# Implications of Epigenetic Learning Via Modification of Histones on Performance of Genetic Programming

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**Abstract.** Extending the notion of inheritable genotype in genetic programming (GP) from the common model of DNA into chromatin (DNA and histones), we propose an approach of embedding in GP an explicitly controlled gene expression via modification of histones. Proposed double-cell representation of individuals features somatic cell and germ cell, both represented by their respective chromatin structures. Following biologically plausible concepts, we regard the plasticity of phenotype of somatic cell, achieved via controlled gene expression owing to modifications to histones (epigenetic learning, EL) as relevant for fitness evaluation, while the genotype of the germ cell – to reproduction of individual. Empirical results of evolution of social behavior of agents in predator-prey pursuit problem indicate that EL contributes to more than 2-fold improvement of computational effort of GP. We view the cause for that in the cumulative effect of polyphenism and epigenetic stability. The former allows for phenotypic diversity of genotypically similar individuals, while the latter robustly preserves the individuals from the destructive effects of crossover by silencing of certain genotypic fragments and explicitly activating them only when they are most likely to be expressed in corresponding beneficial phenotypic traits.

**Keywords:** epigenesis, histones, genetic programming, multi-agent system

## 1 Introduction

Until a few years ago, the role of histones (the family of proteins which DNA is wrapped around forming a super-coiled chromatin fiber) in molecular biology community was viewed as solely to help pack the long DNA into the tiny nucleus of eukaryotes' cells. However, as the results of resent research suggest, the histones play a significant role in regulating the synthesis, repair, recombination and transcription of DNA [8][15][18]. It is recognized that the regulation of DNA-transcription (and consequently, the overall gene expression) via histone code during cell division controls the specialization of the cells with the same DNA into variety of cell types. In addition, the histone code might control the variances in phenotypes (i.e. biochemistry, morphology, physiology and behavior) seen on different stages of life cycle of living organisms as developing, maturing and aging. Moreover, the onset of some genetically

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associated diseases (and even cancer) is viewed as a process triggered by both a sudden activation of the genes that "contribute" to the disease and/or sudden deactivation of the genes that "fight" the disease. Being an interface between the nurture and nature, the changeable histone code might be regarded as an integrating link in the information pathway of epigenesis of living organisms. As illustrated in Figure 1 the interaction between the phenotype and various environmental factors (such as food, viral infections, exposure to toxins, irradiation, light, UV, etc.) leads to corresponding variations in the histone code, which in turn result in modified (beneficial or detrimental) gene expression. Without touching the details of either the chromatin structure or the chemical processes in histones, we would like to generalize the recently emerged findings that transcription of the genes in DNA is controlled by the surrounding chemical structure of histones. The acetylation of histones correlates with transcriptional activity of the corresponding DNA gene, while the metylation - with transcriptional inactivity of the gene.

In our approach, extending the notion of inheritable genotype in GP from commonly considered model of DNA of simulated organisms (i.e. genetic programs) into chromatin (i.e. model of DNA with surrounding histone proteins) we attempt to mimic the naturally observed phenomenon of regulating gene expression via epigenetic modifications of histones (i.e. epimutations) into a software system. The system features epigenesis embedded in evolution (phylogenesis), simulated through GP. Because (i) we are interested in short-term (i.e. within the life cycle of the organisms), adaptive or developmental epimutations; and (ii) these epimutations are presumed to be beneficial to the performance of behavioral (rather than biochemical, morphological or physiological) aspect of the phenotype of simulated organisms, we consider our approach as a form of *epigenetic learning* (EL), incorporated in GP. The *objective* of our research is to explore the effects of EL on the performance, and namely – on the computational effort of evolution (phylogenesis) of emergent social behavior of autonomous software agents.

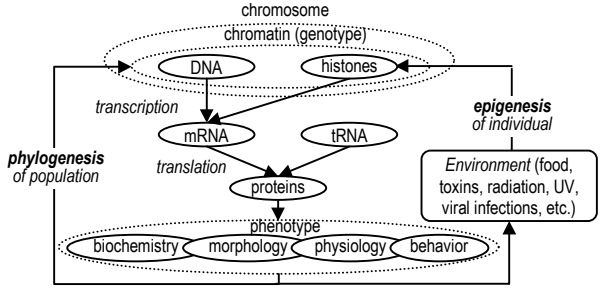


**Fig. 1.** Simplified Information pathways in phylogenesis and epigenesis in eukaryotic organisms. The inheritable genotype is illustrated as chromatin – a fiber of DNA wrapped around (balls of) histone proteins. The latter control the transcription of DNA by activating or silencing the corresponding nearby genes in DNA. Being an interface between the nature and nurture, histones are subject to modifications as a result of interaction between the phenotype and the environment during the lifetime development and adaptation of organisms

Our work can be viewed as related to the various aspects of approaches of employing heuristics [13], phenotype plasticity [4], Baldwin effect [5], and redundant code [14][16] in GP. In contrast to all of these approaches, the mechanism of EL does not imply direct manipulation on either the simulated DNA or the phenotype. Instead, the proposed EL is achieved through controllable and inheritable gene expression mechanism of simulated individuals. In our approach the genes, being silenced can still comprise the genotype without affecting the performance of individual's phenotype. In addition to being biologically more plausible, such an approach might offer (i) better phenotypic diversity of genotypically similar individuals in the populations and (ii) an efficient way to preserve the individuals from the destructive effects of crossover by explicit activation of the growing genetic combinations when they are most likely to be expressed as corresponding beneficial phenotypic traits.

The remainder of this document is organized as follows. Section 2 briefly introduces the task, which we use to test our hypothesis. The same section briefly explains the key properties of the algorithmic paradigm employed to evolve the functionality of agents. The proposed mechanism of EL is introduced in Section 3. The same section presents empirically obtained results of the implications of EL on the performance of evolution. The conclusion is drawn in Section 4.

## 2 Background

In this section, we briefly introduce the application and the main attributes of evolutionary algorithmic paradigm employed in our approach. The general, well defined and well studied yet difficult to solve predator-prey pursuit problem [2] is used to verify the implications of EL on the efficiency of evolution. The problem comprises four predator agents whose goals are to capture a prey by surrounding it on all sides in a world. In our work we consider an instance of the problem, which is more realistic and probably more difficult for predators than is commonly considered in the previous work [6][10]. The world is a simulated two-dimensional continuous torus and the moving abilities of four predator agents are continuous. We introduce a proximity perception model for predator agents in that they can see the prey and only the closest predator agent, and only when they are within the limited range of visibility of their simulated (covering an area of *360* degrees) sensors. The prey employs random wandering if there is no predator in sight and a priori handcrafted optimal escaping strategy as soon as predator(s) become "visible". The maximum speed of prey is higher than the maximum speed of predator (i.e. predator-agents feature inferior moving abilities). In order to allow predators to stalk and collectively approach the prey the range of visibility of predators is more than the range of visibility of the prey. We consider this case as a key prerequisite for creating inherently cooperative environment in that the mission of predators is nearly impossible unless they collaborate with each other.

The evolved social (surrounding) behavior of predator agents emerges from what we regard as Occam's razor in interactions between the predator agents: simple, local, implicit, proximity-defined, and therefore – robust and scalable interactions. Within

the scope of this document, we consider the emergence as phenomena of local interaction creating global properties [1][12]. Without providing explicit domain-specific knowledge about how to accomplish the task (e.g. how to surround the prey) the agents, evolved through GP behave "as if" they had such explicit knowledge, because the original source of problem-specific constrains is an integral part of the GP itself. The interaction between GP and the problem environment allows the appropriate knowledge about how to accomplish the task to emerge as a by-product. With the only difference in the representation of relevant domain-specific knowledge, from the outside the evolved behavior is no different than one that allows the agents to accomplish the task by intentional, deliberate acts (of surrounding). Thus we consider the evolved behavior of agents as *emergent behavior*. Moreover, because in such seemingly intentional, deliberate acts each agent is acting "as if" it is well aware of objectives of other agents, shares these objectives, and anticipates the actions of other agents, the emerged (surrounding) behavior of agents is considered as a form of *social behavior*.

A set of stimulus-response rules is used as a natural way to model the reactive behavior of predator agents [7], which in our approach is evolved using GP. GP is a domain-independent problem solving approach in which a population of computer programs (individuals) is evolved to solve problems [9]. The simulated evolution in GP is based on the Darwinian principle of reproduction and survival of the fittest. The strength of GP to automatically evolve a set of stimulus-response rules featuring arbitrary complexity without the need to a priori specify the extent of such complexity might imply an enormous computational effort caused by the need to explore a huge search space while looking for the potential solution to the problem. The function set of GP comprises IF-THEN statement, arithmetical operations and comparison operators. The terminal set features local, proximity defined sensory- and continuous moving abilities. The representation of genetic programs is based on widely adopted document object model (DOM) and extensible markup language (XML) in a way as proposed in [17]: genetic programs are represented as a DOM-parsing trees featuring corresponding flat XML text. Both the genetic operations and the evaluation of individuals are performed on their respective DOM-parsing trees using off-the shelf, platform- and language neutral DOM-parsers, and XML-text representation is employed as a flat format, feasible for migration of genetic programs among the computational nodes in the distributed implementation of GP. The genetic operations are binary tournament selection, random sub-tree and transposition mutations. The breeding strategy is homogeneous: the performance of a single genetic program, cloned to all the agents is evaluated. We consider such a strategy as adequate to the symmetrical nature of the world, which is unlikely to promote any behavioral specialization among predator agents. The fitness of the genetic program is evaluated as average of the fitness measured over 10 different, randomly created initial situations. The fitness measured during the trial starting with particular initial situation considers the performance of the team of agents [3] and accounts for (i) the average energy loss of the agents during the trial, (ii) the average distance of the agents to the prey by the end of the trial, and (iii) the elapsed time of the trial. The energy loss estimation takes into account both the basal metabolic rate of the agents and the energy loss for moving activities. Smaller values of fitness function correspond to better performing predator agents.

A trace of the entities in the world, where the team of predator agents is governed by sample best-of-run genetic program in one of the initial situations is shown in Figure 2. The prey, originally situated in the center of the world, is captured by time step 118. The emergence of following behavioral traits of predator agents are noticeable: (i) switch from greedy chase into surrounding approach (agent #2, time step 65, on the top, center of the world); (ii) zigzag move, which results in a lower chasing speed indicating "intention" to trap the prey (agent #1, after time step 40, center) and (iii) surrounding approach (agents #0 and #3, top; agent #2, bottom and top) demonstrated during the final stages of the trial.

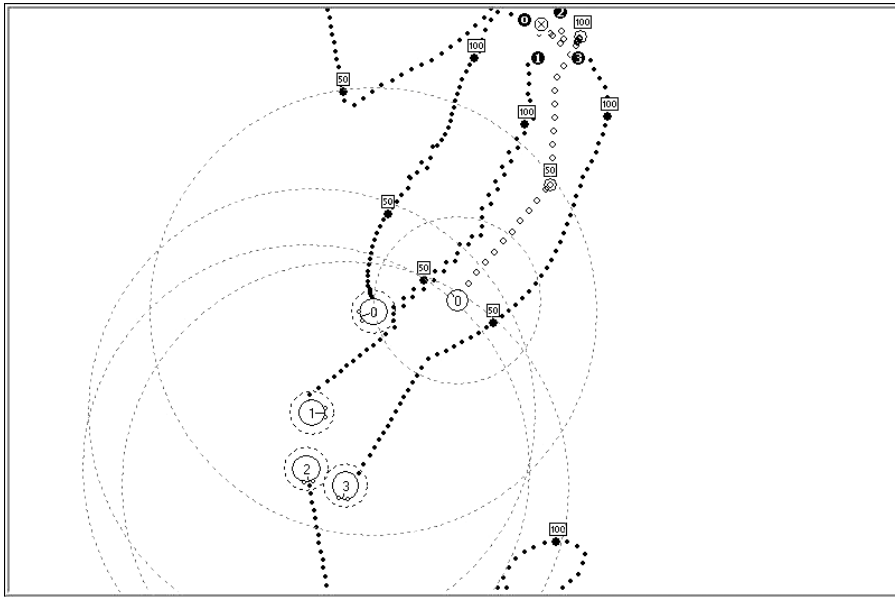

**Fig. 2.** Traces of the entities with predator agents governed by the sample best-of-run genetic program. The prey is captured in 118 simulated time steps (top). Large white and small black circles denote the predator agents in their initial and final position respectively. The small white circle indicates the prey, initially situated in the center of the world. The numbers in rectangles show the timestamp information

## 3 Embedding EL via Epimutations in GP

### 3.1 The Mechanism of EL

**Chromatin Representation.** In the proposed approach, we represent the predator agents as simulated individuals passing through the phases of birth, development and survival (reproduction) or death (Figure 3). At the phase of birth, the individual is

represented as a single embryonic cell expressed by its respective chromatin. The simulated division of the embryonic cell into single germ cell and single somatic cell initiates the EL phase. Both cells are expressed by their respective chromatin structures. In contrast to the germ cell, the somatic cell is subject to EL via iterative epimutations. The completion of the learning phase of the organism is associated with fitness evaluation, based on the performance of the phenotype of modified somatic cell. Reproduction phase concludes the life cycle of the individual when, depending on the relative ranking of the individual in the population and the outcome of the following selection, either (i) a new individual (i.e. embryonic cell) is born by crossover with another individual from the surviving mating pool or (ii) the individual dies. The logical separation of the cells into germ cell and somatic cell where the former is subject to phylogenesis and the latter – to epigenesis and following fitness evaluation reflects our intention to simulate the biologically plausible presumption that the epimutations in somatic cells do not cross the so called Weissman barrier and consequently, are not inherited through the germline.

The representation of chromatin as a genotype of both germ and somatic cell of the organism in GP is based on the representation of DNA paired with isomorphic histone code. Employing the flexibility of XML, we implemented the chromatin in which DNA is organized into tree structure representing the evolved stimulus-response rules, combined with histones expressed as corresponding attributes of IF-THEN nodes of the rules (Figure 4a). The semantics of genotype is shown in Figure 4b. The gene expression mechanism, controlled by histone code implies that during the evaluation of the agent behavior only IF-THEN nodes with histone attributes equal to *"1"* feature transcriptional activity and therefore – only these nodes are parsed, considered as active phenotype and executed (Figure 4c).

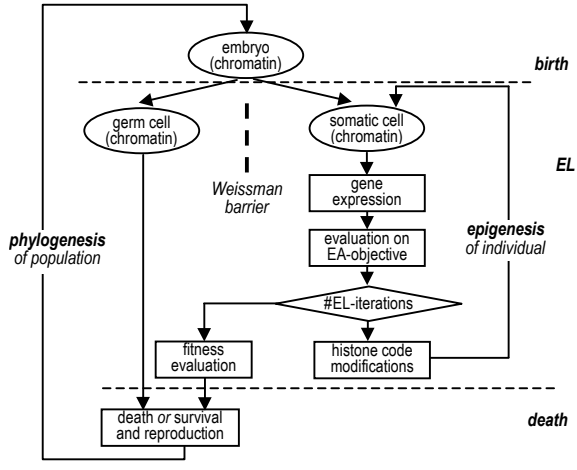


**Fig. 3.** Life cycle of simulated individual. Individual features double cell representation – germ cell and somatic cell where the former is subject to phylogenesis and the latter – to EL and following fitness evaluation. Only the best scoring (on EL objective) epigenetic changes to phenotype of somatic cell are evaluated for fitness

**Algorithm of EL.** We incorporated the EL into the fitness evaluation routine of GP as a special case of random local search embedded within GP (Figure 5). We consider the following relevant aspects of the algorithm of EL: (i) the way of selecting which histone should be modified, (ii) the algorithm of epimutations (histone modification), (iii) the objective of learning (i.e. the learning task), (iv) the learning interval and (v) the amount of EL-iterations.

Random histone is selected for modification and the modification algorithm is simply inverting the value of the selected histone. Both the selection and modification algorithms are implemented in the `Modify_Histones` function as illustrated in Figure 5, line 10.

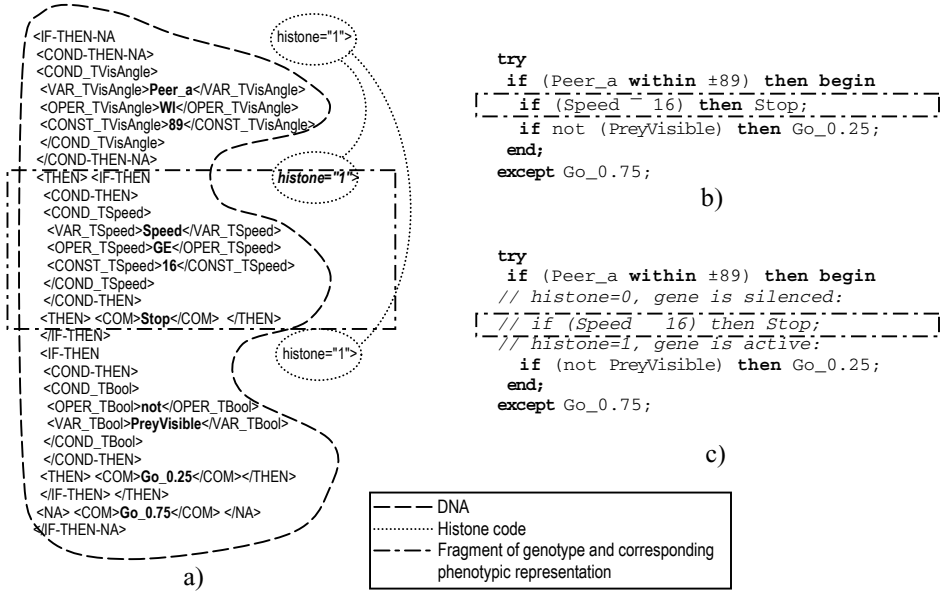


**Fig. 4.** Genetic representation. The genotype of somatic cell before the development phase of the individual is shown in (a). (b) and (c) illustrate the human readable semantics of the phenotype of somatic cell before the EL phase (b) and after EL (c) as a result of silencing an "**`if-then`**" statement due to change of the value of corresponding histone from "1" to "0".

```
 1. Procedure EvalWithEL(GP: TChromatin; EL_Cycles: integer; [out] Fitness: TFitness);
 2. var Dev_GP : TChromatin;
 3.     i, EL_Ability, Dev_EL_Ability : integer;
 4. begin
 5.  Dev_GP:=GP; EL_Ability:=0;
 6.  for i:=1 to EA_Cycles do begin
 7.   Clone_GP_To_All_Agents(GP);
 8.   Eval_EL_Objective([out] Dev_EL_Ability);
 9.   if (Dev_EL_Ability better_than EL_Ability) then Dev_GP:=GP;
10.   if (i < EL_Cycles) then Modify_Histones(GP);
11.  end;
12.  Clone_GP_To_All_Agents(Dev_GP);
13.  Eval_Fitness ([out] Fitness);
14. end;
```

**Fig. 5.** The algorithm of EL embedded in the routine of evaluation of genetic program. The output specifiers of function parameters are explicitly given for better readability

We considered three cases of EL featuring different learning objectives and epigenetic inheritance as follows:

- The learning objective is the same as the evolution attempts to achieve (EL case 1, EL1). The estimation of the learning ability (variable `Dev_EL_Ability`, Figure 5, assigned in line 8) is identical to fitness evaluation. The epimutations in case EL1, although inherited through the EL cycles of somatic cell of simulated individual, are not assumed to be inherited thought the germline,
- The learning objective aims to increase the amount of implicit interactions between predator agents (EL case 2, EL2). Learning ability accounts for the total number of references to any sensory variables related to perceiving the peer predator agents. The epimutations in case EL2 are not assumed to be inherited throught the germline of simulated individuals, and
- EL3: the learning objective is the same as in EL2 and the epimutations are assumed to be inherited thought the germline of simulated individuals.

In all three cases only the best-scoring (on EL objective) adapted individual is being evaluated for fitness. The considered cases of epigenetic inheritance through the development of the somatic cells (EL1 and EL2) is based on our intention to simulate the recognition that in Nature the epimutations are not inherited through the germline of individuals. The introduction of inheritance of epimutations through the germline of simulated individuals (EL3) is motivated by our interest in analyzing the implications of such inheritance on the efficiency of simulated evolution. Germline inheritance of epimutations implies that the histone code of germ cell is assumed to be identical to the mutated (through EL) histone code of somatic cell of the organism.

The case of learning objective, not identical to the fitness is introduced with objective to reduce the computational cost of learning (and consequently, to boost the overall performance of GP with embedded EL) by decreasing the learning interval. Because the qualitative value of the fitness heavily depends on the result of quantitative, discrete event of capturing the prey, the approach of noisy fitness evaluation [11] is hardly applicable for the EL1: the fitness values are simply undefined prior to capturing the prey or, ultimately, before the expiration of the allowed time interval of the trial. Exploring the feasibility of using simple, continuous function, evaluated over reduced learning interval for estimation of learning abilities of agents, we use the amount of implicit interactions among the agents. The benefits of the proposed approach are as follows: (i) it is biologically plausible – compared to the survival process, the learning acts in nature take place in a different time scale; and the learning objective usually features downgraded complexity, risk, and cost; (ii) being continuous, "anytime" indicator of the fitness, the EL objective function could be noisily evaluated over reduced learning interval; and (iii) due to the experimentally verified correlation of learning abilities with the fitness, the learning and evolution would synergistically influence each other.

The learning interval is *0.25* of the trial of fitness evaluation. The decision about the duration of learning interval is based on the anticipation that the degradation of computational effort due to noisy fitness evaluation would be insignificant (indeed, the experimentally obtained standard deviation of the noise in estimating the overall amount of interactions from the amount of interaction obtained during the considered

learning interval is *0.35*) and this degradation is most likely to be overcompensated by the associated 4-fold improvement of computational performance.

The minimally possible amount of learning iterations is attempted: a single learning iteration in EL1, and *2* learning iterations in EL2 and EL3 (variable `EL_Cycles` in Figure 5 equals *1* and *2* respectively).

### 3.2 Effect of EL on the Performance of Evolution: Empirical Results

**Values of Parameters.** The values of parameters of GP used in our experiments are as follows: the population size is *400* genetic programs, the selection ratio is *0.1*, including *0.01* elitism, and the mutation ratio is *0.02*, equally divided between sub-tree mutation, transposition and histone modification. The latter is performed in identical way as in the EL. The termination criterion is defined as a disjunction of the following conditions: (i) fitness of the best genetic program in less than *300* and the amount of initial situations in which the prey is captured (successful situations) equals *10* (out of *10*), (ii) amount of elapsed generations is more than a *100*, and (iii) amount of recent generations without fitness improvement is more than 16. The raw fitness value of *300* roughly corresponds to successful team of predator agents, which in average (over all initial situations) capture the prey by the middle of the trial. The latter equals to *600* time steps, where each step is simulated by *500ms* of "real time" sampling interval. A superior sensory abilities of predators (range of visibility *400mm* vs. *200mm* for prey) and inferior moving abilities have been considered (*20mm/s* vs. *24mm/s*).

**Computational Effort of GP Incorporating EL.** The effect of EL on the computational effort, statistically estimated (in a way as suggested in [9]) from the probability of success p(t) of GP over 20 independent runs is shown in Figure 6. As figure illustrates, probability of success of 0.95 for GP (denoted as P, phylogenesis) is achieved for about 32,000 individuals, while for incorporated EL1 (denoted as P+EL1), EL2 (P+EL2) and EL3 (P+EL3) these values are 24,000 (reduced 1.3 times), 15,000 (2.1 times) and 14400 (2.2 times) individuals respectively. The reasons for improved computational effort of evolution with embedded EL we view in the cumulative effect of polyphenism and epigenetic stability introduced by histone code and exploited by proposed EL. The polyphenism allows for phenotypic diversity of genotypically similar individuals, while the epigenetic stability robustly preserves the individuals from the destructive effects of crossover by silencing of certain genotypic combinations and explicitly activating them only when they are most likely to be expressed in corresponding beneficial phenotypic traits.

The breakdown of computational effort is shown in Table 1. The total equivalent amount of evaluated individuals $E_{TE}$, depicted as an abscissa in Figure 9, which takes into account the reduced learning interval with respect to the trial interval of fitness evaluation, is calculated in accordance with the following rule:

$$E_{TE} = E_P + (T_{EA} / T_{FE}) \times E_{EL}$$

Where $E_P$ and $E_{EL}$ are the amount of fitness evaluations during the phylogenesis and EL (either EL1 or EL2) respectively, and $T_{FE}$ and $T_{EL}$ are the trial interval of fitness evaluation and learning interval respectively. The results, shown in Table 1 indicate that both P+EL2 and P+EL3 compared to P+EL1 not only reduce $E_{TE}$ (which, in general might be due to the reduced learning interval alone). Moreover, EL2 and EL3 reduce $E_P$ too, suggesting the presence of favorable effect of these cases of EL on the efficiency of phylogenesis. This effect overcompensates the expected deteriorative effect of the noisy evaluation of learning objective in EL2 and EL3 on the efficiency of evolution. The effect could be explained by beneficial dependencies between the amount of interactions and fitness. We assume that these dependencies are beyond the correlation (which alone should not result in decrease of $E_P$) as elaborated earlier in 3.1.2. Presumed statistical association of the climb in the learning landscape during EA with a move towards the proximity of optimal solutions in the fitness landscape could be viewed as a reason for the beneficial effect of considered cases of EL on the efficiency of evolution.

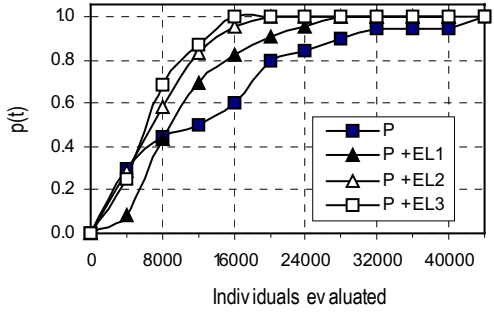


**Fig. 6.** Probability of success *p(t)* for GP employing phylogenesis only (P), EL embedded in phylogenesis with learning objective the same as in the evolution (P+EL1), and learning objective of intensifying interactions (P+EL2 and P+EL3). The inheritance of epimutations in EL2 is through the EL cycles of somatic cell, while in EL3 the inheritance is both through the EL cycles of somatic cell and through the germline of simulated individual

**Table 1.** Breakdown of computational effort of GP

| Case | EL objective | Epigenetic inheritance | EL interval, $T_{EL}$ | EL cycles | Computational effort | | | Speedup |
|---|---|---|---|---|---|---|---|---|
| | | | | | $E_P$ | $E_{EL}$ | $E_{TE}$ | |
| P | - | - | - | - | 32000 | - | 32000 | 1 |
| P+EL1 | Same as fitness | In somatic cells only | $T_{FE}$ | 1 | 12000 | 12000 | 24000 | 1.3 |
| P+EL2 | Interactions | In somatic cells only | $0.25*T_{FE}$ | 2 | 10000 | 20000 | 15000 | 2.1 |
| P+EL3 | Interactions | Both in somatic cells and through the germline | $0.25*T_{FE}$ | 2 | 9600 | 19200 | 14400 | 2.2 |

## 4 Conclusion

We present the results of our work inspired by recently discovered findings in molecular biology suggesting that histones play a significant role in regulating the gene expression in eukaryotes. Extending the notion of inheritable genotype in GP from commonly considered model of DNA into chromatin, we propose an approach of epigenetic programming as way to incorporate the naturally observed phenomenon of regulated gene expression via modification of histones. Considering the individual as comprising of germ cell and somatic cell, both represented as a chromatin, we focus our attention on the development phase of the life cycle of simulated individuals. We mimic the biologically plausible hypothesis that the information contained in chromatin is inheritable both through the development of the somatic cells and through the germline, but that the epigenetic changes to somatic cells' histones are not believed to be inheritable through the germline. Thus, we regard the phenotype of the somatic cell (subject to beneficial EL via histone code modification) as relevant for fitness evaluation of the individual, while the genotype of the germ cell – as a genetic material involved in phylogenesis. The empirically obtained performance evaluation results indicate that epigenesis with biologically plausible epigenetic inheritance through the development the somatic cells contributes to 2.1-fold improvement of computational effort of genetic programming applied to evolve social behavior of predator agents in predator-prey pursuit problem. The simulated epigenetic inheritance through the germline of individuals yields a marginally better (2.2-fold) reduction of computational effort. We associate the benefits of embedding EL in evolution with the cumulative effect of polyphenism and epigenetic stability. The former allows for phenotypic diversity of genotypically similar individuals, while the latter robustly preserves the individuals from the destructive effects of crossover by silencing of certain genotypic combinations and explicitly activating them only when they are most likely to be expressed in corresponding beneficial phenotypic traits. In this context, our approach can be viewed as an attempt to co-evolve the most beneficial genotypic building blocks and the best possible combinations of their expressions.

In the near future we are planning to incorporate evolvable rather than handcrafted learning objective as used in our current approach in order to investigate whether it has even better effect on the performance of the phylogenesis. We are also interested in enhancing the currently used homogeneous breeding strategy into a strategy which allows for genotypically homogeneous team of agents to develop into phenotipically diverse one by means of EL (as in polyphenism, seen in social insects in the nature). In addition, we intend to investigate the feasibility of the proposed approach for modeling the morphogenesis of the somatic cells through EL in evolvable multi-cellular organisms. Finally, considering our approach as a domain-neutral we are planning to verify it on different tasks from various problem domains and to compare the obtained results with results of known approaches of incorporating other models of redundant genetic representations.

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