EPIAL
An Epigenetic Approach for an Artificial Life Model

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Abstract: Neo-Darwinist concepts have always been questioned and, nowadays, one of the sources of debate is epigenetic theory. Epigenetics study the relation between phenotypes and their environment, and the way this relation can regulate the genetic expression, while producing traits that can be inherited by offspring. This work presents an Artificial Life model designed with epigenetic concepts of regulation and inheritance. A platform was developed, in order to study the evolutionary significance of the epigenetic phenomena, both at individual and population levels. Differences were observed in the evolutionary behavior of populations, regarding the epigenetic variants. Agents without epigenetic structures display difficulties thriving in dynamic environments, while epigenetic based agents are able to achieve regulation. It is also possible to observe the persistence of acquired traits during evolution, despite the absence of the signal that induces those same traits.

1 INTRODUCTION

150 years after the publication of *"On the Origin of Species"* (Darwin, 1859), Darwin's theory of evolution by means of natural selection is still a source of inspiration, but also of debate. Neo-Darwinism (Dawkins, 1976), the idea that evolution is gene centric and that the organisms' structures are untouchable by the environment, is due for a revision, as defended by some authors (Jablonka and Lamb, 2005). Different theories claim that the modern synthesis provides for an incomplete view of evolution, regarding the separation between organism and nature (Waddington, 1942). Genetic structures are far more complex than previously thought, due to the non linear nature of the mapping between genotype and phenotype. Epigenetics posit the existence of environmentally based regulatory operations, and the possibility for inheritance of structural marks (Jablonka and Lamb, 2005). Several approaches in Artificial Life (ALife) attempt to model biological phenomena, mostly focusing on the Neo-Darwinist point of view in evolution. Most models perceive the environment solely as a factor of selection, discarding interrelations between agents and their world, such as the influence of the environment in the developmental processes (Rocha, 2007), which could provide for an alternative evolutionary approach (Jablonka and Lamb, 2005). In this work, we present an approach for an ALife model that considers epigenetic concepts, focusing on the regulation of organisms and the possible inheritance of epigenetic acquired marks. By including regulatory elements in the agents' structures, our model enables the study of the evolutionary significance of epigenetic concepts, while contributing to an enriched ALife model. The remainder of this article is organized in the following way: section 2 briefly tackles epigenetic theory; section 3 presents the current state of the art in epigenetic or related ALife models; section 4 describes the developed model, *EpiAL*; in section 5, some experimental results are shown; finally, section 6 discusses some final remarks pointing to some future work directions.

2 EPIGENETICS

Epigenetics is conceived as a set of genetic mechanisms and operations involved in the regulation of gene activity, allowing the creation of phenotypic variation without a modification in the genes' nucleotides. Some of these variations are also possibly inheritable between generations of individuals (Gilbert and Epel, 2009). The focus is on the major importance of development in organisms, but also on the relationship between the mechanisms of devel-

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opment and the genetic system and, ultimately, with evolution itself (Jablonka and Lamb, 2005). In terms of phylogeny, epigenetics refers to the traits that are, or can be, inherited by means other than DNA nucleotides. Epigenetics in relation to ontogeny refers to the influence, through epigenetic effects, of structural genetic parts of an individual during its lifetime (Gorelick, 2004). Although epigenetic marks can be inheritable, their frequency of inheritance is lower than nucleotide sequences (Holliday, 1994). This is due to the fact that epigenetic signals are much easier to alter through environmental disturbances and, therefore, it could result in a high and undesirable variability (Gorelick, 2004). Four types of (cellular) epigenetic inheritance systems (EIS) have been theorized (Jablonka and Lamb, 2005): (i) self-sustaining regulatory loops; (ii) structural templating; (iii) chromatin marking systems; (iv) RNA-mediated inheritance . The one that is used for our work is the chromatin system, in which methylation is one of the possible marks (Jablonka and Lamb, 2005). Methylation of DNA refers to the addition of a methyl group to the base sequence, that although does not change the coding properties of the base, can influence its gene expression (Bender, 2004; Boyko and Kovalchuk, 2008). It is known (Gorelick, 2004) that stress responses (tolerance, resistance, avoidance or escape) from the organisms, which are induced from environmental conditions, can lead to responses of methylation or demethylation of a binding site of chromosomes. The effects of these responses can both be heritable and remain present during more than one generation (Gorelick, 2004). Most individuals, during development, possess mechanisms that erase the methylation marks from the parents, sometimes resetting the genome to the original state (Youngson and Whitelaw, 2008). Nevertheless, there are cases in which these erasure operations are not fully accomplished, with epigenetic variation persisting through meiosis, and being retained by the offspring (Jablonka and Lamb, 2005).

3 STATE OF THE ART

Artificial Life (ALife) is a scientific area whose main goal is the study of life and life-like phenomena by means of computational models, aiming at a better understanding of those phenomena. As a side effect, ALife has also produced nature-inspired solutions to different engineering problems. At the core of ALife activity, we find the development of models that can be simulated with computers. Although some works use epigenetic theory (or related concepts) for problem solving techniques, to the best of our knowledge, none tackles the question of experimenting with epigenetic ideas regarding the evolutionary questions posed by the concept itself. This is a flaw that is pointed out by other authors as well (Rocha, 2007). There are some approaches for problems solving model that take inspiration in epigenetic, or epigenetic related ideas. In (Rocha and Kaur, 2007), the authors model an agent structure that is able to edit the genotype, allowing the same genotype to produce different phenotypic expressions. This edition, however, is not influenced by environmental conditions. A dynamic approach for the environment is presented in (Clune et al., 2007), where an Avida (Ofria and Wilke, 2004) based model promotes a time based symmetric environment in order to induce the agents to produce phenotypic plasticity (Pigliucci, 2001). In (Tanev and Yuta, 2008), epigenetic theory is used in order to model a different sort of genetic programming, with the modelling of different life phases (development, adult life) being used to adapt the agents to the environment. During the simulations, the agents adapt to the environment using epigenetic based processes, that are separated between somatic and germ line structures. Finally, in (Periyasamy et al., 2008), epigenetic concepts are used for the formulation of an Epigenetic Evolutionary Algorithm (EGA). The algorithm is used in order to attempt an optimization for the internal structures of organizations, with a focus on the autopoietic behavior of the systems.

4 EPIAL MODEL

EpiAL aims at studying the plausibility for the existence of epigenetic phenomena and its relevance to an evolutionary system, from an ALife point of view. In this section, we first describe the conceptual design and notions used in *EpiAL*, focusing in the agent, the regulatory mechanisms and the environment. Then we present the dynamics of the system, explaining how to evaluate the agents and the mechanisms of inheritance of *EpiAL*.

4.1 Conceptual Design

In our model, epigenetics is considered as the ability for an agent to modify its phenotypic expression due to environmental conditions. This means that an agent has regulatory structures that, given an input from the environment, can act upon the genotype, regulating its expression. We also consider the possibility for the epigenetic marks to be inherited between generations,

through the transmission of partial or full epigenetic marks (methylation values), allowing the existence of acquired traits (methyl marks) to be transmitted through generations of agents. The proposed model is based on two fundamental entities, the **agent(s)** and the **environment**. Their relation and constitution are conceptually depicted on figure 1. The environment

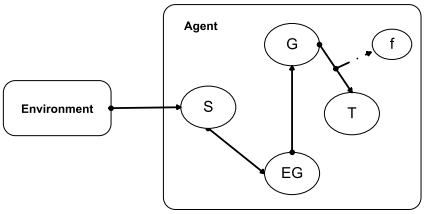


Figure 1: EpiAL conceptual model.

provides inputs that are perceived by the sensors of the agent (S). These sensors are connected to the elements that compose the epigenotype (EG), i.e., the epigenetic code of the agent. The epigenotype is composed of structures that can act over the agents' genotype (G), performing regulatory functions. This regulation occurs in methylation sites that are assigned to each of the genes, controlling their expression. The methylation value for a gene is a real value comprehended between 0 (not methylated at all) and 1 (fully methylated). It is this value that determines, stochastically, the type of expression for each of the genes. Finally, genes are expressed, originating the phenotype of the agents, which is composed of a set of traits (T). This mapping from expressed genotype to phenotype is performed according to a function (**f**) that relates sets of genes with the traits. In figure 2, we show an example where each trait is dependent of 3 genes.

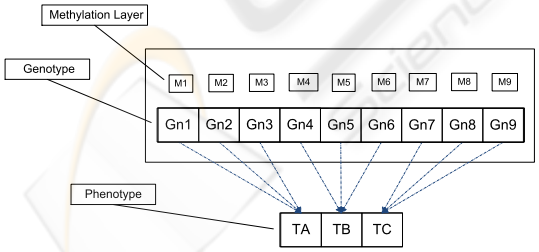
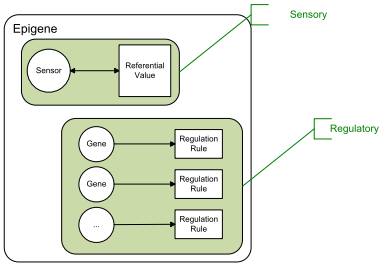


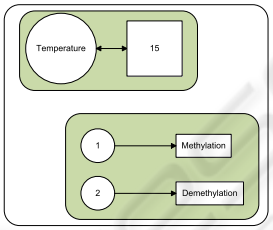
Figure 2: Genotype to phenotype mapping.

4.2 Regulation

The regulatory actions are taken under control of the epigenes. An agent can contain one or several epigenes, that have the structure shown in figure 3. Epigenes are composed of two main parts, sensory and



(a) Generic epigene structure.



(b) Concrete example of an epigene.

Figure 3: Epigene structure.

regulatory (figure 3(a)). The sensory section is a tuple that states (i) the sensor to which the epigene is connected and (ii) the reference value that is going to be used to compare with an environmental effect. The possible reference values (for instance, the mean values for each range of environmental effects) are previously setup by the experimenter. The other constituent of the epigenes, the regulatory section, contains a list of tuples, with each tuple representing a gene and a regulatory operation. During a regulatory phase, the reference value encoded in the epigene is compared against the environmental value perceived by the sensor corresponding to the epigene. If the epigene detects an activation, it acts on the genotype by firing the rules that it encodes. Formulas 1 and 2 are used to define the update of the methylation sites, with $m(g)$ representing the methylation value of gene g, $BaseMethyl$ a methylation constant and $AcValue$ the activation value perceived from the sensory operation, proportional to the level of activation perceived. The rules can be to *methylate* (formula 1) or *demethylate* (formula 2) a certain gene, which means that a methylation value is either increased or decreased for that gene.

$$m(g)_{new} = max(1, m(g)_{old} + (BaseMethyl * AcValue)) \quad (1)$$

$$m(g)_{new} = min(0, m(g)_{old} - (BaseMethyl * AcValue)) \quad (2)$$

4.3 Environment

The environment is modelled as a 2D grid with each location being transposable or not (a wall). Each of the locations also has different attributes - temperature, light and food - that can vary along time. These attributes are used to define the favoured traits for the locations. A certain location in the world favours agents which have the traits more adequate for the current environmental conditions. Therefore, a change in an environmental condition might also imply a change in the trait that is favoured. This is shown in figure 4, where a modification in the temperature state also implies a modification in the set of favoured traits. However, environmental dynamics are also used to promote the regulatory expression of agents. This allows for an influence of the environment over the agents not only by performing selection, but also by inducing possible structural changes (either adaptive or disruptive) within the agent. Because the agents sense environmental conditions, if there is a change in the environment then it is possible that regulatory actions are undertaken in the agents structures.

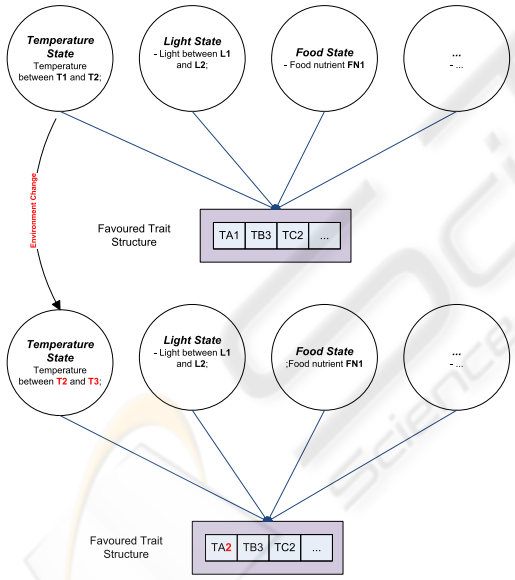


Figure 4: Environmental traits setup of favoured traits.

4.4 System Dynamics

The simulation of the agents in the environment is performed in evolutionary steps, as shown in figure 5. Agents are born and, either during their development phase or their adult life, are subject to regulatory phases. Here, by sensing environmental conditions, they regulate their expression. At the core of

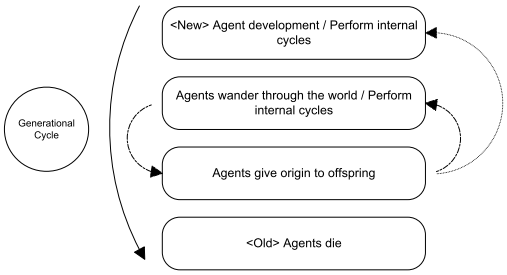


Figure 5: EpiAL system cycles.

the evolutionary system is a Darwinian evolution and, as such, agents are subject to selection, with the best ones being chosen for reproduction and new agents being subject to mutation. The agents live for a number of generations, originate offspring periodically and die of old age, with the possibility for different generations to live at the same time in the environment. The time step of the agents is independent from the one in the environment. An agent can perform several internal cycles of regulation or food digestion during only one environmental cycle.

4.5 Evaluation

As agents do possibly have different performances during their lifetime, due to their different regulation status, it is relevant to possess means for this evaluation to take into account not only the immediate performance, but also an account of the past behaviour of the agent. Moreover, recent values are more important to evaluate an agent. In order to evaluate the agents in *EpiAL*, two measures are used: *direct* fitness evaluation, i.e., the immediate fitness of the agents. This value is obtained by comparing the agents' trait values with the favoured ones for the location (cell) in which the agent currently stands (formula 3). From the formula, it is clear that the lower the sum of the module value of the differences, the better. Therefore, agents attempt to minimize this direct fitness. During the life of the agents, these evaluations are stored. When one desires to evaluate the global performance of an agent, the *weighted* evaluation is performed. This calculation is based on the exponential moving average method, proposed in (Achelis, 2000). In simple terms, this method assigns more weight to recent evaluations. The weighted sum calculated in formula 4 is used to obtain the weighted fitness, as depicted in formula 5 ($f(t)$ is the direct fitness evaluation for time t). This allows to perceive if the current regulatory state of the agent is beneficial or detrimental. At the same time, allows agents that are born later to be evaluated without prejudice from the older agents.

$$Fitness = \sum_{i=1}^{3} |Phenotype_i - CellFavouredTrait_i| \quad (3)$$

$$wSum(t) = w(1)f(1) + w(2)f(2) + \ldots + w(t)f(t) \quad (4)$$

$$WeightedFit = \begin{cases} \frac{1}{wSum} & \text{if } wSum > 0.2 \\ 5 & \text{if } wSum <= 0.2 \end{cases} \quad (5)$$

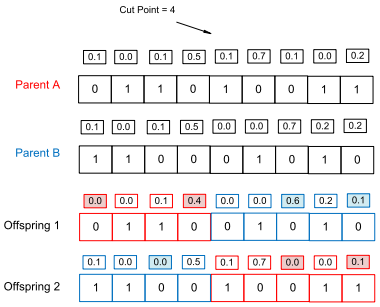


Figure 6: Partial transfer of methylation marks.

4.6 Inheritance

During reproduction, crossover operations are used, so the genetic material of the parents is combined to form the offspring genetic material. The genotype is immutable during an agent's life, but there is, however, the possibility for the methylation marks to be inherited by the offspring. In *EpiAL*, there are three different mechanisms of epigenetic methylation mark transmission: (i) faithful transmission, in which the methylation marks are transmitted entirely to the offspring; (ii) complete erasure, where all the marks are deleted from parent to offspring, being reset in the new organism; or (iii) partial and stochastic erasure, in which some of the marks may be partially erased. This partial erasure is either performed uniformly over the whole genotype or independently for each gene, according to formulas 6 (*DeltaMax* being the maximum erasure value) and 7. Partial inheritance of methyl marks is exemplified in figure 6. Here, methylation values of genes 1, 4 and 9, for the first offspring, and genes 3, 7 and 9, for the second offspring, are slightly decreased, compared to the original parents' marks. They have suffered a partial, stochastic erasure.

$$\Delta Erase = Rand(0, DeltaMax) \quad (6)$$

$$\forall g\text{: } methyl(g)_{new} = methyl(g)_{current} - \Delta Erase \quad (7)$$

5 EXPERIMENTAL RESULTS

Several types of experiments were performed with the *EpiAL* model, in order to study the mechanisms that influence the evolution of the agents. Agents were subject to environments where the three conditions encoded in the world (temperature, light and food) were modified, either periodically or non periodically. Populations without epigenetic mechanisms are compared against epigenetic ones. The epigenetic mechanisms - encoded in the agents' epigenotype - remain static and are not subject to evolution. In table 1 are shown the main parameters used or tested, while table 2 presents the different major mechanisms that were also experimented with in our simulations. These values were applied in several different simulations in which the environmental setup would vary from modifying one or more conditions, periodically or non periodically, with higher or lower modification values. As available space does not permit the exhaustive presentation of all these results, we present two types of experiments that demonstrate the typical behavior of the *EpiAL* platform.

Table 1: Parameters for the simulations.

Parameter	Value
Agent Step	1
Fitness Smooth Factor	0.5
Aging Step	1
Aging Value	0.5/1/1.5
Dying Age Base	100
World Step	1
Mating Step	10
Initial Agents	15
Offsprings (per mating)	6
Agents Initial Age	[-10;-5;-1]
Epigenetic Sensing Factor	[3;4]
Methyl Base Value	[0.1;0.3;0.5;0.7]
Genetic Mutation Rate	[0.01; 0.1]
Losers' Hype (Tournament)	[0.05; 0.15]

Figure 7 shows a simple environment where the temperature is modified, periodically, each 100 iterations.

The results (average fitness values for sets of 30 runs) for this environment are shown in figure 8. Non epigenetic populations, using tournament selection with a mutation rate of 0.01, perform poorly in this sort of environment, whereas the epigenetic pop-

Table 2: Methods for the simulations.

Action	Method
Agent Aging	Fitness Related
Agent Death	Stochastic
Selection	Tournament (2 Pair)
Reproduction	Sexual (Crossover)
Genetic Crossover	Trait Based (Gaps of 3)
Partial Methyl Erasure	Overall

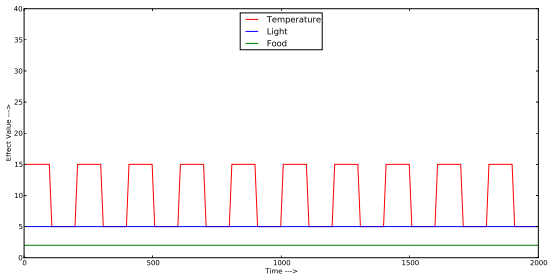


Figure 7: Dynamic, periodic temperature.

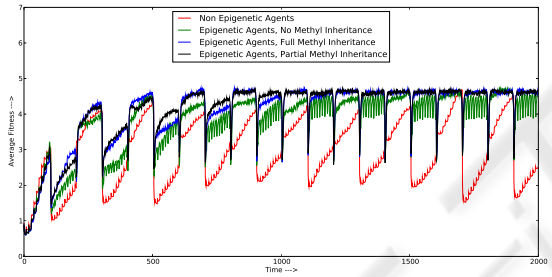


Figure 8: Average fitness results for different populations, regarding the environment shown in 7.

ulations, subject to the same evolutionary operations of selection, crossover and mutation, are able to endure such an environment. Along the evolutionary time, epigenetic agents adapt to the dynamic environment by adapting also to the epigenetic structures they possess. Agents which evolve to take advantage of the epigenetic layer, regarding the environment, are preferentially selected to reproduce. This is performed indirectly, by selecting the agents with the best weighted fitness - i.e., during the agents' lifetime, the ones that performed better, by regulating to in adequate terms with the environment. As such, along time, the population increases their adaptation to the dynamic environment. One can, however, observe different evolutionary behaviors, regarding the different epigenetic inheritance mechanisms. In the case where the methylation marks are not inherited, the 'spiked' behavior is due to the fact that the new agents are born from parents that are regulated with methyl marks for the colder environment, with no change on the genotype. As the epigenetic marks are not transmitted, the agents are born with the genotype for warmer environments - which are the ones actually coded in the genotype -, but are not regulated to colder ones. Thus, there is a drop in the mean fitness values because part of the population is not epigenetically adapted to the colder environment. The case where there is no methyl mark inheritance is the worst of the epigenetic variants, while the cases where the inheritance occurs in full terms, or only partially, are very similar in terms of performance.

We also experimented with non periodic, more dynamic environmental effects, where both temperature and light values are non periodically modified. This is shown in figure 9.

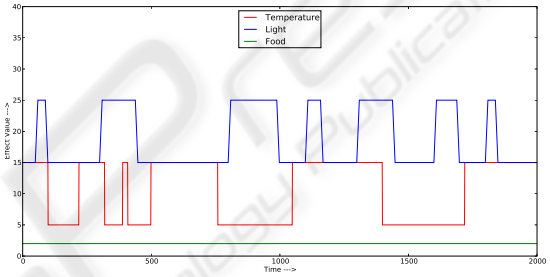


Figure 9: Dynamic, non periodic temperature and light.

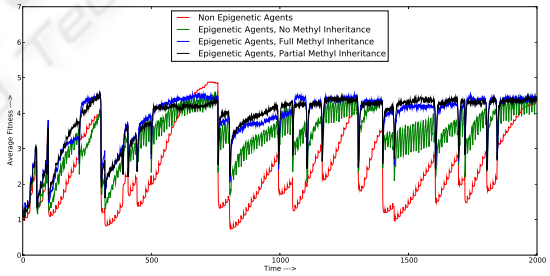


Figure 10: Average fitness results for different populations, regarding the environment shown in 9.

The results for this scenario are shown in figure 10. The results are very similar to the previous ones, with the non epigenetic agents showing bad performance, whereas the epigenetic populations are able to adapt to such an environment. The apparently significant difference in the evolutionary behavior of the agents regarding the possession or absence of epigenetic mechanisms poses some interesting questions that can be tackled with the *EpiAL* model. For instance, we experimented with a basic movement behavior, where some of the agents would be able to move into different locations, while others would be fixed into the place where they are born. At the same

time, the environment changes not as a whole, but only in some specific locations (the environmental modification in these areas occurs as depicted in figure 7). Some of the agents can, therefore, move out of unfavorable locations, while others have to endure the conditions from their birth location. The results for this sort of simulation is presented in figure 11.

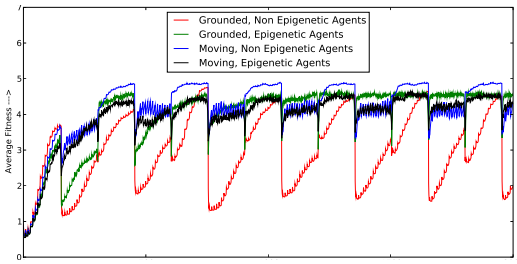


Figure 11: Average fitness results for different populations, regarding an environment modified in some of the areas according to dynamics in figure 7.

Results indicate that the impact of either possessing epigenetic mechanisms or not, regarding populations that can move is not nearly as significant as for populations that cannot move. The moving populations have a fairly similar performance whether they are epigenetic or not. In the case of the grounded populations, however, as they cannot move from the modified areas, they are subject to harsher environments, unless they regulate their genotypes to the new conditions. This is in agreement with the epigenetic theory, in which plants, organisms that, indeed, cannot move, posess biological mechanisms that are much more plastic than the ones in animals. Some of these mechanisms can be considered epigenetic (Boyko and Kovalchuk, 2008).

Regarding the results of the model in general, a legitimate question arises, related to whether there is a *memory role* at play, a way in which the agents remember the environmental modifications and inherit those memories. Memory, in the terms that the agents remember that cycles occur at a certain time, is discarded by the exposure to non periodic environments (figure 10) and the consequent adaptation of the epigenetic agents. There are no hard coded mechanisms that the agents can take advantage of, in order to remember timed, cyclic conditions in the environment and transmit that information to their offspring. Nevertheless, it can be stated that the main role is played by both *regulation* and a *genetic memory* factor. If we consider that the construction of the methylation marks are a mechanism of life-time adaptation, and if those marks are inherited, it is only fair to state that there is some 'knowledge' inherited by the offspring. However, and because the mechanics were built around the regulatory theory of epigenetics, that sort of 'memory' is derived from regulatory mechanisms. The agents have no means to remember a specific state from the environment, unless the epigenetic components allow them to mark their genotypes with such knowledge. And, even then, such knowledge has to evolve (genetically, at least) in order to be of any use. Methylation, by itself, is worthless if the genetic elements are not evolved to cooperate with the epigenetic mechanisms. Despite some evidence regarding the partial inheritance of these acquired marks (as studied in (Gorelick, 2004), for instance), the *EpiAL* model enables the possibility to consider that this genetic memory does not operate. The results obtained from the experiments have shown that, although these results are usually worse than the simulations with methyl mark inheritance, there can be improved results from this solely regulatory behavior, compared with the absence of epigenetic mechanisms at all. As such, we can consider that the key role of the epigenetic dimension modelled in *EpiAL* is mostly regulatory, with the genetic memory variants improving on the results obtained by regulatory mechanisms.

6 CONCLUSIONS AND FUTURE WORK

EpiAL, the model hereby presented, is designed with a biological enhancement regarding epigenetic mechanisms. The dynamics of the environment are able to handle multiple conditions, like temperature, light and food, in cyclic or non periodic modifications. The artificial agents, in turn, possess mechanisms to incorporate and process these environmental conditions, allowing an epigenetic influence in their coding structures. This enables the simulation with different mechanics regarding the epigenetic effects, ranging from the regulatory aspects to the inheritance methods. Using an abstraction for the phenomena of methylation in the genome, the model is able to represent regulatory operations for adapting to different, dynamic environments and allows different inheritance patterns to be experimented with. The results show that there could be a significant difference regarding the agents' possession of epigenetic mechanisms. The non epigenetic populations find it hard to thrive in dynamic environments, while the epigenetic populations are able to regulate themselves to dynamic conditions. Moreover, results regarding a simple behavior in the agents, i.e., movement, have been presented, in the light of epigenetic constraints. However, different sorts of experimentations can be performed with the actual implementation of the model. It would also be inter-

esting to perceive if nocive effects of the epigenetic mechanisms can be found, namely the application of mutational events either to the methylation sites or the epigenetic structures themselves. It would also be interesting to perceive if the application of these mechanisms could be used in the scope of problem solving techniques. This work is but a first step, in which we attempted to show that there is a difference, in evolutionary terms, in considering agents with an epigenetic variant. By pursuing this work further, we can hope to achive a better understanding of the field of epigenetics. The subject of epigenetics is young and still maturing, but, as a hot subject in biology, it provides an example of an excellent opportunity to capitalize over the knowledge achieved in the past years, regarding the modelling of biological phenomena. We intend to pursue the continuous development of the model, with a focus on two dimensions: the first is regarding the biological knowledge that we believe the *EpiAL* model can assist in studying and better understanding. The emergent fields of developmental biology (evo-devo) tackle this issues and have use for simulation tools that can assist in theoretical speculation. The other dimension is related to problem solving techniques. Problems with dynamic environments are tackeld by several algorithmic approaches, and we believe that the conceptual basis of the *EpiAL* model has some evolutionary and adaptational mechanisms that could provide a different approach in tackling these problems. This twofold path is but another hint that ALife models can be used concurrently with the discoveries found on the field of epigenetics and developmental biology, providing an actual relation of biomutualism between the fields of computation and biology.

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