GENE EXPRESSION PROGRAMMING AND THE EVOLUTION OF COMPUTER PROGRAMS

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In this chapter an artificial problem solver inspired in natural genotype/phenotype systems – gene expression programming – is presented. As an introduction, the fundamental differences between gene expression programming and its predecessors, genetic algorithms and genetic programming, are briefly summarized so that the evolutionary advantages of gene expression programming are better understood. The work proceeds with a detailed description of the architecture of the main players of this new algorithm (chromosomes and expression trees), focusing mainly on the interactions between them and how the simple yet revolutionary structure of the chromosomes allows the efficient, unconstrained exploration of the search space. And finally, the chapter closes with an advanced application in which gene expression programming is used to evolve computer programs for diagnosing breast cancer.

1. Evolutionary Algorithms in Problem Solving

The way nature solves problems and creates complexity has inspired scientists to create artificial systems that learn by themselves how to solve a particular problem. The first attempts were done in the 1950s by Friedberg (Friedberg 1958; Friedberg et al. 1959), but ever since highly sophisticated systems have been developed that apply Darwin's ideas of natural evolution to the artificial world of computers and modeling. Of particular interest to this work are the genetic algorithms (GAs) and the genetic programming (GP) technique as they are the predecessors of gene expression programming (GEP), the most recent development in evolutionary computation and the theme of this chapter. A brief introduction to these three techniques is given below.

1.1. Genetic Algorithms

Genetic algorithms were invented by John Holland in the 1960s and they also apply biological evolution theory to computer systems (Holland 1975). Like all evolutionary computer systems, GAs are an oversimplification of biological evolution. In this case, solutions to a problem are usually encoded in strings of 0's and 1's (chromosomes), and populations

of such strings (individuals or candidate solutions) are used in order to evolve a good solution to a particular problem. From generation to generation candidate solutions are reproduced with modification and selected according to fitness. Modification in the original GA was introduced by the genetic operators of mutation, crossover, and inversion.

It is worth pointing out that GAs' individuals consist of naked chromosomes or, in other words, GAs' individuals are simple replicators. And like all simple replicators, the chromosomes of genetic algorithms function simultaneously as genotype and phenotype: they are both the object of selection and the guardians of the genetic information that must be replicated and passed on with modification to the next generation. Consequently, the whole structure of the replicator determines the functionality and, therefore, the fitness of the individual. For instance, in such systems it would not be possible to use only a particular region of the replicator as a solution to a problem: the whole replicator is always the solution: nothing more, nothing less.

1.2. Genetic Programming

Genetic programming, invented by Cramer in 1985 (Cramer 1985) and further developed by Koza (1992), solves the problem of fixed length solutions through the use of nonlinear structures (parse trees) with different sizes and shapes. The alphabet used to create these structures is also more varied, creating a richer, more versatile system of representation. Notwithstanding, the created individuals also lack a simple, autonomous genome. Like the linear chromosomes of genetic algorithms, the nonlinear structures of GP are also cursed with the dual role of genotype/phenotype.

The parse trees of genetic programming resemble protein molecules in their use of a richer alphabet and in their complex and unique hierarchical representation. Indeed, parse trees are capable of exhibiting a great variety of functionalities. The problem with these complex replicators is that their reproduction with modification is highly constrained in evolutionary terms because the modifications must take place on the parse tree itself and, consequently, only a limited range of modification is possible. Indeed, special kinds of genetic operators were developed that operate at the tree level, modifying or exchanging particular branches between trees.

Although at first sight this might appear advantageous, it greatly limits this technique (we all know the limits of grafting and pruning in nature). Consider for instance crossover, the most used and often the only search operator used in genetic programming. In this case, selected branches are exchanged between two parent trees to create offspring (Figure 1). The idea behind its implementation was to exchange smaller, mathematically concise blocks in order to evolve more complex, hierarchical solutions composed of smaller building blocks.

The mutation operator in GP is also very different from natural point mutation. This operator selects a node in the parse tree and replaces the branch underneath by a new randomly generated branch (Figure 2). Notice that the overall shape of the tree is not greatly changed by this kind of mutation, especially if lower nodes are preferentially chosen as mutation targets.

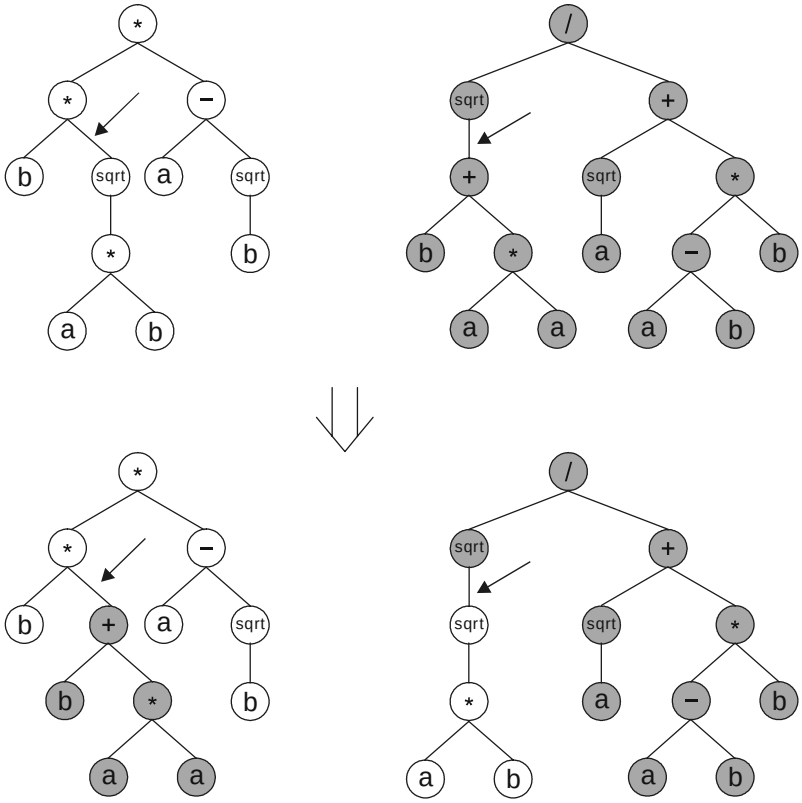


Figure 1. Tree crossover in genetic programming. The arrows indicate the crossover points.

Permutation is the third operator used in genetic programming and the most conservative of the three. During permutation, the arguments of a randomly chosen function are randomly permuted (Figure 3). In this case the overall shape of the tree remains unchanged.

In summary, in genetic programming the operators resemble more of a conscious mathematician than the blind way of nature. But in adaptive systems the blind way of nature is much more efficient and systems such as GP are highly constrained. For instance, the implementation of other operators in genetic programming such as the simple yet high-performing point mutation (Ferreira 2002c) is unproductive as most mutations result in syntactically incorrect structures (Figure 4). Obviously, the implementation of other operators such as transposition or inversion raises similar difficulties and the search space in GP remains vastly unexplored.

Although Koza described these three operators as the basic GP operators, crossover is practically the only genetic operator used in most GP applications (Koza 1992). Consequently, no new material is introduced in the genetic pool of GP populations. Not surprisingly, huge populations of parse trees must be used with the aim of creating all the neces-

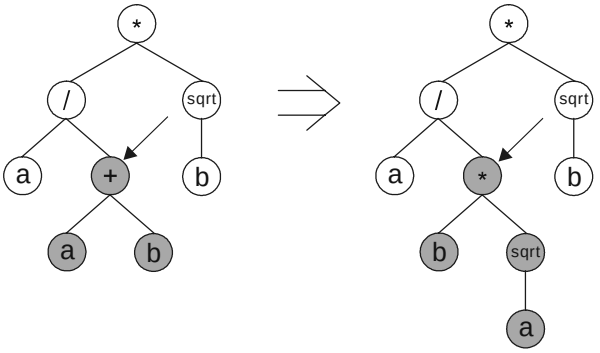


Figure 2. Tree mutation in genetic programming. The arrow indicates the mutation point. The new branch randomly generated by the mutation operator in the daughter tree is shown in gray.

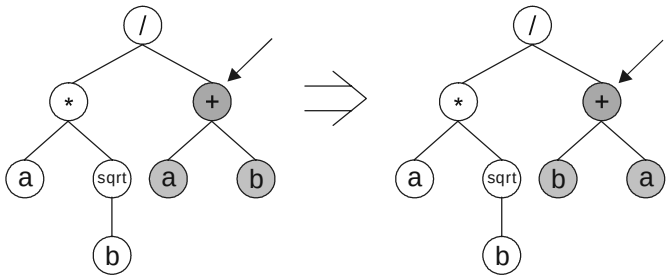


Figure 3. Permutation in genetic programming. The arrow indicates the permutation point. Note that the arguments of the permuted function traded places in the daughter tree.

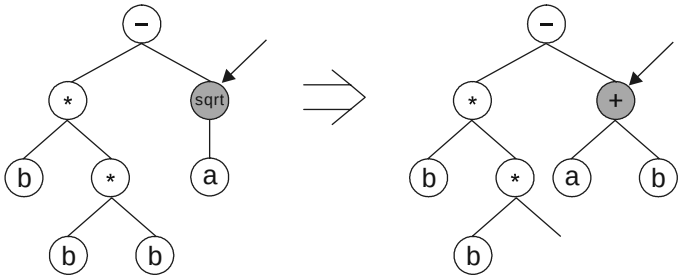


Figure 4. Illustration of a hypothetical event of point mutation in genetic programming. The arrow indicates the mutation point. Note that the daughter tree is an invalid structure.

sary building blocks with the inception of the initial population in order to guarantee the discovery of a good solution only by moving the initial building blocks around.

Finally, due to the dual function of the parse trees (genotype and phenotype), genetic programming is incapable of a simple, rudimentary expression: in all cases, the entire parse tree is the solution.

1.3. Gene Expression Programming

Gene expression programming was invented by myself in 1999 (Ferreira 2001), and incorporates both the simple, linear chromosomes of fixed length similar to the ones used in genetic algorithms and the ramified structures of different sizes and shapes similar to the parse trees of genetic programming. This is equivalent to say that in gene expression programming the genotype and phenotype are finally separated and the system can now benefit from all the advantages this brings about.

Thus, the phenotype of GEP consists of the same kind of ramified structure used in genetic programming. But the ramified structures created by GEP (expression trees) are the expression of a totally autonomous genome. Therefore, with gene expression programming, the second evolutionary threshold – the phenotype threshold – is crossed (Dawkins 1995). This means that, during reproduction, only the genome (slightly modified) is passed on to the next generation and we no longer need to replicate and mutate rather cumbersome structures: all the modifications take place in a simple linear structure which only later will grow into an expression tree.

The fundamental steps of gene expression programming are schematically represented in Figure 5. The process begins with the random generation of the chromosomes of a certain number of individuals (the initial population). Then these chromosomes are expressed and the fitness of each individual is evaluated against a set of fitness cases (also called selection environment). The individuals are then selected according to their fitness (their performance in that particular environment) to reproduce with modification, leaving progeny with new traits. These new individuals are, in their turn, subjected to the same developmental process: expression of the genomes, confrontation of the selection environment, selection, and reproduction with modification. The process is repeated for a certain number of generations or until a good solution has been found.

The pivotal insight of gene expression programming consisted in the invention of chromosomes capable of representing any parse tree. For that purpose a new language – *Karva* language – was created in order to read and express the information encoded in the chromosomes. The details of this new language are given in the next section.

Furthermore, the structure of the chromosomes was designed to allow the creation of multiple genes, each coding for a smaller program or sub-expression tree. It is worth emphasizing that gene expression programming is the only genetic algorithm with multiple genes. Indeed, the creation of more complex individuals composed of multiple genes is extremely simplified in truly functional genotype/phenotype systems. In fact, after their inception, these systems seem to catapult themselves into higher levels of complexity such as the multicellular systems, where different cells put together different consortiums of genes (Ferreira 2002a).

The basis for all this novelty resides on the revolutionary structure of GEP genes. The simple but plastic structure of these genes not only allows the encoding of any conceivable program but also allows their efficient evolution. Due to this versatile structural organization, a very powerful set of genetic operators can be easily implemented and used to search

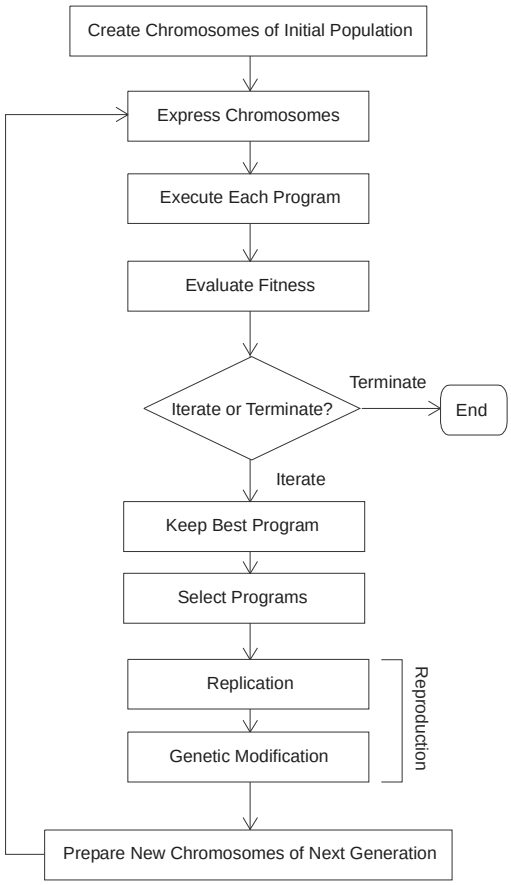


Figure 5. The flowchart of gene expression programming.

very efficiently the solution space. As in nature, the search operators of gene expression programming always produce valid structures and therefore are remarkably suited to creating genetic diversity.

2. The Architecture of GEP Individuals

We know already that the main players in gene expression programming are the chromosomes and the expression trees (ETs), being the latter the expression of the genetic information encoded in the former. As in nature, the process of information decoding is called translation. And this translation implies obviously a kind of code and a set of rules. The genetic code is very simple: a one-to-one relationship between the symbols of the chromosome and the nodes they represent in the trees. The rules are also very simple: they determine the spatial organization of nodes in the expression trees and the type of interaction between sub-ETs. Therefore, there are two languages in GEP: the language of the genes

and the language of expression trees and, thanks to the simple rules that determine the structure of ETs and their interactions, we will see that it is possible to infer immediately the phenotype given the sequence of a gene, and vice versa. This means that we can choose to have a very complex program represented by its compact genome without losing in meaning. This unequivocal bilingual notation is called *Karva* language. Its details are explained in the remainder of this section.

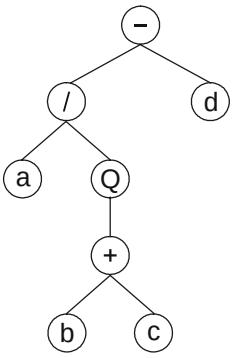
2.1. Open Reading Frames and Genes

The structural organization of GEP genes is better understood in terms of open reading frames (ORFs). In biology, an ORF or coding sequence of a gene begins with the start codon, continues with the amino acid codons, and ends at a termination codon. However, a gene is more than the respective ORF, with sequences upstream of the start codon and sequences downstream of the stop codon. Although in GEP the start site is always the first position of a gene, the termination point does not always coincide with the last position of a gene. Consequently, it is common for GEP genes to have non-coding regions downstream of the termination point. (For now we will not consider these non-coding regions, as they do not interfere with expression.)

Consider, for example, the algebraic expression:

$$\frac{a}{\sqrt{b+c}} - d \tag{1}$$

It can also be represented as a diagram or ET:



where “Q” represents the square root function.

This kind of diagram representation is in fact the phenotype of GEP chromosomes. And the genotype can be easily inferred from the phenotype as follows:

```
01234567
-/daQ+bc
```
(2)

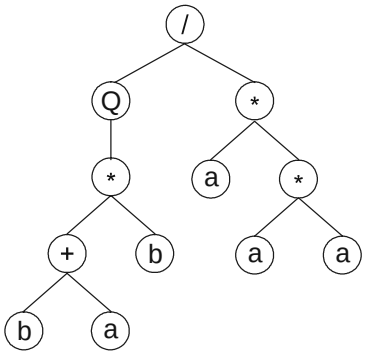
which is the straightforward reading of the expression tree from left to right and from top to bottom (exactly as we read a page of text). The expression (2) is an open reading frame,

starting at "-" (position 0) and terminating at "c" (position 7). These open reading frames were named *K-expressions* from Karva language.

Consider another open reading frame, the following K-expression:

```
012345678901
/Q**a*+baaba
```
(3)

Its expression as an ET is also very simple and straightforward. In order to express the ORF correctly, we must follow the rules governing the spatial distribution of functions and terminals. First, the start of a gene corresponds to the root of the expression tree which is placed in the topmost line. Second, in the next line, below each function, are placed as many branch nodes as there are arguments to that function. Third, from left to right, the nodes are filled consecutively with the next elements of the K-expression. Fourth, the process is repeated until a line containing only terminals is formed. In this case, the following expression tree is formed:



which mathematically corresponds to $\frac{\sqrt{(b+a)b}}{a^3}$.

Looking at the structure of GEP ORFs only, it is difficult or even impossible to see the advantages of such a representation, except perhaps for its simplicity and elegance. However, when open reading frames are analyzed in the context of a gene, the advantages of this representation become obvious. As previously stated, GEP chromosomes have fixed length, and they are composed of one or more genes of equal length. Consequently, the length of a gene is also fixed. Thus, in gene expression programming, what varies is not the length of genes which is constant, but the length of the ORF. Indeed, the length of an open reading frame may be equal to or less than the length of the gene. In the first case, the termination point coincides with the end of the gene, and in the latter, the termination point is somewhere upstream of the end of the gene.

What is the function of these non-coding regions of GEP genes? We will see that they are the essence of gene expression programming and evolvability, for they allow the modification of the genome using several genetic operators without restrictions, always producing syntactically correct programs. Thus, in GEP, the fundamental property of genotype/

phenotype systems – syntactic closure – is intrinsic, allowing the totally unconstrained restructuring of the genotype and, consequently, an efficient evolution.

In the next section we are going to analyze the structural organization of GEP genes in order to understand how they invariably code for syntactically correct programs and why they allow an unconstrained application of virtually any genetic operator.

2.2. Structural Organization of Genes

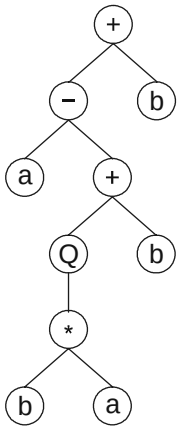
The genes of gene expression programming are composed of a head and a tail. The head contains symbols that represent both functions and terminals, whereas the tail contains only terminals. For each problem, the length of the head *h* is chosen, whereas the length of the tail *t* is a function of *h* and the number of arguments *n* of the function with more arguments (also called maximum arity) and is evaluated by the equation:

$$t = h\,(n\text{-}1) + 1 \tag{4}$$

Consider a gene for which the set of functions F = {Q, *, /, -, +} and the set of terminals T = {a, b}. In this case *n* = 2; if we chose an *h* = 11, then *t* = 11 (2 - 1) + 1 = 12; thus, the length of the gene *g* is 11 + 12 = 23. One such gene is shown below (the tail is shown in bold):

```
01234567890123456789012
+-ba+Qb*ba/abaaaabbaabb
```
(5)

It codes for the following expression tree:

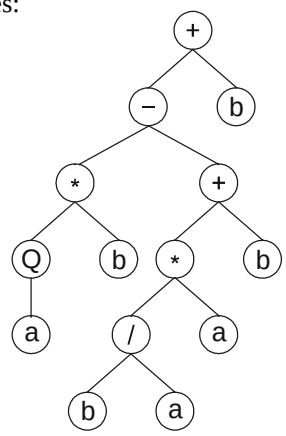


or the equivalent mathematical expression $\left(a-\sqrt{ba}\right)$. In this case, the open reading frame ends at position 9, whereas the gene ends at position 22.

Suppose now a mutation occurred at position 3, changing the “a” into “*”. Then the following gene is obtained:

```
01234567890123456789012
+-b*+Qb*ba/abaaaabbaabb                                    (6)
```

And its expression gives:

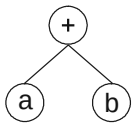


which mathematically corresponds to the expression $b\left(\sqrt{a}-1\right)$. In this case, the termination point shifts four positions to the right (position 13), enlarging and changing significantly the daughter tree.

Obviously the opposite also might happen, and the daughter tree might shrink. For example, consider again gene (5) above, and suppose a mutation occurred at position 1, changing the "-" into "a":

```
01234567890123456789012
+aba+Qb*ba/abaaaabbaabb                                    (7)
```

Its expression results in the following ET:



In this case, the ORF ends at position 2, shortening the original ET in seven nodes.

So, despite their fixed length, each gene has the potential to code for expression trees of different sizes and shapes, where the simplest is composed of only one node (when the first element of a gene is a terminal) and the largest is composed of as many nodes as the length of the gene (when all the elements of the head are functions with maximum arity).

It is evident from the examples above, that any modification made in the genome, no matter how profound, always results in a structurally correct program. Obviously, the structural organization of genes must be preserved, always maintaining the boundaries between head and tail. We will be able to fully appreciate the plasticity of GEP chromosomes in the section *Genetic Operators and Evolution* where the mechanisms and effects of different genetic operators will be thoroughly analyzed.

2.3. Multigenic Chromosomes

The chromosomes of gene expression programming are usually composed of more than one gene of equal length. For each problem or run, the number of genes, as well as the length of the head, are a priori chosen. Each gene codes for a sub-ET and the sub-ETs interact with one another forming a more complex multi-subunit expression tree.

Consider, for example, the following chromosome with length 39, composed of three genes, each with length 13 (the tails are shown in bold):

```
012345678901201234567890120123456789012
*Qb+*/bbbabab-a+Qbabbababa/ba-/*bbaaaaa
```
(8)

It has three open reading frames, and each ORF codes for a sub-ET (Figure 6). The start of each ORF is always given by position 0; the end of each ORF, though, is only evident upon construction of the corresponding sub-ET. As shown in Figure 6, the first open reading frame ends at position 9; the second ORF ends at position 5; and the last ORF ends at position 2. Thus, GEP chromosomes contain several ORFs of different sizes, each ORF coding for a structurally and functionally unique sub-ET. Depending on the problem at hand, these sub-ETs may be selected individually depending on their respective outputs, or they may form a more complex, multi-subunit expression tree and be selected as a whole. In these multi-subunit structures, individual sub-ETs interact with one another by a particular kind of posttranslational interaction or linking. For instance, algebraic sub-ETs can be linked by addition or multiplication whereas Boolean sub-ETs can be linked by OR, AND or IF.

The linking of three sub-ETs by addition is illustrated in Figure 6, c. Note that the final ET could be linearly encoded as the following K-expression:

```
01234567890123456789
++/*-baQba++Qb*/abbba
```
(9)

However, the use of multigenic chromosomes is more appropriate to evolve solutions to complex problems, for they permit the modular construction of complex, hierarchical structures, where each gene codes for a smaller and simpler building block. These smaller building blocks are separated from each other, and thus can evolve independently. Not surprisingly, these multigenic systems are much more efficient than unigenic ones (Ferreira 2001, 2002a).

3. Genetic Operators and Evolution

Genetic operators are the core of all evolutionary algorithms, and two of them are common to all evolutionary systems: selection and replication. Indeed, all artificial systems use a scheme to select individuals more or less according to fitness. Some schemes are totally deterministic, whereas others include a touch of unpredictability. Gene expression programming uses one of the latter, namely, a fitness proportionate roulette-wheel scheme (see e.g. Goldberg 1989) coupled with the cloning of the best individual (simple elitism) as it mimics nature very faithfully and produces very good results.

a. 0123456789012012345678901201234567890 12
Qb+/**bbbabab**-a+Qba**bbababa**/ba-/***bbaaaaa**

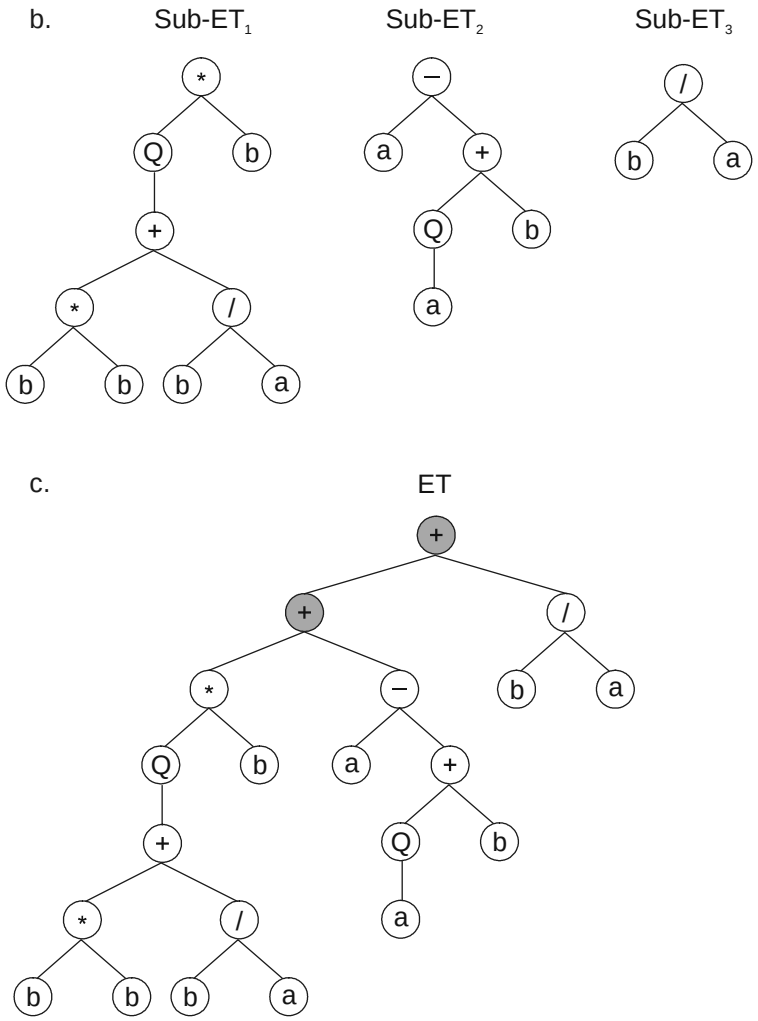


Figure 6. Expression of GEP genes as sub-ETs. **a)** A three-genic chromosome with the tails shown in bold. Position zero marks the start of each gene. **b)** The sub-ETs codified by each gene, which correspond respectively to $b\sqrt{b^2+b/a}$, $a-\left(\sqrt{a}+b\right)$, and b/a. **c)** The result of posttranlational linking with addition, which obviously corresponds to $b\sqrt{b^2+b/a}+a-\left(\sqrt{a}+b\right)+b/a$. The linking functions are shown in gray.

Thus, according to fitness and the luck of the draw, individuals are selected to be replicated. Although crucial, replication is the most uninteresting operator. During replication, chromosomes are dully copied and passed on to the next generation. The fitter the individual the higher the probability of passing on its genes to the next generation. So, during replication, the genomes of the selected individuals are copied every time the roulette picks them up. And the roulette is spun as many times as there are individuals in the population so that the same population size is maintained from generation to generation.

Although the center of the storm, by themselves, selection and replication, do nothing in terms of adaptation. In fact, by themselves they can only cause genetic drift, making populations less and less diverse with time until all the individuals are exactly the same. So, the corner stone of all evolutionary systems is genetic modification. And different algorithms create this modification differently. For instance, genetic algorithms normally use mutation and recombination; genetic programming uses almost exclusively tree recombination; and gene expression programming uses mutation, inversion, transposition, and recombination.

With the exception of GP, which is severely constrained in terms of tools of genetic modification, in both GAs and GEP it is possible to implement easily a vast set of search operators because the search operators act on simple linear chromosomes. In fact, a varied set of search operators was implemented in gene expression programming in order to shed some light on the dynamics of evolutionary systems, but what is important is to provide for the necessary degree of genetic diversification in order to allow an efficient evolution. Nevertheless, mutation (by far the most efficient operator) by itself is capable of wonders. However, the interplay of mutation with other operators not only allows an efficient evolution but also allows the duplication of genes and their subsequent differentiation, the creation of small repetitive sequences, and so forth, making things really interesting.

In the remainder of this section we will see how the search operators work and how their implementation in gene expression programming is a child's play due to the simple fact that the genome is completely autonomous and consequently is not tied up in the structural complexities of the computer programs encoded within.

3.1. Mutation

In gene expression programming, mutations can occur anywhere in the chromosome. However, the structural organization of chromosomes must remain intact, that is, in the heads of genes any symbol can change into another (function or terminal), whereas in the tails terminals can only change into terminals. This way, the structural organization of chromosomes is preserved, and all the new individuals produced by mutation are structurally correct programs.

Consider the following three-genic chromosome:

```
012345678901201234567890120123456789012
/bQa***bbbbaba---+*Q-abbbabaQ*a+***baabbba
```

Suppose a mutation changed the "*" at position 5 in gene 1 to "a"; the "-" at position 1 in gene 2 to "Q"; and the "a" at position 2 in gene 3 to "*". In this case the following chromosome is obtained:

```
012345678901201234567890120123456789012
/bQa*abbbbaba-Q+*Q-abbbabaQ***+***baabbba
```

Note that if a function is mutated into a terminal or vice versa, or a function of one argument is mutated into a function of two arguments or vice versa, the expression tree is usually modified drastically. Note also that the mutation on gene 1 is an example of a neutral mutation, as it occurred in the non-coding region of the gene. It is worth emphasizing that the non-coding regions of GEP chromosomes are ideal places for the accumulation of neutral mutations which are known to play an important role in evolution (Kimura 1983; Ferreira 2002b).

In summary, in gene expression programming there are no constraints both in the kind of mutation and the number of mutations in a chromosome as, in all cases, the newly created individuals are syntactically correct programs.

3.2. Inversion

We know already that the modifications bound to make a big impact occur usually in the heads of genes. Therefore, the inversion operator was restricted to these regions. Here any sequence might be randomly selected and inverted.

In gene expression programming, the inversion operator randomly chooses the chromosome, the gene to be modified, and the start and termination points of the sequence to be inverted. It is worth pointing out that this is the first time the inversion operator is described in gene expression programming.

Consider, for instance, the following three-genic chromosome:

```
012345678901201234567890120123456789012
/+aQ*aaabaaab/aa/baaababab-Q++aQababaab
```

Suppose that the sequence "aQ*" in gene 1 (positions 2-4) was picked up to be inverted. Then the following chromosome is formed:

```
012345678901201234567890120123456789012
/+*Qaaaabaaab/aa/baaababab-Q++aQababaab
```

It is worth pointing out that, since the inversion operator was restricted to the heads of genes, there is no danger of a function ending up in the tails and, consequently, all the new individuals created by inversion are syntactically correct programs.

3.3. Transposition and Insertion Sequence Elements

The transposable elements (also called transposons) of gene expression programming are fragments of the genome that can be activated and then jump to another place in the chromosome. In GEP there are three kinds of transposable elements: (1) short fragments with a function or terminal in the first position that transpose to the head of genes except the root (insertion sequence elements or IS elements); (2) short fragments with a function in the first position that transpose to the start position of genes (root IS elements or RIS elements); (3) and entire genes that transpose to the beginning of chromosomes.

3.3.1. IS Transposition

Any sequence in the genome might become an IS element and, therefore, these elements are randomly selected throughout the chromosome. A copy of the transposon is made and inserted at any position in the head of a gene, except the first position. The transposition operator randomly chooses the chromosome, the start and termination points of the IS element, and the target site. It is worth pointing out that the implementation of this operator as described here, slightly differs from the original implementation (Ferreira 2001) where the length of the IS elements was a priori chosen.

Consider the following three-genic chromosome:

```
012345678901201234567890120123456789012
+*+-Q/baaaabbQ+aa*abaaaaba*+-a/-aabbbba
```

Suppose that the sequence “a/-” in gene 3 (positions 3-5) was picked up as an IS element to be then inserted between positions 1-2 in gene 2, obtaining:

```
012345678901201234567890120123456789012
+*+-Q/baaaabbQ+a/-abaaaaba*+-a/-aabbbba
```

Note that, in this case, a perfect copy of the transposon appears at the site of insertion. Note also that a sequence with as many symbols as the IS element is deleted at the end of the head (in this case, the sequence “a*a” was deleted). Thus, despite this insertion, the structural organization of chromosomes is maintained and, therefore, all the new individuals created by IS transposition are syntactically correct programs.

3.3.2. Root Transposition

All root IS elements start with a function, and therefore must be chosen among the sequences of the heads. For that, a point is randomly chosen in the head and the gene is scanned downstream until a function is found. This function becomes the start position of the RIS element. If no functions are found, the operator does nothing.

The RIS transposition operator randomly chooses the chromosome, the gene to be modified, and the start and termination points of the RIS element. It is worth noticing that this

operator is slightly different from the original RIS transposition (Ferreira 2001) as the length of the transposon is randomly chosen by this simpler RIS transposition.

Consider the following three-genic chromosome:

```
012345678901201234567890120123456789012
*Q/+b*bababaaQ*aQ*QaaababaQa*/+abbbaaab
```

Suppose that the sequence "/+b" in gene 1 was randomly chosen to become an RIS element. The transposon copies itself and then transposes to the root of the gene, giving:

```
012345678901201234567890120123456789012
/+b*Q/bababaaQ*aQ*QaaababaQa*/+abbbaaab
```

Note that during transposition, the whole head shifts to accommodate the RIS element, losing, at the same time, the last symbols of the head (as many as there are in the transposon). In this case, the sequence "+b*" was deleted and the transposon became only partially duplicated. As with IS transposition, the tail of the gene subjected to RIS transposition and all nearby genes remain unchanged. Note, again, that all the programs newly created by this operator are syntactically correct as it also preserves the structural organization of the chromosome.

3.3.3. Gene Transposition

In gene transposition an entire gene works as a transposon and transposes itself to the beginning of the chromosome. In contrast to the other forms of transposition, in gene transposition, the transposon (the gene) is deleted at the place of origin.

The gene transposition operator randomly chooses the chromosome to be modified and then randomly chooses one of its genes (except the first, obviously) to transpose. Consider the following chromosome composed of three genes:

```
012345678901201234567890120123456789012
-ab+a-babaaaaQ+bab/babbbba*-*Q*-abbabab
```

Suppose gene 3 was chosen to undergo gene transposition. In this case the following chromosome is obtained:

```
012345678901201234567890120123456789012
*-*Q*-abbabab-ab+a-babaaaaQ+bab/babbbba
```

Apparently, gene transposition is only capable of shuffling genes and, for sub-ETs linked by commutative functions, this contributes nothing to adaptation in the short run. Note, however, that when the sub-ETs are linked by a non-commutative function, the order of the

genes matters and, in this case, gene transposition becomes a macromutator. However, gene transposition becomes particularly interesting when it is used in conjunction with recombination, for it allows not only the duplication of genes but also a more generalized shuffling of genes or smaller building blocks.

3.4. Recombination

In gene expression programming there are three kinds of recombination: one-point recombination, two-point recombination, and gene recombination. In all types of recombination, two chromosomes are randomly chosen and paired to exchange some material between them, creating two new daughter chromosomes.

3.4.1. One-point Recombination

In one-point recombination the parent chromosomes are paired and split up at exactly the same point. The material downstream of the recombination point is afterwards exchanged between the two chromosomes.

Consider the following parent chromosomes, each composed of three genes:

```
012345678901201234567890120123456789012
*b-Qb/aaabaabQ**Q+*bbaaabb*Q--QQaabbbbb
-/bQa+aabbbba/Q*b/aababaaa-/a/a/abaaabb
```

Suppose bond 4 in gene 2 (between positions 3 and 4) was randomly chosen as the crossover point. Then, the paired chromosomes are both cut at this bond, and exchange between them the material downstream of the crossover point, forming the offspring below:

```
012345678901201234567890120123456789012
*b-Qb/aaabaabQ**Q/aababaaa-/a/a/abaaabb
-/bQa+aabbbba/Q*b+*bbaaabb*Q--QQaabbbbb
```

It is worth emphasizing that GEP chromosomes can cross over any point in the genome, continually disrupting old building blocks and continually forming new ones. Furthermore, due to both the multigenic nature of GEP chromosomes and the existence of non-coding regions in most genes, entire genes and intact open reading frames can be swapped between parent chromosomes. Thus, the disruptive tendencies of one-point recombination (splitting of building blocks) coexist side by side with its more conservative tendencies (swapping of genes and ORFs), making one-point recombination (and of course two-point recombination too) a very well balanced genetic operator. Furthermore, like all the other recombinational operators, when one-point recombination is used together with gene transposition, it is also capable of duplicating genes.

3.4.2. Two-point Recombination

In two-point recombination two parent chromosomes are paired side by side and two points are randomly chosen as crossover points. The material between the recombination points is afterwards exchanged between the parent chromosomes, forming two new daughter chromosomes.

Consider the following pair of recombining chromosomes:

```
01234567890120123456789012012345678901 2
/bQbb*aabaaaaQ*a/b+bbbaaabQ+/aa+babaabb
+-Qa/Qaabbaba+Q-+/+abbbaaa//+-/+bababab
```

Suppose bond 7 in gene 1 (between positions 6 and 7) and bond 4 in gene 3 (between positions 3 and 4) were chosen as crossover points. Then, the following daughter chromosomes are created:

```
01234567890120123456789012012345678901 2
/bQbb*aabbaba+Q-+/+abbbaaa//+-a+babaabb
+-Qa/QaabaaaaQ*a/b+bbbaaabQ+/a/+bababab
```

It is worth emphasizing that two-point recombination is more disruptive than one-point recombination in the sense that it recombines the genetic material more thoroughly, constantly destroying old building blocks and creating new ones. But like one-point recombination, two-point recombination has also a conservative side and it is good at swapping entire genes and open reading frames. And, as observed for one-point recombination, two-point recombination can also give rise to duplicated genes if it were used together with gene transposition.

Notwithstanding, if the goal is to evolve good solutions, one-point or two-point recombination should never be used as the only source of genetic variation as they tend to homogenize populations (Ferreira 2002c). However, together with mutation, inversion and transposition, these operators are an excellent source of genetic variation and are more than sufficient to evolve good solutions to virtually all problems.

3.4.3. Gene Recombination

In the third kind of GEP recombination, entire genes are exchanged between two parent chromosomes, forming two daughter chromosomes containing genes from both parents. The exchanged genes are randomly chosen and occupy exactly the same position in the parent chromosomes.

Consider the following parent chromosomes:

```
01234567890120123456789012012345678901 2
/+*--bbaaabab*+b--aabaaaabQ**+*bababbab
Q//b-baababaa/ab/QQbaababaQ*+a++bbaaaaa
```

Suppose gene 2 was chosen to be exchanged. In this case the following offspring is formed:

```
012345678901201234567890120123456789012
/+*--bbaaabab/ab/QQbaababaQ**+*bababbab
Q//b-baababaa*+b--aabaaaabQ*+a++bbaaaaa
```

Note that, with this kind of recombination, similar genes can be exchanged but, most of the times, the exchanged genes are very different from one another and new material is introduced in the population.

It is worth emphasizing that this operator is unable to create new genes: the individuals created by gene recombination are different arrangements of existing genes. Obviously, if gene recombination were used as the unique source of genetic variation, more complex problems could only be solved using very large initial populations in order to provide for the necessary diversity of genes. However, GEP evolvability is based not only in the shuffling of genes (achieved by gene recombination and gene transposition), but also in the constant creation of new genetic material which is carried out essentially by mutation, inversion and transposition (both IS and RIS transposition) and, to a lesser extent, by recombination (both one-point and two-point recombination).

4. Evolving Computer Programs for Diagnosing Breast Cancer

In this section we are going to use gene expression programming to design a computer program that can be used to diagnose breast cancer. The data sets used both for training and testing were obtained from PROBEN1 – a set of neural network benchmark problems and benchmarking rules (Prechelt 1994). Both the technical report and the data sets are available through anonymous FTP from Neural Bench archive at Carnegie Mellon University (machine **ftp.cs.cmu.edu**, directory **/afs/cs/project/connect/bench/contrib/prechelt**) and from the machine **ftp.ira.uka.de** in directory **/pub/neuron**. The file name in both cases is **proben1.tar.gz**.

In this diagnosis task the goal is to classify a tumor as either benign (0) or malignant (1) based on nine different cell analysis (input attributes or terminals).

The model presented here was obtained using the **cancer1** data set of PROBEN1 where the binary 1-of-*m* encoding in which each bit represents one of *m*-possible output classes was replaced by a 1-bit encoding (“0” for benign and “1” for malignant). The first 350 samples were used for training and the last 174 were used to test the performance of the model in real use. This means that absolutely no information from the test set samples or the test set performance are available during the adaptive process. Thus, both the classification accuracy and classification error on the test set can be used to evaluate the generalization performance of the evolved models.

For this problem a very simple function set was chosen, composed only of the four arithmetic operators, that is, F = {+, -, *, /}, where each function was weighted five times; the set of terminals consisted of the nine attributes used in this problem and were represented

by T = {d_0, ..., d_8} which correspond, respectively, to clump thickness, uniformity of cell size, uniformity of cell shape, marginal adhesion, single epithelial cell size, bare nuclei, bland chromatin, normal nucleoli, and mitoses.

In classification problems where the output is often binary, it is important to set criteria to convert real-valued numbers into zero or one. This is the 0/1 rounding threshold R_t that converts the output of a chromosome into "1" if the output is equal to or greater than R_t, or into "0" otherwise. For this problem we are going to use $R_t = 0.1$.

The fitness function used to evaluate the performance of each candidate model is very simple and is based on the number of samples correctly classified. Thus, the fitness f_i of an individual program corresponds to the number of hits and is evaluated by the formula:

$$\text{if } n > C_p, \text{ then } f_i = n; \text{ else } f_i = 0 \tag{10}$$

where n is the number of sample cases correctly evaluated, and C_p is the number of samples in the class with more members (predominant class).

As it is customary in genetic programming (Koza 1992) and gene expression programming (Ferreira 2001), the parameters used per run are summarized in a table (Table 1). Note that, in this case, a small population of 50 individuals and chromosomes composed of three genes with an $h = 8$ and sub-ETs linked by addition were used. The program below

Table 1
Settings used in the breast cancer problem.

Number of generations	500
Population size	50
Number of training samples	350
Number of testing samples	174
Function set	(+-*/)5
Terminal set	d0 - d9
Rounding threshold	0.1
Head length	8
Number of genes	3
Linking function	+
Chromosome length	51
Mutation rate	0.044
Inversion rate	0.1
IS transposition rate	0.1
RIS transposition rate	0.1
One-point recombination rate	0.3
Two-point recombination rate	0.3
Gene recombination rate	0.1
Gene transposition rate	0.1

was discovered after 423 generations (genes are shown separately and a dot is used to separate each element):

```
*.+.d0.*.*.*.+.*.d7.d0.d8.d3.d5.d4.d3.d5.d6
*.+.*.d0.*.*.*.-.d5.d4.d1.d5.d1.d0.d2.d1.d1
*.d5.*.+.d6.*.+.d5.d2.d2.d1.d1.d7.d0.d7.d4.d0          (11a)
```

It has a fitness of 340 evaluated against the training set of 350 fitness cases and maximum fitness on the test set of 174 examples. This means that this model is very good indeed, with a classification accuracy of 100% and a classification error of 0% in the test set. In the training set a classification accuracy of 97.14% and a classification error of 2.86% were obtained.

Note that for the expression of chromosome (11a) to be complete the sub-ETs must be linked by addition and the 0/1 rounding threshold must be taken into account. With the software *APS 3.0* by *Gepsoft*, the model (11a) above can be automatically converted into a fully expressed computer program or function, such as the C++ function below:

```
int apsModel(double d[])
{
    const double ROUNDING_THRESHOLD = 0.1;
    double dblTemp = 0;
    dblTemp =  ((((d[0]*d[8])*(d[3]+d[5]))+((d[4]*d[3])*d[7]))*d[0]);
    dblTemp += ((d[0]+((d[0]-d[2])*d[5]))*((d[4]*d[1])*(d[5]*d[1])));
    dblTemp += (d[5]*(((d[5]*d[2])+(d[2]+d[1]))*d[6]));
    return (dblTemp > ROUNDING_THRESHOLD ? 1:0);
}                                                          (11b)
```

Similarly, all models evolved by gene expression programming can be immediately converted into virtually any programming language through the use of grammars, including the universal representation of parse trees (Figure 7). These trees can then be used to grasp immediately the mathematical intricacies of the evolved models and therefore are ideal for extracting knowledge from data.

As you can clearly see in Figure 7, all the cell analysis seem to be relevant to an accurate diagnosis of breast cancer. This is, indeed, one of the great advantages of gene expression programming: the possibility of extracting knowledge almost instantaneously as the models evolved by GEP can be represented in any conceivable language, including the universal diagram representation of expression trees.

5. Conclusions

In this chapter the details of implementation of gene expression programming were thoroughly explained, giving other researchers the possibility of implementing it themselves. Furthermore, this new algorithm was summarily compared to genetic algorithms and genetic programming in order to bring into focus the fundamental differences between the three techniques and, consequently, enable readers to appreciate the advantages a full-fledged

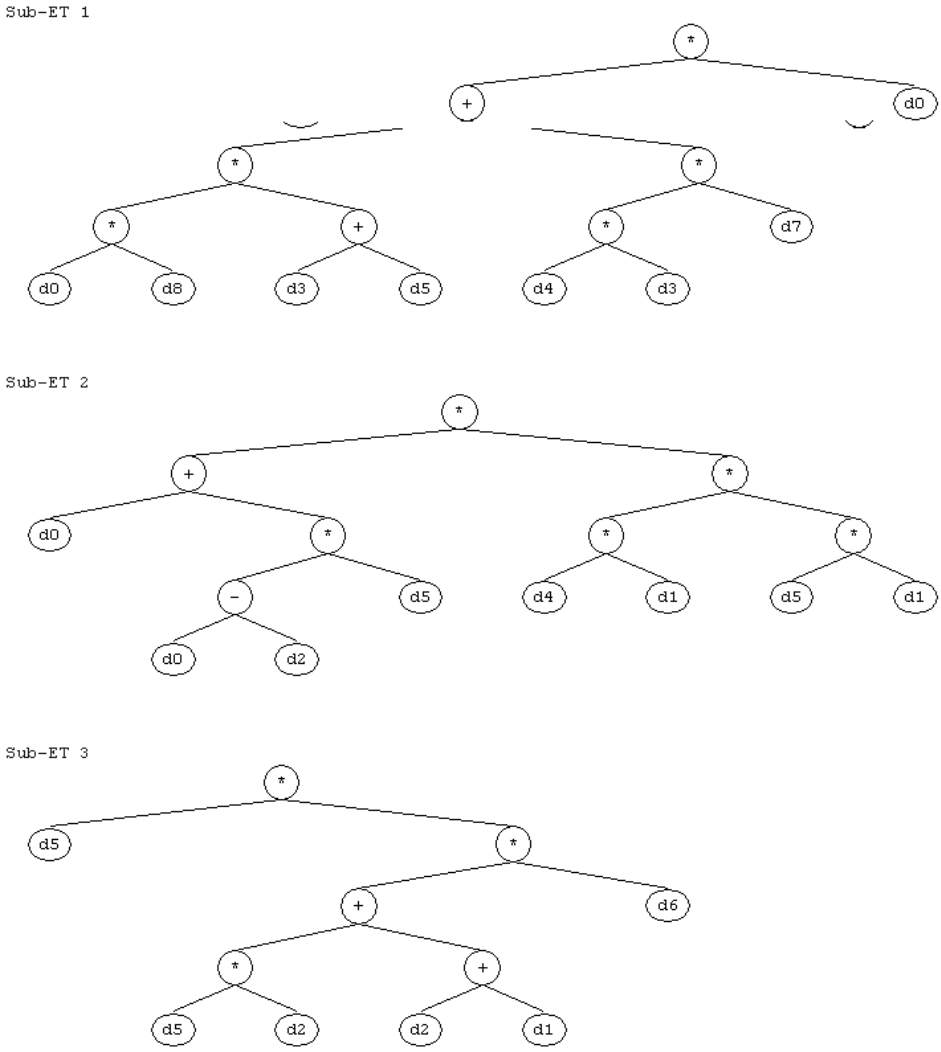


Figure 7. The sub-ETs of the model (11b) evolved by gene expression programming to diagnose breast cancer. (Expression trees drawn by *Gepsoft APS 3.0*.)

genotype/phenotype system brings into evolutionary computation. In addition, the classification task solved in this work clearly demonstrates the modeling prowess of this new technique: the compact computer programs evolved by gene expression programming in its native Karva code can be immediately used to generate highly sophisticated computer programs in virtually any programming language through the use of grammars as is already done in commercially available software.

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