatalytic system. Thus persistent architectures appeared as entities engaged in the trick of conjuring up a virtual reality at the inside for the purpose of coping effectively with the outsides.

On the background of this discussion it might be fruitful to introduce the term *the extended membrane* as the inner locus for life. The extended membrane encompasses the totality of membranes that make up an organism (including its skin, plumage, etc.) and is responsible for the actual execution of life as process, semiotic agency. It is the extended membrane that directs ontogeny in a selforganized process scaffolded by an internal system of 'labels', genes, kept orderly in the genome.

#### CODE-DUALITY

Claus Emmeche and I have suggested the term code-duality to grasp the over-all semiotic logic of reproduction and ontogenesis (Hoffmeyer and Emmeche 1991). Here the term code is used simply in the sense of a set of signs acting in concerted ways in a given context. Thus the genome may be seen as a digital code embracing the totality of DNA based - and thus sequential - signs, whereas most other sign processes in the natural world are analogically coded, i.e. their codification relies on the principle of likeness, such as e.g. the key and lock principle involved in the

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<sup>8</sup> The total area membranes in the human body (including subcellular membranes) is in the order of magnitude of one or several km<sup>2</sup> (Hoffmeyer 2000a) Most of the persons metabolism at rest is spent on upholding these widespread inner surface areas.

passage of messages across cell membranes. Analog coding necessarily implies spatial and temporal continuity.

Whereas the notion of the genetic code may have paved the way for our seeing the genome as a digitally coded string of labels, an inventory control system so to say, where single genes operate like menu topics whose activation occasions the delivery of specific protein resources, the idea of body dynamics as dependent on analogly coded sign systems may perhaps seem less obvious. And certainly Pattee's distinction between a linguistic and a dynamic mode bears this out. It is however important to stress the interdependence of the analog and the digital as two equally necessary forms of referential activity arising like twins in the individuation of that logic which we call life. The digital code is the seat for self-referential activity, i.e. the redescription in a sequential alphabet of all the macromolecular constituents of the organism, whereas the analog codes are engaged in non-self referential activity, i.e. the semiotic looping of organism and environment into each other through the activity of their interface, the closed membrane<sup>9</sup>. To claim that only the digital twin is semiotic whereas the analog twin remains in the sphere of classical dynamics is to block the only possibility for transcending Pattee's semantic cut position. Having emphasized (in the preceding section) the dynamic role of the extended membrane, i.e. the analog coded system, let me here clarify the distinctive role of the genetic or digital code system. As pointed out in (Hoffmeyer and Emmeche 1991) digital codes have at least three characteristic advantages which make them the obvious instruments for life's self-referential tasks. These three characteristics are:

#### *Freedom from the constraints of nature*

Digital codes allow for impossible messages because there is no strict binding between the code itself and the message it carries. In linguistic messages anything goes; Socrates may have lunch with Meryl Streep and the wives of pilots may give birth to children carrying wings. The same is true of genomes. Impossible genetic instructions are created all the time through processes of genetic recombination such as, e.g. crossing over, resulting in early abortions or the birth of non-vital descendants. The incredible combinatorial capacity of living systems for creating endless chains of novelties is due to this freedom.

#### *Objectivity and temporality*

Digital codes are codes for memory. Only because Plato wrote down Socrates' dialogues do we know them today. Had the dialogues not been coded in language but

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<sup>9</sup> here non-self should be understood as a hierarchical concept, i.e. at the cellular level other cells are 'non-self' whereas at the organismic level other organisms are 'non-self'

in pieces of mime they would probably have died with Socrates himself or would have survived a few generations at most. The key here is that digital codes are objective in the sense that they depend on a shared convention. Thus, Anthony Wilden pointed out the following distinction between analog and digital codes: "a digital code is 'outside' the sender and receiver and mediates their relationship; an analog code is the relationship which mediates them" (Wilden 1980) 173). Genomes are not normally thought to be outside the sender or the receiver, since they are normally exchanged via processes of mitosis or meiosis. But if, as we try to do here, life is seen as unfolding across membranes, then even the inside of the membrane is in a way an outside. The important thing in this context however is that DNA is actually protected from the vicissitudes of life by its relative chemical inertness and by a sophisticated apparatus of enzymatic repair systems. In many sexual reproducing species furthermore the germ line is kept separate from the somatic cell lines so that no Lamarckian inheritance is normally believed to take place. Digital codes thus are necessary to assure the temporal semi-stability needed for evolution - nothing can evolve if it is not remembered (because then we talk about substitution).

### *Abstraction*

Digital codes are eminent tools for the construction of meta-messages, i.e., messages necessary for interpreting other messages. Gregory Bateson showed that meta-messages may also be communicated in the analog as when young monkeys were engaged in so-called "play", i.e., an activity in which they exchanged signals similar to those seen during combat. As Bateson observed, when the monkeys snapped at one another while creating an imaginary combat situation, this snap would actually signify the following "meta-message": "this is not a bite" (Bateson 1972)177-193). The absence of a bite is announced by the presence of the snap. The snap is an indication of something that is *not* there. But Bateson also commented that this is probably as far as an analogically coded communication can go in the direction of the abstract category of "not". For real abstractions to take place digital codes are needed. We still do not know the full syntactic structure of the genetic code, but regulatory genes are examples of meta messages, and the occurrence of atavisms such as the three toed horse seems to indicate that exclusion is not the only way to get rid of outmoded ontogenetic instructions. Negation may suffice. Abstraction thus furnishes plasticity in the absence of which the evolutionary process might perhaps not have been as rich as it actually is.

These three essential aspects of digital codes not only make these codes indispensable tools for the evolutionary process but they also explain why digital codes are fundamentally passive. We do not believe in spells because there is no consistent way

that the mere pronunciation of words could cause desired physical events to take place, and likewise we should not believe that genes by themselves *do* anything. In both cases it takes an interpretant to mediate between the message and the active world, in both cases large amounts of "tacit knowledge" (in the sense of Polanyi (Polanyi 1967) are required by the system if the digital message shall be of any use (and the never-failing availability of this "tacit knowledge" was of course "taken for granted" when the message was first coined in DNA).

The invention of "digitallity", I have suggested, was the step which some 4 billion years ago allowed certain swarms of communicating closed membrane systems floating in the prebiotic mud to escape the indifference of the mere moment and to enter a temporal world of genuine selfhood (Hoffmeyer 2001a).

#### DEMYSTIFYING GENETIC INFORMATION

Current theories need "information flow" to recreate next generation writes Susan Oyama, "because we have been taught to see phenotypes themselves as evolutionary dead-ends, that information must pass by means of the germ cells, diminutive reproductive life boats, that must, if they can, abandon that doomed body before it goes down" (Oyama forthcoming). What really went wrong with the Weismannian separation of the germ line from the somatic line was not, however, so much the separation itself<sup>10</sup> as it was the implied reification of the digital code. Later generations of biologists repeated this fundamental reification, when they saw chromosomes, genotypes, DNA segments or so-called replicators as exerting causal power over heredity. The inherent preformationism of this view requires a causal power to reside in the replicator/genome, and this is where the metaphor of "information flow" enters the scheme. The preformationist assumption needs a causal agent to account for the ontogenetic miracle, and since this agent obviously cannot be the gene as a substantial structure the agent must reside in the gene in a hidden form, i.e. as information. By postulating that ontogeny is then caused by a transport process, whereby this information 'flows' from the genes to the unfolding body, the mystification is consummated. The in-built inconsistencies of the information concept as this concept is presently used in molecular biology has been thoroughly analyzed by Sahotra Sarkar (Sarkar 1996; Sarkar 1997)<sup>11</sup>.

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<sup>10</sup> As shown by Leo Buss strict Weismannian separation does in fact not occur in most taxonomic groups (Buss 1987)

<sup>11</sup> Sarkar draws the conclusion that the information concept has not been of any help to molecular biology and that there is in fact no need to transcend the well established conceptual system of biological chemistry. We draw the opposite conclusion and present an explicit semiotic understanding inside which so-called information is understood as signs or sets of signs, encoded messages.

As we can now see Weismannism did in fact have a healthy core, namely code-duality, i.e. the presence inside living entities of a separate, and fairly wellprotected, digitally organized system of signs directed specifically towards the need to control the production of the constituents of the entity itself. The appearance of multicellularity implied that no single cell would any longer need the whole self-referential system, rather differentiation implies a tissue specific inactivation of parts of the system (e.g. via chromatin modification such as methylation). The Weismannian separation of a specific totipotent germline at an early embryonic stage was one among other solution to this problem and became adopted as such by the species of most animal taxa.<sup>12</sup>

While this fact support the anti-Lamarckian intuition of Weismannism it does not by itself imply that the organism ends up as a dead end in the evolutionary process, although that was what Weismannism came to suppose. Code-duality implies no such thing, since it maintains that the ontogenetic process is the result of the interpretative activity of embryonic or somatic cells or of semiotically integrated living systems. Thus the deterministic ascription of causative power to the genome depends on an unjustified reification of this code as a replicator unit whereby its causative power is transformed from the indeterminate semiotic domain to the determinate biochemical domain.

We shall therefore suggest that the existence of a digitally coded and relatively independent system for self-reference is recognized as a very significant property of living systems. The role of DNA is not to govern the construction or activity of living systems, but it certainly does play a very special role in the semiotics of life. By seeing DNA as a truly unique but *semiotic* resource for the ontogenetic process it becomes possible to balance its uniqueness against its dependence on the semiotic competence of the extended membrane and thereby its dependence on organism-environment interaction.

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<sup>12</sup> That animals and not plants or fungi adopted early segregation as a strategy for assuring the interests of the multicellular system towards the potentially conflicting interests of somatic cell lines, may according to Leo Buss (Buss 1987) have been due to the absence of rigid cell walls in animal cells, which makes these cells mobile and thus capable of invading favorable positions in the embryo. Early segregation could not of course prevent mutant cell lines from exploiting this opportunity, but by monopolizing totipotence the eventual success of mutant cell lines in thus getting access to next generation would be eliminated.

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