Embryonic Machines That Divide and Differentiate

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Abstract. After defining a Universe for computer science in opposition to the Universe of biology, this paper presents the roles that cellular division plays in both of them. Based on the nine construction rules of the so-called Tom Thumb algorithm, cellular division leads to a novel self-replicating loop endowed with universal construction and computation. The self-replication of the totipotent cell of the "LSL" acronym serves as an artificial cell division example of the loop and results in the growth and differentiation of a multicellular organism.

1 Introduction

The *Embryonics* project (for *embryonic electronics*) aims at creating radically new computing machines inspired by Nature and able to grow, to self-repair, and to self-replicate.

The embryonic development of living beings is extremely complex. If numerous partial results have already been reported [14], there exist yet major controversies about the basic mechanisms which trigger the development of an organism and, more precisely, about the internal increase of complexity of a growing being [1].

Embryonic development can be roughly described as the construction of a three-dimensional carbonic organism from a one-dimensional blueprint, the genome, assuming that a number of external conditions are satisfied (food, temperature, etc.). Of course, the developmental process of complex organisms involves processes that are not completely specified within the genome, but are rather heavily influenced by the environment (homozygote twins grow up to become different individuals). However, for simpler organisms this observation is not necessarily as true: for example, the nematode worm *Caenorhabditis elegans*, a real star in the studies of the molecular biology of development, invariably develops into an adult hermaphrodite of exactly 945 cells, as long as environmental conditions are acceptable. Developmental processes based exclusively on the information stored in the genome are therefore possible, and it is then reasonable to begin exploring a developmental approach in an entirely new milieu by limiting the scope of research to the relatively simpler mechanisms involved in genome-based development.

A.J. Ijspeert et al. (Eds.): BioADIT 2004, LNCS 3141, pp. 201–216, 2004.

These mechanisms fascinate engineers who dream of developing computing machines mimicking living organisms in a completely different environment, the two-dimensional world of silicon. Our Embryonics project aims at creating such machines which, starting from a one-dimensional blueprint, an *artificial genome*, will be able to grow and give birth to computers endowed, as their living models, with original properties such as self-repair and self-replication. These *embryonic machines* would be best suited for harsh environments: space exploration, atomic plants, avionics, etc.

We shall briefly visit the Universe of biology and recall some fundamental mechanisms, notably cellular division and cellular differentiation which constitute our main source of inspiration. We will then come back to the Universe of computer science to embed these mechanisms into silicon, and to show how it is possible to design actual computing machines able to self-replicate.

In Sect. 2, after a short reminder of cellular division in living beings, we will show that a new algorithm, the *Tom Thumb algorithm*, will make it possible to design a self-replicating loop that can easily implement artificial cellular division in silicon. This algorithm will be illustrated by means of a minimal unicellular organism, the *Annulus elegans*, composed of four molecules. This mother cell will grow and then divide, triggering the growth of two daughter cells. This example is sufficient for deriving the nine rules which constitute the Tom Thumb algorithm. Sect. 3 deals with the generalization of the methodology previously described and its application to the growth and cellular differentiation of a multicellular organism, the *Acronymus elegans*, which implements the "LSL" acronym (for Logic Systems Laboratory). Sect. 4 will conclude by a brief discussion about the internal increase of complexity, as well as by a first and rudimentary calculation of the complexity of *Annulus elegans* and *Acronymus elegans*.

2 The Tom Thumb Algorithm for Artificial Cellular Division

2.1 Cell Division in the Universe of Biology

Before describing our new algorithm for the division of an artificial cell, let us remember the roles that cellular division plays in the existence of living organisms [2](p. 206).

"When a unicellular organism divides to form duplicate offspring, the division of a cell reproduces an entire organism. But cell division also enables multicellular organisms, including humans, to grow and develop from a single cell, the fertilized egg. Even after the organism is fully grown, cell division continues to function in renewal and repair, replacing cells that die from normal wear and tear or accidents. For example, dividing cells in your bone marrow continuously supply new blood cells. The reproduction of an ensemble as complex as a cell cannot occur by mere pinching in half; the cell is not like a soap bubble that simply enlarges and splits in two. Cell division involves the distribution of identical genetic material (DNA) to two daughter cells. What is most remarkable about

cell division is the fidelity with which the DNA is passed along, without dilution, from one generation of cells to the next. A dividing cell duplicates its DNA, allocates the two copies to opposite ends of the cell, and only then splits into two daughter cells".

In conclusion, we can summarize the two key roles of cell division.

- The construction of two daughter cells in order to grow a new organism or to repair an already existing one (genome *translation*).
- The distribution of an identical set of chromosomes in order to create a copy of the genome from the mother cell aimed at programming the daughter cells (genome *transcription*).

Switching to the Universe of computer science, we will propose a new algorithm, the *Tom Thumb algorithm*, which, starting with a minimal cell made up of four artificial molecules, the *Annulus elegans*, constructs both the daughter cells and the associated genomes. A tissue of such molecules will in the end be able to constitute a multicellular organism endowed with cellular differentiation.

2.2 Definition of the Universe of Computer Science

The implementation of developmental mechanisms in the world of silicon represents a complex challenge. Cellular division, notably, is a process that is inherently *physical*, in that it involves, if not the creation, at least the manipulation of matter. Unfortunately, current technology does not allow such manipulation where electronic circuits are concerned, and developmental approaches in the world of computer science must then be applied to *information* rather than matter.

Fortunately, the technology of field-programmable gate arrays (FPGAs) allows a simple transition between information (the bitstream that configures the circuit) and matter (the actual circuit implemented on the FPGA). This transition is the key background for the approach described in this article, where the basic unit, our *artificial cell*, is represented as a string of hexadecimal characters which in fact represents the configuration required to implement the actual cell (i.e., the logic gates that implement the cell's functionality) in a custom FPGA of our own design.

In general, our approach is based on a hierarchical system of growing complexity, with organisms (computing machines dedicated to a user-defined task) being made up of cells (small processing elements), themselves assembled starting with simpler components, the molecules (the elements of our custom FPGA). Our developmental mechanisms shall then operate by allowing the set of molecular configurations that implement a cell to replicate itself, implementing a process not unlike the cellular division that underlies the growth of biological organisms. A different set of mechanisms will then be used to assign a specific function to each of the cells (cellular differentiation).

A practical way to verify the realization of such novel mechanisms in the world of computer science is to approach the problem through the creation of an *artificial Universe*, defined by a container, a content, and a set of rules.

The container is a two-dimensional flat space, divided in rows and columns (Fig. 1a). Each intersection of a row and a column defines a rectangle or *molecule*, which divides in three memory positions: left, central, and right. Time flows in discrete clock times, the *time steps*, identified by integers ($t = -1, 0, 1, 2, ...$).

The content of this Universe is constituted by a finite number of symbols, each represented by a hexadecimal character ranging from 0 to E, that is, from 0000 to 1110 in binary (Fig. 1b). These symbols are either *empty data* (0), *molcode data* (for molecule code data, $M = 1$ to 7) or *flag data*, each indicating one of the four cardinal directions: north, east, south, west ($F = 8$ to E). Molcode data will be used for configuring our final artificial organism, while flag data are indispensable for constructing the skeleton of the cell. Furthermore, each character is given a status and will eventually be *mobile data* (white character), indefinitely moving around the cell, or *fixed data* (grey character), definitely trapped in a memory position of the cell (Fig. 1c). The original genome for the minimal cell is organized as a string of six hexadecimal characters, i.e. half the number of characters in the cell, moving counterclockwise by one character at each time step ($t = 0, 1, 2, ...$) (Fig. 1a).

The set of rules defines the behavior of the content of the Universe. It is defined by a set of 9 rules, used to construct the cells and to implement cellular division (growth).

A Universe is, of course, defined as a function of the kind of cells required to execute a given application. To provide an overview of the approach, in the present article the Universe is defined so as to implement the cells of the very simple organism *Annulus elegans*. It should be noted, however, that our approach is perfectly scalable: should an application need more complex organisms, it is possible to extend both the size of the molecules' memory and the number of molecules in each cell without altering the basic algorithm in the least.

2.3 Constructing the Cell

The three first rules (rules 1 to 3) allow for the construction of a first path closing on itself: a *loop* (Fig. 3) which will constitute the mother cell. At each time step, a character of the original genome, always beginning by a flag F, is shifted from right to left and stored in the lower leftmost molecule (Fig. 1a and 3). The construction of the cell, i.e. storing the fixed data and defining the paths for mobile data, depends on three patterns (Fig. 2).

- If the three memory positions of a molecule are empty (blank squares), the flag is shifted by one position to the right. Similarly, if the two rightmost memory positions of a molecule are empty, the flag is shifted by one position to the right (shift data: rule 1).
- If the rightmost memory position is empty and the two leftmost memory positions hold flags (F), the characters are shifted by one position to the right (load flag: rule 2). In this situation, the rightmost F' character is trapped in the molecule (fixed data), and a new connection is established from the central position toward the northern, eastern, southern or western molecule, depending on the fixed flag information ($F' = 8$ or 9, A or E, B, C or D).

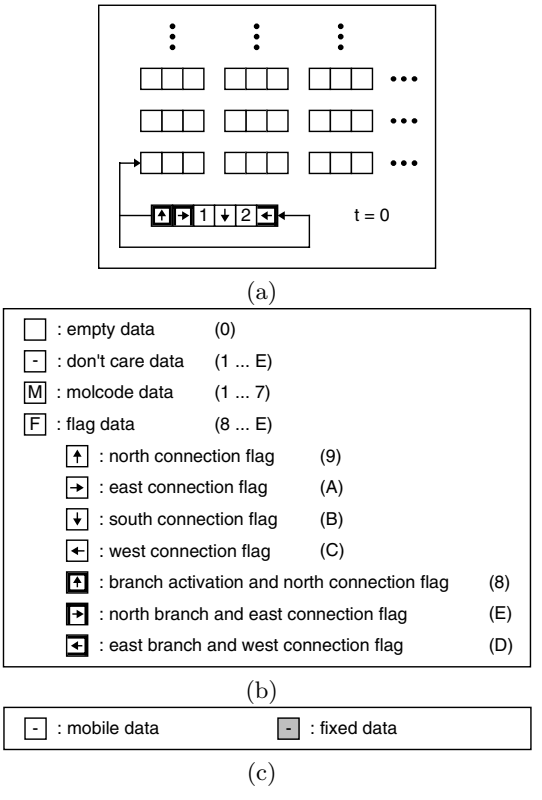


Fig. 1. Our artificial Universe. (a) The container with the genome of a minimal cell. (b) Graphical and hexadecimal representations of the symbols. (c) Graphical representation of the status of each symbol.

– If the rightmost memory position is empty, while the central and leftmost memory positions hold a flag (F) and a molcode (M) respectively, then the characters are shifted by one position to the right (load molcode and flag: rule 3). In this case, both characters are trapped in the molecule (fixed data), and a new connection is launched from the leftmost position toward the northern, eastern, southern or western molecule, depending on the fixed flag information ($F = 8$ or 9, A or E, B, C or D).

At time $t = 12$, twelve characters, i.e. twice the contents of the original genome, have been stored in the twelve memory positions of the cell (Fig. 3). Six characters are fixed data, forming the phenotype of the final cell, and the six remaining ones are mobile data, composing a copy of the original genome, the genotype. Both *translation* (i.e. construction of the cell) and *transcription* (i.e. copy of the genetic information) have been therefore achieved.

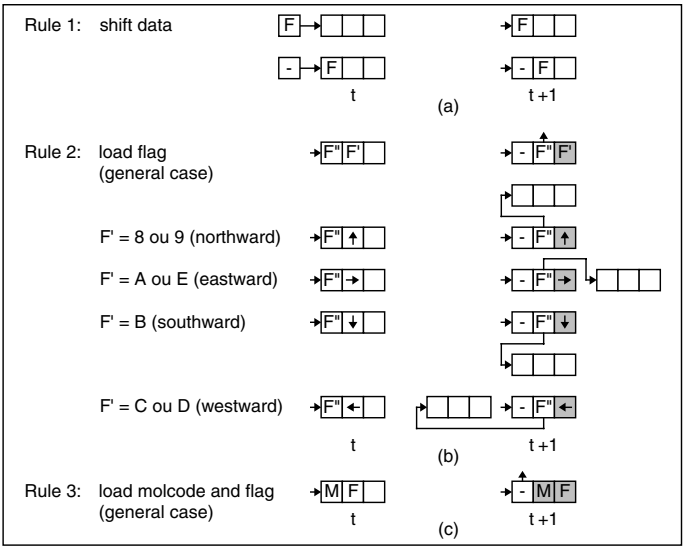


Fig. 2. The three rules for constructing a cell.

The fixed data trapped in the rightmost memory position(s) of each molecule remind us of the pebbles left by Tom Thumb for memorizing his way. The minimal artificial organism will be henceforth designated as *Annulus elegans*.

In order to grow an artificial organism in both horizontal and vertical directions, the mother cell should be able to trigger the construction of two daughter cells, northward and eastward. Two new rules (rules 4 and 5) are thus necessary.

At time $t = 8$ (Fig. 3 and 4a), we observe a pattern of characters which is able to start the construction of the northward daughter cell (rule 4). The upper leftmost molecule is characterized by two specific signals, i.e. a fixed flag indicating a north branch ($F = \mathrm{E}$) and a branch activation flag ($F = 8$) ready to enter the leftmost memory position.

At time $t = 17$ (Fig. 3 and 4b), another particular pattern of characters will start the construction of the eastward daughter cell (rule 5). The lower rightmost molecule is characterized by two specific signals, i.e. a fixed flag indicating an east branch ($F = \mathrm{D}$), and the branch activation flag ($F = 8$) in the leftmost memory position.

2.4 Growing a Multicellular Organism

In order to analyze the growth of a multicellular artificial organism, we are led to carefully observe the interactions of the different paths created inside and outside each individual cell. Numerous hazards are threatening the development of the different cells, and four new rules (rules 6 to 9) are necessary for avoiding collisions at the crossroads.

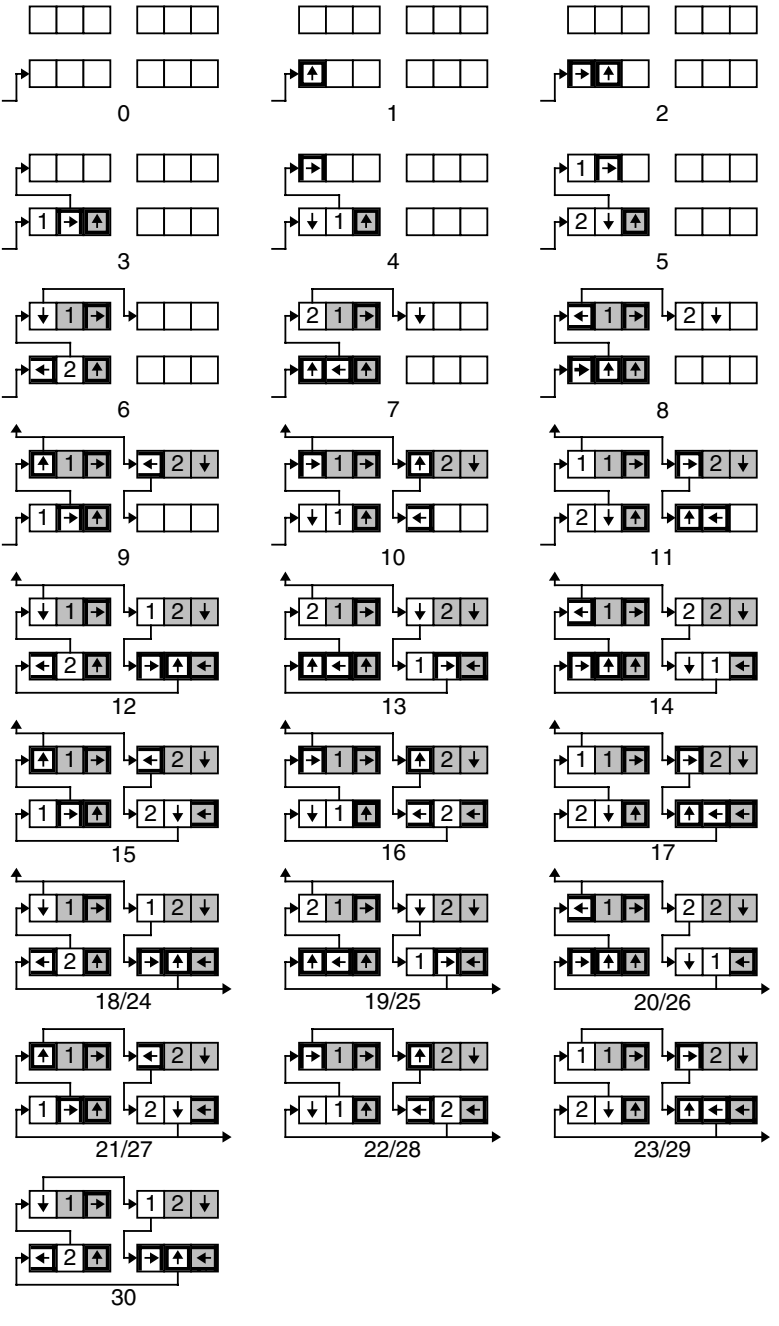


Fig. 3. Constructing the minimal cell.

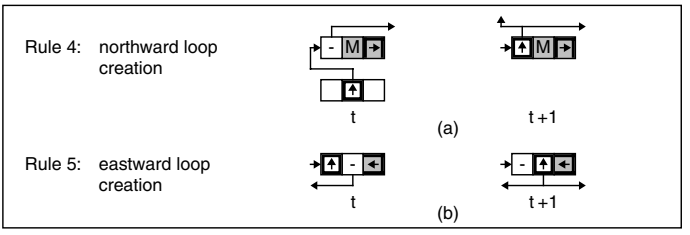


Fig. 4. The two rules triggering the paths to the north and east molecules.

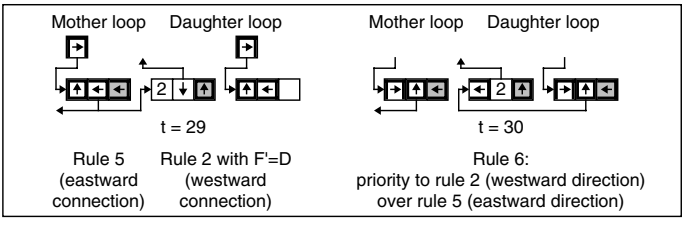


Fig. 5. Rule 6, defining the priority of the east-west direction over the west-east one.

Rule 6, detailed in Fig. 5, arbitrates the conflict between an eastward branch launched by the mother cell (rule 5) and the simultaneous construction of a westward path starting from a daughter cell, at the right of the mother cell (rule 2 with $F' = 2$). In such a case, we will choose the priority of the east-west direction over the west-east direction. This conflict may be represented by the simplified schema of Fig. 6a where only the daughter loop is represented. Such a schema can also be used for representing rule 7 (Fig. 6b: priority east-west over south-north), rule 8 (Fig. 6c: priority south-north over west-east), and rule 9 (Fig. 6d: priority east-west over south-north and west-east).

The diverse priorities defined by rules 6 to 9 may be described by the following relation:

$$(\text{east-west}) > (\text{south-north}) > (\text{west-east})$$

which expresses the following choice: a closing loop has priority over all other outer paths, which makes the completed loop entirely independent of its neighbors (rules 6, 7 and 9), and the organism will grow by developing bottom-up vertical branches (rule 8). This choice is quite arbitrary and may be changed according to other specifications.

It is now possible to come back to the detailed representation of a multicellular organism made up of 2×2 minimal cells (Fig. 7) and exhibit it at different time steps in accordance with the above mentioned priorities.

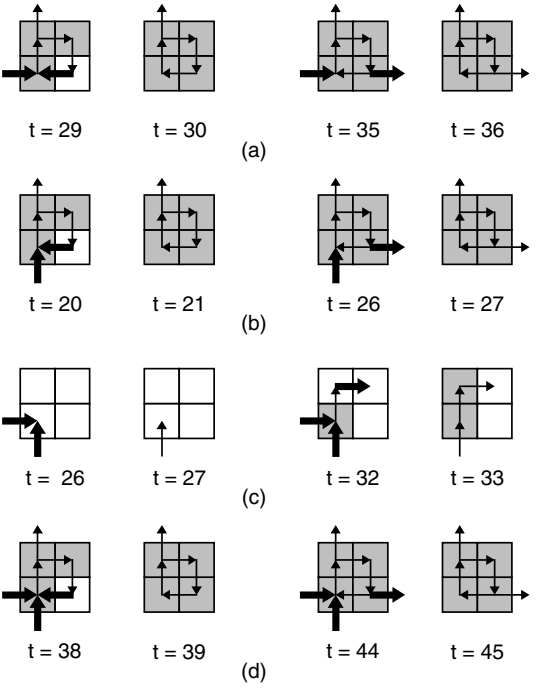


Fig. 6. The four priority rules. (a) Rule 6: east-west over west-east. (b) Rule 7: east-west over south-north. (c) Rule 8: south-north over east-west. (d) Rule 9: east-west over south-north and west-east.

3 Toward Differentiated Multicellular Organisms

3.1 Cell Differentiation in the Universe of Biology

The nematode *Caenorhabditis elegans* is a small worm that has recently come to occupy a large place in molecular biology of development. Thanks to its very particular characteristics (notably, the worm is transparent), it has been possible to reconstruct the entire anatomical history of each cell as the fertilized egg develops into a multicellular adult [13].

Two amazing conclusions emerged when the information gathered from detailed anatomical studies of living worms was combined with more classical anatomical studies obtained by electron microscopy of serial thin sections of the worm at different developmental stages. First, each cell in the adult worm is derived from the *zygote*, the first mother cell of the organism, by a virtually invariant series of cell divisions called a *cell lineage*. Second, as a direct consequence of the invariant cell lineages, individual nematodes are anatomically invariant carbon copies of each other. The mature adult hermaphrodite always consists of exactly 945 cells.

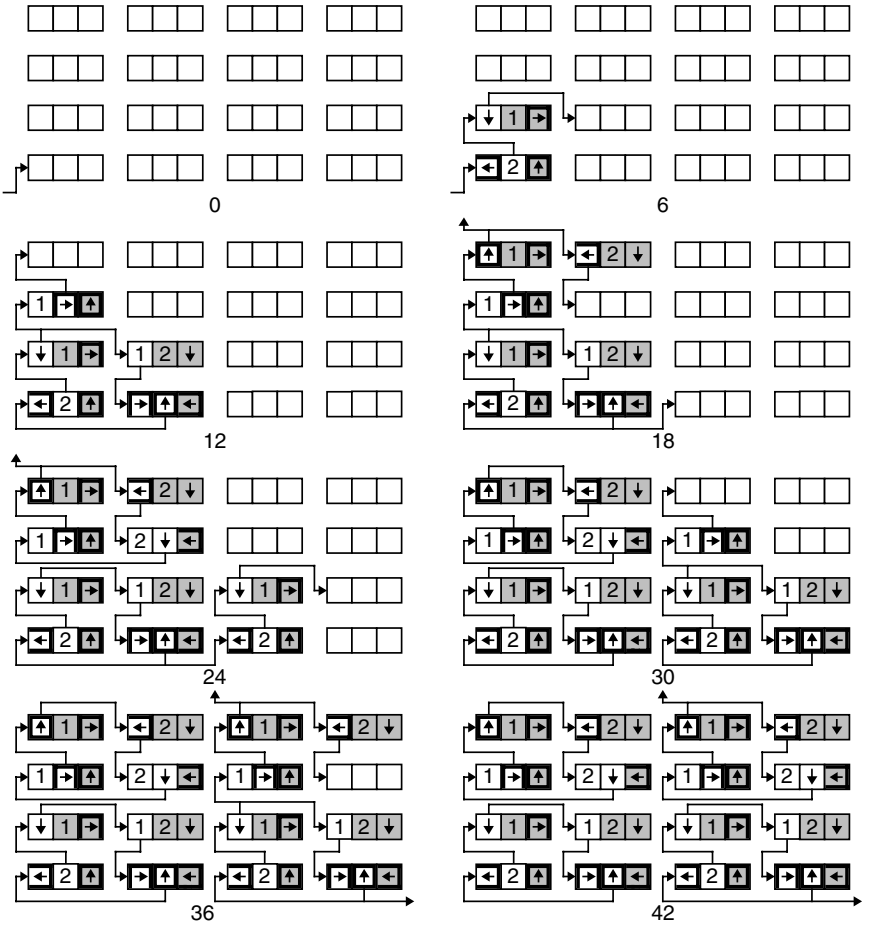


Fig. 7. Constructing a multicellular organism made up of 2×2 minimal cells.

Cell differentiation can proceed in at least two very different styles—*mosaic* and *regulatory*—which presumably reflect profoundly different molecular mechanisms. In *mosaic development*, or temporal development (so called because the organism is assembled from independent parts), the differentiation of a cell does not depend on the behavior or even the existence of neighboring cells: apparently, internal events within each cell determine its actions; such events could be triggered by cell division itself or by the ticking of an internal biological clock that is set in motion by fertilization. In *regulatory development*, or spatial development, differentiation is partially or completely dependent on the interaction between neighboring cells.

Mosaic development governed by strict cell lineages is the overwhelming rule in *C. elegans*, and regulative development the exception. In other multicellular

organisms (*Homo sapiens sapiens* included), the reverse is almost certainly true. The price of such mosaicism may be very small size (perhaps only a limited number of cell divisions can be so rigidly programmed) and only modest complexity (cell-cell interactions may be required to construct a more elaborate anatomy).

As we are dealing with the construction of rather complex computing machines, we are led to choose the model of regulatory development, or spatial development, in the framework of the Embryonics project.

3.2 Cell Differentiation in the Universe of Computer Science

Even if the final goal of our project is the development of complex machines, in order to illustrate the basic mechanisms of Embryonics we shall use an extremely simplified example, the display of the acronym "LSL", for Logic Systems Laboratory.

The machine that displays the acronym can be considered as a one-dimensional artificial organism, *Acronymus elegans*, composed of three cells (Fig. 8a). Each cell is identified by a X coordinate, ranging from 1 to 3 in decimal or from 01 to 11 in binary. For coordinate values $X = 1$ and $X = 3$, the cell should implement the L character, while for $X = 2$, it should implement the S character. A totipotent cell (in this example, a cell capable of displaying either the S or the L character) comprises $6 \times 7 = 42$ molecules (Fig. 8b), 36 of which are invariant, five display the S character, and one displays the L character. An incrementer—an adder of one modulo 3—is embedded in the final organism; this incrementer implements the truth table of Fig. 8c and is represented by the logic diagram and symbol of Fig. 8d. According to the table, the value of the binary variable $X0$ is sufficient to distinguish the display of character L ($X0 = 1$) from the display of character S ($X0 = 0$ or $X0' = 1$).

These specifications are sufficient for designing the final architecture of the totipotent cell (Fig. 9). According to the Little Thumb algorithm, half of the molecules of the cell, i.e. 21, are genotypic (G) and have no functionality: they are used for storing a copy of the original genome. The others are phenotypic molecules, divided into six categories (from 1 to 6) depending on their functionality:

1. Two busses for the horizontal transfer of the X coordinate.
2. Modulo 3 incrementation.
3. One bus for the vertical distribution of the $X0$ logic variable.
4. Permanent display of characters L and S.
5. Display of S character only ($X0 = 0$ or $X0' = 1$).
6. Display of L character only ($X0 = 1$).

The final totipotent cell is therefore made up of $6 \times 7 = 42$ molecules connected according to the pattern in Fig. 10a: bottom-up in the odd columns, top-down in the even columns, with the lower row reserved for closing the loop. It is then possible to define all the flags in the rightmost memory position of each molecule (grey characters in Fig. 10a) without forgetting the branch activation

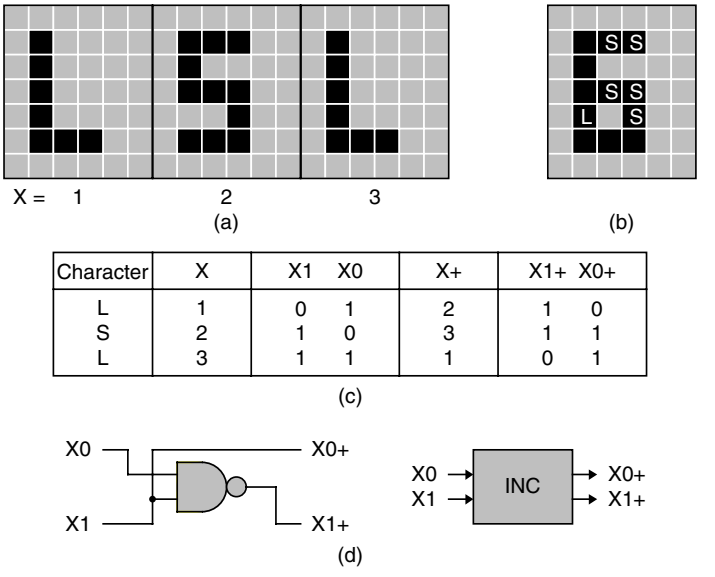


Fig. 8. Specifications of the *Acronymus elegans*. (a) Three cell artificial organism. (b) The totipotent cell. (c) Truth table of the coordinate incrementer. (d) Logic diagram and symbol of the incrementer.

and north connection flag in the lower molecule of the first column ($F = 8$), the north branch and east connection flag in the upper molecule of the first column ($F = \mathrm{E}$), and the east branch and west connection flag in the lower molecule of the last column ($F = \mathrm{D}$).

According to our algorithm, the 21 phenotypic molecules (Fig. 9) occupy a fixed, pre-determined position in the totipotent cell (Fig. 10a). The other 21 genotypic molecules are used for storing and circulating the final genome whose detailed information, i.e. $21 \times 3 = 63$ hexadecimal characters (Fig. 10b), is derived by reading clockwise the fixed characters (grey characters in Fig. 10a) of the whole loop, starting with the lower molecule of the first column. Finally, we just assume that each genotypic molecule will not affect the display in order to respect the original specifications.

Last, it was possible to embed the basic molecule in each of the 2000 field-programmable gate arrays of the BioWall [11] and to show the growth of a first multicellular artificial organism, *Acronymus elegans*, followed by its self-replication in both vertical and horizontal dimensions (Fig. 10c). We therefore obtain a population of identical organisms, i.e. clones, thus creating a fourth level in our hierarchy, a population of organisms.

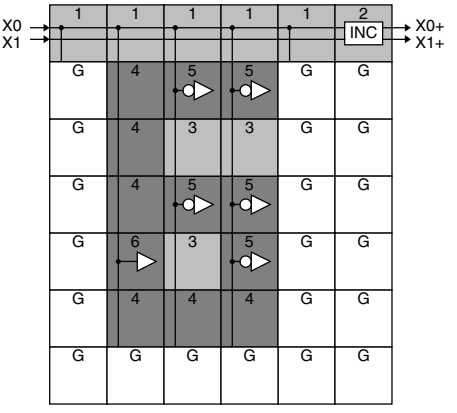


Fig. 9. The genotypic and phenotypic molecules of the totipotent cell.

4 Conclusion

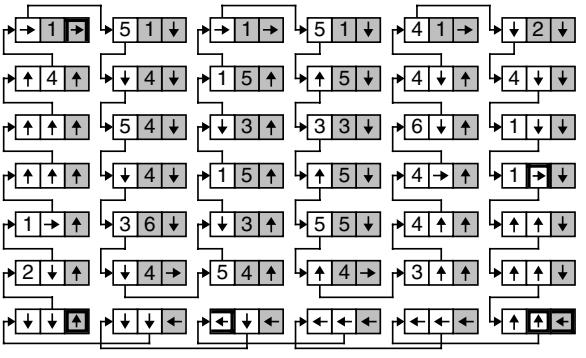
4.1 Present and Future Applications

Several years before the publication of the historical paper by Crick and Watson [12] revealing the existence and the detailed architecture of the DNA double helix, von Neumann was already able to point out that a self-replicating machine required the existence of a one-dimensional description, the genome, and a universal constructor able to both interpret (translation process) and copy (transcription process) the genome in order to produce a valid daughter organism. Self-replication allows not only to divide a mother cell (artificial or living) into two daughter cells, but also to grow and repair a complete organism. Self-replication is now considered as a central mechanism indispensable for circuits that will be implemented through the nascent field of nanotechnologies [4] [10], particularly when the fault-tolerant properties associated with our developmental approaches are taken into consideration [9].

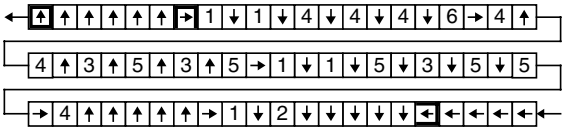
A first field of application of our new self-replicating loop is quite naturally classical self-replicating automata, such as three-dimensional reversible automata [5] or asynchronous cellular automata [8].

A second, and possibly more important field of application is Embryonics, where artificial multicellular organisms are based on the growth of a cluster of cells, themselves produced by cellular division [6] [7]. It is within this context that cellular differentiation will become a key aspect of our growth mechanism, as each newly-created cell identifies its position and its designated role within the complete organism.

Finally, other possible open avenues concern the evolution of such loops and/or their capability to carry out massive parallel computation [3].



(a)



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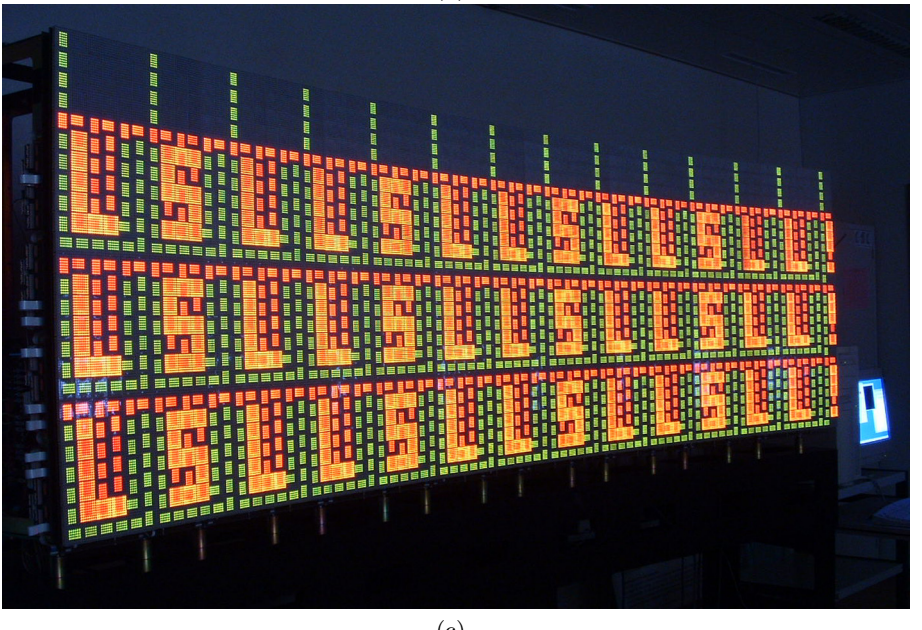

(c)

Fig. 10. Realization of the *Acronymus elegans*. (a) The $6 \times 7 = 42$ molecules of the totipotent cell. (b) Genome. (c) BioWall implementation (Photograph by A. Badertscher).

4.2 Emergence and Complexity

If we assume the existence of a silicon substrate organized as a homogeneous matrix of basic elements or "molecules", we observe that the injection of a finite

string of discrete symbols, the genome, successively produces the emergence of cells (by cellular division), of multicellular organisms (by cellular differentiation) and, finally, of a population of identical organisms, i.e. clones (by cyclic repetition of the coordinates). This emergence is not magic, and follows from a deterministic use of logic symbols considered as the configuration of the molecules, themselves implemented by field-programmable gate arrays (FPGAs). Emergence is then the trivial result of a chain of several mechanisms (cellular division and differentiation, repetition of coordinates). This appearance of a complex system (a population of *Acronymus elegans* in our example) from rather simple molecules and a short genome, simply creates the illusion of an internal growth of complexity.

4.3 Measurement of Complexity

The measurement of the complexity of embryonic machines, in the Universe of computer science, is rather delicate. We will try to propose a first and somewhat rough approximation. Referring to the definition of the complexity due to Kolmogorov, we measure the complexity $K(G)$ of the genome of our artificial organism as the length of the smallest program able to generate this genome, to which we add the complexity $K(C)$ necessitated by the configuration transforming an element of the FPGA (in our case, a Xilinx Spartan XCS10XL circuit) into a molecule.

This mode of calculation accounts for the complexity of the software (the genome) and the hardware (the FPGA), and allows for comparing the complexity of concurrent realizations on the same silicon substrate. In the case of *Annulus elegans* (Fig. 1a), we have $K(G) = 6 \times 4 = 24$ bits, with $K(C) = 24'896$ bits, i.e. a total of $K(G) + K(C) = 24'920$ bits, while in the case of *Acronymus elegans* (Fig. 10b), we have $K(G) = 252$ bits with $K(C) = 26'808$ bits, i.e. a total of $K(G) + K(C) = 27'060$ bits. We observe, in the last case, that the configuration of the molecule is a hundred times more complex than that of the genome necessitated by the construction of the "LSL" acronym. This enormous difference can also be found in biology, where most of the genetic material is aimed at producing the ribosome, which is roughly equivalent to our artificial molecule able, in the Embryonics project, to decode and interpret the artificial genome.

Finally, we hope that our reader will be convinced that computer science may achieve its own growth by renewing its inspiration from the observation of the marvelous machines which populate the living world.

Acknowledgments. This work was supported in part by the Swiss National Science Foundation under grant 20-100049.1, by the Leenaards Foundation, Lausanne, Switzerland, and by the Villa Reuge, Ste-Croix, Switzerland.

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