ELSEVIER

Review

Cryptobiosis: A new theoretical perspective

Yair Neuman*

Office for Interdisciplinary Research, Ben-Gurion University, Beer-Sheva, Israel

Available online 9 December 2005

Abstract

The tardigrade is a microscopic creature that under environmental stress conditions undergoes cryptobiosis [Feofilova, E.P., 2003. Deceleration of vital activity as a universal biochemical mechanism ensuring adaptation of microorganisms to stress factors: A review. Appl. Biochem. Microbiol. 39, 1–18; Nelson, D.R., 2002. Current status of the tardigrada: Evolution and ecology. Integrative Comp. Biol. 42, 652–659]—a temporary metabolic depression—which is considered to be a third state between life and death [Clegg, J.S., 2001. Cryptobiosis—a peculiar state of biological organization. Comp. Biochem. Physiol. Part B 128, 613–624]. In contrast with death, cryptobiosis is a reversible state, and as soon as environmental conditions change, the tardigrade "returns to life." Cryptobiosis in general, and among the tardigrade in particular, is a phenomenon poorly understood [Guppy, M., 2004. The biochemistry of metabolic depression: a history of perceptions. Comp. Biochem. Physiol. Part B 139, 435–442; Schill, R.O., et al., 2004. Stress gene (hsp70) sequences and quantitative expression in Milensium tardigradum (Tardigrade) during active and cryptobiotic stages. J. Exp. Biol. 207, 1607–1613; Watanabe, M., et al., 2002. Mechanisn allowing an insect to survive complete dehydration and extreme temperatures. J. Exp. Biol. 205, 2799–2802; Wright, J.C., 2001. Cryptobiosis 300 years on from van Leuwenhoek: what have we learned about tardigrades? Zool. Anz. 240, 563–582]. Moreover, the ability of the tardigrade to bootstrap itself and to return to life seems paradoxal like the legendary Baron von Munchausen who pulled himself out of the swamp by grabbing his own hair. Two theoretical obstacles prevent us from advancing our knowledge of cryptobiosis. First, we lack appropriate theoretical understanding of reversible processes of biological computation in living systems. Second, we lack appropriate theoretical understanding of bootstrapping in living systems. In this short opinion article, I would like to present the idea that although cryptobiosis is obscure from a certain point of view, it makes sense within a scientific perspective suggesting that "organization becomes cause in the matter" [Strohman, R.C., 2000. Organization becomes cause in the matter. Nat. Biotechnol. 18, 575–576]. I present Bateson's idea that organisms have a "recursive hierarchical" form of organization [Neuman, Y., 2004. Meaning making in the immune system. Perspect. Biol. Med. 48, 320–327; Neuman, Y., in press. A theory of meaning. Inform. Sci.] and suggest that this form of organization allows bootstrapping through reversible process of computation as discussed by theoretical physicists [Bennett, C.H., 1982. The thermodynamics of computation—a review. Int. J. Theoret. Phys. 1, 905–940; Landauer and Bennett, 1985].
© 2005 Elsevier Ltd. All rights reserved.

Keywords: Cryptobiosis; Recursive-hierarchy; Physics of computation; Boundary

*Tel.: +972 8 646 1843; fax: +972 8 647 2897.

*E-mail address:* yneuman@bgumail.bgu.ac.il.

Contents

1. Introduction: the "mystery" of cryptobiosis

Authors submitting manuscripts for "Progress in Biophysics and Molecular Biology" are required "to treat their subject matter in a manner that is authoritative yet also easily comprehensible to those who are not experts in the field." The aim of this article is to present a new perspective for studying cryptobiosis. The subject matter of this article is limited, but it draws on several fields, and its implications go far beyond these fields. In order to do justice to the ideas presented in this article and to meet the requirements of the journal, the ideas presented in this article are discussed on a conceptual level per se without dwelling too deeply on the technicalities and the particularities of each field. Moreover, the ideas presented in this paper are in an embryonic form and therefore they rely heavily on analogies and metaphors as explanatory tools.

The "Tardigrade" (i.e. the "slow walker") is a microscopic creature (250–500 µm) which is also known as the "water bear." This microscopic creature is scarcely familiar to molecular biologists, biophysicists, and laymen alike although it can be found almost everywhere on earth from the top of the Himalaya to the bottom of the oceans. The tardigrade has its own phylum "Tardigrade" and its unique characteristics (Nelson, 2002): a thick cylindrical bilateral symmetrical body with four segments and a head with eyes, four pair of legs, feet with claws or toes, ventral nervous system, and a multi-lobed brain. The next picture is a scanning electron micrograph of a tardigrade (http://www.biology.missouri.edu/courses/Bio10/Tardigrada.html).

The Tardigrade is known for its ability to survive in extreme environments including complete dehydration, boiling water at 151 °C, and an amount of radiation which is thousands of times stronger than the amount of radiation which is lethal to human beings (Picture 1).

Organisms have different mechanisms of adjusting to environmental stress conditions. The tardigrade is described in this paper because it is capable of entering a latent state—*cryptobiosis*—when environmental
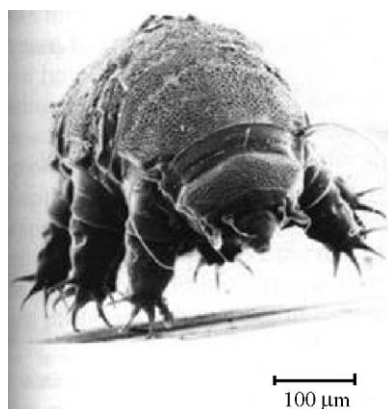
Picture 1. The Tardigrade.

conditions are unfavorable (Nelson, 2002). David Keilin (1959 quoted in Clegg, 2001, p. 213, emphasis mine) coined the term 'cryptobiosis'—hidden life—and defined it as

> the state of an organism when it shows *no visible signs of life* and when its metabolic activity becomes hardly measurable, or comes reversibly to a standstill.

The fact that the metabolic activity of the organism is "hardly measurable" does not logically imply that it is completely inhibited as argued by some researchers such as Feofilova (2003). It is possible that during cryptobiosis metabolism exists at a very low level that is not detectable by a measurement procedure. This possibility will be explored in this paper. However, modern scientific knowledge is based on the positive products of measurement procedures and not on speculations resulting from the limits of the measurement procedures. Therefore, we should accept, at least as a starting point, the common knowledge of the field suggesting that when a tardigrade is in a latent state of cryptobiosis "metabolism, growth, reproduction, and senescence are reduced or cease temporarily" (Nelson, 2002, p. 655). In fact, it is argued that cryptobiosis involves a "complete or a near-complete inhibition of metabolic activity (0%)" (Feofilova, 2003). Since metabolism is a defining characteristic of life one can argue that cryptobiosis is a kind of *temporary death*.

Beyond the quantitative metabolic aspect of cryptobiosis we should realize the qualitative aspect of cryptobiosis. Each organism finally dies and death is clearly an irreversible state. To exclude miraculous stories, as those described in the Bible and the New Testament, a dead organism cannot be revived. Death is irreversible and it is the final station of the organism's journey along the arrow of time. However, an organism that is in a state of cryptobiosis is in a unique state that is somehow a state of a *potentially reversible death*. Indeed, due to its reversibility, cryptobiosis is considered to be a unique biological state between life and death (Clegg, 2001).

The depression of metabolism in the face of environmental stress is acknowledged as "a normal part of the life cycle of many animals, and it has been reported in most of the major invertebrate's phyla and in all vertebrate classes" (Guppy, 2004, p. 435). The ubiquity of cryptobiosis may lead us to expect a wealth of knowledge about the mechanisms underlying cryptobiosis. Surprisingly, there are only 32 references to Cryptobiosis in the PubMed (August, 2005). This state probably indicates the theoretical obscurity of cryptobiosis and the fact that it is poorly understood.

This conclusion is supported by biologists who study cryptobiosis. As argued by Wright (2001, p. 564): "Tardigrade cryptobiosis remains poorly understood." Schill et al. (2004, p. 1607) argue that cryptobiosis in tardigrades and other invertebrates is characterized by several major events that "still remain largely unidentified," and Watanabe et al. (2002) argue that the underlying molecular and metabolic mechanisms of cryptobiosis largely remain a "mystery." Concerning metabolic depression it was recently argued by Guppy (2004, p. 436) that "to date, no molecular mechanism or process associated with the control of metabolic depression has been comprehensively delineated, and the fundamental phenomenon of metabolic depression remains biochemically obscure."

The tardigrade, although not showing (or hardly showing) any signs of life at the metabolic level, is capable of "reviving" itself by responding to cues of a friendly environment. In this case, a drop of water is enough for signaling the tardigrade that it can come back to life. The organism should respond to this signal, and make sense out of it. Here we encounter a difficulty. If we accept the argument that cryptobiosis is a unique biological state in-between life and death how is it possible for the organism to interpret the signal? How is it possible for the tardigrade to extract itself from a state in which metabolism does not exist or almost does not exist? How can it move from a state in which no free energy is allegedly available to maintain biological functions?

The "mystery" of cryptobiosis may be attributed to the lack of appropriate conceptual tools for approaching these questions. The following sections aim to point at possible directions of inquiry. More specifically, I speculate that: (1) cryptobiosis involves a shift toward a form of reversible computation; and (2) the bootstrapping from an irreversible computation to a regular irreversible computation takes place in the topology of a recursive-hierarchy. These speculations are valuable for several reasons. First, they are speculations that may turn into hypotheses that will direct empirical research. Second, they may challenge theoretical biologists by initiating a discussion about the meaning of a bootstrapping process in living systems. Third, they may show that, as Strohman (2000) argued, "organization becomes cause in matter" and that this kind of organization should be the subject of a scientific inquiry.

2. Recursive-hierarchy

Gregory Bateson was the son of the distinguished geneticist, William Bateson, who named his son Gregory after Gregor Mandel. Bateson was a polymath whose work produced insights into a variety of domains to include family therapy and theoretical biology. One of Bateson's most fruitful ideas, later described as a 'recursive-hierarchy' (Harries-Jones, 1999; Neuman, 2004), was that all living systems are multi-level and recursive. For example, Bateson noticed that informational content in biological systems always assume a context of interpretation where the term context is used in the sense of a higher order form or constraint. The context is the one that restrains (to use Bateson's terminology) or constrains (to use a terminology I have used elsewhere—Neuman, 2004) the entropy of the system and its natural tendency toward disorder.

The abstract idea of constraints may be illustrated through a simple mechanical example of Brownian Ratchets (Dill and Bromberg, 2003, p. 330). The example concerns the way molecular machines produce directed motion. Brownian motion in itself cannot be used for a directed motion because it is random. However, the Brownian ratchet model suggests how random diffusion coupled with energy-driven, but non-directional binding and release events, can lead to directed motion. Let us consider a molecule M that moves itself along a partner molecule P having a chain of binding sites. Before time $t = 0$ the system is stable and M is bound at a location where the binding free energy—$F(x)$—is a minimum. At time $t = 0$ energy is put in the system to release M from its binding site on P. M is free to move either in the $+x$ or $-x$ direction along P. M remains free and diffuses. This diffusion leads to a Gaussian distribution along x. During that time some of the molecules will diffuse to $x \geqslant a$, where 'a' is used to denote the location of the next maximum to the right. Those molecules will rebind and slide energetically downhill to the next energy well to the right of the binding site. A smaller number of molecules will diffuse to the left. The diffusion is symmetrical in x. However, the ligand binding potential is not. The free energy is asymmetric. At the time of the diffusion more particles fall into the energy well to the right (or more accurately to a direction which is determined by the asymmetry) of the binding site. Therefore, if there is an appropriate time lag between the cycles, repeated cycles of release, diffusion and rebinding will lead to the directed movement of M. Two things should be emphasized. First, the Brownian ratchet model does not violate the second law of thermodynamics. Second, and much more relevant for our case, the molecule M in the ratchet model is not directed to a given direction by external forces neither by its own erratic movement. The directional movement of the molecule is achieved by imposing energetic constraints on the Brownian movement. This is a simple mechanical example illustrating the way higher order constraints of the system "determine" the behavior of a lower level entity.

The context is a "collective term for all those events which tell the organism among what *set* of alternatives he must make his next choice" (Bateson, 2000, p. 289). Rather than allowing Brownian erratic movement to control the system's behavior, the context as a higher form of organization directs the system's trajectory into a given attractor. This idea was found to be fruitful in explaining processes at different scales of analysis. For example, it was used to explain immune recognition as a meaning-making process (Neuman, 2004, 2005), and the way meaning is related to information (Neuman, in press).

A context is always embedded within another context and therefore we have a *hierarchy of constraints of constraints*. The fact that contexts are embedded within contexts does not point only at the hierarchical structure of living systems. There is also a dynamic aspect to this embeddings and embodiment, and this dynamic aspect is constituted through feedback loops in which information is fed back and forth between the different levels of the system to assure the stability of each level and to constitute the working whole. Therefore, organisms can be described as *recursive-hierarchical* systems (Harries-Jones, 1999; Neuman, 2004) that are capable of self-determination through embedded levels of constrains constituted by feedback loops. The important implication of this statement is that a system of a recursive-hierarchy is a system capable of self-determination and therefore has the potential of bootstrapping. As already envisioned by Bateson (2000, p. 411):

If, in the communicational and organizational processes of biological evolution, there is something like *levels*—items, patterns and possibly patterns of patterns—then it is logically possible for the evolutionary system to make something like positive choices.

Notice that Bateson uses the expression "positive choices" not in the intentional sense, but in the sense of self-determination of higher levels on the behavior of a lower level.

Bateson's idea of a recursive-hierarchy should not be confused with the idea of strong downward causation in which "a given entity or process on a given level may causally inflict changes or effects on entities or processes on a lower level" (Emmeche et al., 2000, p. 19). The idea of strong downward causation, in which a higher-order level determines the behavior of a lower level, is problematic and incompatible with our knowledge of physics. Bateson's idea is closer to the idea of medium downward causation in which "an entity on a higher level comes into being through a realization of one amongst several possible states on the lower level with the previous states of the higher level as a factor of selection" (Emmeche et al., 2000, p. 24) meaning that the higher level serves as a *boundary condition* or *constraint condition* on the behavior of the lower level. That is the higher level is characterized by "organizational principles" (Emmeche et al., 2000, p. 25) that have an effect on the distribution of lower level events and substances. For example, although fluctuations appear on the quantum level, stability appears on the molecular level due to the constraints imposed by the molecular organization on the atomic and sub-atomic degrees of freedom. This idea is highly relevant for the tardigrade case. It implies that although micro-level metabolic activity may be significantly reduced, high-level form of organization may still be maintained to allow at the right moment a shift to normal metabolic activity.

After illustrating the meaning of constraints, it is the time to explain the meaning of a bootstrapping procedure. The term "bootstrapping" alludes to the legendary Baron Münchhausen who was able to lift himself out of a swamp by pulling up on his own hair or his own bootstraps (http://en.wikipedia.org/wiki/BootstrappingBootstrapping). The term acquired different senses in a variety of domains. For example, in computer science, this term refers to any process where a simple system activates a more complicated system. It is the problem of starting a certain system without the system already functioning, a process that may be portrayed as allegedly illogical or paradoxical the same as the Baron's legend. However, solutions, accordingly called bootstrapping, exist; they are processes whereby a complex system emerges by starting simply and, bit by bit, develop more complex capabilities on top of the simpler ones. The tardigrade's shift from normal activity to cryptobiosis may be portrayed as a logical biological process of slowing down metabolic processes. However, a shift from a state of cryptobiosis to a state of normal metabolic activity is a bootstraping procedure. It is not simply a shift from a low level of metabolic activity to a higher level of metabolic activity, but a qualitative shift from one state to another more complicated state that involves higher-order behaviors such as reproduction and predation. The next section explains the possible logic underlying the tardigrade's bootstraping process.

3. Organization becomes cause in the matter

Bateson's idea of a recursive-hierarchy might be misinterpreted as an expression of a general non-scientific holism. However, this idea has been fully realized in modern conceptions that consider organization as cause. In 2000, Richard Strohman published an insightful commentary in "Nature Biotechnology" entitled: "Organization becomes cause in the matter." Strohman's commentary may be used to apply Bateson's ideas to the tardigrade and the mystery of cryptobiosis.

Strohman's point of departure is the perspective of complex systems and "the middle way" (Laughlin et al., 2000) or the search for the laws operating at levels and scales of organization intermediate between the microscopic state of fundamental particles and the macroscopic state of higher level organization. Following Laughlin et al. (2000), Strohman (2000, p. 575) argues that:

> …in biology, molecular genetic reductionism has mostly distracted us from study of mesoscopic realms between genotype and phenotype where complex organizational states exists, and where, as we now realize, there also exist networks of regulatory proteins capable of reorganizing patterns of gene expression, and much other 'emergent' cellular behavior, in a context-dependent manner.

Strohman argues further that it is the mesoscopic level which is responsible for the emerging features of biological systems, and pays his intellectual debt to the work of Michael Polanyi, whose idea of boundary condition (Polanyi, 1968) is in line with Bateson's idea of a recursive-hierarchy, and the idea of medium downward causation. A similar idea also appears in Yates (1993, p. 212) who argues that "every 'level' in a

natural system is constrained by the next level below and the next level above; it is in a middle of a sandwich, with every level equally sovereign with respect to the global stability of the organism. Command, control, communication, and co-operatively permeate 'laterally' (heterarchically) and 'vertically' (bottom-up and top-down)." Strohman also points at *metabolic* networks as an arena in which the new venture of mesoscopic analysis may show its power. This idea brings us back to the tardigrade and the way it depresses its metabolism. However, before delving into this point, let me quote an excerpt from a manuscript written by a leading experimental immunologist. This manuscript, which is a theoretical treatise in both immunology and theoretical biology, deals with life as an emergent property (Cohen, 2000). This statement is worth reading because it reminds us that 'life' is in the organization and that in a very deep sense, organization is the cause in the living matter:

> The clearest example of an emergent property is life itself. Life is not inherent in any single element constituting the living cell. DNA is not alive, neither are proteins, carbohydrates or lipids. Indeed, for a single short moment, a living cell and a dead cell may, upon analysis, be found to contain precisely the same catalogue of "dead" chemicals in identical concentrations. Bacteria have been resurrected after 35 million years of suspended life in the guts of ancient bees entrapped in amber. While not quite dinosaurs, 35 million year old bacteria are still a marvel. Today they surely live; what was their state for 35 million years? What distinguishes the living from the dead? Nothing more than *actions and interactions*. Life emerges from inert matter as a consequence of metabolism, the continuous transfer of energy and information systematically packaged in cells in a way that leads to self-perpetuation (§47).

Cohen's statement naturally leads us to the next section.

4. A recursive hierarchical metabolism?

Metabolism involves the "autonomous use of matter and energy in building, growing, developing, and maintaining the bodily fabric of a living thing" (Boden, 1999, p. 237). Bergareche and Ruiz-Mirazo (1999, p. 53, emphasis mine) define metabolism in the most abstract sense as

> …any material organizational apparatus of energy management which can implement an operationally close constructive–relational system, so that the network of components production relations held in it *recursively* maintains and renews the aforementioned apparatus.

This abstract definition of metabolism suggests that *metabolism operates as a recursive-hierarchical structure*, which as we have realized before, has the potential of bootstrapping through a medium version of downward causation. If during cryptobiosis the tardigrade is capable to maintain a minimal level of metabolic activity just for keeping the organization of the metabolic network then this organization (i.e. a higher level of the metabolic network) may serve to return the metabolic activity of the cells to a normal level. This suggestion assumes the possibility to constitute a minimal maintenance activity of the network at a minimal energy expense, and a unique topology of the metabolic network that materialize the recursive-hierarchical structure. It is not quite clear what is the meaning of metabolic constraints at a higher level. A possible interpretation is that while energy-consuming activity of translation from the DNA is depressed, a minimal level of energy is used for maintaining the organization of the network in-itself, maybe through the mitochondria that has its own DNA. A more biologically oriented explanation is currently not at hand and may be the aim of a future work. The next sections point at the viability of this possibility in the context of the physics of computation.

5. A lesson from the physics of computation

Landauer and Bennett (1985) describe a process of computation, in the most general sense, as a process in which an "output" is produced from an "input" through an algorithm, and "information" is considered in the most general sense of differentiated states. They argue that this process of computation has a clear physical meaning. Processes of computation do not take place in a Platonic space of ideas but are physically grounded. This perspective led them to offer a thermodynamic approach to computation. According to this approach

(Bennett, 1982, p. 906) "The digital computer may be thought of as an engine that dissipates energy in order to perform mathematical work." This approach has some interesting insights with clear implications for biology.

For example, one of the insights of the physics of computation concerns the price of eliminating information (to include biological information) from the system. Landauer (1961) argued that the elimination of information from a given system is an activity that consumes energy and dissipates heat into the environment. "When an information is erased there is always an energy cost of $kT \ln 2$ per classical bit to be paid" and "amount of heat equal to $kT \ln 2$ is dumped in the environment at the end of the process" (Plenio and Vitelli, 2001, p. 27).

The association between the dissipation of energy and the loss of information can be easily illustrated by using the original example of Landauer and Bennett (1985). Let us assume that we drop two identical elastic rubber balls from 1 m and from 10 m. The potential energy of the balls turns into a kinetic energy of movement. When the balls hit the ground they jump back and the height of their jump indicate the height from which they were dropped. Whenever a ball hits the ground some amount of energy is being lost and we may say that heat (i.e., energy in transfer) was released to the environment. After a while the two balls will rest peacefully on our playground, indicating nothing about the height from which they were dropped. Heat was released and information was lost. In this sense, Heat is not only the "graveyard" of energy that could have done some work (i.e., free energy) but the graveyard of information too.

Landauer's argument is thought provoking for two reasons. The first reason is that it associates the abstract mathematical term "information" with the physical (and the bio-physical) realm. Information, whether in the digital computer or in the DNA has physical meaning. The second reason is that it associates the loss of information with the release of heat into the environment. This reason is highly relevant for understanding cryptobiosis. If (almost) no computation is conducted, (almost) no information is lost, (almost) no heat is generated, and the organism may maintain its organization at minimal energy expense. It is possible that in a state of cryptobiosis all processes of computation cease in the sense that computation from the DNA is stopped and almost no energy is wasted. This process will become more comprehensible when the ideas of reversible computation will be discussed below.

The physics of computation suggests that computation, which is usually discussed in a purely functional way, is a physically grounded process which is subject to the laws of thermodynamics. Landauer and Bennett (1985) push this idea forward to biological systems, and we can argue that the organism is a unique type of highly complex metabolic engine that dissipates energy to perform "biological work." In this context, the difference between *reversible* and *irreversible* processes is of great importance.

In thermodynamics, a reversible process changes the state of a system in such a way that the net change in the combined entropy of the system and its surroundings is zero. It is a process in which no heat is lost from the system as a "waste" and the machine is as efficient as it can possibly be. In other words, the process does not result in the increase in physical entropy and the loss of information.

A reversible computing is a computational process which is reversible at least to some close approximation, and it has the merit of improving the energy efficiency of the computer or the organism using it. *It must be emphasized that the idea of reversible computation does not contradict the second law but just questions the limits of the price organisms (and other computational devices) should pay* for it as open systems. Indeed, Bennett presents some theoretical models that perform computation with (approx.) zero energy dissipation. Although these theoretical models have not been actualized yet by human beings, there is no theoretical obstacle for their existence at the molecular level during cryptobiosis. It is possible to imagine a reversible process of computation that strives for a minimal level of energy expenditure. It is also possible that cryptobiosis involves such a process of reversible computation. This speculation is grounded in the slowdown of all metabolic processes during cryptobiosis. This slowdown may reflect a shift to reversible computing which is capable of maintaining a very low and economic activity of metabolic activity at a minimal cost of energy expense. This activity may maintain the organization that at the right time will support the bootstrapping procedure, the emergence of a higher-order state, and the shift to normal metabolism.

Computation as it is commonly materialized in the electronic computer is irreversible and the dissipation of energy and the loss of information are inevitable. Cognitive systems also involve irreversible processes of computation in which micro-level differentiations are lost in favor of higher-level outputs. For example, seeing involves an irreversible process of computation in which lower-level changes in the activity of retinal cells is

integrated at a higher level and produce the perceived image. Irreversibility is a defining property of a hierarchical system. When we shift from one level of organization to a higher level of organization, a certain level of differentiation and information is by definition lost in the transition at the cost of energy dissipation. However, in the case of a recursive-hierarchical structure this does not have to be necessarily the case, and the dissipation may be reduced to the limit line.

In sum, if the metabolic network of the tardigrade is built according to the topology of recursive-hierarchy, and if it shifts to a reversible process of computation during cryptobiosis, then metabolic activity would not be detectable (or extremely low) although it will be efficient enough to bootstrap the organism.

If cryptobiosis works according to the logic of reversible computation, which is materialized in the recursive hierarchical structure of the metabolic network, then the ability of the tardigrade to bootstrap itself turns from a ''mystery'' into a process which is comprehensible according to scientific terms.

We may conclude our analysis so far by suggesting that while death is the ultimate expression of an irreversible process called life, cryptobiosis as a state in-between life and death involves a temporary shift to a reversible form of biological computation. The organism is able to bootstrap itself when macro-level constraints re-organize and allow the highly efficient metabolic computation to re-use resources of energy from the environment.

6. From Baron von Munchausen to the Klein bottle

Our scientific knowledge is mediated and impeded by the models we use, including visual models of representation. For example, according to the Darwinian theory, the environment is portrayed as a kind of a *strainer*. Random mutations of the DNA results in different phenotypes that pass or do not pass through the strainer. The general epigenetic conception puts much more weight on the shoulders of the environment. The environment is not portrayed as a strainer but as a *landscape* in which the potentialities of the organism are channeled. This metaphor was introduced by Waddington whose visual image of an epigenetic landscape has become well known. Here is an epigenetic landscape as it was presented in Waddington (1957) ''The Strategy of the Genes'' (Picture 2).

The developing embryo, according to Waddington, is like a ball channeled by the structure of the landscape. This portrait does not give the organism, whether at the genetic, embryo or mature level, any freedom to act. A ball has no freedom, but only the degrees of freedom a priori forced on it by the environment. It is only a passive respondent to the environment. From the perspective of *life-here-and-now* (Luigi, 1998) the tardigrade seems to challenge this visual image. This organism has the ability to turn from life to quasi-death and vice versa by responding to environmental cues. It is not a passive object that ends its life when the environment becomes too stressful. It is an organism that actively, and if I may add creatively, responds to the stressful environment by turning into a unique state from which it can actively bootstrap itself. If we are looking for a
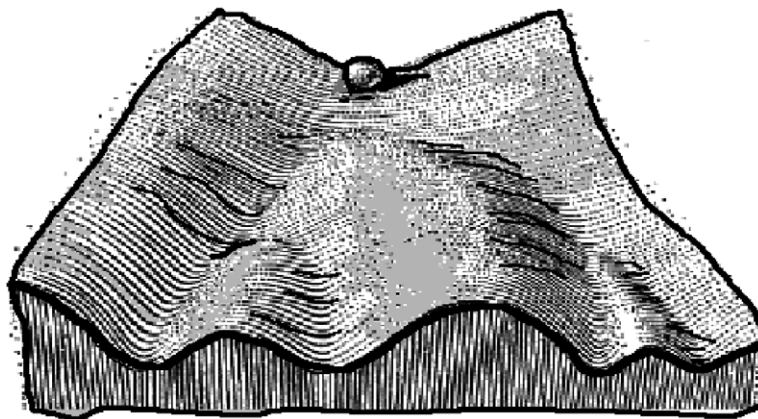

Picture 2. Waddington's landscape.

graphical image of a bootstrapping process then we may use the image of the Baron von Munchausen pulling himself out of the swamp by grabbing his own hair.

Indeed, the tardigrade is like the Baron von Munchausen. However, the Baron's image portrays the bootstrapping process as an illogical act. Is there another graphical representation that can do justice to bootstrapping? The visual representation which is perfectly fit to describe the bootstrapping activity of the tardigrade is the *Klein bottle*, a higher dimensional topological version of the Möbius strip. The Möbius strip is a one sided surface in the sense that a bug can traverse the entire surface without crossing an edge. The sketch of the Möbius strip is shown in Picture 3.

The Möbius band is interesting since it is non-orientable. In geometry and topology, a surface is called non-orientable, if a figure such as the letter ''R'' can be moved about on the surface so that it becomes mirror-reversed. Otherwise, the surface is said to be orientable. A non-orientable surface may allow us to restore the symmetry of an object sliding on it. It is an example of a topology that may allow symmetry restoratation and, therefore, reverse computation. Another example of a non-orientable surface is the Klein bottle, which is, roughly speaking, the product of two Möbius strips glued together along each of their lone edges (a proper Klein bottle can only exist in four dimensions; it can be only imperfectly represented in three). The representation of the Klein bottle is shown in Picture 4.

What is important to notice about the Klein bottle is that it is a topological structure that passes through itself so that outside and inside meet. The philosopher Steven Rosen (1988, 1994, 2004), made a substantial contribution for our understanding of the philosophical meaning and implications of the Klein bottle for physics and other domains. For us, it is only important to realize that the idea of boostraping is not as illogical as illustrated in the Baron's picture. The movement from the inside to the outside (and vice versa), or out of the system and into the system, the bootstraping process, can be smoothly conducted without encountering a paradoxical point of discontinouity. The Klein bottle is the ultimate visual representation of a recursive-hierarchcial structure (Rosen, 2004). Moreover, while moving along this re-entering structure we may restore the symmetry of the object we transform. Symmetry is reversibility and, therefore, the Klein bottle is an illustration of a topological structure that is capable of re-entering (and therefore bootstraping) and reversible computation. Can it be that the metabolic network of the tardigrade is built along the lines of the Klein bottle?
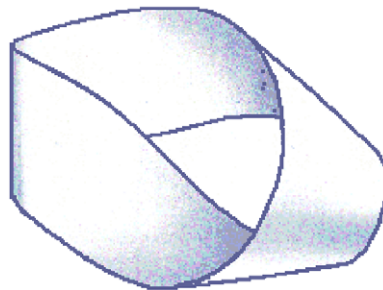
Picture 3. The Möbius strip.

Picture 4. The Klein bottle.

What does it mean for understanding reversible processes of computation? These questions may sound like wild speculation, but one should be attentive to the relation between thermodynamics and topology, a relation that has been almost exclusively studied by theoretical physicists, and seek creative ways to answer them. In this sense, rather than providing conclusive answers to the "mystery" of cryptobiosis, this article has the modest purpose of pointing at possible directions for inquiry. It is like a traffic sign pointing at the right direction rather than being the direction itself. As such it should be judged.

References

Bateson, G., 2000. Steps to an Ecology of Mind. The University of Chicago Press, Chicago.

Bennett, C.H., 1982. The thermodynamics of computation—a review. Int. J. Theor. Phys. 21, 905–940.

Bergareche, A.M., Ruiz-Mirazo, K., 1999. Metabolism and the problem of its universalization. BioSystems 49, 45–61.

Boden, M.A., 1999. Is metabolism necessary? Br. J. Philos. Sci. 50, 231–248.

Clegg, J.S., 2001. Cryptobiosis—a peculiar state of biological organization. Comp. Biochem. Physiol. Pt. B 128, 613–624.

Cohen, I.R., 2000. Tending Adam's Garden. Academic Press, New York.

Dill, K.A., Bromberg, S., 2003. Molecular Driving Forces: Statistical Thermodynamics in Chemistry and Biology. Garland Science, New York.

Emmeche, C., Køppe, S., Stjernfelt, F., 2000. Levels of emergence, and three versions of downward causation. In: Andersen, P.B., Emmeche, C., Finnemann, N.O., Christiansen, P.V. (Eds.), Downward Causation. Minds, Bodies and Matter. Aarhus University Press, Aarhus, pp. 13–34.

Feofilova, E.P., 2003. Deceleration of vital activity as a universal biochemical mechanism ensuring adaptation of microorganisms to stress factors: A review. Appl. Biochem. Microbiol. 39, 1–18.

Guppy, M., 2004. The biochemistry of metabolic depression: a history of perceptions. Comp. Biochem. Physiol. Pt. B 139, 435–442.

Harries-Jones, P., 1999. A Recursive-Vision: Ecological Understanding and Gregory Bateson. Toronto University Press, Toronto.

Landauer, R., 1961. Irreversibility and heat generation in the computing process. IBM J. Res. Dev. 5, 183–191.

Landauer, R., Bennett, C., 1985. The fundamental physical limits of computation. Sci. Am. 253, 48–56.

Laughlin, R.B., et al., 2000. The middle way. Proc. Natl. Acad. Sci. USA 97, 32–37.

Luigi, L.P., 1998. About various definitions of life. Origins Life Evol. Biosphere 28, 613–622.

Nelson, D.R., 2002. Current status of the tardigrada: evolution and ecology. Integr. Comp. Biol. 42, 652–659.

Neuman, Y., 2004. Meaning making in the immune system. Perspect. Biol. Med. 47, 317–328.

Neuman, Y., 2005. Meaning making in language and biology. Perspect. Biol. Med. 48, 320–327.

Neuman, Y., in press. A theory of meaning. Inform. Sci.

Plenio, M.B., Vitelli, V., 2001. The physics of forgetting: Landauer's erasure principle and information theory. Contemp. Phys. 42, 25–60.

Polanyi, M., 1968. Life's irreducible structure. Science 160, 1308–1312.

Rosen, S.M., 1988. A neo-intuitive proposal for Kaluza–Klein unification. Found. Phys. 18, 1093–1139.

Rosen, S.M., 1994. Science, Paradox and the Moebius Principle. State University of New York Press, New York.

Rosen, S.M., 2004. What is radical recursion? SEED J. 4, 38–57.

Schill, R.O., et al., 2004. Stress gene (hsp70) sequences and quantitative expression in Milensium tardigradum (Tardigrade) during active and cryptobiotic stages. J. Exp. Biol. 207, 1607–1613.

Strohman, R.C., 2000. Organization becomes cause in the matter. Nat. Biotechnol. 18, 575–576.

Waddington, C.H., 1957. The Strategy of the Genes. George Allen and Unwin Ltd., London.

Watanabe, M., et al., 2002. Mechanism allowing an insect to survive complete dehydration and extreme temperatures. J. Exp. Biol. 205, 2799–2802.

Wright, J.C., 2001. Cryptobiosis 300 years on from van Leuwenhoek: What have we learned about tardigrades? Zool. Anz. 240, 563–582.

Yates, F.E., 1993. Self-organizing systems. In: Boyd, C.A.R., Noble, D. (Eds.), The Logic of Life. Oxford University Press, Oxford, pp. 189–219.