Embryonics: Electronic Stem Cells

Lucian Prodan[1], Gianluca Tempesti[2], Daniel Mange[2], and André Stauffer[2]
[1] "Politehnica" University (UPT), Timisoara, Romania
E-mail: lprodan@cs.utt.ro, WWW: http://www.cs.utt.ro
[2] Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland
E-mail: name.surname@epfl.ch, WWW: http://lslwww.epfl.ch

Abstract

Embryonics is a long-term research project attempting to draw inspiration from the biological process of ontogeny, to implement novel digital computing machines endowed with better fault-tolerant capabilities. This article discusses the degree of bio-inspiration attained while also attempting to start a similarity debate on various implementation decisions, on why and how nature developed its subtle, intricated means of growing, healing and reproducing.

Motto: "What makes stem cells special is that they're immortal, and they can become anything they want to be." — Dr. James Thomson, University of Wisconsin.

Introduction

The incredibly huge number of some 60 trillion (60×10^{12}) cells make up a human being, with as many as 10 billion (10^{10}) cells with 100 trillion (10^{14}) interconnections concentrated in each of our brains (Mange & Tomassini 1998). Intelligence, creativity, the capacity of abstractization and ultimately conscience are all possible thanks to this marvelously complex human machine. Yet its entire structure emerges from a single cell, the zygote, giving birth to a completely functional organism that will continue to develop and enhance its features throught its entire life.

However, there is a key question that arises, driving biologists and not only: how can all this be possible? How can this be, that a single cell would divide for such a large number of times even us humans find difficult to imagine? And what mechanisms direct the division process so perfectly that when it ends the result is a healthy organism? Would it be possible to exploit these mechanisms to inspire engineers, perhaps including novel computational implementations? It seems that nature has created a remarkable circle: we became complex enough to develop sciences and now scientists have reached the point that enables them to study how nature can reach such complexity.

A special type of cell appears to answer some of the previous questions, a cell that can give birth to other identical cells, and all being able to become specialized cells themselves, such as muscular or nerve cells. But it is not all that easy to discover nature, let alone to penetrate its mysteries. After nearly 20 years of hard work, two teams of scientists have succeeded in growing and replicating these mother cells (Thomson & others 1998). Called "stem cells", these basic units ultimately mature and differentiate to become the building material of all types of body tissue (May 2000).

The fact that scientists are all driven by common questions is remarkably demonstrated by recent history, the research on novel bio-inspired computing systems having roughly the same age as modern biology. In the late 1940's von Neumann began to develop a theory of automata in order to contribute to a better understanding of both natural automata (living beings) and of artificial automata (computational systems) (Sipper *et al.* 1998). In more recent years there has been significant research carried out in a new project, aiming at creating bio-inspired computer hardware, called Embryonics (Tempesti 1998; Tempesti, Mange, & Stauffer 1998).

The purpose of this article is not to delve into the ethical issues' debate — related to cloning or using the DNA molecule as a threat (Alexander 2000) — but to take a comparative look to the recent findings in the field of cellular biology and their virtual mirror, the world of Embryonics. Intriguingly, there are many more similarities and common ideas than it is possible to explain by a mere coincidence. Section 2 briefly describes the discovery of a new kind of cell. Section 3 presents the path to a new kind of bio-inspired computer hardware within the Embryonics research environment, together with a deeper look inside the characteristics of the newly discovered cell and how the two relate to each other. Finally, Section 4 presents the conclusions and some general guidelines for the future of the Embryonics.

Nature Reveals Its Ways

Each and every living multi-cellular organism consists of groups of specialized cells that make up tissues and organs. Throughout its entire life, the perfect operation of this magnificent massively parallel biological system is

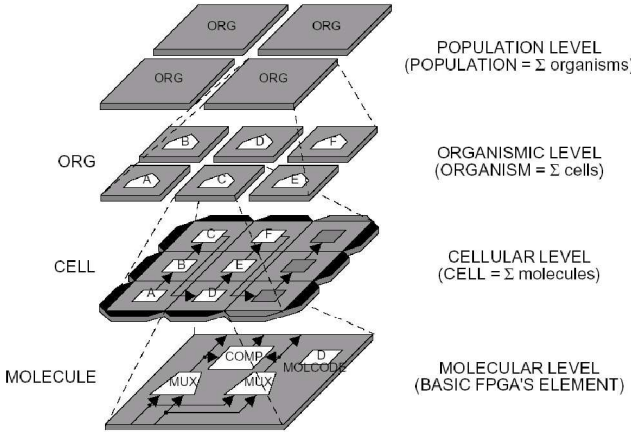

Figure 1: The 4 levels of organization of Embryonics.

ensured by a ceaseless process of cellular division, activated in order to overcome wounds and illnesses. A great majority of such cases are successfully repaired, with the exception of extreme situations such as the complete destruction of a vital organ or tissue. When this occurs, there are no possibilities of healing, which leads to the death of the entire organism.

At its very beginning, each organism originates from a single cell, the zygote. Its development process takes place through successive cellular divisions and differentiations, proof for the existence of a very special cell, capable of differentiating into any kind of needed, specialized cell. Christened *stem cell*, its unique transforming capacity could provide a solution for an organism's survival to extreme stress such as loss of a vital organ, giving it a huge potential in biology and medicine. Because this cell is the precursor to all other cell types in the human body, this accomplishment has set the stage for a revolution in medicine and basic biology (Thomson & others 1998; Anonymous 2001).

The zygote has the potential to form an entire organism as it has the remarkable feature of being *totipotent*, meaning that its potential is total (Anonymous 2000). Immediately following the fertilization, it starts to divide into identical totipotent cells that begin to specialize after several cycles of cell division, forming a hollow sphere of cells, called a blastocyst (May 2000).

But mastering the conditions necessary to witness the delicate phenomenon of cellular division is no simple matter. Yet the experiments made at Johns Hopkins University successfully verified that stem cells have the true potential of developing into basic cells found in all mammalian embryos (Shamblott & others 1998). However, directing the specialization process of the stem cells is another problem. We do know now that stem cells can in fact become any type of cell, either resulting new stem cells or specialized cells. What we are uncertain of is what exactly *instructs* a stem cell to specialize into a specific type of cell. Research conducted at Stanford reveals that in fact there are some stem cell "guardians", surrounding areas composed of stem cells, that determine which type of ordinary cell they will specialize in (Vaughan 2000).

As far as we know, the most interesting characteristics of the stem cells are the following:

- they can give rise to specialized cells;
- undifferentiated, they seem to have the ability to divide for apparently indefinite periods in culture;
- any of these cells can potentially develop into a fetus.

These are sufficient arguments to consider the fantastic potential of stem cells that lies in their ability to be ultimately directed to become specific types of cells or tissue. If, on one hand, this feature could be used to treat a host of cell-based diseases, on the other hand it might have a significant impact on the world of computer engineering.

The Embryonics Project — Biological Connections

As a long term research project, Embryonics has been developing for some years now becoming a consistent repository of bio-inspired solutions in computer engineering. Along with the proposed POE model (Sipper *et al.* 1997, also this volume, p**??**), the Embryonics project aims at developing ontogenetic hardware, i.e. hardware capable of self-replicating, self-repairing and evolving from its very own genetic material.

Fault tolerance has become a major requirement in modern computing. A great deal of research effort has been spent to achieve this feature and considerable boost comes from technological advancements, enabling system designers to consider new reconfiguration techniques applied to an entire computing universe made by connecting many identical entities (Mange *et al.* 1998; Negrini, Sami, & Stefanelli 1989; Shibayama *et al.* 1997). While the struggle for performance is still present, the term's definition has become somewhat loose due to a sufficient level of brute computing force available from nearly any digital machine. Today we witness the shift toward the first priority of the quest for *distributed, highly redundant and massively reconfigurable systems* and the Embryonics project makes no exception. Recent reliability analysis also show that embryonic structures open a new direction for building highly capable fault tolerant systems (Ortega & Tyrrell 1999).

Characteristics such as replication (self-replication), which can be seen as a special case of growth, and regeneration (self-repair), or recovery after wounds or illnesses, are part of the ontogeny process and are extremely attractive for many applications. The Embryonics project presents a consistent view of ontoge-

netic hardware and beyond (Gilbert 1991; Wolpert 1991; Prodan *et al.* 2001).

Embryonics quasi-biological artificial organisms are made up of a finite number of functionally identical cells (Mange & Tomassini 1998; Mange *et al.* 1998; Prodan *et al.* 2000; 2001), each of which is in turn made up of a finite number of functionally identical molecules (Figure 1). Each cell is a simple processor (a binary decision machine) realizing a unique function within the organism, defined by a set of instructions (program), which we call the *gene* of the cell. The functionality of the organism is therefore obtained by the parallel operation of all the cells while all the genes make up the genetic program or the *operative genome*. Cells are delimited by the existence of a rectangular cellular *membrane*, specified by a special part of the genome, called the *polymerase genome*. Each cell determines which gene is to be executed based on its coordinates inside the organism and stores a complete copy of the operative genome, thus making possible any task transfer. This feature makes the cells capable of *virtually replacing each other* (in the event of a detected malfunction) just like in real biological organisms.

The process of a cell deciding which gene to execute based on the coordinates from within its local environment, i.e. the surrounding cells, determines its functionality, not unlike cellular specialization in biological organisms. Furthermore, the access to the whole genetic program provides our electronic cell with *universality*, much as biological stem cells have the potential of becoming *any* type of specialized cell.

There are no limits on how large Embryonics cells can be. Then, the universality of the cell becomes actually the capacity of executing variable tasks — the more computationally complex the task, the more molecules required for the cell structure. Furthermore, by carefully selecting which portion of the code is to be executed by molecules, their universality is also assured — a molecule can effectively replace any other one by simply adapting its internal code.

Every living cell's innermass is delimited from the surrounding environment by the cellular membrane, which also acts as an *interface* with the exterior, allowing a limited exchange of substances. If the biological world allows and depends on exchanging substances, the world of silicon has more restrictive rules: the material replacing substances, but nonetheless allowed and dependent on its exchange, is *information*. Much as in nature, where substances entertain life by carrying energy and information, in the world of silicon electronic signals carry in a similar way the same ingredients, entertaining artificial life.

The artificial membrane (also called the space divider) has a triple role (Figure 2). Firstly, it acts like a spatial barrier, logically separating resources (molecules)

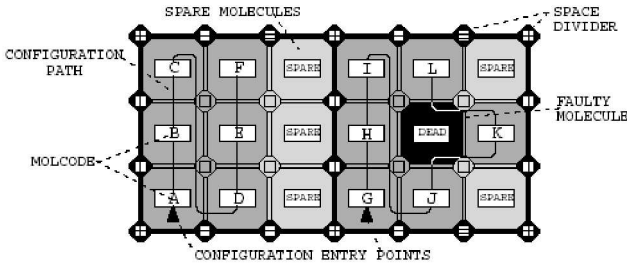

Figure 2: Self-repair at the molecular level

belonging to different cells and ensuring an individual identity in the surrounding environment. Secondly, it acts as a guide for the entering configuration, which contains the operative part of the genome (genes from A to D for the left cell and from G to L for the right cell, Figure 2). All molecules pertaining to a cell are configured with the corresponding gene in a chain-like process, which does not allow information to get outside the cell and be wasted; in a similar manner, the existence of the cellular membrane in biological cells restricts the access of the environment to their inner part both ways, thus preventing any unwanted loss of substances or possible intrusions to or from the environment. Thirdly, its presence triggers a mechanism determining which gene is to be executed by each molecule. This can be seen as a specialization at the molecular level, the surrounding membrane directing the whole process in a similar way the stem cells' "guardians" (Vaughan 2000) control cell specialization in biology.

What makes living beings so complex is the subtle cooperation between various mechanisms helping to preserve the innate features of an organism and continuously adapting them to a quite considerable extent to environmental challenges. Life is a quite dramatic and long testing process, so it is perhaps best for biological entities to employ self-developed procedures in order to check for abnormalities and trigger the repair processes.

As in nature, where multiple self-testing happens in each and every living being, Embryonics also relies on more than one such mechanisms (Mange *et al.* 1998; Tempesti 1998; Tempesti, Mange, & Stauffer 1998). The very first self-testing procedure employs test-vectors and applies to the core of the molecule. An off-line testing procedure was considered to be sufficient, and takes place before any critical data is loaded. Nature does a similar process at the lowest level possible, contained by the very intimate structure of the DNA itself. The two strands that make up the DNA continuously test each other by subtle chemical bonds, preventing and detecting a majority of possible errors. During operation, the molecular core can act as an active memory, much as the DNA does. The self-testing is ensured by "breaking" its internal register into two halves storing complementary data and acting in a similar way the two DNA strands

do (Prodan *et al.* 2001).

Another part of the molecule, the functional unit, is implemented as an on-line self-testing device, using the voting majority technique. Once the testing features in place, any detected error should allow the recovery, or healing of the organism. Due to the vast complexity of biological organisms, healing (self-repairing) mechanisms can only be effective if the task is hierarchically decomposed and dealt with accordingly.

Embryonics uses a hierarchy composed of two self-repairing mechanisms. The cellular structure is built of active and spare molecules. In the event of functional failure of an active molecule, all its functions are taken by the nearest spare molecule by means of shifting part of the cellular active resources one position. This is the self-repairing mechanism at the molecular level (Figure 2). A similar process takes place in nature, where the cell is capable of fabricating the resources needed. This is obviously impossible with current technology, the only way of providing additional resources at the molecular level being as spares. During its artificial life, the electronic organism may experience the situation when inside a cell a new fault is detected, but no more spares are available. This is the moment the second self-repair mechanism enters the stage, at the cellular level: the faulty cell "dies", then it is isolated, and all active cells are shifted a position by rerouting all the interconnections (Mange *et al.* 1998; Negrini, Sami, & Stefanelli 1989). This is again inspired by nature, where foreign bodies (objects or mutating cells) are isolated and eventually eliminated. Self-replication can be seen as a special case of growth; after configuring an initial cellular structure, the self-replication process considers this as a pattern and colonizes the whole environment (Sipper 1998; Tempesti 1998).

Conclusions

This article presented the essential bio-inspired features of the Embryonics project. It all started as a long-term research project, and, while it still remains largely so, the bio-inspired hardware developed allows us to build computing machines endowed with improved robustness, copied and adapted from biology to electronics. The technological advancements also give us now the opportunity to implement digital systems based on novel, complex operating principles but also put a higher pressure onto the design process and necessary trade-offs. Successful bio-inpired hardware may emerge only together with successful theory on nature's ways and the ways of implementing them in silicon.

All discussed issues lead us to believe that real bio-inspired hardware systems might just be closer than we think, thus narrowing the gap between biology and biologically inspired digital systems.

References

Alexander, D. 2000. The human genome project. *Science & Christian Belief* 12(2):98.

Anonymous. 2000. Stem cells: A primer. Technical report, National Institutes of Health. http://www.nih.gov/news/stemcell/primer.htm.

Anonymous. 2001. Opportunities and challenges: A focus on future stem cell applications. In *Stem Cells: Scientific Progress and Future Research Directions*. National Institutes of Health, Department of Health and Human Services.

Gilbert, S. F. 1991. *Developmental Biology*. MA: Sinauer Associates Inc., 3rd edition.

Mange, D., and Tomassini, M., eds. 1998. *Bio-inspired Computing Machines: Towards Novel Computational Architectures*. Lausanne, Switzerland: Presses Polytechniques et Universitaires Romandes.

Mange, D.; Sanchez, E.; Stauffer, A.; Tempesti, G.; Marchal, P.; and Piguet, C. 1998. Embryonics: A new methodology for designing field-programmable gate arrays with self-repair and self-replicating properties. *IEEE Transactions on VLSI Systems* 6(3):387–399.

May, M. 2000. Mother nature's menders. the battle against aging. *Scientific American*. Special Issue "The Quest to Beat Aging".

Negrini, R.; Sami, M. G.; and Stefanelli, R. 1989. *Fault Tolerance Through Reconfiguration in VLSI and WSI Arrays*. Cambridge, MA: MIT Press.

Ortega, C., and Tyrrell, A. 1999. Reliability analysis in self-repairing embryonic systems. In *Proc. 1st NASA/DoD Workshop on Evolvable Hardware*, 120–128.

Prodan, L.; Tempesti, G.; Mange, D.; and Stauffer, A. 2000. Biology meets electronics: The path to a bio-inpired FPGA. In *Proc. 3rd International Conference on Evolvable Systems: From Biology to Hardware*, 187–196.

Prodan, L.; Tempesti, G.; Mange, D.; and Stauffer, A. 2001. Embryonics: Artificial cells driven by artificial DNA. In *Proc. 4th International Conference on Evolvable Systems: From Biology to Hardware*, 100–111.

Shamblott, M., et al. 1998. Derivation of pluripotent stem cells from cultured human primordial germ cells. *Proc. Natl. Acad. Sci. USA* 95:13726–13731.

Shibayama, A.; Igura, H.; Mizuno, M.; and Yamashina, M. 1997. An autonomous reconfigurable cell array for fault-tolerant LSIs. In *Proc. 44th IEEE International Solid-State Circuits Conference*, 230–231.

Sipper, M.; Sanchez, E.; Mange, D.; Tomassini, M.; Perez-Uribe, A.; and Stauffer, A. 1997. A phylogenetic, ontogenetic, and epigenetic view of bio-inspired hardware systems. *IEEE Transactions on Evolutionary Computation* 1(1):83–97.

Sipper, M.; Tempesti, G.; Mange, D.; and Sanchez, E. 1998. Von Neumann's legacy: Special issue on self-

replication. *Artificial Life* 4(3).

Sipper, M. 1998. Fifty years of research on self-replication: an overview. *Artificial Life* 4(3):237–257.

Tempesti, G.; Mange, D.; and Stauffer, A. 1998. Self-replicating and self-repairing multicellular automata. *Artificial Life* 4(3):259–282.

Tempesti, G. 1998. *A Self-Repairing Multiplexer-Based FPGA Inspired by Biological Processes*. Ph.D. Dissertation, EPFL, Lausanne. No. 1827.

Thomson, J., et al. 1998. Embryonic stem cell lines derived from human blastocysts. *Science* 282:1145–1147.

Vaughan, C. 2000. Stem cells' "guardians" found to control cell specialization. *Stanford Report*.

Wolpert, L. 1991. *The Triumph of the Embryo*. New York: Oxford University Press.