3

Emergence and the human genome

George Gericke
Clinical Geneticist: AMPATH National Reference Laboratory,
Highveld Technopark, Centurion, South Africa.

Introduction

In human biology, interest in the phenomenon of emergence appears to be related to the emergence of life on earth, the evolution of modern human beings and the ascent (emergence) of human consciousness and free will. Of particular interest is the intricate relationship between certain human genomic characteristics and human behaviour. Some of us are also interested in causal principles and teleology, while others may deem these topics as being too esoteric for biologists. What do the concepts of 'emergence' and 'self-organisation' mean in terms of human genome functioning? Can continued unravelling of the mysteries of the human genome contribute to the development of thoughts relating to these matters? A meaningful attempt to address these issues requires both an understanding of the fundamental concepts of emergence and self-organisation, as well as a critical appraisal of how such information can be linked with genome processes in ways that could potentially contribute to the broader debate. These considerations are not traditionally within the purview of the biological scientist. Although it is necessary to be fully cognisant of the dangers of attempting to use information outside one's own field, it is nevertheless necessary to take into account as much as possible of the context within which the genome operates as an open system. Many of the ideas expressed in this document have been subjected to rigorous debate, or represent accepted scientific views. Note that some of the deductions presented here are based on the personal perspectives of the author and must be regarded as speculative.

Reductionism – which way?

Many biologists, with good reason, may be intuitively uncomfortable when holistic views dominate the discussion of complex systems in a way which appears to undermine a history of significant advances made via reductionist approaches. Stating that an emergent behaviour or state is not captured by the behaviour of the parts is a serious misunderstanding indeed. Collective behaviour, in this instance, is implicitly contained in the behaviour of the parts if they are studied in the context in which they are found. However, the concept of emergence of unpredictable radical novelty describes a totally unique global behaviour or state that arises from the interactions of the local parts, where the global behaviour cannot be traced back to known, prior actions of the individual parts. It is in the process of attempting to understand such a new picture, through the use of the fixed, available pieces of the puzzle, that we run into trouble, since the end product will no longer resemble the picture on the box. The first known 'reductionist' to hypothesise that matter can be broken down to smaller parts until a point is reached when the parts cannot be further divided was the ancient Greek philosopher Democritus, who coined the term atomos ('a', meaning 'not' and temnein, meaning 'to cut'). But modern science continued to cut even deeper than was thought possible and uncovered a strange new world of subnuclear particles. However, the noted quantum physicist and science philosopher, David Bohm, criticised reductionist views among his colleagues who assume that "… there seems to be an unshakable faith that either the known set of separately existent, indivisible, and unchangeable 'elementary particles', or some other kind yet to be discovered, will eventually make possible a complete and coherent explanation of everything" (Bohm 1980). Bohm continues: "Indeed, the attempt to live according to the notion that the fragments are really separate is, in essence, what has led to the growing series of extremely urgent crises that is confronting us today." Brian Goodwin (1994) describes a similar sentiment evolving among biologists: "The emergent qualities that are expressed in biological form are directly linked to the nature of organisms as integrated wholes; these can be studied experimentally and simulated by the use of complex non-linear models."

Genome emergence in the context of human intervention

Modern humans are instrumental in having created unique, nutritional, economic, cultural, intellectual and emotional contexts within which our genes are now expressed. Of profound importance is the extent of free will, a free will that emerged with our cognitive and consciousness traits. With the unprecedented technological advances made during the last century, for the first time a biological organism can, in theory, deliberately design its own future evolution. This is likely to remain limited by an ultimate unpredictability due to emergent novelties arising during the process. The effect(s) of a strong human strategic guiding influence, however, implies a tremendous moral responsibility to help shape future outcomes which will enhance the continued existence of life on earth. According to Stuart Kaufmann, "... we are beginning to see the first glimmerings of a new scientific world view ... which ... finds a natural scientific place for value and ethics, and places us as co-creators of the enormous web of emerging complexity that is the evolving biosphere and human economics and culture" (Kaufmann 2008). Even though the attainment of such lofty ideals may not be readily apparent in everyday life, it remains necessary to constantly define higher goals that we could work towards through willed effort.

Teleology?

Being *Homo sapiens*, we cannot easily shrug off teleological considerations. We need to consider the following: "How are we doing so far, and where do we want to go from here?" These issues may be more important for our survival than agonising about *why* we are here, and *how* did we come to be here, which, in terms of emergence principles, may not be traceable in retrospect (however interesting these burning questions will remain as challenges to be resolved). "One of the most moral acts is to create a space in which life can move forward" (Pirsig 1991). Another caveat is that we will have to carefully consider the appropriateness of the extrapolation of the principles of self-organisation and emergence as described in experimental physical, chemical and 'lower' biological systems to the way *thinking beings* act as active, participating agents. Even though self-organising processes are evident in terms of collective human behaviour, we *can* intuit/deduce probable unwanted outcomes of current events and trends, and link these with an ever-increasing technological ability to modify microlevel interactions, change or at least influence macrolevel outcomes (or vice versa?). When considering complex emergent characteristics of human thought and cultural dynamics, the principle of an acausal dynamics needs to be applied with circumspection. "Related to the supposed provisionality of emergents is the issue of their ontological status. Are emergent phenomena part of the real, authentic 'furniture of the world', or are they merely a function of our epistemological, cognitive apparatus with its ever-ready mechanism of projecting patterns on to the world"? (Goldstein 1999). Before we embark on a journey of discovery, it may be prudent to consider the wisdom of David Bohm's words (1994): "Thought is constantly creating problems ... and then trying to solve them. But as it tries to solve them it makes it worse because it doesn't notice that it's creating them, and the more it thinks, the more problems it creates." Knowledge is always provisional and our thoughts are not only stimulated, but also constrained by a (reductionist!) focus on spontaneous emergence and self-organisation in terms of complexity in the universe. Even though emergent processes are real and important, there remains a distinct possibility that they do not capture all the variables in current models. As stated by Louis de Broglie in the foreword to David Bohm's book *Causality and chance in modern physics* (1984), it is possible that: "... looking into the future to a deeper level of physical reality, we will be able to interpret the laws of probability and quantum physics as being the statistical results of the development of completely determined values of variables which are at present hidden from us". David Bohm's main focus in his work hinged on an attempt to develop a non-local, hidden variable deterministic theory whose predictions agreed perfectly with nondeterministic quantum theory.

Emergence and self-organising processes in relation to biology and evolution

A prime reason why it appears to be important for the geneticist to understand 'emergence' is based on the view that emergence addresses a component believed to be missing from Darwinian mutation and selection:

> ... if there is order for free – if you have complex systems with powerfully ordered properties – you have to ask a question that evolutionary theories have never asked: Granting that selection is operating all the time, how do we build a theory that combines self-organization of complex systems – that is, this order for free – and natural selection? There's no body of theory in science that does this. One thing we have to do is broaden evolutionary theory to describe what happens when selection acts on systems that already have robust self-organizing properties (Kaufmann 1995).

This is a feature of 'open-ended' evolution - 'novelty' appears outside our current experience or that of the system – Chris Lucas <www.calresco.org/genetic.htm> also believes that the concept of genetic 'selection', useful though it is in an isolated sense, can now be seen as just a passive simplification for what is always a complex, co-evolutionary and adaptive emergent system. This system makes use of dynamic self-organising processes and selection at many levels (chemical, regulatory, learning, co-evolutionary) and needs to be understood in a rather deeper sense than the shallow linear reductionism often employed by neo-Darwinists. Since genes operate according to the laws of physics and biochemistry, it is relevant to more closely examine the principles that operate in self-organising and emergent behaviour in complex systems. Genes interact extensively, so a resultant genotype representative of a particular biological organism needs to be considered, from a whole systems perspective, as an emergent dynamic whole. Although it is common knowledge that cellular systems are dynamic and regulated processes, to this date they are not adequately investigated and represented as such. The kinds of experimental techniques which have been applied in molecular biology underscored a material reductionism, which describes gene expression by means of molecular characterisation. Instead of trying to identify genes as causal agents for some function, role, or change in phenotype, these observations should instead be related to sequences of events. In other words, in systems biology, instead of looking for *a gene* that is the reason, explanation or cause of some phenomenon, an explanation has to be found in a causal *dynamics* (Wolkenauer 2001). In the context of a dynamical system, the concept of emergence has been studied via four main research approaches (Wolf & Holvoet 2005):

- ***Complex adaptive systems theory***, which explicitly uses the term 'emergence' to refer to the macro-level patterns arising from interacting agents.
- ***Nonlinear dynamical systems theory*** and ***chaos theory*****,** which promulgates the central concept of attractors, i.e. a specific behaviour to which the system evolves. One kind of attractor is the so-called strange attractor that the philosopher of science David Newman (1996) classifies as an authentically emergent phenomenon. There is a '*sensitive dependence on initial conditions*', where infinitesimally small first-order modifications can have unexpected outcomes with major effects.
- ***The synergetics school***, founded by the German physicist Hermann Haken (1981). This approach describes the idea of an order parameter that influences which macro-level coherent phenomena a system exhibits.
- ***Far-from-equilibrium thermodynamics***, which was introduced by Ilya Prigogine and which refers to emergent phenomena as dissipative structures arising at far-from-equilibrium conditions. The concepts of process, change and fluctuation, which play such a crucial role in the systems view of living organisms, are emphasised in Eastern mystical traditions.

Other study fields could be added to this list include*cybernetics*. The term 'cybernetic' [Greek *kybernetes*, pilot, steersman] was coined by the mathematician Norbert Wiener to encompass "the entire field of control and communication theory, whether in the machine or in the animal". This was in 1948 at the time general information theory as a scientifically well grounded concept was introduced by Claude Shannon. " ... In an extended sense, cybernetics may be said to include the timeliest applications of the quantitative theory of information" (McCulloch 1965). In *fractal science*, the main feature of self-generated complexity is the presence of an iterative mechanism which transforms the initial boundary limiting information to a new emergent with certain degrees of freedom ('*sensitive dependence on initial conditions'* as also found in chaos theory). Fractal processes exhibit properties such as self-similarity and scaling in time and space (Lebovitch & Shehadeh 2005).

In critically considering the meaning of emergence, it is useful to keep the essential features, as shown in Table I, in mind. It may be thought-provoking to constantly attempt to compare these principles with analogous biological phenomena, despite the fact that the terminology is different from the language traditionally used by biologists.

Table I

Essential components of the process of emergence

Scale – requires **critical mass** in the number of system elements (order emerges from many interactions over space and time).
Simplicity – requires that each element behave rather simply (difficult to construct elements to act on complete information). This is also a requirement for scalability in terms of fractal theory (see below).
Locality – requires interaction among "neighbours" attained in scale free networks.

Randomness – requires chance interactions among elements (optimises degree of information dissemination).
Feedback – requires ability to sense environmental conditions (allows some estimation of global state; positive and negative feedback).
Adaptation – requires that each element can vary its behaviour (allows system state to change with time)

Emergence: from cybernetics to thermodynamics

After Ilya Prigogine's 1977 Nobel Prize, scientific researchers started to migrate from a cybernetic view to a thermodynamic view of the concept of self-organisation. Both cybernetics and thermodynamics, however, remain useful constructs in the context of attempting to understand the emergence of unique features in self-organising systems. Since feedback from outside the system is also involved, complex systems cannot be closed. Also, according to the cybernetic relationship between endogenous goals and the external environment – Peter Corning <www.asc-cybernetics.org/foundations/cyberneticians.htm>. One of the most striking features of complex systems, especially in the biological realm, is their ability to modify their functioning according to context shifts (adapt). An adapted state refers to the need to reach a balance between selection of a specific behaviour and the consideration of a large variety of behaviours. An adapted state may also be viewed as a new emergent attractor. In a self-organising system, the emergence should be adaptive in order to have a system that self-organises in the presence of a changing situation (Glansdorff & Prigogine 1978). In biology, it is clear that the adapted (homeostatic) state in a healthy individual would not be indefinitely maintained owing to constant changes in the metabolic context. A system remaining in equilibrium will not possess the internal dynamics it needs to enable it to respond to its environment. A system in chaos ceases to function as a system. The most productive state to be in is at the edge of chaos, where there is maximum variety and creativity, leading to new possibilities. While the environment may not be causal, there are at least many influences that would influence emergence and self-organisation; in other words, how are energy demands met to drive these dynamic systems? Shalizi, CR (2001) states: "... self-organisation increases [statistical] complexity, (an increase in entropy due to an increase in interactive elements), while emergence, generally speaking, reduces it ..." Could emergence of a novel feature or state then represent an attractor, the homeostatic state attained when the non-closed space within which the self organising interactions occurred, for instance, runs out of energy? The process can then be reinitiated in relation to energy availability. According to Boltzmann's widely accepted reduction of the second thermodynamics law to a stochastic collision function, transformations from an incoherent to a coherent state are 'infinitely improbable'. Yet it is precisely the transformation of the incoherent into the coherent, the progressive ***emergence of new levels of*** macroscopic constraints, that brings the visible universe into being (Swenson 1989). Is this the life struggle observed through biological evolution to compete for energy in order to allow new emergents for sustenance of life on earth?

Open systems allow 'scaling' processes/Does 'scaling' open a possibility of higher order control?

In fractal theory, self-similarity implies that the patterns of fluctuations at faster time scales mimic the patterns of fluctuations at slower time scales. Scaling means that measures of the patterns (e.g. the amount of variability present) depend on the resolution (from cosmic to subatomic level), or the time scale at which the measurements have been taken. Assuming that we live in a highly interconnected universe, including features such as 'action at a distance' (quantum non-locality), and also assuming that these are purportedly thermodynamically open systems, this means that there is a 'vertically scaled' context within which these processes occur (ignoring 'horizontal' influences for the time being). Our observation all around us of order and organisational processes which are not under our control leads us to assume that there must be a Higher Level Entity/Person who is 'in control', although we can now observe that order may arise through *acausal processes.* Advances in semiconductor technology are contributing to the increasing complexity in the design of embedded systems and Abubakr and Vinay (2007) demonstrated that conceptually evolvable embedded systems can be characterised by an acausal nature. They noted that, in acausal systems, future input needs to be known, and they envisaged a mechanism such that the system predicts the future inputs and exhibits a pseudo-acausal nature. This led to their proposal of an embedded system that uses the theoretical framework of acausality. Their paper described a novel architecture that allows for hardware evolvability and autonomous behaviour alongside pseudo-acausality. While higher level properties are considered to display causal effects on the lower level, i.e. *downward causation*, the concepts of 'above' and 'below' are perhaps irrelevant in an information loop. Did the alchemists perhaps unwittingly have the right idea, even though traditional science would rather pretend the alchemists did not exist? The principle of *As above, so below is* regarded as one of the most important in all of alchemy, but is also a central principle of the new complexity sciences. In alchemy, the principle is more subtle, indicating a self-similarity both within and across different systems: of form, but also more appropriately, of forming processes. Despite the importance of this principle, which in its most general terms can be called a correspondence principle in both alchemy and complexity science, its usage in each context differs significantly – Seth Miller <www.academia.edu/.../As_Above_So_Below>. According to cybernetic modelling, the circularity arising from feedback loops imply circular self-scaling, i.e. no beginning and no end. We live in a quantum universe, and it is the 'quantum dance' of uncertainty which upsets our traditional thinking patterns. It is in the world of quantum physics that the strangest discoveries have been made and it is apparent that the very smallest subnuclear particles behave according to a very different set of rules of cause and effect. "In relativity, movement is continuous, causally determinate and well defined, while in quantum mechanics it is discontinuous, not causally determinate and not well defined" (Bohm 1980). In one sense, human beings are microcosms of the universe; therefore what a human being is, is a clue to the universe (Bohm & Hiley 2009). In other words, perhaps we need to be less sensitive about adopting an anthropocentric perspective in our attempts to try to understand the cosmos?

Human evolutionary considerations

Organismal DNA represents one level of interlinked, multilayered information system along the lines of David Bohm's concept of implicit order/an undivided whole. Exobiological research deals with the contiguity of life sciences using the tools of cosmology, physics, and chemistry (Flores & Raulin 1998). Biological evolution can perhaps be stated to reflect the process of optimising complex information – gaining mechanisms in different life forms. With more information, competitiveness for energy acquisition is increased (to sustain self-organising/emergent processes?). There are both vertical (time related) and horizontal influences (space-related competitiveness) at work. Speech, writing and reading in such a schema may be regarded as inevitable outcomes of a need for enhanced information management, linking information that has been compartmentalised externally to human individuals with an internal sensor and interpreter (the brain). Evolution of the human brain may thus have been required to fulfil the need for a suitable biological template with increased genetic and neural structure interconnections, which resulted in its ability to "look in on itself". This brain development was a necessity for linking "meaningfully" the information from internal and external compartments; effectively, a channel bandwidth increase for conveyance of information. The term 'autopoiesis' (from Greek αυτο- (auto-*'self'*, and *ποίησις (poiesis)*, meaning 'creation, production') was introduced in 1972 by the Chilean biologists Humberto Maturana and Francisco Varela to define the self-maintaining chemistry of living cells (Maturana & Varela 1973). Since then, the concept has also been applied to the fields of system theory and sociology. A related model – called structural coupling of autopoiesis – offers an interesting perspective on such processes. Autopoietic systems are 'structurally coupled' with their medium, embedded in a dynamic of changes that can be recalled as sensory-motor coupling. This continuous dynamic is considered as a rudimentary form of knowledge or cognition and can be observed throughout all life forms. Language is said to arise as a phenomenon proper to living systems from the reciprocal structural coupling of at least two organisms with nervous systems, and self-consciousness arises as an individual phenomenon from the recursive structural coupling of an organism with language with its own structure through recursive self-description.

Emergence vs self-organisation

When properly defined, emergence and self-organisation are not regarded as identical concepts (Wolf & Holvoet 2005). There may be instances of self-organisation without emergence and there may be instances of emergence without self-organisation. *Emergence* emphasises the presence of a novel coherent macro-level emergent property/behavior/structure, as a result of the interaction between micro-level parts. *Self-organisation* emphasises dynamical and adaptive increase in order or structure, without external control.

> The idea that the dynamics of a system can tend, of themselves, to make it more orderly is by Descartes, in the fifth part of his Discourse on Method. He presents it hypothetically, as something God could have arranged to have happen, if He hadn't wanted to create everything Himself. Descartes elaborated on the idea at great length in a book called Le Monde, which he never published during his life, probably to avoid reaction from organised religion. What Descartes introduced was the idea that the ordinary laws of nature ***tend*** to produce organization. In this vein, it has been indicated that it is a mistake to assume that the principle of self-organisation represents a break with a so called "Cartesian, mechanistic, reductionist tradition of science (Shalizi 2001).

Another contribution to a self-organising phenomenon in modern society comes from the 'invisible hand', a term coined by economist Adam Smith in his 1776 book *An inquiry into the nature and causes of the wealth of nations*. In this work, Smith states: "Every individual necessarily labours to render the annual revenue of the society as great as he can. He generally neither intends to promote the public interest, nor knows how much he is promoting it. By pursuing his own interest he frequently promotes that of the society more effectually than when he really intends to promote it." (Is this analogous to Dawkins' concept of the 'selfish gene'?) A full understanding of the link between emergence and self-organisation appears to remain an unresolved research question. Combining self-organisation and emergence in one system thus raises the question of how both phenomena should be linked to each other (Wolf & Holvoet 2005). A first point of view considers self-organisation as a *cause*, i.e. emergent properties in complex systems are the result of a self-organising process, possibly combined with selective pressures towards a certain emergent behaviour. Thus, the interactions between the individual entities are the self-organisation. *Self-organisation is situated at the micro-level of the emergent process.* A second point of view considers self-organisation as an *effect*, i.e. emergence results in self-organisation. Thus, in this view, self-organisation becomes an emergent property.

Why does self-organisation occur in complex systems?

In the scientific realm, knowing that self-organisation *can* occur in systems with certain qualities, is not inevitable, and it's still not clear *why* it sometimes does. In other words, no one yet knows the *necessary* and *sufficient* conditions for self-organisation – Ethan Decker <sev.lternet.edu/~bmilne/bio576/instr/html/SOS/sos.html>. Prigogine (1984) argued that macro-scale emergent order is one way in which a system dissipates micro-scale entropy creation caused by energy flux, but this view has no support in theory. There are a number of hypotheses about *why* self-organising systems move towards critical states, such as the law of maximum entropy production (Swenson 1989) and perpetual disequilibration (Ito & Gunji 1994), but these also have yet to move beyond conjecture. The two most likely mechanisms at this stage are generally considered to be natural selection and physical laws, such as spontaneous and successive symmetry-breaking, coupled with the progressive attraction of matter away from equilibrium (which appears to be the fundamental principle for transformation from an incoherent to a coherent state). This immediately raises the question of where, given the known laws of physics, such progressive goal-directed behaviour can come from (Swenson 1998):

(i) What universality governs the instability (symmetry-breaking) of the incoherent regimen?
(ii) What *extremum* principle governs the selection of microstates by the attractor?

System-induced symmetry breaking

In 'spontaneous' ordering, advantageous or disadvantageous characteristics may appear via a 'spontaneous' symmetry breaking. Stephens, Olmedo and Vargas (1998) postulated that adaptation can also occur due to an *induced* symmetry breaking by the action of genetic operators other than selection. What cause(s) internal to the system can be identified? One example that comes to mind concerns so-called fragile prone genomic regions associated with chromosomal and gene rearrangements during evolution, individual development as well as disease processes that occur when physiological thresholds are exceeded. Chromosomal 'fragile sites' are regions of the genome that exhibit altered DNA structures and chromosomal breakage with structural and functional diversifying consequences under conditions of cellular stress; a large number of genes can be involved in the process (Gericke 2006; Dillon et al 2013). In a network context, it was demonstrated that coordinated regulation of fragile gene expression occurs as a response to a stress stimulus in a manner similar to controlled chromosomal breakage and rejoining in the immune system to attain antibody diversity (Re et al 2006; Dillon et al 2013). In this regard, memory of novel input to the brain may be managed in a way that is similar to a foreign antigen-host antibody reaction; both involve pattern recognition and memory formation through the same genetic rearranging mechanisms (Gericke 2008, 2010). Many of the genes spanning the fragile site/rearranging regions have been functionally linked with the generation of antibody diversity and neural function, and it is now accepted that chromosomal breakage occurs during normal neurodevelopment (Yurov et al 2007; Gericke 2008).

'Nonlinearity/connectivity' is a characteristic of both self-organisation and emergence

Because emergence and self-organisation are often described in combination with each other, a characteristic specific for the combination of the phenomena is nonlinearity. In other words, the parts need to interact – parallelism is not enough. When there has been a nonlinear 'alignment' with positive feedback, the only possibility to escape that alignment, and end up in a new alignment that is adapted to the new situation, is to use negative feedback. In more complex self-organising systems, there will be several interlocking positive and negative feedback loops, so that changes in some directions are amplified, while changes in other directions are suppressed. Unanticipated, emergent structures can play a determining role in the evolution of such systems, which is why such systems show a great deal of unpredictability (Riley et al 2012). David Green (1993) believes that, in highly-connected landscapes, information travels very quickly and the system becomes more chaotic whereas, in sparsely-connected landscapes, the system quickly settles into a stable or periodic state. He suggests that the number of connections to each unit in a self-organising system might be the sole parameter that determines the self-organising dynamics of the system. Research on deterministic chaos performed at Duke University by Cavalcante et al (2010) focused on deterministic chaos exhibited by systems that can be efficiently modelled by Boolean networks. Boolean data represent the primary result of conditional statements which allow different actions and change informational flow if several cells are able to communicate. While differential equations have been used to develop accurate or predictive models of individual genes in a particular organism and context, Boolean networks modelling hundreds and thousands of interacting genes have been successful in capturing evolutionary aspects at the genome level (Kauffman 1995). This level of structural interaction is true for all complex systems - the interactions are a 'many to many' process, not a simple hierarchical control structure as traditionally envisaged. It is truly a highly nonlinear configuration, where feedback processes (both positive and negative) interact. Unlike most optimisation methods working from a single point in the decision space and employing a transition method to determine the next point, in a densely interconnected system, genetic algorithms work from an entire 'population' of points simultaneously. These genetic algorithms try many directions in parallel and employ a combination of several, genetically-inspired methods to determine the next population of points (Cantú-Paz & Goldberg 1999).

Lower level coding gene 'building blocks' and higher level networked regulatory switches

The genetic makeup of coding DNA results in an impressive redundancy, with many genes coding for the *same* protein, a feature which increases network robustness and protects against isolated mutations. Since many proteins have similar selective or functional effects, it becomes evident that genetic variation, in itself, does not guarantee any phenotypic variation on which selection may act. Furthermore, the number and structures of coding genes do not differ dramatically in genomes of different living beings. The ability to sequence complete genomes led to the realisation, for instance, that humans and worms have approximately the same number of protein coding genes and, more recently, that human and chimpanzee genomic-coding regions are 99.7% identical (Licatalosi & Darnell 2010). In the 1960s, while investigating regulatory proteins and the interactions of allosteric enzymes, Jacob and Monod introduced the distinction between 'structural genes' (coding for proteins) and 'regulatory genes', which control the rate at which structural genes are transcribed (Jacob & Monod 1961). This control of the rate of protein synthesis gave the first indication of such processes being most appropriately viewed as dynamic systems. The coding genes represent a linking element within a hierarchical as well as a horizontally networked information system and are themselves influenced by a whole range of upstream and downstream regulatory mechanisms. So even though all animals have basically the same set of genes, with gene crosstalk organised as a scale-free network, the combinatorial logical possibilities are almost infinite, because a few changes in the wiring network can lead to massive changes in emergence of new characteristics (de-Leon BT & Davidson 2007).

Nonlinearity and genome networks

How do overall features or traits arise if neither selection nor individual genes are specific enough? The answer appears to lie in the origin of nonlinear networks with many interacting components functioning as a higher level of self-organising processes. In the human brain, there are approximately 100,000 connecting neurons (interneurons) per neuron, compared with about 20,000 interneurons per neuron in the mouse (Wills 1993). So, although our genes are remarkably similar to other life forms, we are more 'interconnected', a feature which would allow emergence of new human-specific features. New brain regions appear to have evolved as a result of anatomical duplications. Increased structural and functional complexity required evolutionary recruitment of an increasing number of gene promoters (gene switches) as members of progressively intricate gene expression networks employing different patterns of expression of stable household genes. Gene copy number variation has been considered to underlie a significant proportion of normal human variation, including differences in cognitive, behavioural, and psychological features (Lee & Lupski 2006). Duplicated genes, and sometimes segmentally duplicated genomic regions harbouring a large number of different genes following chromosomal breakage mostly at the specific fragile sites alluded to above, are involved in network establishment in the genome. Two key evolutionary processes shaping genomic networks are (Berg et al 2004):

(i) Gene duplications – an initial event increases the probability of a second event.
(ii) Gain and loss of network interactions through mutations, which are referred to as 'link dynamics'.

Duplicate genes rapidly diverge in their expression profiles in the network and, compared with singletons, contribute to maintaining network robustness (Chung et al 2006). Also, according to modelling analyses, duplication plays an important role in feed-forward loop evolution (Cordero & Hogeweg, 2006). The organisation of low copy repeat segmental duplication segments within genes, when compared between humans and baboons indicate that, in humans, the duplications are similar in structure to baboon-duplicated segments, but with a much greater variation in size and are distributed to many more different genomic map positions (Goidts et al 2006). These features have been proposed to form the basis for species-specific network connections as key drivers of evolutionary change and complex behavioural phenotypes which arise as an emergent property of such networks (Anholt 2004). It has been found that regulatory circuits of development behave as evolutionary units (Boldogkoi 2004). These data demonstrate that: (1) instead of being based on the action of individual genes, gene networks are more likely to be responsible for the determination of traits and behaviours; and (2) evolution proceeds through continuous restructuring of the composition of gene networks (Boldogkoi 2004). The regulatory genome supplies an enormous computational capability with the capacity to process, in parallel, a vast number of regulatory inputs, and comprises many thousands of processing units that create a network (Ben-Tabou de-Leon et al 2007). Such principles may reflect the human ability to *combine and recombine* highly differentiated actions, perceptions, and concepts in order to construct larger, more complex, and highly variable units in a variety of behavioural domains including language, social intelligence, tool-making, and motor sequences (Gibson 2002). It has been suggested that speech development and visual interpretation are characterised by multipart representations formed from elementary canonical parts (e.g. phonemes in speech, geons in visual perception) (Corballis 1992). In these new combinations, they similarly gave rise later to the introduction of iconic symbols used in art, writing and reading when information management became too complex for gestures and oral traditions. The different levels cannot easily arise by means of standard mutation and crossover operations. Instead, they seem to require a new form of evolution, sometimes called 'compositional evolution', 'cooperative co-evolution', 'synergistic selection' or 'holistic Darwinism', that allows separately evolved functional building blocks to combine in modular fashion, improving overall combinatorial fitness.

RNA level networks can create novelty beyond DNA capability

RNA is formed on a DNA template and plays a role in transferring information from DNA to the cell's protein-forming system. The current belief is that biological complexity has RNA complexity at its core (Caetano-Anollés & Seufferheld 2013; Penn et al 2013). According to this view, it is the intricate unfolding of the genetic information in DNA into diverse RNA species – mediated by RNA-protein interactions – that leads to the biological variation that is not evident from the analysis of DNA sequence alone. It has been suggested that the RNA regulatory network of higher eukaryotes can re-wire itself, and that this network employs various and evolvable mutational strategies in response to external pressures enabling intracellular, RNA-mediated learning processes. In neurons, RNA is centrally involved in directing various epigenetic processes, implying that the transcriptional state of the cell is the primary determinant of epigenetic memory. Selected successful strategies and pathways may then be recorded (hard-wired) into the DNA genome via an enzyme, reversing transcriptase**.**

Understanding the 'interactome'

The existence of multiple interconnected biological information tiers in any individual complicates the full biological understanding of complex life forms. These tiers include: the 'traditional' human genome, with the transcribed genes (transcriptome), resulting proteins (proteome) and the resultant sum of metabolic features (metabolome); the altered breakage sited (fragilome); and the genetic linking factors (connectome) etc. Analysing the biology of an organism requires various combinations of these 'omic' features to derive a comprehensive understanding of systems biology. Insight into the full systems biology of any individual would also require elucidation of the features of our mitochondrial genome located in the cytoplasm of the cell as opposed to DNA's intranuclear habitat; it would also require the presence and effects of genomic endogenous retroviral and other sequences scattered throughout the noncoding part of the DNA molecule and our privately unique microbiomes (complement of bacterial genes) found at different body sites. These 'levels of influence' can be expanded, and of course are not *all* being investigated simultaneously and linked in this combinatorial fashion, even in current biological research. An excellent review of the 'interactome' concept was published in *Nature Genetics* (Barabási et al 2011). The potential complexity of the human interactome (all the interactions between biological entities in cells and organisms considered as a whole) is daunting. Understanding such links will help us understand how different medical disorders, often addressed by different medical subdisciplines, can be linked at the molecular level to help us understand why certain groups of diseases arise together (Barabási et al 2011).

Do emergents harbour memories of self-organising events?

Early attempts to identify "universal laws of form" in order to explain observed forms of living organisms and Plato's theory of forms appear to be in line with an idea put forward by Goethe: that a special status should be accredited to a key phenomenon to which all associated effects can be traced. Goethe called this an *Urphänomen*, or *Primal Phenomenon*. The genetic code may be another significant example of this assimilation of the primal into the derivative state (Barlow 2012). Because of the association of "universal laws of form" with Lamarckism the proponents of this view fell into disrepute until the early 20th century, when pioneers such as D'Arcy Wentworth Thompson revived them (Arthur 2006). *The modern understanding is that there are indeed universal laws (arising from fundamental physics and chemistry) that govern growth and form in biological systems.* According to David Bohm's theory of implicate and explicate orders, in the enfolded [or implicate] order, space and time are no longer the dominant factors determining the relationships of dependence or independence of different elements. Instead, an entirely different sort of basic connection of elements is possible, from which our ordinary notions of space and time, along with those of separately existent material particles, are abstracted as forms derived from the deeper order. These ordinary notions in fact appear in what is called the 'explicate' or 'unfolded' order, which is a special and distinguished form contained within the general totality of all the implicate orders (Bohm 1980). From the micro-level to the macro-level, the parts give rise to an emergent structure (see 'micro-macro effect' above). In the other direction, the emergent structure influences its parts. Coherence refers to a logical and consistent correlation of parts. Emergents appear as integrated wholes that tend to maintain some sense of *identity* over time (i.e. a *persistent* pattern). Are there historically derived *engramms* in Nature? "... Narrowly defined cybernetics is but the art of the helmsman, to hold a course by swinging the rudder so as to offset any deviation from that course. For this the helmsman must be so informed of the consequences of his previous acts that he corrects them – communication engineers call this 'negative feedback" (McCulloch 1965). What are 'forms'? Plato says that they are perfect templates that exist somewhere in another dimension. These forms are the ultimate reference points for all objects we observe in the physical world. They are more real than the physical objects observed by us – Michael Vlach <www.theologicalstudies.org/resource-library/philosophy-dictionary/158-platos-theory-of-forms>. Do these appear to us as the 'laws of nature'?

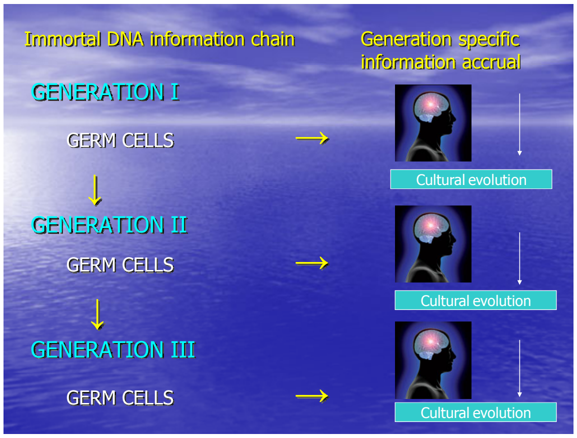
Retained memory is probably an important feature of evolutionary advances in system states or behaviours, in case the utility of the exploratory aspect for novelty is lost in the self-organising processes. Relevant considerations therefore include the following: Is a new (biological) state *completely novel*? Does it reflect the manifestation/uncovering of inherent hidden potential (Plato's *horseness* or Goethe's *Urphänomen*)? Or does emergence require interaction of these aspects? In biology, a central question for a long time was "Does ontogeny recapitulate phylogeny?" in the sense that many mammalian embryos were observed to bear a striking similarity to one another during the earliest stages of development. The Haeckelian form of recapitulation theory (Ernst Haeckel 1834-1919) German biologist, naturalist, philosopher, physician, professor and artist who discovered, described and named thousands of new species) is now considered defunct (Hall 2009). However, embryos do undergo a period where their morphology is strongly shaped by their phylogenetic position, rather than selective pressures. Fractal systems, too, evolve historically, meaning their past or history, i.e., their experience, is added onto them and determines their future trajectory.

Genomic memory

The genes that exist today reflect the set of environments that they have experienced in the past. This includes the internal environments provided by the bodies the genes have inhabited, and also external environments, desert, forest, seashore, predators, parasites, social companions, etc. When we are talking about development, it is appropriate to emphasise non-genetic as well as genetic factors (Dawkins 1999). While the poetic sounding statement is indeed true, neo-Darwinists still expect that random variation itself will remain sufficient to explain the emergence of novel features. The modern synthesis of evolutionary genetics in the 1930s to 1940s tended to entrench the view that genetic variation is random and stochastic, and not moulded by the environment. “For modern biology, there is no molecular mechanism enabling instructions from the environment to be imprinted into DNA directly, that is, without the roundabout route of natural selection. Not that such a mechanism is theoretically impossible. Simply it does not exist” (Jacob 1982, as quoted in Torrance 1994). A new compartment had to be created to deal with the ‘problem’ of explaining the transmission of cultural traits. The ‘meme’ was subsequently called into being to fulfil the need for a cultural descriptor that is transmitted by repetition in a manner analogous to the biological transmission of genes, yet passed from one person to another by non-genetic means (by imitation); “memes are the cultural counterpart of genes ‘meme’” 1976; *mīmeîsthai* to imitate, copy; coined by R. Dawkins (Blackmore 1999).

Figure 1

The traditional view of a unilateral flow of inherited DNA-based information from the germline to the soma (i.e. “the brain” in this instance). Cultural evolution is believed to occur in the non-biological realm and is ascribed to ‘meme flow’.



Gene-environmental interaction may in reality represent a more complex concept than extra-biologically compartmentalised memes operating as independent ‘units of imitation’ would allow. In his classic *Adaptation and natural selection: a critique of some current evolutionary thought* (1966), George Williams expressed the idea that, without genes to specify what constitutes an environment, environments would not exist. Furthermore, in the cultural realm, it is possible that the information continuum between genes, brain and environment may follow quantum rules and that such systems exhibit correlated properties that result in coordinated behaviour (entanglement) without signal transfer or interaction. Emergent cultural traditions in such a schema cannot be solely meme-based. In 1995, Stuart Kauffman (1995) developed a Boolean network called a ‘coupled fitness landscape’. To some extent, evolution is influenced by the decisions made by the life forms that comprise it; we change our destiny (say) by active decisions (conscious, unconscious or random as the case may be) which change the shape of our fitness landscape, and this, in turn, alters that of all the associated species: “we cannot study evolution on the basis that the fitness landscape is fixed and not altered by the organisms present, the full two-way co-evolutionary perspective is always necessary”. Could learned emergent properties be passed on biologically? The problem as usually stated is that the inheritance of any such ‘learned’ behaviours (as proposed by Lamarck) seems impossible, because there is no mechanism to incorporate such changes into the genes and only the germline genes (not the body) in fact survive. Lamarck adopted and elaborated a mechanism of variation and inheritance that was commonly accepted in the nineteenth century and which influenced generations of biologists, stretching into the early twentieth century. For example, in *On the origin of species*, Darwin repeatedly used the phrase ‘conditions of life’ and referred to the effects of use and disuse to explain the source of variation on which natural selection acts, much like the strengthening of brain synapsis during repetitive learning.

Epigenetics

Conflicting ideas about the influence of the environment on genomic processes arose, historically, through an inability to differentiate between genetic (Darwinian mutation and selection) and epigenetic (‘Lamarckian’ regulatory switching) functions (Morange 2002). The term ‘epigenetics’ was coined by Conrad Waddington (1949) to describe the mechanism by which multicellular organisms develop different tissue types from a single genotype, and how the environment influences this process; we now recognise that this process is associated with detectable molecular marks. Today, it is accepted that proteins, on binding to a DNA sequence, can alter the frequency and quality of genetic change that occurs in the coding part of the sequence. This represents a reverse flow of information from proteins to DNA. In neurophysiology, an analogy can be found in ‘Hebbian learning’, named after a concept introduced by Donald Hebb in his 1949 book *The organization of behavior*. The theory is often summarised as *cells that fire together, wire together*. According to Skrebitsky and Chepkova (1998), the frequency of use-dependent alterations in synaptic efficacy are believed to form the basis for complex brain functions because learning and memory significantly contribute to the development of neuronal networks through the formation of Hebbian synapses in cortical and hippocampal pathways. Pallas (2001) stated: "Afferent inputs direct the formation of their own processing circuitry, a possibility that has important implications for brain development, plasticity and evolution." So, although our brain function is heavily influenced by inherited stable coding gene functioning required for basic metabolic functions, there is another layer of learned, environmentally-induced effects on brain gene expression. In recent years, the plasticity of the phenotype, including neurodevelopment, has become recognised as a key element in the evolution of species also (West-Eberhard 2003). In this sense, the 'genome learns from its experience' as indicated in the poem, *Children live what they learn.* Based on frequency dependent neuronal input during neurodevelopment, children assume certain characteristic behavioural traits as adults when the environment interacts in highly specific ways with their inherited brain gene repertoire.

Memory appears to be built on novelty-induced brain DNA structural alterations

In the brain, structural genetic rearrangement appears to be closely linked with sensory experiences that physiologically invoke the stress and fear circuitry pathways, even under normal circumstances (Cui et al 2008). The emerging idea is that lifelong behavioural memory storage may involve lasting changes in the physical, three-dimensional structure of DNA itself (Gericke, 2010). From his quite different perspective, David Bohm (2002) remarkably states: "... the manifest content of consciousness is based essentially on memory, which is what allows such content to be held in a fairly constant form. ... there will be a strong background of recurrent stable, and separable features, against which the transitory and changing aspects of the unbroken flow of experience will be seen as fleeting impressions that tend to be arranged and ordered mainly in terms of the vast totality of the relatively static and fragmented content of memories". The recombinase activation gene RAG-1 involved with immune recombination (antibody diversification) in white blood cells has also been localised in neurons in the brain regions that are involved in spatial learning and memory and the modulation of emotionally relevant information (Cushman et al 2003). The processes involving genomic rearrangement following breakage at chromosomal fragile sites in the brain thus appear to be similar to immune-like modular rearrangement of antibody components associated with pattern recognition and memory formation in the immune system. Under circumstances of excessive intrauterine traumatic stress-inducing experiences, 'unstable', immune-like chromosome rearranging processes in the brain may result in immune activation with neuro-inflammatory and auto-immune sequelae in later life (Dietert & Dietert 2008).

Runaway brain evolution requires a compound interest approach for information storage

Since *Homo habilis* first handled stone tools ~2.5 million years ago with an unprecedented increase in brain capacity during this species' existence, and since the advent of modern humans – generally believed to be about 100,000 years ago – there since appears to have been a logarithmic surge, particularly in recent times, of more widely distributed gains in intelligence and creativity. A significant further advance can be observed to have occurred during the Renaissance and the Age of Reason/Age of Enlightenment. The human species attained 'runaway' characteristics that enabled the growth of scientific analysis, with its enormous impact on human culture in the 100 to 150 years preceding current times (Wills 1993). What could have contributed to these increasingly accelerated developments in the brain? One explanation could lie in our increased ability to relay lifetime gained information to the germ cells with an exponential growth in stored information, similar to a compound interest scenario when investing money. This line of thinking is in direct opposition to the findings of August Weismann in 1883 (Stanford 2005), who claimed that this direction of informational flow was not possible.

About 70 years ago, the Swiss psychiatrist Eugen Bleuler actively pursued an existing, systematically developed theory in Europe called *mnemism* (Möller & Hell 1999). According to mnemism, all organic life – independent of the possibility of a self-reflecting consciousness – is able to learn experiences made by an analysis of environment and to pass this learning on to following generations. The assumption of the efficacy of specific, not necessary consciously remembered *engramms* of memory, allows a concept of mnemic memory to be compatible with the concept of collective unconscious put forward by Jung. Jung believed that the archetypes of the collective unconscious not only have a powerful influence on the behaviour of individuals, but also govern large-scale historical movements. From this point of view, entire nations and cultural groups might be enacting, in their behaviour, important mythological themes. In the decade preceding the outbreak of World War II, Jung found in the dreams of his German patients many elements from the Nordic myth of Ragnarok, or the twilight of the gods. From these observations he concluded that this archetype was emerging in the collective psyche of the German nation; he also accurately predicted that it would lead to a major world catastrophe which would ultimately turn out to be self-destructive (Grof 1995). In *Moses and Monotheism*, Freud writes, "when I speak of an old tradition still alive in a people, of the formation of a national character, it is such an inherited tradition, and not one carried on by word of mouth that I have in mind ..." (Freud, S 1939). Similar psychohistorical influences implying transgenerational memories, underlying some current conflicts, have also been brought to light in the theories of war historians such as Volkan (Volkan 1979).

Brain to germline information feedback to pass on to future generations?

A compound interest type of information accumulation facilitating 'runaway brain evolution in modern man is more likely to have happened with a strong brain to germline information feedback loop. This concept is still highly controversial and not considered likely by the majority of molecular biologists. But is it *possible* that mechanisms have evolved to transfer individual-acquired brain information to germline genetic information management systems? The latter would then be expected to also play a major role in specifying the type of brain that would be needed. A survey of positively selected genes in the genomes of humans and chimpanzees indicated that genes with maximal expression in the brain show little or no evidence for positive selection, while genes with maximal expression in the testis tend to be enriched with positively selected genes. Many of the genes that present a signature of positive selection in the evolution of the human lineage are involved in sensory perception and spermatogenesis (Nielsen et al 2005). Recent brain evolution may thus have accelerated through significant network modification in the germline. All of this may be aimed at ensuring strong, competitive selection for brain modifying genes. Additional findings underscore the importance of the linkage of germline and somatic genomic rearranging events (Cunningham et al 2003), the identification of translin (testis-brain RNA-binding protein) recognition sites at breakpoints (Gajecka et al 2006) and the finding that DNA-damaging reagents initiate a signalling pathway for the active nuclear transport of translin, support the hypothesis that translin has a pivotal function in recognition of the generated single-stranded DNA ends following staggered breaks at recombination hotspots (Kasal et al 1997). Stated differently, the brain may (only) represent an organ that is required by the germline to enrich/diversify the immortal information chain running from generation to generation. In this role, consciousness of 'consciousness' is obviously an asset. Consciousness would then be something the brain may become aware of, if not primarily located within the brain itself. David Bohm believed that the working of the brain, at the cellular level, obeyed the mathematics of certain quantum effects. He therefore postulated that thought was distributed and non-localised in the same way that quantum entities do not readily fit into our conventional model of space and time (Bohm & Hiley 2009).

Germ cell neurotransmitters

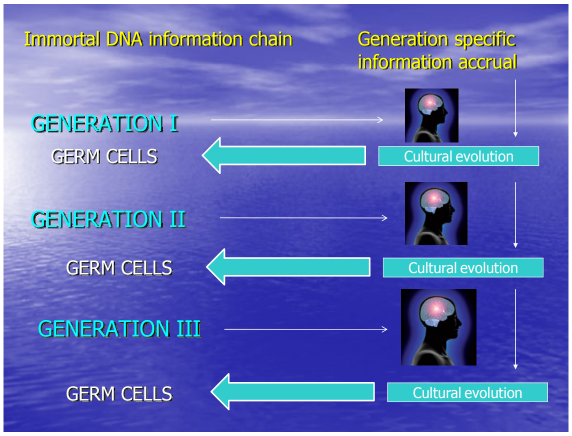
There is evidence for common neurotransmitter signalling molecules in neurons and sperm (Schuel & Burkman 2005). Many neuropeptides operate as local regulators of testicular germ cell development and function (Li & Arimura 2003; Lewis & Maccarrone 2009). Do the brain and gonadal neurotransmitters operate in series or in parallel? Do gonadal cells directly pick up the same environmental cues and process them on a different level than the brain, or is brain-processed information relayed to germ cells utilising certain signalling processes (e.g. the immune-like mechanism considered below)?

Germline immunoglobulin (antibody) genes capture acquired information from antigen-antibody interaction

If immune antigen-antibody events can be transmitted to the germline to be inherited by future offspring to protect against re-exposure to the same antigens, and if the brain uses a similar immune-like pattern recognition and memory system, can brain-stored survival information also be transmitted to the germline? Only about half of the human germline V antibody repertoire has been used in mature immunoglobulin V(D)J rearrangement, so there appears to be further capacity for information storage (Weiller et al 1998). A major part of acquired information could be silenced (methylated) and stored in a 'repository' to enable future activational recall if required. Genetic buffering represents a means whereby a species may accumulate a significant amount of unexpressed genetic potential for reacting to changes in environmental conditions (Rutherford & Lindquist 1998). This could imply that there is a need for the germline to play a major role in informational silencing of a maintained excess informational load which could, theoretically, be stored in RNA caches and managed as RNA mediated epigenetic programming of genome rearrangement pathways, broadly similar to findings in the ciliate organism *Oxytricha trifallax* (Nowacki et al 2008). In humans, the prolonged influence exerted postreproductively on the type of environment in which younger individuals may transmit their acquired behavioural response experiences (memories) to the germlines of their offspring may result in a behavioural selection process operating transgenerationally (Graves 2001). Our changing environmental context actively selects gene activity and our behaviours – which then, in turn, determine our next environmental context and the subsequent genetic processes. This mutual triggering effect is the 'structural coupling' of autopoietic thought and is an active and increasingly recognised area of modern biological research (Maturana 1975). Jablonka and Lamb (2002) summarised a body of work suggesting that 'heritable epigenetic variations' are advantageous "when organisms live in environments in which certain traumatic events occur regularly but unpredictably, … by favouring the preparation of offspring for exposure to repeated similar environmental exigencies."

Figure 2

Proposed bidirectional information flow: a) accepted germline to brain flow of inherited DNA-based germline information and b) unproven brain to germline flow of individually acquired information trapped in DNA higher order structures, suggested to enable a compound interest type of information accrual which has been responsible for recent runaway brain evolution (See discussion). In such a model, cultural evolution would straddle DNA based germline biological feedback and non-biological intergenerational meme flow.



Teleological considerations – free will to design a better future life on earth?

We are regularly confronted with a repeated iteration of the most extreme levels of mindless violence – both in real life and in computer games; science fiction, today, is based on contrived soap opera plotting and provides us with bleak depictions of post-apocalyptic decay. To what extent does depression and criminal behaviour in youth reflect an increasing unease in their collective unconscious as a result of this constant and unprecedented bombardment of symbols of violence, death and destruction during sensitive neurodevelopmental phases in the human brain? When we write these computer games and create these negative images, will the games/soap operas/science fiction/post apocalyptic doom depictions also 'write us' – i.e. is this the way we *want to* define ourselves, because then future biological life *will* in all likelihood mirror this? "Wenn du lange in einen Abgrund blickst, dann blickt der Abgrund auch in dich hinein" – "If you gaze long into an abyss, the abyss gazes also into you" (Friedrich Nietzsche (1844-1900)). We urgently need to assess and rectify, if necessary, the future semiotics which may influence human behaviour and societies. "Many of the people with whom we have worked saw humanity at a critical crossroad facing either collective annihilation or an evolutionary jump in consciousness of unprecedented proportion" (Grof 1988). This may, however, not be possible. Not enough people may subscribe to this ideal since, every day, most people simply have to fight in order to survive. What worked before (cunning and deceit) still seem to be required at certain levels of society (if not to fight poverty, then to fuel greed), but these qualities are now putting our future at risk. Stanislav Grof (1988) continues "… if a sufficient number of people undergoes a process of deep inner transformation, we might reach a level of consciousness evolution that will bring us to the point of deserving the name given to our species – Homo sapiens". How many people would be required for such behaviour to become an 'attractor'? Critical mass models have become a major part of theoretical sociology's literature on crowd behaviour and collective action.

Can we shape future neurobehavioural evolution by managing our semiotics?

"More than any other social species we engage in collective thinking, and in doing so we create a world of culture and values that becomes an integral part of our natural environment. Thus biological and cultural characteristics of human nature cannot be separated. Humankind emerged through the very process of creating culture and needs this culture for survival and further evolution" (Capra 1982). Semiotics is an investigation into how meaning is created and how meaning is communicated. It is a way of seeing the world, and of understanding how the landscape and culture in which we live have a massive impact on all of us unconsciously. Our sense of self as a constancy is a social construction which is 'over-determined' by a host of interacting codes within our culture (Chandler 2007). In the process of adopting a 'way of seeing', we also adopt an ‘identity’. Biosemiotics (from the Greek *bios* meaning ‘life’ and *semeion* meaning ‘sign’) is a growing field that studies the production, action, and interpretation of signs and codes in the biological realm. Biosemiotics attempts to integrate the findings of scientific biology and semiotics, proposing a paradigmatic shift in the occidental scientific view of life, demonstrating that semiosis (sign process, including meaning and interpretation) is its immanent and intrinsic feature – The International Society for Biosemiotic Studies (ISBS) <biosemiotics.org/>.

Mastering moral deficiencies through programmed machine interaction?

Most transhumanist views seem to be pessimistic and apocalyptic, and focus on a time when machines may transit to a ‘runaway positive feedback loop’ in high-level autonomous computation. On the other hand, we may not be able to overcome the evolutionary mismatch of an advanced intellect hampered by low-level emotional control *without the assistance of machine-enhanced moral behavioural brain programming* to keep political and other leaders on ‘the straight and narrow’ with regard to their responsibilities towards the societies they are supposed to serve. Evolution has made us big-brained and small-jawed – this reflects a preferred transition to intellectual rather than physical competition for energy resources. Yet, without adequate mature emotional control mechanisms, we still resort to techniques of cunning and deceit and destruction. A more useful scenario could relate to enhanced and interdependent human-machine interfacing to overcome the dangers to society inherent in the ‘Machiavellian’ hypothesis of human brain development which includes strategies of achieving social success through the use of deception, manipulation, alliance formation, exploitation of the expertise of others, etc. (Gavrilets & Vose 2006). This is reminiscent of a Survivor Earth reality show in which we all star. Will we be deluding ourselves when considering such technologically assisted interventions because too many variables will remain outside our control and life will keep self-organising on its own despite our grand intentions? Should we attempt to attain an optimal future through the stringent application of leadership based on principles known to be important in directing (optimising) the behaviour of self organising systems, albeit *with* machine assistance *or* ‘unplugged’?

Concluding remarks

Through an appreciation of the functioning of our genome, with its full ramifications, and by accepting our responsibility in terms of moulding the future context in which the contained and novel added information will unfold in the genome, we can participate with a stronger commitment to our emerging destiny. My motivation has been somewhat similar to Murphy and Ellis’s reasoning in their book *On the moral nature of the universe,* where they strive to develop a comprehensive vision of humanity’s place in the cosmos, as well as an understanding of the process of discovery and an account of hierarchies and dual control (Murphy & Ellis 1996), which also bear on the phenomenon of emergence. These authors affirm that the complexity of reality allows for causation to occur both from the top down and the bottom up, which makes room for higher level/‘divine’ action as well as human freedom. But ‘cause’ and ‘effect’ and teleology remain complex considerations:

> The most valuable feature of the cybernetical analysis of phenomena in general, and of second order cybernetics in particular is that it leads us not to think in terms of single causes and effects, but rather of equilibria between constraints. This helps to avoid the widespread illusion that we could gather ‘information’ concerning a reality supposed to be causing our experience; and it therefore focuses attention on managing in the experiential world we do get to know. In terms of teleological considerations, the future cannot be assessed or measured from a desired future end-state of the present action, but from the representation of a state such actions have reliably produced in the past (Von Glasersfeld E 2000).

This includes actions we should actively try to avoid in order to create a better type of future, at least as far as the component is concerned that may be influenced by human control.

Works consulted

Abubakr, M & Vinay, RM. 2007. *Architecture for Pseudo Acausal Evolvavle Embedded Systems.* Cornel University Library. arXiv.org>cs>arXiv:0704:0985.

Anholt RR. 2004. Genetic modules and networks for behavior: lessons from Drosophila. *Bioessays* 26(12):1299–306.

Aoki K., Inazawa J., Takahashi, T., Nakahara, K. & Kasai, M. 1997. Genomic structure and chromosomal localization of the gene encoding translin, a recombination hotspot binding protein. *Genomics* 15:43(2):237-41

Arthur, W. 2006. D'Arcy Thompson and the theory of transformations. *Nat Rev Genet* 7(5):401-6.

Barabási, AL., Gulbahce, N., & Loscalzo, J. 2011. Network medicine: a network-based approach to human disease. *Nat Rev Genet* 12(1):56-68.

Barlow, PW. 2012. The primal integrated realm and the derived interactive realm in relation to biosemiosis, and their link with the ideas of J.W. von Goethe. *Communicative & Integrative Biology* 5(5):434-439

Ben-Tabou de-Leon, S., Davidson, EH. 2007. Gene regulation: gene control network in development. *Annu Rev Biophys Biomol Struct* 36:191.

Berg, J., Lässig M., Wagner, A. 2004. Structure and evolution of protein interaction networks: a statistical model for link dynamics and gene duplications. *BMC Evol Biol* 4(1):51.

Blackmore, S. 1999. The Meme Machine. New York: Oxford University Press.

Blanden, RV., Rothenfluh, HS., Zylstra, P., et al 1998. The signature of somatic hypermutation appears to be written into the germline IgV segment repertoire. *Immunol Rev* 162:117–32.

Bohm, D. 1980. *Wholeness and the Implicate Order*. London: Routledge.

Bohm, D. 1984. *Causality and Chance in Modern Physics*. London: Routledge 978-0-415-17440-4.

Bohm, D. 1994. *Thought as a System*. London: Routledge .

Bohm, D. 2002. *Wholeness and the Implicate Order*. London: Routledge.

Bohm, D. & Hiley, B. 2009. *The Undivided Universe: An Ontological Interpretation of Quantum Theory, Taylor & Francis e-library*, first edition. London: Routledge.

Boldogköi, Z. 2004. Gene network polymorphism is the raw material of natural selection: the selfish gene network hypothesis. *J Mol Evol* 59(3):340-57.

Caetano-Anollés, G. & Seufferheld, MJ. 2013. The coevolutionary roots of biochemistry and cellular organization challenge the RNA world paradigm. *J Mol Microbiol Biotechnol* 23(1-2):152-77.

Cantú-Paz, E. & Goldberg, DE. 1999. On the scalability of parallel genetic algorithms. *Evolutionary Computation* 7(4):429-449.

Capra, F. 1982. *The Turning Point: Science, Society, and the Rising Culture*. New York: Simon and Schuster.

Cavalcante, HL de S., Gauthier, DJ., Socolar, JES. & Zhang, R. 2010. On the origin of chaos in autonomous Boolean networks. *Philos Transact A Math Phys Eng Sci* 28:368 [1911]:495-513.

Chandler, D. 2007. *Semiotics: The Basics*. Routledge, London.

Chung, WY., Albert, R., Albert, I., et al 2006. Rapid and asymmetric divergence of duplicate genes in the human gene coexpression network. *BMC Bioinformatics* 7:46.

Cohen, Robert, S. & Marx W. Wartofsky (eds.) 1973. Boston Studies in the Philosophy of Science 42. ([1st edition 1973]. Dordecht: D. Reidel Publishing Co.

Corballis, MC. 1992. On the evolution of language and generativity. *Cognition* 44(3):197-26.

Cordero, OX. & Hogeweg, P. 2006. Feed-forward loop circuits as a side effect of genome evolution. *Mol Biol Evol* 23(10):1931–6.

Corning, P. American Society for Cybernetics: Notable cyberneticians. www.asc-cybernetics.org/foundations/cyberneticians.htm. Accessed 28/04/2013.

Cui, H., Sakamoto, H., Higashi, S., et al 2008. Effects of single-prolonged stress on neurons and their afferent inputs in the amygdala. *Neuroscience* 152(3):703–12.

Cunningham, LA., Cote´, AG., Cam-Ozdemir, C., et al 2003. Rapid, stabilizing palindrome rearrangements in somatic cells by the center-break mechanism. *Mol Cell Biol* 23(23):8740–50.

Cushman, J., Lo J., Huang, Z., Wasserfall, C., & Petitto, JM. 2003. Neurobehavioral changes resulting from recombinase activation gene 1 deletion. *Clin Diagn Lab Immunol* 10(1):13-8.

Dawkins, R. 1989. *The Selfish Gene*. Oxford University Press.

Dawkins, R. 1999. *The Extended Phenotype*. Oxford University Press.

Decker, EH. Landscape Ecology & Macroscopic Dynamics: Self-Organizing Systems. sev.lternet.edu/~bmilne/bio576/instr/html/SOS/sos.html. Accessed 05/05/2013.

Dietert, RR., Dietert, JM. 2008. Potential for early-life immune insult including developmental immunotoxicity in autism and autism spectrum disorders: focus on critical windows of immune vulnerability. *J Toxicol Environ Health B Crit Rev* 11(8):660–80.

Dillon, LW., Pierce, LC., Ng, MC. & Wang, YH. 2013. Role of DNA secondary structures in fragile site breakage along human chromosome. *Hum Mol Genet* 1;22(7):1443-56.

Flores, JC., & Raulin, F. 1998. *Exobiology: matter, energy, and information in the origin and evolution of life in the universe : proceedings of the Fifth Trieste Conference on Chemical Evolution: an Abdus Salam memorial*, Trieste, Italy, 22-26 September 1997. Dordrecht: Kluwer Academic Publishers.

Freud, S. 1939. *Moses and Monotheism*. Translated from the German by Katherine Jones. Hogarth Press.

Gajecka, M., Glotzbach, CD. & Shaffer LG 2006. Characterization of a complex rearrangement with interstitial deletions and inversion on human chromosome 1. *Chromosome Res* 14(3):277–82.

Gao, JB., Cao, YH., Tung, WW. & Hu, J. 2007. *Multiscale Analysis of Complex Time Series: Integration of Chaos and Random Fractal Theory, and Beyond*. Hoboken, NJ: Wiley Interscience.

Gavrilets, S. & Vose, A. 2006. The dynamics of Machiavellian intelligence. *PNAS* 103(45): 16823–16828

Gell-Mann, M. 1994. *The Quark and the Jaguar.* WH. Freeman, New York, USA.

Gericke, GS. 2006. Chromosomal fragility, structural rearrangements and mobile element activity may reflect dynamic epigenetic mechanisms of importance in neurobehavioural genetics. *Medical Hypotheses* 66:276-285.

Gericke, GS. 2008. An integrative view of dynamic genomic elements influencing human brain evolution and individual neurodevelopment. *Medical Hypotheses* 71:360-373.

Gericke, GS. 2010. Common chromosomal fragile sites may be involved in normal and traumatic cognitive stress memory consolidation and altered nervous system immunity. *Medical Hypotheses* 74(5):911-8.

Gibson, KR. 2002. Evolution of human intelligence: the roles of brain size and mental construction. *Brain Behav Evol* 59(1-2):10-20.

Glansdorff, P. & Prigogine, I. 1978. *Thermodynamic study of structure, stability and fluctuations*. Wiley, New York.

Goidts, V., Cooper, DN., Armengol, L. et al, 2006. Complex patterns of copy number variation at sites of segmental duplications: an important category of structural variation in the human genome. *Hum Genet* 120(2):270–84.

Goldstein, J. 1999. Emergence as a Construct: History and Issues. *Emergence* 1(1):49-72.

Goodwin, B. 1997. *How the Leopard Changed Its Spots: The Evolution of Complexity*. Scribner, 1994.

Goodwin, BC. 2000. The life of form. Emergent patterns of morphological transformation. *Comptes rendus de l'academie des sciencies III - Sciences de la vie-life sciences* 323 (1):15-21.

Graves, JA. 2001. From brain determination to testis determination: evolution of the mammalian sex-determining gene. *Reprod Fertil Dev* 13(7–8):665–72.

Green, DG. 1993. Emergent behaviour in biological systems. in D. G. Green and T. J. Bossomaier (eds.), *Complex Systems - From Biology to Computation*. IOS Press, Amsterdam.

Grof, S. 1988. *Human Survival and Consciousness Evolution* (SUNY Series in Transpersonal and Humanistic Psychology). State University of New York Press.

Grof, S. 1995. Consciousness Evolution and Planetary Survival: Psychological Roots of Human Violence and Greed. Paper presented at the Thirteenth International Transpersonal Conference entitled Spirituality, Ecology, and Native Wisdom in Killarney, Ireland, June 1995. www.stanislavgrof.com/pdf/ConsciousnessEvolution.pdf.

Hall, BK. 2009. Embryos in evolution: evo-devo at the Naples Zoological Station in 1874. *Theory Biosci* 128(1):7-18.

Hebb, DO. 1949. *The Organization of Behavior: A neuropsychological theory*. New York: Wiley.

Hsu, E., Pulham, N., Rumfelt, LL., et al 2006. The plasticity of immunoglobulin gene systems in evolution. *Immunol Rev* 210:8–26.

Ito, K. & Gunji, Y-P. 1994. Self-organization of living systems towards criticality at the edge of chaos. *Biosystems* 33:17-24.

Jablonka, E., Lamb, MJ. 2002. The changing concept of epigenetics. *Ann N Y Acad Sci* 981:82-96.

Jacob, F. & Monod, J. 1961. Genetic regulatory mechanisms in the synthesis of proteins. *J Mol Biol* 3:318-356.

Kaufmann, S. 2008. *Reinventing the Sacred: A New View of Science, Reason, and Religion*. New York: Basic Books.

Kauffman, S. 1993. *The Origins of Order: Self-Organization and Selection in Evolution*. Oxford University Press.

Kauffman, SA. 1995. *At Home in the Universe: The Search for Laws of Self-Organisation and Complexity*. Oxford University Press, New York.

Lebovitch, LS. & Shehadeh, LA. 2005. Introduction to fractals, in *Tutorials in contemporary nonlinear methods for the behavioral sciences*, Riley M. A., Van Orden G. C., (eds). 178–266. Available: http://www.nsf.gov/sbe/bcs/pac/nmbs/nmbs.jsp. Accessed May 13 2013.

Lee, JA. & Lupski, JR. 2006. Genomic rearrangements and gene copy-number alterations as a cause of nervous system disorders. *Neuron* 52(1):103–21.

Lewis, SE. & Maccarrone, M. 2009. Endocannabinoids, sperm biology and human fertility. *Pharmacol Res* 60(2):126-31.

Li, M. & Arimura, A. 2003. Neuropeptides of the pituitary adenylate cyclase-activating polypeptide/vasoactive intestinal polypeptide/growth hormone-releasing hormone/secretin family in testis. *Endocrine* 20(3):201-14.

Licatalosi, DD. & Robert, B. & Darnell, RB. 2010. RNA processing and its regulation: global insights into biological networks. *Nature Reviews Genetics* 11:75-87.

Lucas, C. Genetic Algorithms - Nature's Way. Available: www.calresco.org/genetic.htm Accessed 28/04/2013.

Maturana, HR. 1975. The organization of the living: A theory of the living organization. *International Journal of Man-Machine Studies* 7;3:313–332.

McCulloch, WS. 1965. *Embodiments of Mind: A collection of 21 essays and lectures*. M.I.T. Press, Cambridge, Massachusetts.

Miller, ST. As Above, So Below: A Brief Sketch of Ideas Concerning Reproductive and Creative Self-Similarity Across Five Realms. Available: www.academia.edu/.../As_Above_So_Below_A_Brief_Sketch_of_Ideas_... *Accessed 02/05/2013*

Möller, A. &, Hell, D. 1999. The general psychological concept in the later work of Eugen Bleulers. Comparison with a summarized description from a forgotten theory 60 years after the final publication (1939). *Fortschr Neurol Psychiatr* 67(4):147–54.

Morange, M. 2002. The relations between genetics and epigenetics: a historical point of view. *Ann N Y Acad Sci* 981:50-60.

Murphy, N. & Ellis, GFR. 1996. *On the Moral Nature of the Universe: Theology, Cosmology and Ethics.* Minneapolis: Fortress Press, 1996.

Newman, D. (1996). Emergence and Strange Attractors. *Philosophy of Science* 63:245–61.

Nielsen, R., Bustamante, C., & Clark, AG., et al 2005. A scan for positively selected genes in the genomes of humans and chimpanzees. *PLoS Biol* 3(6):e170.

Nowacki, M., Vijayan, V., Zhou, Y., et al 2008. RNA-mediated epigenetic programming of a genome-rearrangement pathway. *Nature* 451(7175):153–8.

Oldham, MC., Horvath, S. & Geschwind, DH. 2006. Conservation and evolution of gene coexpression networks in human and chimpanzee brains. *PNAS.* 103(47): 17973-17978.

Pallas, SL. 2001. Intrinsic and extrinsic factors that shape neocortical specification. *Trends Neurosci*. Jul 24(7):417-23.

Penn, AC., Balik, A., Greger, IH. 2013. Reciprocal regulation of A-to-I RNA editing and the vertebrate nervous system. *Front Neurosci* 18(7):61.

Pirsig, RM. 1991. *Lila: An Inquiry into Morals*. New York: Bantam Books.

Prigogine, I. & Stengers, I. 1984. *Order Out Of Chaos*. Bantam Books Inc., New York, USA.

Re, A., Cora, D., Puliti, AM., et al 2006. Correlated fragile site expression allows the identification of candidate fragile genes involved in immunity and associated with carcinogenesis. *BMCBioinformatics* 7:413.

Roth, DB. 2000. From lymphocytes to sharks: V(D)J recombinase moves to the germline. *Genome Biol* 1(2).

Rothenfluh, HS., Gibbs, AJ., Blanden, RV., et al 1994. Analysis of patterns of DNA sequence variation in flanking and coding regions of murine germ-line immunoglobulin heavy-chain variable genes: evolutionary implications. *Proc Natl Acad Sci USA* 91(25):12163–7.

Riley, MA., Bonnette, S., Kuznetsov, N., Wallot, S. & Gao, J. 2012. A tutorial introduction to adaptive fractal analysis. *Front. Physiol.* 28 September.

Rutherford, SL., Lindquist, S. 1998. Hsp90 as a capacitor for morphological evolution. *Nature Nov* 26;396(6709):336-42.

Schuel, H., Burkman, LJ. 2005. A tale of two cells: endocannabinoid-signaling regulates functions of neurons and sperm. *Biol Reprod* 73(6):1078-86.

Shalizi, CR. 2001. Causal Architecture, Complexity and Self-Organization in Time Series and Cellular Automata. PhD thesis, University of Wisconsin at Madison. Available: http://cscs.umich.edu/˜crshalizi/thesis/.

Shannon, CE. 1948. A Mathematical Theory of Communication. *The Bell System Technical Journal* 27:379-423.

Smith, A. 1976. *The Wealth of Nations* edited by R. H. Campbell and A. S. Skinner. The Glasgow edition of the Works and Correspondence of Adam Smith, vol. 2a, Vol. 1 [1776]. Oxford University Press.

Skrebitsky, VG. & Chepkova, AN. 1998. Hebbian synapses in cortical and hippocampal pathways. Rev *Neurosci* 9(4):243-64.

Stanford, PK. 2005. August Weismann's theory of the germ-plasm and the problem of unconceived alternatives. *Hist Philos Life Sci* 27(2):163-99.

Steele, EJ., Lindley, RA. & Blanden, RV. 1998. *Lamarck's signature: how retrogenes are changing Darwin's natural selection paradigm.* Sydney: Allen & Unwin.

Stephens, CR. Garc´ıa Olmedo I, Vargas, JM. & Waelbroeck, H. 1998. Self-Adaptation in Evolving Systems. *Artificial Life* 4(2):183-201.

Suseendranathan, K., Sengupta, K., Rikhy, R. et al 2007. Expression pattern of Drosophila translin and behavioral analyses of the mutant. *Eur J Cell Biol* 86(3):173–86.

Swenson, R. 1989. Emergent attractors and the law of maximum entropy production: Foundations to a theory of general evolution. *System Research* 6(3):187–197.

Torrance, RM. 1994. The Spiritual Quest: Transcendence in Myth, Religion, and Science. Berkeley: University of California Press,

Vlach, M. *Plato's Theory of Forms*. Available: www.theologicalstudies.org/resource-library/philosophy-dictionary/158-platos-theory-of-forms. Accessed 18/05/2013.

Volkan, V. 1979. *Cyprus – War and Adaptation: A Psychoanalytic History of Two Ethnic Groups in Conflict.* Virginia: Virginia. University Press.

Von Glasersfeld, E. 2000. Reflections on Cybernetics. *Cybernetics And Human Knowing* 7(1):93–95.

Waddington, CH. 1942. The epigenotype. *Endeavour* 1:18–20.

Waldrop, MM. 1992. *Complexity: the emerging science at the edge of order and chaos*. New York: Simon & Schuster Inc.

Weiller, GF., Rothenfluh, HS., Zylstra, P. et al 1998. Recombination signature of germline immunoglobulin variable genes. *Immunol Cell Biol* 76(2):179–85.

West-Eberhard, MJ. 2005. Phenotypic accommodation: adaptive innovation due to developmental plasticity. *J Exp Zool B Mol Dev Evol* 304(6):610-8.

Wiener, N. 1961. *Cybernetics: or Control and Communication in the Animal and the Machine.* 2nd Ed.Cambridge Massachusetts: MIT Press.

Williams, GC. 1966. *Adaptation and Natural Selection: A Critique of Some Current Evolutionary Thought*. New Jersey: Princeton University Press.

Wills, C. 1993. *The Runaway Brain*. London: Harper Collins

Wolf, T. & Holvoet, T. 2005. Emergence Versus Self-Organisation: Different Concepts but Promising When Combined. In Engineering Self Organising Systems: Methodologies and Applications. *Lecture Notes in Computer Science* 3464:1–15.

Wolkenhauer, O. 2001. Systems Biology: The Reincarnation of Systems Theory Applied in Biology? Briefings in *Bioinformatics, Henry Stewart Publications* 2(3):258-270, September (Special Issue: Modelling Cell Systems).

Yurov, YB., Lourov, IY., Vorsanova, SG., et al 2007. Aneuploidy and confined chromosomal mosaicism in the developing human brain. *PLoS ONE* 2(6):e558.