Enzyme Genetic Programming

Modelling Biological Evolvability in Genetic Programming

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This thesis is dedicated to all my family and friends.

(So you'd better read it! — I'll be asking questions!)

Abstract

This thesis introduces a new approach to program representation in genetic programming in which interactions between program components are expressed in terms of a component's behaviour rather through its relative position within a representation or through other non-behavioural systems of reference. This approach has the advantage that a component's behaviour is expressed in a way that is independent of any particular program it finds itself within; and thereby overcomes the problem when using conventional program representations whereby program components lose their behavioural context following recombination. More generally, this implicit context representation leads to a process of meaningful variation filtering; whereby inappropriate change induced by variation operators can be wholly or partially ignored. This occurs as a consequence of program behaviours emerging from the self-organisation of program components, ignoring those components which do not fit the contexts declared by the other components within the program. This process results in gradual change within the behaviour of a program during evolution. This thesis also presents results which show that implicit context representation leads to better size evolution characteristics than conventional genetic programming; and that functional redundancy and Lamarckian reinforcement learning both improve evolutionary search, agreeing with previous research by other authors.

Contents

List of Tables

List of Figures

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I would also like to offer special thanks to all my colleagues at York, past and present, for their help and friendship; to Steve Smith and Keith Downing, my examiners, for their constructive advice; and to Spike the goose and his feathered friends, for being there when I needed someone to talk to.

Declaration

Some of the research presented in this thesis has previously been published by the author [Lones and Tyrrell, 2001c,b,a, 2002b,a, 2003b,a]. All work presented in this thesis as original is so to the best knowledge of the author. References and acknowledgements to other researchers have been given as appropriate.

Hypothesis

This research follows from the notion that models of biological representations can be used within genetic programming to represent executable structures; motivated by the expectation that these models will capture useful biological properties that will improve the evolution of executable structures. More specifically, it is asserted that:

- Representations from engineering domains are not designed to respond to random change in a meaningful way. In genetic programming, this is demonstrated by the poor response of conventional representations towards recombination operators.
- Biological representations are a product of evolution and are therefore well adapted for representing evolving artefacts. In particular, they are believed to confer evolvability — the capacity to exhibit change in an appropriate direction — to the artefacts that they represent.
- Many biological structures are known to carry out activities of a computational nature. This includes metabolic, signalling, gene expression and neural pathways. It has also been shown that models of these structures can be used to represent non-biological computational artefacts.

Following from these assertions, it is hypothesised that models of biological representations can be used to represent computer programs and other artificial executable structures within genetic programming, thereby improving the evolvability of these structures.

1 Introduction

1.1 Genetic Programming

Genetic programming (GP) is an evolutionary computation approach to automatic programming; designing programs to solve a particular task through the use of an algorithm modelled upon processes and mechanisms of biological evolution. Genetic programming has several apparent advantages over better known automatic programming techniques. Unlike formal methods, GP requires no knowledge about the problem that it is attempting to solve other than a measure of how good a solution is, and once a GP run has been initiated it requires no human interaction. Unlike inductive logic programming, GP does not attempt to carry out an exhaustive search of the problem's solution space; but rather exploits its search history to identify those areas which are more likely to contain global optima.

However, GP is far from perfect. For much of its execution, it fails to effectively exploit its search history: since its model of biological recombination does not, on the whole, produce better programs from existing programs. GP has a bloat problem: the programs that it generates tend to become larger and larger at a rate which rises in line with a quadratic function; filling up the available space and making it near-impossible to find small, efficient solutions. Like other evolutionary computation approaches, GP has a scalability problem: increasing problem size leads to an unmanageably high increase in space and time resource requirements.

Nevertheless, the GP approach is not futile. It is still a young field of research, it is attracting a growing research community, and there are many avenues of research yet to be explored. Moreover, it already shows a lot of promise. GP has been used to solve a huge variety of problems: from designing robot controllers to discovering new quantum algorithms to understanding the role of genetic motifs and protein structures in biology. One of its particular strengths is its ability to find solutions to problems which a human would probably never consider: making it possible to solve problems in fields which humans do not thoroughly understand (like biology); or find hard to understand (like quantum computing); and to discover new, more efficient solutions to problems which humans have already solved (such as computer algorithms); not to mention its ability to inform humans through reverse-engineering of these solutions.

1.2 Biological Modelling

Modelling biology on computers has been a prevailing theme for much of the history of computation. It is the ambition of many computer scientists to create computers which are as powerful and flexible as animal brains. Accordingly, it is logical to draw information from systems which have already achieved this feat: biological systems. Nevertheless, the interests of computer scientists in biology are not limited to neural processes. Biological systems have many properties which are the envy of computer science; for example: growth, learning, reconfigurability, self-repair, fault tolerance, and reproduction — though of course there are many biological processes, mechanisms and artefacts which at the moment would have no conceivable benefit within the silicon environment of a computer.

Biological modelling gave birth to evolutionary computation, yet there are mixed views within the EC community regarding biological modelling within evolutionary computation. A number of researchers cite the 'No Free Lunch' theory [Wolpert and Macready, 1995] whilst warning against the futility of introducing greater complexity to evolutionary algorithms: yet this same theory also predicts that evolutionary computation can be no better than random search across the whole spectrum of problem domains. Clearly, EC is considerably better than random search upon the kinds of problems that computer scientists actually want to solve. Other researchers have championed the value of biological modelling within EC; testifying to the obvious superiority of biological evolution over simulated evolution.

1.3 Evolvability

Evolvability is the relative capacity for something to exhibit appropriate change. For a biological organism, evolvability is the relative likelihood that random genetic change could lead to an improvement in the organism's fitness. For computer software, evolvability is the ease with which new functionality can be introduced by a human programmer. For a human language, evolvability is a measure of its ability to express new concepts and accept new constructs and methods of communication as required. These examples illustrate that evolvability is meaningful within many domains. In fact, the concept of evolvability can be thought of as a pattern which can be applied to any domain where an entity or group of entities is subject to a process of change; and particularly where a domain has some notion of a particular direction of change being more valuable than another.

What is perhaps less appreciated is that concepts of how to achieve evolvability can also be applied across domains. For example, in software systems modularity is seen as a source of evolvability since it limits the effect of change to a local region of the program. This limits the global impact of change within the program, making it easier to apply change, and making it less likely that any errors will propagate to other parts of the program. Likewise, biological organisms develop in a compartmental fashion, allowing individual compartments to be evolved separately and making it less likely that genetic errors will propagate within the whole organism [Conrad, 1990].

The work reported in this thesis is motivated to a large degree by the premise that principles of biological evolvability can be applied within non-biological artefacts in order to improve the way in which they evolve. This premise is motivated by a number of observations: (i) the way in which biological organisms are represented is believed to be a product of evolution and therefore presumably superior to many other potential representations; (ii) these representations are evidently capable of describing and supporting the evolution of highly complex systems i.e. biological organisms; (iii) these representations are capable of describing systems of computation; and (iv) many principles of evolvability are known to be applicable across domains. That biological representations can describe computation is perhaps not obvious but is supported by the developing community of computer scientists who use models of biological processes to carry out information processing and other overtly computational tasks.

1.4 Enzyme Genetic Programming

The product of this work is a GP system called enzyme genetic programming. Enzyme genetic programming has many similarities with conventional GP systems: in that it uses a population based evolutionary algorithm; it applies recombination and mutation operators to create new programs; it specifies a problem using a fitness function, a function set and a terminal set; and it generates programs represented by parse trees. However, it does not use parse trees to represent programs during evolution but rather uses a new program representation modelled upon the way in which enzyme systems are represented in biology. The consequences of this new representation for evolution are examined at length in the pages to come.

1.5 Contributions

This work makes the following principle contributions to knowledge:

- The development and understanding of a new **implicit context** form of program representation in which program components interact through behavioural descriptions rather than through relative positions or arbitrary references.
- The implementation of a genetic programming system based upon an implicit context representation, showing how this new form of representation may be used in practice.
- The development of the concept of **meaningful variation filtering**, whereby a representation can filter out the effects of inappropriate variation events whilst promoting meaningful change.
- The demonstration that implicit context representation leads to meaningful program recombination as a result of meaningful variation filtering.
- The realisation that functional redundancy within an implicit context representation is structured as a subsumption hierarchy and supports meaningful variation filtering through the action of variation operators upon this structure.

1.6 Thesis Organisation

This thesis is organised into three main segments. Chapters 1 to 5 introduce the concepts of biological representation, evolution, and evolvability. Chapters 6 and 7 review related work in genetic programming and evolutionary computation. Chapters 8 to 10 describe the novel contributions of this research. Specifically:

Chapter 1 is this introduction.

Chapter 2 introduces evolution; describing how evolution can be understood as a general process which exhibits common behaviours across domains.

Chapter 3 reviews the fundamental components of biological representation.

Chapter 4 discusses how these components are organised into higher-level structures.

Chapter 5 introduces the concept of evolvability and discusses the sources of evolvability within biological systems.

Chapter 6 reviews fundamental topics in genetic programming: focussing on its limitations and derivative approaches.

Chapter 7 reviews approaches to improving the evolvability of evolutionary computation, placing particular emphasis upon genetic programming and the role of biological modelling.

Chapter 8 introduces enzyme genetic programming; discussing the motivation behind the approach and its implementation.

Chapter 9 presents experimental analysis of enzyme genetic programming, discusses the experimental results, and identifies key evolutionary behaviours.

Chapter 10 summarises, draws conclusions, and offers some speculative suggestions for future research.

Appendix A describes the activity model, an approach which predates the current version of enzyme genetic programming.

2 Evolution

Evolution is a process that leads to change. In particular domains, the term evolution is used to refer to specific processes of change. In the study of social development, for instance, evolution is used to describe the development of societies. In mathematics, evolution is an iterative process which finds the root of a number. Stellar evolution, in astronomy, is the process of star formation. Software evolution, in software engineering, is the change in functionality over the lifetime of a software system. Biological evolution is the change in genetic constitution of a population of organisms over time.

Even in Darwin's era, there was nothing new about the idea of evolution. Evolution has been acting, and could easily be seen to be acting, in myriad systems since the dawn of history. The thing that shocked Victorian people was the idea that biological populations, too, were subject to evolution and therefore not entirely shaped by the will of God — or, to take the 'theory of evolution' [Darwin, 1859] to its ultimate conclusion, formed entirely by a process of selection acting upon essentially random variation.

This chapter has several objectives. First, to introduce the properties of a range of example evolutionary systems. Second, to present commonalities that exist between the properties of these systems and establish a general view of evolutionary systems. Third, to develop a standard taxonomy and terminology of evolutionary systems.

Above all, the aim of this chapter is to demonstrate that it is possible to introduce the key concepts of evolution without having to talk about biological evolution: and, in this way, show that ideas concerning evolution have relevance to a broader range of domains than biology alone.

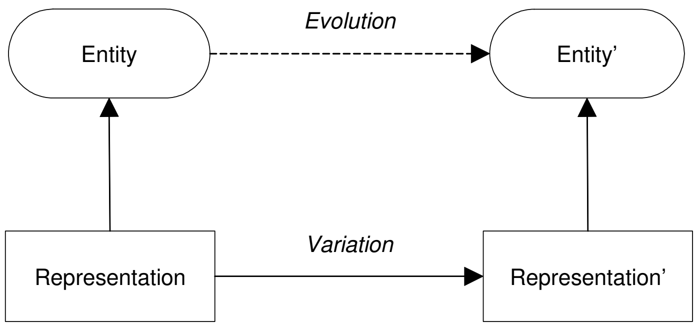


Figure 2.1. An evolutionary system. Entities evolve through a process of variation acting upon their representation.

2.1 Evolution of Individuals

The simplest evolutionary systems consist of a single entity undergoing change. A good example is a geographical landscape. In an abstract sense, a geographical landscape is a three-dimensional shape. This shape was formed, or evolved, by natural processes such as rain, wind, frost and earthquakes introducing change within the conformation of the rocks that make up the landscape. In essence, the eventual shape was decided by the action of these natural processes of variation upon the properties of the constituent rocks: a product of both the kind of change introduced by the natural processes *and* the kind of change permitted by the rocks. Different rocks react to natural processes in different ways and, consequently, lead to different landscapes. For instance, chalk can be dissolved by water, sand is easily shaped by wind, and certain rocks (such as granite) are particularly prone to frost shattering.

This example illustrates the three basic elements of an evolutionary system — the entity being evolved, its representation, and the mechanisms of variation. In this case, the entity is the shape of a geographical landscape, the representation is the constituent rocks, and the mechanisms of variation are natural environmental processes. It also illustrates how the evolutionary change of an entity is a result of the mechanisms of variation acting upon its representation, a pattern which is illustrated in figure 2.1.

Another example of this pattern is software evolution [Lehman and Parr, 1976]. Here, the entity being evolved is a software system. Its representation is the way in which the software is implemented — for example: the granularity of the language it is written in, its internal structure of decomposition, its choice of data structures and algorithms. The mechanism of variation is the programmer or programmers responsible for maintaining and updating the code. Again, it is the action of the mechanism of variation (the programmers) upon the representation (the implementation) that decides how the software system evolves.

However, this example has a significant difference to the previous example: evolution is *directed*. In geographical landscapes, evolution is the consequence of rocks annealing to environmental processes. There is no external pressure for the system to evolve in any particular direction. In software systems, on the other hand, evolution in the direction of increased functionality is the objective of the programmers who modify the implementation. Consequently, programmers introduce variation that they believe will increase the functionality of the software system. This directed variation leads to directed evolution.

2.1.1 Evolvability

Evolvability [Conrad, 1990, Kirschner and Gerhart, 1998, Nehaniv, 2003] is a measure of an evolutionary system's ability to evolve in an appropriate direction. To re-iterate a point made earlier, the evolution of an entity is a consequence of the mechanisms of variation inducing change within the entity's representation: a result of both the mechanisms of variation's ability to express change and the representation's ability to accept change. Accordingly, the evolvability of an evolutionary system is a function of both the evolvability accorded by the entity's representation and the evolvability accorded by the mechanisms of variation.

In the context of the software evolution example, this entails that the degree to which the evolution of a software system can be directed is a function of not only the programmers' ability to conduct appropriate change but also the implementation's capacity to accept appropriate change. This is not to say that any programmer could not make an appropriate change to the functionality of any existing software system given enough time and energy, but rather that certain approaches to implementation (those which accord greater evolvability) accept these changes more easily than others and that certain forms of code maintenance (those which accord greater evolvability) generate these changes more easily than others.

In this example, the evolvability accorded by an implementation could be measured by the number of lines of code which have to be added or changed in order to produce the desired functionality. An implementation accords evolvability if it is designed in such a way that a minor change in functionality can be achieved with a minor change in its code. An implementation does not accord evolvability if a minor change in functionality can only be achieved through a major re-write of its code. This principle is widely recognised within software engineering where programmers are encouraged to write code in such a way that functionality can be adapted with minimal code change. Mechanisms to achieve this include abstraction, which achieves robustness through functional redundancy; modularisation, which limits the propagation of code changes; and re-use, which removes the need to duplicate changes.

An interesting property of software systems (which is also true of biological systems) is that these architectural mechanisms are recorded within the code of the implementation alongside the code which implements the software's functionality. Consequently, when programmers modify code they are targeting both functional and architectural components of the representation. Therefore, for programmers who maintain software to do so in a way that accords evolvability, they must make appropriate changes to both functional and architectural components of the representation. Again (although to a lesser degree) this principle is recognised within software engineering and programmers are encouraged to modify code in a way that both implements the required changes in functionality *and* preserves, or improves, the evolvability accorded by the implementation. Mechanisms such as code re-factoring exist to help programmers achieve this.

2.1.2 Evolutionary Spaces and Landscapes

When talking about evolution, it is often useful to visualise the evolutionary process as movement within an abstract space of all possible conformations of the evolving entity or its representation. It is also conventional, though not always appropriate, to organise these spaces so that neighbouring points represent entities that differ by an amount equivalent to the change introduced by a single variation event; although since there are often multiple sources of variation, this is usually only meaningful if a separate space is envisaged for each source of variation. Nevertheless, such spaces are useful for measuring the evolvability of an evolutionary system since, by measuring the distance between the locations of different entities, it can be seen how much effort will be required to evolve one entity into another.

Within some evolutionary systems it is convenient to assign values of worth to each possible conformation of an evolving entity. For example, within a software system undergoing evolution, each possible version of the software can be given a value that reflects how likely it is to sell within the software marketplace. For such evolutionary systems it is useful to extend the notion of evolutionary space by giving each point a value which reflects its worth: in effect, adding another dimension. Since points close together within the evolutionary space refer to similar entities with typically similar values of worth, this augmented space tends to have what looks like a continuous hyper-surface in the value dimension with peaks in regions of high value entities and valleys in regions of low value entities. In analogy to this appearance, these spaces are often referred to as *landscapes* [Conrad, 1979, Jones, 1995].

Evolution is often described as a search process. Nevertheless, for most evolutionary systems evolution does not lead to behaviours which would be normally be thought of as search (although you could describe evolution as searching for the natural biases caused by an entity's representation and mechanisms of variation). However, certain evolutionary systems do carry out search behaviours and often this search can be described as directed movement within an evolutionary landscape: moving from a location corresponding to a low valued solution to a location corresponding to a high valued solution.

2.1.3 Neutral Evolution

Sometimes when the representation of an entity experiences variation, the entity itself does not change. This is called *neutral evolution* [Kimura, 1983]. It occurs when there is a one-to-many mapping between entity and representation: such that a single entity can be described by many representations. Neutral evolution is the result of variation switching between members of this set of equivalent representations.

Returning to the real-world example of a software system, a typical neutral evolution event would involve turning a piece of code into a function and replacing its original

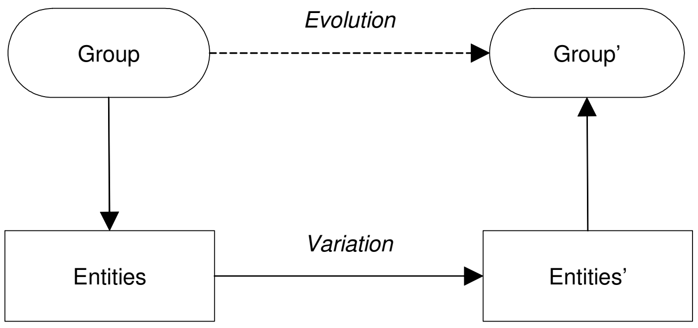


Figure 2.2. Evolution of a group of entities. Groups evolve as processes of variation act upon their entities.

occurrence with a call to this function, a technique called re-factoring. This structural change does not affect the functionality of the software and so, from an external perspective, the change appears neutral. This example also illustrates the potential benefit of neutral evolution. The structural change has not improved the functionality of the software but it has improved the evolvability accorded by the representation — since future code additions will be able to use this re-factored code with a single function call.

A sequence of neutral variation events constitutes a *neutral walk* [Huynen et al., 1996]. Within a directed evolutionary system, appropriate neutral walks can be very useful: taking the representation from a state of poor evolvability to a state of high evolvability, and giving the system access to future evolutionary paths which were not readily accessible using the original representation. Within evolutionary landscapes, areas of neutrality can be seen as plateaus and ravines connecting entities of equal value. Whilst this is a special case of neutrality (since entities of equal value aren't necessarily equal in other respects) it allows visualisation of potential neutral walks within the landscape and, in particular, can indicate which neutral walks lead from low-lying areas (containing solutions of low value) to areas of more mountainous terrain (containing solutions of high value).

2.2 Evolution of Groups

Consider a group of evolving entities. Over the course of time, the entities within the group evolve. This may cause the collective properties of the group to change:

causing, in effect, an evolutionary process at the group level. This process of group evolution, shown in figure 2.2, obeys the same pattern as the evolution of individual entities (shown in figure 2.1) whereby evolution occurs as a consequence of mechanisms of variation acting upon a representation — but in this case, the representation is the entities that comprise the group.

As an example, consider a group of software systems, each of which has limited functionality. Over time, the developers of the software systems will modify their implementations in order to improve their functionality. Consequently, the level of functionality of the group will appear to evolve in a positive direction. If there is a tendency for developers to develop certain kinds of functionality, perhaps in response to market demands, then the type of functionality of the group will appear to evolve in a particular direction. If developers choose their objectives non-deterministically, then the functionality of the group will tend to become increasingly diverse. The evolution of these collective properties is a result of variation acting upon the entities within the group.

2.2.1 Co-operative Evolution

Exchange of information — or more generally, interaction — between members of a group can alter the dynamics of the group-level evolutionary process. This is of particular interest within groups undergoing directed evolution, where the direction (and speed) of evolution is highly dependent upon the nature of interaction between members of the group.

Co-operative evolution occurs when entities within a group share information about how to increase their value. Co-operation works via mechanisms of variation which attempt to identify valuable components of entities and copy these components into other entities. The effect of co-operative evolution is to improve the collective search capacity of the group above that of a group of non-interacting evolving entities. Figure 2.3 shows a simple example of co-operative evolution.

A good example of co-operative evolution is the evolution of ideas [Dawkins, 1976]. Ideas evolve via variation produced by the mechanisms of human thought. These mechanisms include generalisation, taking an existing idea and making it more widely

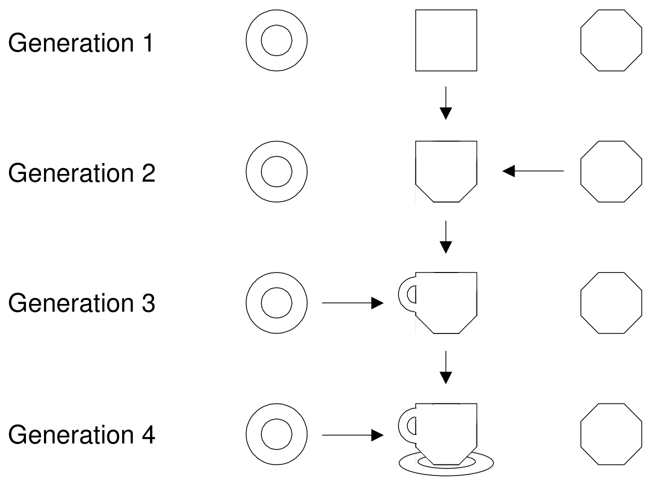


Figure 2.3. Evolving Teacups. Co-operative interactions during evolution.

applicable; and clarification, taking an existing idea and making it easier to understand. However, there are also mechanisms which transfer information between existing ideas — in effect, from one evolutionary system to another. These include composition, joining an existing idea to another one; mimicry, applying the structure of an existing idea to another existing idea; and inspiration, which might involve taking components and structures from multiple existing ideas to form a new idea.

Effective co-operative evolution depends upon a number of factors. One of these is the ability of variation mechanisms to identify which components of which entities are particularly valuable. Another is the ability of an entity's representation to accept components copied from other entities. Again, effective evolution depends upon both the mechanisms of variation's ability to express appropriate change and the ability of an entity's representation to accept appropriate change. For example, the co-operative evolution of a group of software systems depends both upon the programmers' ability to recognise which components of which software systems lead to useful functionality, and the capacity of the software systems' implementations to augment code copied from other software systems without requiring additional re-writing or re-structuring.

2.2.2 Competitive Evolution

The complement of co-operative evolution is competitive evolution. In a group undergoing competitive evolution, entities only remain in the group if they are able to compete effectively against the other entities in the group. As a consequence, the average ability of entities to compete will tend to increase over time as those entities which compete poorly are removed. Competition may occur either as a result of competitive interactions within the group or as a result of some external selective mechanism. In a software marketplace, for example, competition between software systems is determined by customer preferences. Those which are preferred by customers will survive and continue to be evolved; those which are not preferred by customers may be discontinued and removed from the marketplace. Accordingly, the average quality of software systems will tend to increase over time.

2.3 Summary

Evolution is a process which leads to change within an entity or group of entities over a period of time. Evolution results from some process or processes of variation acting upon the representation of an entity or group of entities. Importantly, an entity can undergo a certain evolutionary change if and only if this change is possible as a result of processes of change acting upon the entity's representation. Evolvability is the capacity for an evolutionary system to evolve in a particular direction; and is determined by the nature of the entity, by the flexibility of the entity's representation, and by the ability of the variation operators to induce appropriate change. Directed evolution, which can lead to evolution carrying out a process of search, can be encouraged within groups of entities through both co-operative and competitive mechanisms.

2.4 Perspectives

The interest of the scientific and engineering communities in developing a unified view of evolution is a recent phenomenon [Nehaniv, 2003]. Nevertheless, there is considerable commonality between the evolutionary processes which occur in different kinds of system: and a growing view that lessons learnt from one evolutionary domain can be applied within other evolutionary domains. The issue of evolvability is particularly relevant; since an understanding of evolvability is essential in understanding how best to design and represent artefacts — such as software systems and engineered products — which are subject to a process of change over time. Evolvability is also of paramount importance within evolutionary computation systems. In the past, the choices of representation within evolutionary computation have been somewhat arbitrary from an evolvability perspective. Typically an evolutionary computation practitioner will use the form of representation which is most natural or most common for a given entity; without thinking about whether or not it is evolvable. In part this is due to a lack of understanding regarding what is and what is not evolvable. This thesis presents a biologically motivated approach to the development of an evolvable representation for evolutionary computation: an approach motivated by the relatively large amount of information concerning evolvability which may be mined from biological systems. However, this is not the only approach, and it is conceivable that other, perhaps equally fruitful approaches, could be developed by looking at how evolution occurs in a much broader range of both natural and artificial systems.

3 Biological Representation

The functioning of biological systems can be described at many levels from the interactions between individual biochemicals up through interactions at increasingly higher levels of organisation: biochemical pathways, organelles, cells, tissues, organs, organisms, populations, species, communities and ecosystems; and interactions with the abiotic environment including, for some species, cultural artefacts.

This chapter aims to show how functionality is represented at a low level within biological systems. It is divided into two sections. The first section describes the low-level components from which biological systems are constructed. The second section describes the processes by which these components are constructed and replicated. Unless otherwise indicated, this material can be found in biological textbooks such as Lodish et al. [2003], Brown and Brown [2002], and Lewin [2000].

3.1 Biological Components

3.1.1 Proteins and Enzymes

Proteins are the main functional element of the body and play a role within almost every biological process. Specified by a sequence of amino acids, each species of protein has a unique three dimensional structure. It is this structure which determines the protein's effect upon other biological elements and, accordingly, its function within the biological system.

Amino acids are a group of molecules unified by a common structure. Of the many possible amino acids, only twenty varieties are normally found in biological systems.

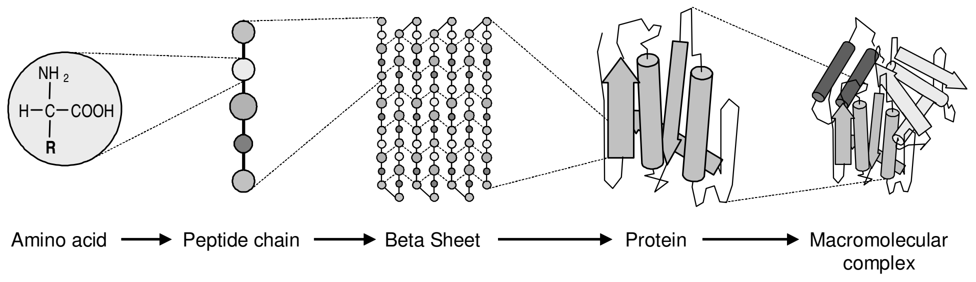


Figure 3.1. Hierarchical levels of protein structure. From left to right: amino acid, primary, secondary, tertiary, and quaternary structures.

Each of these is distinguished by a characteristic chemical residue called the side chain which through variance in size, shape, charge, reactivity and hydrophobicity, gives each amino acid a particular chemical signature. A protein is a complex of one or more *polypeptides* — sequences of amino acids linked together by peptide bonds — arranged in a three-dimensional structure. This structure, termed the *native state*, is an attribute solely decided by the nature of the polypeptide sequences and hence, to a great extent, the chemical behaviour of each amino acid[1].

A protein's structure is specified by four hierarchical levels: the primary, secondary, tertiary and quaternary structures (see figure 3.1). Primary structure is the linear amino acid sequence(s). Secondary structure describes local organisation within the polypeptide chain caused by attractions and repulsions between chemicals in different amino acids. There are a number of basic components which may form within the chain. The term *random coil* refers to those parts of the chain where no specific pattern of structure emerges. *α-helices* and *β-strands* are the most common structural components within a protein. An α-helix is the result of hydrogen bonding between oxygen and hydrogen atoms along the polypeptide backbone, causing the local chain to form a stable helix. This α-helix acts like a sturdy and inflexible rod, making it a good structural member for mechanical action. Where α-helices have one side hydrophilic (soluble in water) and the other hydrophobic (insoluble in water), a state termed *amphipathic*, they may combine with other α-helices to form a higher-dimensional, tougher helix. β-strands are sections of polypeptide which do not coil, but remain straight and non-helical. Though fairly weak by themselves, they hydrogen bond with other

[1]Other factors deciding the final shape include the nature of the peptide bonds — which behave like inflexible double bonds due to resonance from the nearby C=O bond — and the possible presence of prosthetic groups (see later).

β-strands (running parallel or anti-parallel) to form β-sheets. The presence of amino acid residues on both sides of the sheet can allow for interesting behaviours to emerge — for instance if those on one side are hydrophilic and the other side hydrophobic. Tougher structures result when sheets form stacks.

Turns, composed of three or four amino acids, are sharp bends in the chain resulting from hydrogen bonding between the residues at either end of the sequence. *Motifs* are distinctive combinations of secondary structures, with characteristic function and primary structure. An example is the zinc finger, a motif consisting of one α-helix and two β-strands. These form a cage around a single zinc atom; the assembled motif resembling, and offering similar function to, a finger. The zinc atom involved in this motif is an example of a *prosthetic group* — a tightly bound non-peptide molecule or metal which provides structural support, a binding site, or some other function to the protein.

Tertiary structure defines the folded form of the protein when introduced to an aqueous environment — where hydrophobic interactions pull the secondary structure into a more compact form. Typically, the protein will configure itself into a number of distinct regions, called *structural domains*, which encompass a section of the polypeptide chain containing numerous secondary structures. A cluster of structural domains which together provide a localised function within the protein are deemed a *functional domain*. Functional domains which recur in many proteins (and therefore exist as building blocks) are known as *tertiary domains*.

Where a protein consists of more than one polypeptide, a final layer of structure — quaternary structure — describes the positioning of polypeptide subunits. In certain circumstances, multiple proteins may form an aggregate structure. These are called *macromolecular assemblies*.

Enzymes

Enzymes are proteins which act to catalyse other chemical reactions. For a chemical reaction to take place, an activation energy must be met. Usually, this is provided by the kinetic energy of the reactants. However, for many reactions, the kinetic energy required is substantial and is only available at hot temperatures. In biological

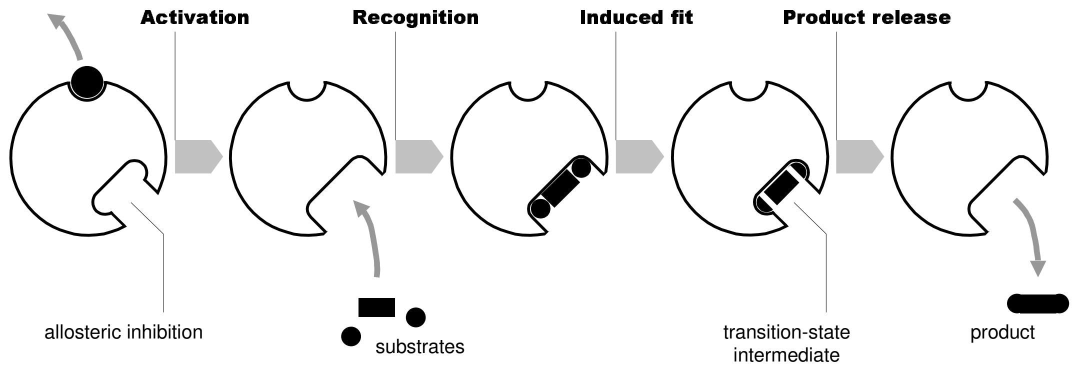


Figure 3.2. Enzyme activity

systems, ambient temperature is relatively low, making most reactions energetically unfavourable. To make these reactions possible, either the activation energy must be met — not usually possible — or it must be lowered. This is the function of enzymes (see figure 3.2). Enzymes possess *specificity*, an ability to recognise[2] only certain chemicals and bind exclusively to these. The chemicals recognised, the *substrates*, are the reactants needed for the reaction. By bringing these together, the kinetic energy required for the reaction to occur is reduced, and hence the activation energy of the reaction is lowered.

Most important reactions do not take place immediately. Rather, the reaction progresses through a number of transition states. During this process, the substrates are converted through a series of transition-state intermediates until, after the final transition stage, they become the reaction's final products. For an enzyme to effectively catalyse a reaction, it must not only bind to substrates, but also to transition-state intermediates.

Binding of substrates occurs at active sites on the enzyme. Active sites are produced by a precise arrangement of amino acid residues which, when in contact, bond non-covalently with complementary sites on the substrate's surface. This is called the *lock-and-key* mechanism. Recognition of a substrate may also cause structural change in the enzyme, *induced fit*, which brings the substrate into closer contact with the active site. Non-covalent bonding holds the substrate in place. However, the enzyme may also form covalent bonds with a substrate. It is these bonds which change the nature

[2]Recognition here, and elsewhere in molecular systems, refers to a stable non-covalent bonding between large macromolecules — a result of diffusion rather than active convergence.

of the substrate, converting it into a transition-state intermediate. Subsequent changes in the substrate occur either by contact with other reactants, or by further enzymatic action (making and breaking of covalent bonds). In order for the correct bonds to be made, amino acid residues alone may be insufficient. In these circumstances, prosthetic groups may be used. Prosthetic groups used in this way are called *co-enzymes*.

Since chemical reactions require energy and resources, for purposes of efficiency it is desirable that reactions only take place as and when they are required. Consequently, the function of enzymes are regulated so that reactions are only catalysed when the current chemical conditions make them useful. This is achieved through effector-binding sites which, when bound, either inhibit or activate the enzyme. The molecules which bind to these sites are called *effectors*. In the case where the (inhibiting) effector is the product of the reaction which the enzyme catalyses, this is called *feedback inhibition*. Moreover, in real biological systems, products of reactions often become reactants of other reactions. In these cases, the product of the final reaction may be the effector of the enzyme involved in the first reaction. Hence, this enzyme will only become functional when the end product is in short supply and, in effect, the entire pipeline will be disabled at other times (since the first reaction produces the reactants for the second, and so on). Inhibition and activation occur through conformational change induced by bonding at the effector site. This change of shape for purposes of regulation is called *allostery*.

3.1.2 Nucleic Acids

While proteins provide the functional elements of a biological system, it is nucleic acids which specify and aid construction of these units. These roles are provided, respectively, by *deoxyribonucleic acid* (DNA) and *ribonucleic acid* (RNA), both of which are polyesters composed of nucleotides. *Nucleotides*, like amino acids, are small molecules with common structure, differentiated between by side groups. These side groups are called *bases*, and are of two types — *purines* and *pyramidines*. Purines are substantially larger than pyramidines. The purines found in biological systems are Adenine and Guanine, each identified by their initial letters, A and G. The pyramidines are Cytosine (C), Thymine (T) and Uracil (U). Nucleotides with Thymine bases are only found in DNA and those with Uracil are found only in RNA. Nucleotides are formed when

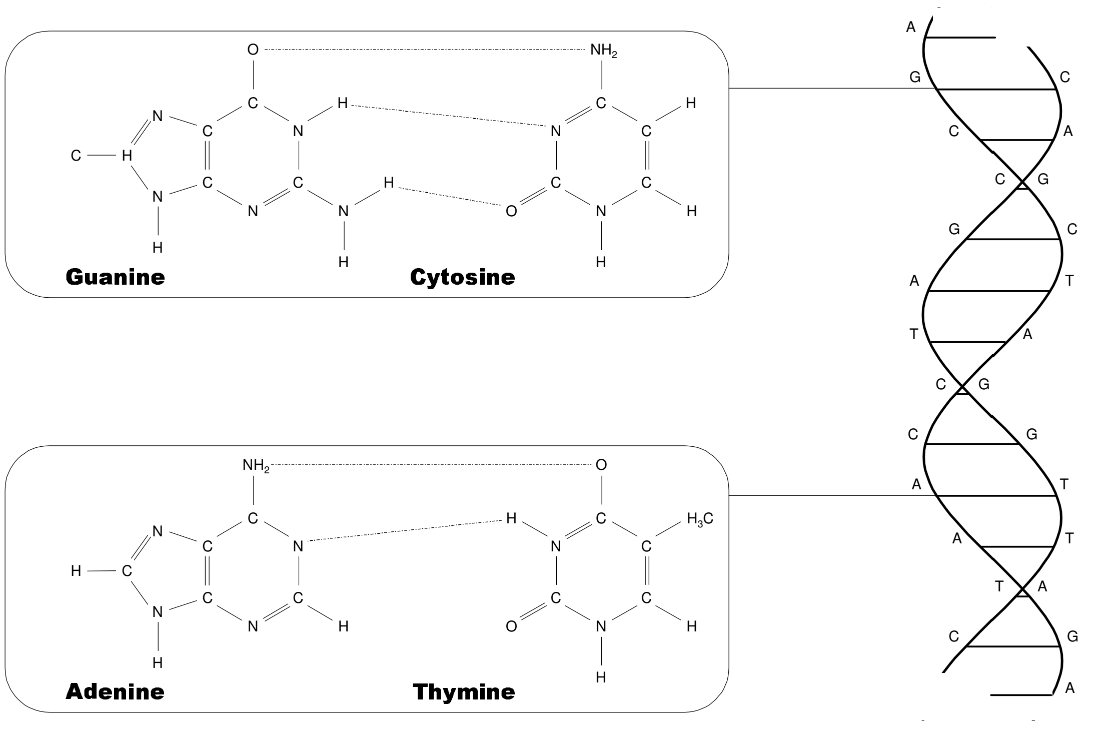


Figure 3.3. Nucleotides of DNA

nucleosides, consisting of a sugar and a base and found free-floating in cellular fluids, are joined together by phosphate bonds. A nucleotide is then the aggregate of a sugar, a base and one phosphate bond. The two ends of the unit are called 5′ and 3′. A 5′ is always connected to a 3′, and hence the entire nucleic acid has chemical polarity, running from a 5′-end at the beginning to a 3′-end at the finish.

DNA is formed from two anti-parallel polynucleotide strands, fused together by various non-covalent bonding actions. Most important of these is hydrogen bonding between bases in the two strands, forcing the amalgam into a double-helical arrangement (see figure 3.3). The linking of two bases — a purine in one strand with a pyramidine in the other — is called *base-pairing*. Base pairs in DNA are almost always either AT (Adenine bonded with Thymine) or GC (Guanine and Cytosine). The natural form of DNA is called B-DNA. In addition to hydrogen bonding between base pairs, the structure is stabilised by hydrophobic interaction and Van der Waals bonding[3] between helical sections, or *turns*. The helix makes a complete turn every ten base pairs, which is about 3.5nm. However, A-form DNA — which only remains sta-

[3]A week form of non-covalent bonding whose net effect can be quite appreciable between large complementary-shaped molecules.

ble in non-aqueous environments — turns every eleven base pairs. This is a more compact form of DNA, with a turn of about 2.3nm, but only occurs when DNA is removed from solution. Both A- and B-DNA are right-handed varieties. A further form, Z-DNA, is left-handed, but has never been observed in natural biological systems. DNA in eukaryotes, such as animals and plants, is found in linear form. However, in prokaryotes and viruses DNA is circular, with the 5′-end attached to the 3′-end. Sometimes sections of circular DNA may become underwound. This state is energetically unfavourable, and so the entire strand is pulled towards a more favourable state — either by reducing the overall twist or by forming *supercoils* (where the degree of supercoiling is measured as *writhe*).

DNA is an information store, a purpose to which it is well-suited due to its relative long-life and stability. RNA sacrifices long-life for lability; a fact reflected in its multitude of uses within biological systems. It can occur in single-stranded and double-stranded varieties, linear or circular, can hybridise with DNA, and can combine with proteins to form ribonucleoprotein complexes. Like proteins, RNA can form three-dimensional structures: allowing expression of catalytic and auto-catalytic behaviours (for instance, breaking and splicing other RNA molecules). These structures are described by three levels of organisation. Primary structure describes the base sequence, secondary specifies two-dimensional structure such as loops and hairpins, and tertiary describes interacting two-dimensional features which form three-dimensional structures such as *pseudoknots*.

The purpose of DNA in biological systems is to store a description of the organism in which the DNA is found. This information, called the *genome*, is expressed by a language written in the *genetic code* — the alphabet of bases found in DNA — namely, A, C, G and T. However, this information is not a blueprint, but rather a highly decentralised developmental plan which describes, by specifying systems of proteins, how the organism will function at a local level. The overall nature of the organism is then emergent from the sum of these local functions.

3.1.3 Genes

According to Mendel [1965], the founder of genetic science, a gene is a unit of inheritance, a 'particulate factor that passes unchanged from parent to progeny'. From a functional viewpoint, a gene is a stretch of polypeptide chain encoding one protein, or more exactly, a fragment of DNA which can be transcribed by messenger RNA.

Although the language and chemical structure of prokaryotic and eukaryotic DNAs are virtually the same, there are two major differences in genetic structure. The first of these concerns the unit of transcription. In prokaryotes, it is normal for several genes to be encompassed by the same transcription unit. This means that a single mRNA can encode several different proteins, each of which can be synthesised independently by a ribosome. In eukaryotes, by contrast, ribosomes may only begin synthesis at the beginning of an mRNA strand, entailing that eukaryotic mRNA may only transcribe from a single gene. This is called *monocistronic* RNA. Prokaryotic mRNA is *polycistronic*. The cluster of genes from which this is transcribed is an *operon* — with transcription starting from a short stretch of DNA called a *promoter*. If this promoter is mutated, then all the genes in the operon may become non-functional, a fact which makes prokaryotic DNA less fault-tolerant than its eukaryotic cousin. However, this approach is slightly more efficient than having many separate transcription and synthesis events — and efficiency is very important to a prokaryote, where evolutionary pressure selects against any waste of energy. Moreover, low-level efficiency is relatively unimportant to a eukaryotic organism, for which behavioural effectiveness is the dominant evolutionary selector. This, too, explains the second major difference between prokaryotic and eukaryotic DNA. Prokaryotic DNA is tightly packed, with almost all the polypeptide used to encode functional genes. By comparison, eukaryotic DNA consists mostly of non-coding DNA, the relative quantity of which varies widely between species and does not correlate with the size or complexity of the organism. Eukaryotic genes consist of *exons*, coding segments, and *introns*, non-coding segments. During transcription, both coding and non-coding parts are copied to mRNA. Before protein synthesis, mRNA excises its non-coding introns to form a continuous stretch of coding RNA.

Solitary genes are genes which occur only once in the genome, accounting for between twenty-five and fifty percent of all genes. A *gene family* is a set of nearby[4] genes which encode similar, but not identical, amino acid sequences (a protein family). Polypeptide sequences which are similar to genes but are non-functional are called *pseudo-*

[4]This proximity suggests that similar genes may be a result of unequal crossover — crossover between chromosomes which are not properly aligned.

genes. Quite often, sequences of bases occur over and over again in a repeated array. Depending on whether the sequence is a gene or is non-coding, these are called either *tandemly repeated genes* or *repetitious DNA fragments*. Tandemly repeated genes encode proteins for which demand is greater than that which can possibly be transcribed from a single gene in a given time period. To meet demand, transcription of many identical genes occurs in parallel.

More generally, there are three classes of eukaryotic DNA. These are identified, and named, according to how fast they re-associate after their strands have been separated. Where there are tandem arrays of short sequences (5–10 base pairs), sections of one strand can bond to many sections on the other, pulling the strands together very quickly. Such DNA is called *rapid reassociation rate*, or *simple sequence*, DNA. Due to the way it forms bands around other DNA when centrifuged, it is also known as *satellite* DNA. Regions of fewer repeats are *minisatellites*, with small differences in the length of minisatellites between members of the same species providing the basis for genetic fingerprinting. A single variety of simple sequence DNA can occupy up to one percent of the genome in total, and is often found in specific areas of the chromosome.

Intermediate reassociation rate, or *intermediate repeat*, DNA represents many occurrences of larger base sequences. Compared to simple sequence DNA, there are relatively few varieties of these, although each variety occurs in large numbers. Repeating sequences of between 150 and 300 base pairs are classed as short interspersed elements, *SINES*, whereas those of 5000 to 7000 base pairs are *LINES*, long interspersed elements. Intermediate repeat DNA is either found in large tandem arrays (e.g. functional gene tandem arrays) or scattered randomly around the genome. This latter class includes mobile DNA elements — DNA sequences that are able to move or copy themselves to other regions of DNA. These sequences, which have no real purpose other than self-replication[5], occupy about thirty percent of the human genome. Slow reassociation rate DNA, or single copy DNA, occupies between fifty and sixty percent of the genome. Of this, only five percent encodes genes — the rest being spacer DNA with mostly no known function.

Although seen as a molecular parasite, using the organism's transcription facility without giving anything in return, mobile DNA is thought to have evolutionary sig-

[5]Which gives mobile DNA the alternative name of selfish DNA. This should not be confused with Dawkins' [1976] idea of the selfish gene, which is unrelated.

nificance. On the whole, transposition of mobile DNA is balanced by mutation, which destroys existing copies with no disadvantage to the organism. However, it does lead to variance in the lengths of chromosomes — meaning that it is possible that two chromosomes of unequal length will be crossed over. The result of this is *unequal crossover*, which can lead to duplication and mutation of existing genes. Mobile DNA can also carry with it parts of genes it has overwritten. If these parts are then copied into other genes when the mobile DNA moves, *exon shuffling* takes place — the creation of novel genes from combinations of pre-existing exons [Gilbert, 1978].

There are two broad classes of mobile DNA, categorised by their transposition mechanism. *Transposons* remain as DNA throughout the move. They are either excised or copied from their original location and then inserted at their new location. *Retrotransposons* transpose via an RNA intermediate, and hence are always copied rather than moved. RNA polymerase encodes the retrotransposon as RNA. An enzyme called reverse transcripterase then copies this to a new segment of DNA which is then inserted into the chromosome. Retrotransposons are either viral or non-viral, with viral retrotransposons encoding a viral shell which, when synthesised, allows the retrotransposon to leave the cell and infect other cells and organisms. Non-viral retrotransposons are either LINES or SINES. LINES encode reverse transcripterase. SINES, however, use the reverse transcripterase synthesised by LINES, meaning they can be much shorter (in effect, they are hyperparasites).

Prokaryotes also contain selfish DNA. In bacteria, insertion sequences (IS elements) are 1.5kb segments of single-strand DNA which invade normal double stranded DNA (*homoduplex*), forming a *heteroduplex* with one strand containing the extra IS element. Insertion sequences include instructions for synthesising transposase, which allows the IS element to move within the bacterial DNA. However, since bacterial DNA is tightly packed, these moves are likely to generate fatal mutations. For this reason, surviving IS elements transpose very rarely.

The introduction of new, useful, genes as well as occasional beneficial effects of mutation and exon shuffling are rare chance events. The role of mobile DNA is, on the whole, non-functional. By contrast, local cellular processes sometimes carry out rearrangements of DNA with a specific functional intent. These include *inversion* of DNA sequences, gene conversion, amplification and segment deletion. The role of inversion is varied, and depends upon the organism. For instance, in the bacterium salmonella, it is used to alter the expression of certain surface proteins. Once the host organism has produced antibodies for the primary infection, bacteria which experience this inversion will not be recognised, producing a secondary infection for the body to combat. *Gene conversion* results in a component of an active gene being updated with an inactive part from elsewhere in the chromosome, changing the protein produced by the gene. The uses of this mechanism, again, are varied. *Gene amplification*, also called *polytenation*, causes parts of chromosomes to be replicated. The replicants are either than released, or remain connected. This is the mechanism used to produce lots of copies of the rRNA gene. It is a dynamic alternative to tandem arrays. Finally, *segment deletion* is involved in the separation and rearrangment of segments of DNA, allowing many forms to be generated from a set of DNA segments (e.g. antibodies).

3.1.4 Chromosomes

In many organisms, genomic DNA is arranged into chromosomes. Dividing the genome into storage units in this manner makes the large amount of data easier to store and handle. However, the genome is very large. In its natural form, even split into sub-units, the DNA is far too voluminous to fit into a single cell, let alone a nucleus. In prokaryotes, which have relatively small genomes, the natural random coil formed by the single circular chromosome would be one thousand times larger than a bacterial cell. Much of this expanse is due to electric charge repulsion between the negatively charged phosphate groups in the DNA backbone. The prokaryotic solution to this problem is to introduce positively charged polyamine groups, which associate with the phosphate groups to shield the charges. Additionally, numerous small proteins bind to the DNA, folding it into a more compact structure, and finally, special enzymes induce supercoiling.

The eukaryotic solution to the compaction problem is called *chromatin*, a complex of DNA and structural proteins. These proteins, H1, H2A, H2B, H3 and H4 are all members of the *histone* family and retain a high degree of similarity between species. Two each of H2A, H2B, H3 and H4 form a histone octomer, a roughly cylindrical shaped object that acts like a reel around which DNA can be wound. A *nucleosome* is a histone octomer with slighty less than two windings of DNA (146 bases). This is the primary structural unit of chromatin. Further organisation produces a solenoid form, *euchromatin*, with six nucleosomes per turn. This structure is stabilised by an association of histone H1 with each nucleosome — forming chromatosomes. During interphase (the period between cell divisions), euchromatin is the normal level of chromosome structure, the non-condensed form of chromatin. During metaphase (cell division), when chromosomes become visible to the light microscope, the chromosome experiences several degrees of supercoiling, forming a compact structure called *heterochromatin*, the condensed form. This is supported by an internal scaffold[6] of non-histone proteins. The number, size and shape of heterochromatin complexes during metaphase is an organism's *karyotype*. During interphase, some sections of the chromosome remain as heterochromatin, occuring in regions where no transcription takes place. When interphase chromosomes are stained by certain dyes, these regions of heterochromatin form dark bands. Staining of metaphase chromosomes also produces characteristic bands. However, the cause of this banding is unknown, yet provides a useful roadmap within the organism's karyotype.

Most sequences of bases in DNA are either protein encoding genes or non-coding redundant regions. However, other sequences are designed with a functional role. These have arrangements of bases which are recognised by various types of binding proteins, such as transcription sites. Three such regions are of particular importance for chromosome duplication and segregation — autonomously replicating sequences (ARSs), the centromere and the telomeres. ARSs are origins of replication. These are bound to by special proteins which start the replication process. Centromeres have binding sequences for proteins which hold and follow the microtubule spindle. Telomeres[7] protect the ends of chromosomes, and are placed after replication. They also provide a binding point outside of the main chromosome where replication of the chromosome ends can occur from. Otherwise, it would not be possible to replicate the last few bases of a linear chromosome, creating shorter chromosomes each generation.

[6]During interphase, chromosomes remain associated with this scaffold. Binding sites between the chromosome and scaffold are called scaffold-associated regions (SAR's), occuring between transcription regions. During transcription, the solenoid in the transcription region unwinds to allow access by transcription proteins.

[7]Telomeres consist entirely of guanine bases, forming a loop at the end of the chromosome. The sides of the loop are bound together by non Watson-Crick G-G bonds.

3.1.5 Cells

Cells are the fundamental unit of most biological systems (or *the* unit, in the case of some). It is local processing done by cells which, when combined with communication between cells, lead to the emergent behaviour of a single organism. This local processing, called the *metabolism*, is in turn the sum of all chemical processes which occur within the cell.

Within the biological community, the prevailing view is of a single heritage to all cells. However, from the current standpoint in evolution, cells can be seen as falling into two broad categories — *prokaryotic* and *eukaryotic*. Organisms which consist of these types of cell are called, respectively, prokaryotes and eukaryotes. Prokaryotes encompass the most primitive organisms on Earth, the bacteria. This cell lineage can be further divided into eubacteria and archaebacteria, the latter of which is considered by some as a separate lineage to the prokaryotes. Eubacteria are common, and consequently well studied. Archaebacteria live in unusual environments such as swamps and sulphur springs, and at the cellular level have many features in common with eukaryotes. Eukaryotes include animals, plants and fungi.

Both prokaryotic and euakaryotic cells are contained within a *plasma membrane*. The plasma membrane is a semi-permeable layer which maintains the integrity of its contents by controlling inward and outward movement of chemicals. Prokaryotic cells are fairly unstructured. Eukaryotic cells, however, contain extensive internal membranes which organise the cell into compartments of local metabolic processing, *organelles*. The largest of these, and the structure which gives the eukaryotic cell its name, is the *nucleus*, the location of the cell's DNA. However, exactly which organelles are found in a cell depends upon the cell's type — which is likely to be decided by the surrounding tissue. In fact, not all eukaryotic cells have a nucleus. The red blood cell, for example, has, and needs, very little by way of internal structure since it does not divide and does not communicate with other cells. Most animal cells, however, contain at least a nucleus; mitochondria, to provide energy; centrioles, which are used in cell division; and lysosomes, which handle recycling. Plant cells have similar components, but use chloroplasts rather than mitochondria to provide energy, and often contain vacuoles for storage of nutrients and fluids. The region of the cell outside the organelles is termed the *cytosol*, where much of the cellular metabolism takes place. Until fairly recently, this space was assumed to be fairly unstructured. However, higher resolution microscopes have shown the cytosol to contain a filamentous *cytoskeleton* which defines a grid-like structure within the cell and holds the organelles in place. It is theorised that the proteins and enzymes within the cytosol are also well organised spatially, possibly by binding to particular fibres in the cytoskeleton.

Most important cellular functions are anabolic, requiring complex molecules to be assembled from simpler ones — and since these reactions are energetically unfavourable, energy must be provided for them to occur. For most reactions, this is provided by a chemical called *adenosine 5′-triphosphate* (ATP) which, when catabolised, releases energy which may then be used in a nearby anabolic reaction. Cells do not have direct access to ATP from their environment, but must rely on some other form of energy as a source. For example, animals obtain energy from food in the form of sugars which are eventually converted to glucose and distributed to all cells of the body via the blood stream. Plants, on the other hand, rely upon light energy. The conversion of these energy sources into ATP is handled by organelles within the cell. In animal cells, this function is provided by *mitochondria*, large organelles covering up to a third of the cellular space in total. Mitochondria have their own DNA[8], used to synthesise proteins (ATP synthase) which convert large glucose molecules into many small, easy to use, ATP molecules. This occurs on the surface of a large folded inner membrane. Plants have similar organelles called *chloroplasts*. These contain DNA used to synthesise pigment (chlorophyl) and enzymes which, together, convert light into ATP.

3.2 Biological Processes

3.2.1 DNA Replication

The process of DNA replication is said to be *semiconservative*. From two existing complementary strands, two new strands are synthesised (see figure 3.4). This produces two daughter molecules, each consisting of one old strand and one new. Synthesis of a new strand starts at a replication origin, of which there may be many, somewhere

[8]This DNA is passed, through mitochondria in the female egg cell, from a mother to her offspring. It is unrelated to nuclear DNA and, since since sperm do not contain mitochondria, does not recombine with male mitochondrial DNA. Mitochondria are thought to be prokaryotes that formed a symbiotic relationship with the eukaryotic cell. (This also applies to chloroplasts).

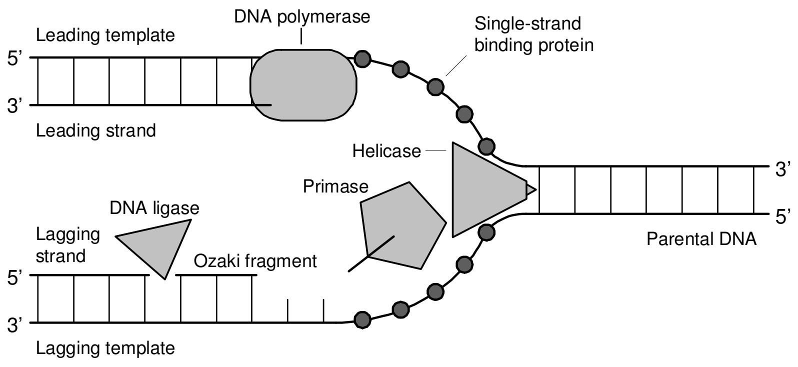


Figure 3.4. DNA Replication

within the existing strand. From this point, the replication process may be either omnidirectional (moving one way along the strand, but not the other) or bidirectional. The former occurs in some bacteria, a circular genome meaning that replication will eventually reach the other end even if only one replication origin is involved. Bidirectional replication is normal for eukaryotes with linear genomes. At the start of replication, the two existing strands are still connected together, with disconnection occurring incrementally at the same time as replication. This means that synthesis of both strands can take place at the same place at the same time, producing something that looks like a bubble. In some viruses this is not the case, and synthesis of the two strands begins in different places.

The region of DNA served by a single replication origin is a *replicon*. The current point where the strands are separated up to, and new DNA is being synthesised, is called a growing fork. For bidirectional replication, there are two of these. The region between the forks, or between the fork and the origin, is called a *replication bubble*. In humans, replication forks move at about one hundred base pairs per second. The entire genome is about 3x10^9 base pairs, divided into between 10,000 and 100,000 replicons. Replication of the entire genome takes about eight hours, with redundancy in the number of replication origins meaning replicons need not be active throughout this entire period.

A growing fork moves in one direction along the existing DNA. However, DNA can only be grown in one direction, from the 3′-end to the 5′-end. Since the strands in DNA are anti-parallel, and both strands will be copied at the growing fork, only one of the new strands (the leading strand) can be grown throughout from 3′ to 5′. The strategy used for the other new strand (the lagging strand) is to grow small fragments of DNA as groups of bases become available. These *Ozaki fragments* are then joined together to form a complete strand.

Replication origins (ARSs) consist of tandemly repeated short sequences which are recognised by multimeric origin-binding proteins. These proteins bootstrap the replication process by assembling the replication enzymes at the right locations. The first of these enzymes detaches the two strands at the replication point, forming a small gap called an open complex. *Helicase* then binds to this open complex, taking on the role of strand separator at the leading edge of the growing fork. As the strands are separated, small molecules — *single-strand binding proteins* (SSBs) — bind to the exposed strands, preventing the DNA from re-annealing. *Primase*, working to the rear of helicase (and forming a macromolecular complex called a *primosome*), is responsible for creating new RNA primers as necessary (only once on the leading strand, and many times on the lagging strand). DNA *polymerase* III uses these RNA primers, growing new complementary DNA bases according to the exposed strands, whilst removing SSBs. DNA polymerase I removes the RNA primers from DNA strands and DNA ligase joins DNA fragments together. In prokaryotes, DNA is particularly amenable to supercoiling, making it difficult to separate and process individual strands. The solution to this is an enzyme called *topoisomerase*, which removes supercoils at the growing fork and re-establishes them later.

During synthesis, it is possible that errors may occur. To combat this, DNA polymerase offers a proofreading capability which inspects the newly synthesised strand as it forms. If an error is found, the incorrect section of the new strand is removed and the synthesis action of polymerase is reactivated to update the strand with the correct information. More generally, environmental influences may cause errors to occur in DNA at any point of its lifetime. The damage caused may be missing, altered or invalid bases, bulges, bonding between side chains, strand breakage, strand cross-linking or fragmentation. The damage is either repaired directly, or more commonly, an excision-repair mechanism removes the damaged section and updates it using DNA polymerase. Some researchers also hypothesise that DNA sequences contain error correcting codes which minimise the impact of the errors that are not repaired by the excision-repair mechanism [Battail, 2003].

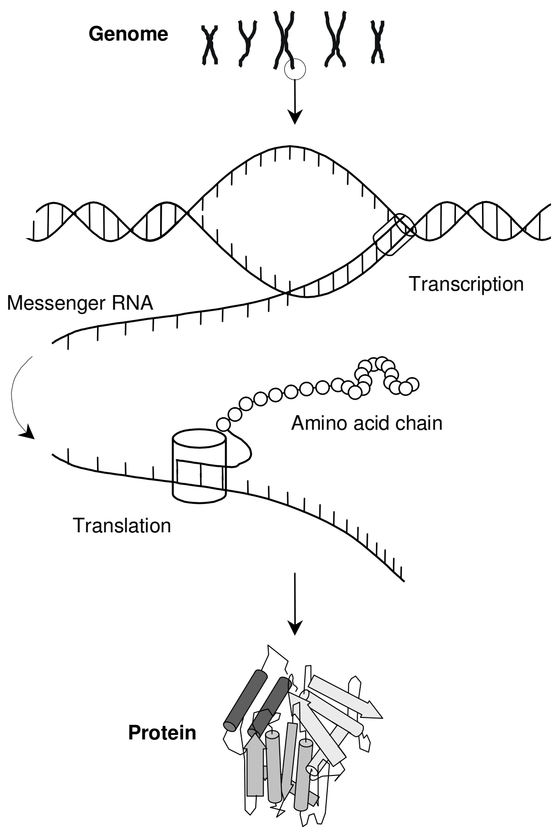


Figure 3.5. Protein synthesis through transcription and translation

3.2.2 Transcription

Transcription is the synthesis of a messenger RNA strand from a DNA template. Transcription is similar to DNA replication in that RNA polymerase recognises start sequences in the genetic code, binds and reads DNA, and constructs complementary RNA sequences. The process is similar in both prokaryotes and eukaryotes, although substantially more complicated in the latter.

Prokaryotic genes occur in conserved structures known as *operons*, genetic units that tie groups of genes into a single transcription event. An operon is a tightly packed polypeptide sequence consisting of a control region followed by a group of genes. The control region consists of a *promoter*, where RNA polymerase first binds, and an *operator*, which enables or disables transcription of the operon. Promoter sequences contain distinctive base-sequence patterns which are recognised by initiation units within RNA polymerases. There are a number of different types of RNA polymerase, and each binds to a particular pattern. The strength with which an RNA polymerase binds, and therefore the frequency at which an operon is transcribed, depends upon how accurately a promoter implements this pattern. Hence, genes which should be transcribed often have very accurate, or strong, promoters whereas those which are seldom transcribed have only a passing resemblance to the ideal pattern. For most operons, the important promoter sequences lie around ten and thirty-five bases downstream of the genes. The parts of the RNA polymerase that bind to these regions are collectively called the *initiation factor*, or σ. The complex of subunits that continue transcription after binding form the *core polymerase*. Together, the intitiation factor and the core polymerase form a *holoenzyme*, a complete and functional molecule.

Operon expression is controlled by molecules (usually enzymes) called regulators that, through binding to control locations, turn transcription on or off. Positive regulators are called activators. By binding to both promoter sequences and RNA polymerase, these strengthen the hold between the two, making transcription more likely. Hence, activators make a promoter stronger. Repressors, negative regulators, do not effect the promoter but rather bind to the operator region, blocking RNA polymerase and preventing transcription. Operators typically consist of an inverted repeat sequence (a sequence followed by its repeat in reverse), each repeat forming a half-site. Repressors are dimeric, consisting of two units, each unit binding non-covalently to a different half-site — the bond made stable by α-helices which the repressor inserts into major grooves of the DNA helix. A set of operons controlled by the same regulator is called a regulon. Each member of the regulon may have a different affinity for the regulator, in the same way that different promoters have differing affinities for a certain RNA polymerase. Certain molecules, by binding to recognition sites on the repressor, may cause the positions of its binding α-helices to change, deactivating the repressor. This allows repression to be enabled or disabled according to the chemical environment. Hence, gene expression is dynamic, changing according to the products of other genes and the current needs of the molecular system.

Not all prokaryotic genes follow the schemes outlined above. In particular, some genes are transcribed by non-standard RNA polymerases with altered σ-factors. These bind at many different sites, some within the normal promoter region and others in more distant places. Also, some RNA polymerases cannot use ATP directly, requiring the help of protein intermediaries. These intermediaries also bind to the DNA, often quite a distance from the operon being transcribed. Although the exception for prokaryotes, where much gene regulation is simply metabolic response to the presence of nutrients, these more complicated systems are the norm for eukaryotes. Here, complexity reflects the fact that genes, cells, tissues and organs all have highly-linked actions and responses, meaning that the influences on gene expression may be far from simple.

In eukaryotes, genes are transcribed on an individual basis rather than arranged into operons. RNA polymerase II is responsible for the transcription of protein-encoding genes, whereas polymerases I and III operate solely upon RNA-template genes. Eurakyotic RNA polymerases do not contain an initiation factor or carry out ATP-hydrolysis, relying upon DNA-binding proteins to provide these facilities. This results in a very flexible process, with some initiation complexes consisting of many large protein complexes. These factors bind to DNA promoters at various locations, and through sequential interactions, guide the activity of the RNA polymerase. Eukaryotic promoters are of several types. The strongest are *TATA-boxes* and *initiators*, similar in structure to prokaryotic promoters. An interesting exception is the *CpG* (where 'p' denotes the phosphate bond) *island*, a CG repeating sequence which occurs just upstream of the first exon. The sequence CG is statistically under-represented in the eukaryotic genome, and hence stretches are easily recognised as promoters and unlikely to be confused with other genetic information[9].

Promoter sites are found anywhere between tens and tens of thousands of base pairs away from exon sites. Promoter sites at a distance of less than two hundred base pairs are called *promoter-proximal elements*, and those at a greater distance, *enhancers*. Enhancers can occur upstream of exons, within introns, or even downstream of the entire gene. Typically, multiple activator proteins will bind to a single enhancer site, sometimes forming heterodimer complexes with members of the same class. Activators are often modular, with distinctive (even separable) DNA-binding and activation domains. Repressors are less-well understood than activators, yet appear to have a similar structure and capability to regulate from distant binding sites[10].

[9]The CG dinucleotide is highly susceptible to mutation, whereby methylation causes C to mutate into T. This explains its under-representation. A special DNA repair system protects those stretches of CpG used as promoters.

[10]These regulation proteins are able to bend DNA. During transcription activation, this allows distant proteins to move close together, causing large loops of DNA to appear.

The purpose of transcription regulation in eukaryotes is different to prokaryotes. Prokaryotes are single-celled and chiefly concerned with metabolising a variety of nutrients. Eukaryotes, on the other hand, are multi-cellular. Transcription regulation is the mechanism used to make cells specialised, with the pattern of gene expression in a cell reflecting its lineage and hence its type with respect to the surrounding tissues. Regulators are inherited from the cytosol of its parent cell, and these, through transcription regulation, decide the format of the cell's metabolitic activity. Other regulators are universal, passing configuration signals throughout the organism. These either act directly, by binding to promoter regions, or indirectly, through signal transduction pathways. For example, lipid-soluble hormones pass through cell walls and excite receptors which then release inhibitors which block the action of transcription factors. Furthermore, lipid-insoluble hormones excite receptors on cell surfaces, which then transmit signals through the plasma membrane to excite receptors within the cell etc etc. In practice, far more complicated pathways exist (see section 4.2 for a full discussion of signalling pathways).

Transcription in eukaryotes is made more complex by the structural organisation of chromatin. Areas of heterochromatin, which are very compact, are inaccessible to transcription factors. This entails that transcription cannot take place during cell-division. Furthermore, certain sections of chromatin remain condensed during interphase. These areas are not transcribed — even though theoretically-active genes exist within them. Some of these areas have become unused over evolutionary time, making it more efficient for them to remain compressed. Other areas are only found compressed in certain cells. This form of regulation is equivalent to regulator molecules in the cytosol, making the cell specialised. Human females inherit two X-chromosomes from their parents. Early on in development, one of these chromosomes becomes, and remains, condensed. Hence, only one of the human X-chromosomes, decided randomly, is transcribed in a given human.

Finally, mitochondria and chloroplasts have gene transcription systems similar to prokaryotes. Both these organelles have small genomes encoding a small number of proteins. Mitochondria, in particular, have very simple transcription systems — with mitochondrial RNA polymerase being the simplest protein that can carry out all stages of transcription.

3.2.3 Cell Division

For prokaryotes, cell-division and reproduction[11] are typically the same thing. The circular DNA within the cell becomes attached to the cell membrane. The DNA replicates, separates, and the new strand becomes attached to the plasma membrane at a different, but nearby, point. The membrane between the two attachment points and the membrane on the opposite side of the cell then move together. When they join, the cell separates into two daughter cells — each with its own DNA and a fifty percent share of the original cytosol.

The cell cycle for eukaryotes is somewhat more complicated and can be expressed by two different processes, mitosis and meiosis. *Mitosis* is normal cell division, accounting for regeneration and growth and producing daughter cells that are genetically identical. *Meiosis* is the production of germ cells (eggs and sperm) to meet reproductive needs, generating daughter cells that are genetically different.

Mitosis

The mitotic cell cycle consists of four phases, illustrated in figure 3.6. At the beginning is a gap of inactivity, during which the cell goes about its normal metabolic functions. At some point in time, depending upon the type of cell and how frequently it should divide, the cell enters the synthesis phase — during which nuclear DNA is replicated to produce two identical sets. Following from this is another, shorter, gap of inactivity, concluded by the *mitotic phase*. The mitotic phase, in turn, is carried out in four stages.

In eukaryotes, it is normal for nuclear DNA to be split into a number of units, each contained within its own macromolecular complex. This complex is called a *chromosome* and consists of a single molecule of DNA bonded to various proteins and structural members. In sexual species, there are two sets of chromosomes — the maternal and the paternal — inherited, respectively, from the organism's mother and father. After the synthesis stage of mitosis — where chromosomes are duplicated — each chromosome remains attached to its duplicate, forming a structure called a *sister chromatid*. Since this is the only time when chromosomes become easily visible in a microscope,

[11]Sexually reproducing bacteria do so by horizontal gene transfer, whereby a section of DNA from one bacteria invades the DNA of another. This can occur whenever the bacteria are in proximity.

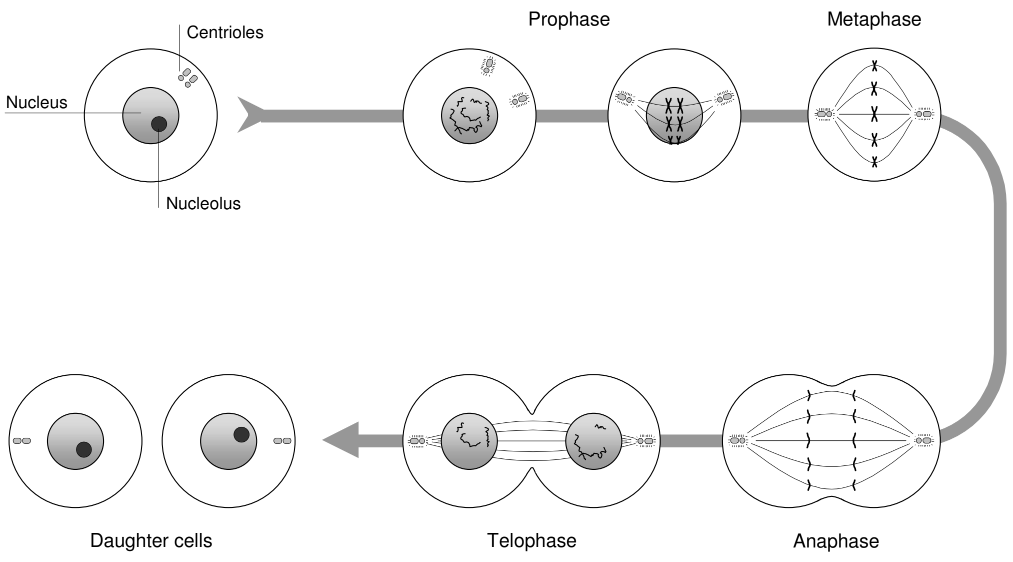


Figure 3.6. Mitotic cell division

this X-shaped form has become the standard representation of a chromosome — even though it really represents two chromosomes.

So, before the mitotic phase, the cell has twice the normal quantity of DNA, arranged into sister chromatids in the nucleus. The first stage of mitosis is *prophase*, during which the centriole organelle replicates — each centriole moving to opposite ends of the cell. Between the two centrioles, and spanning the length of the cell, microtubule spindles develop, each attaching itself to the middle of a sister chromatid and providing tracks along which the chromatids may move.

Metaphase, the second stage of mitosis, is characterised by the disappearance of a distinct nucleus. By the end of metaphase, the sister chromatids have become aligned along the cell's equatorial plane. This is followed by *anaphase*. Here, the sister chromatids become detached, each moving in a different direction along the microtubule spindles. Finally, in *telophase*, *cytokinesis* — division of the cell's cytoplasm — occurs, chromosomes group together, and nuclei reform in each of the daughter cells. During cytokinesis, mitochondria or cytoplasts, which have their own cycle of prokaryote-like division, are shared roughly equally between the daughter cells. Both daughter cells are now roughly identical, containing all the important organelles and a normal quantity of DNA.

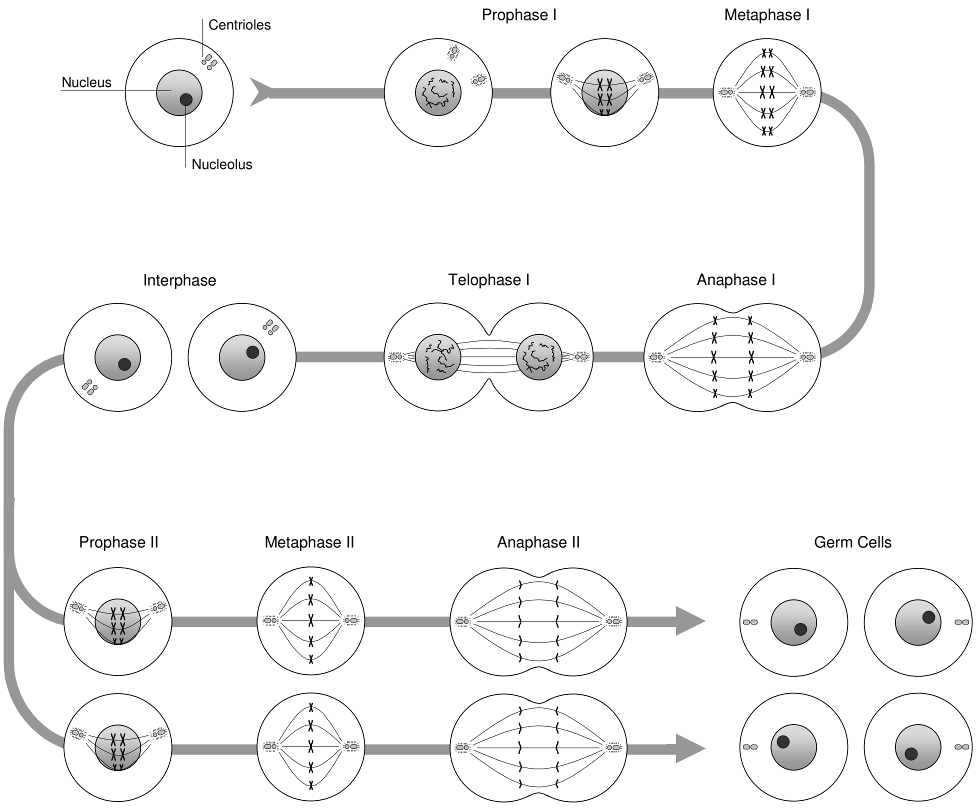


Figure 3.7. Meiosis

Meiosis

Meiosis is the production of sex (or germ) cells; cells which contain half the chromosomes of their parent (stem) cell. During reproduction, germ cells from the mother and father organisms join to form a *zygote*, a cell containing a full set of chromosomes which define the genome of a new organism. The mechanism of meiosis (see figure 3.7) is similar to mitosis. Up until early metaphase (where sister chromatids have been formed and the nucleus has denatured), the process is identical. However, instead of the chromatids aligning linearly along the equator, they line up in homologous pairs; with each maternal sister chromatid lying next to its corresponding paternal sister chromatid. Each sister chromatid in this pair will move, non-deterministically, to a different daughter cell during anaphase; and following this chromosome segregation, each daughter cell will contain exactly one of each chromosome type.

During late metaphase, and before chromosome segregation takes place, the aligned chromatids experience recombination: during which genetic material is transferred between the chromatids. Recombination involves a process called *crossover*: the exchanging of sections of DNA between the chromosomes; and although not explicitly transferring genes, this is the most likely outcome. The mechanism of crossover is explained in the following section. Following recombination, within anaphase and telophase, each homologue of a sister chromatid pair moves towards a different end of the cell and cytokinesis occurs. Unlike in mitosis, the sister chromatids do not split into separate chromosomes. The result is two daughter cells, each containing the normal amount of DNA, arranged into sister chromatids. Since the aim is to have half the normal amount of DNA, a second phase of cell division occurs with the chromatids detaching and segregating as in mitosis: finally resulting in four germ cells being produced from a single stem cell, each of which is genetically different to all the others.

Recombination

Recombination occurs at the end of metaphase when pairs of homologous sister chromatids have become aligned at the cellular equator. This alignment is called *synapsis*. Crossover is the swapping of genetic material between chromatids bought into close contact by synapsis. A number of points are randomly selected along the length of the two chromatids and sections of the DNA occurring between every other pair of points are swapped. Compared to the length of the chromatids, these crossover points are innumerous and are most likely to occur within regions of non-coding DNA. Therefore, the effect is that genes, or groups of genes, move between pairs of chromosomes. Most of the time, the integrity of genes are unaffected. Sometimes a crossover point will occur within a gene and, most likely, this will result in a novel gene formed from parts of the paternal and maternal versions. However, since chromosomes do not always align perfectly, there is some chance of this new gene not working correctly.

The Holliday model was the first to offer a satisfactory explanation of the mechanism behind crossover. At synapsis, both chromosomal duplexes align. Under the control of enzymes, a nick is made in a single DNA strand in one of the chromosomes. At this point, a small section of the nicked strand becomes detached from its complementary strand and invades the other chromosome, which is nicked at the same point, ligating to the corresponding strand. The same effect happens with the displaced strand from the other chromosome, forming a *crossed-strand Holliday structure*. This crossed section linking the chromosomes is mobile, able to move in either direction along the DNA complex. Under enzymatic influence, the crossed section moves a random distance — a process called *branch migration* — further detaching sections of single-strand DNA and carrying them over to the other chromosome. Rotation around the crossed section, the crossover point, results in an *isomeric Holliday structure*, a cross-shaped formation characteristic of recombination. Further nicks and resealings, driven by enzymatic action, produce one of two different end structures — recombinative or non-recombinative. Both of these contain heteroduplexes, sections of non-complementary duplex DNA. These will either be repaired by the DNA excision-repair mechanism, or remain heteroduplex until the next cell division. At this point, each daughter chromosome will gain a different section of DNA corresponding to the two halves of the heteroduplex. In recombinant DNA, sections of duplex DNA have transferred between chromosomes. Heteroduplexes occur around the joining point. In non-recombinative DNA, only small sections of single-strand DNA have been transferred between chromosomes. The excision-repair mechanism can update from either the existing strand, replacing the transferred single-strand, or from the invading strand. If crossover occurs within a gene, this latter action will cause gene conversion, the updating of an exon with new code.

4 Biochemical Pathways

Having introduced the key components of biological systems — cells, genes and proteins — these elements can now be bought together to describe higher-level structures which form the basis of control and function within biological organisms. These structures, called *biochemical pathways*, form networks of computation and communication which permeate organisms, bringing about order through the control and co-ordination of the activity of local systems.

There are three categories of biochemical pathway (see figure 4.1). *Metabolic* networks exist within cells, emerging from interactions between locally-transcribed proteins. *Signalling* networks comprise cellular responses to inter-cellular signals. *Gene expression* networks describe regulatory interactions between genes and gene-products. Marijuán [1995] describes these activities, respectively, as *self-organisation*, *self-reshaping* and *self-modification*. Self-organisation reflects how a distributed system of independent components can carry out a unified process. Self-reshaping is the ability of an existing system to carry out multiple processes to satisfy varying needs. Self-modification is the ability of a system to change its constitution in order to solve unforeseen problems. Interactions between the three classes of pathway unifies these processes and bring out the emergent behaviour of the whole organism.

4.1 Metabolic Networks

The previous chapter introduced the structure and function of individual proteins and enzymes, their capacity to interact — through sharing of products and substrates — and their mechanisms of regulation: activation, inhibition and allosterism. This sec-

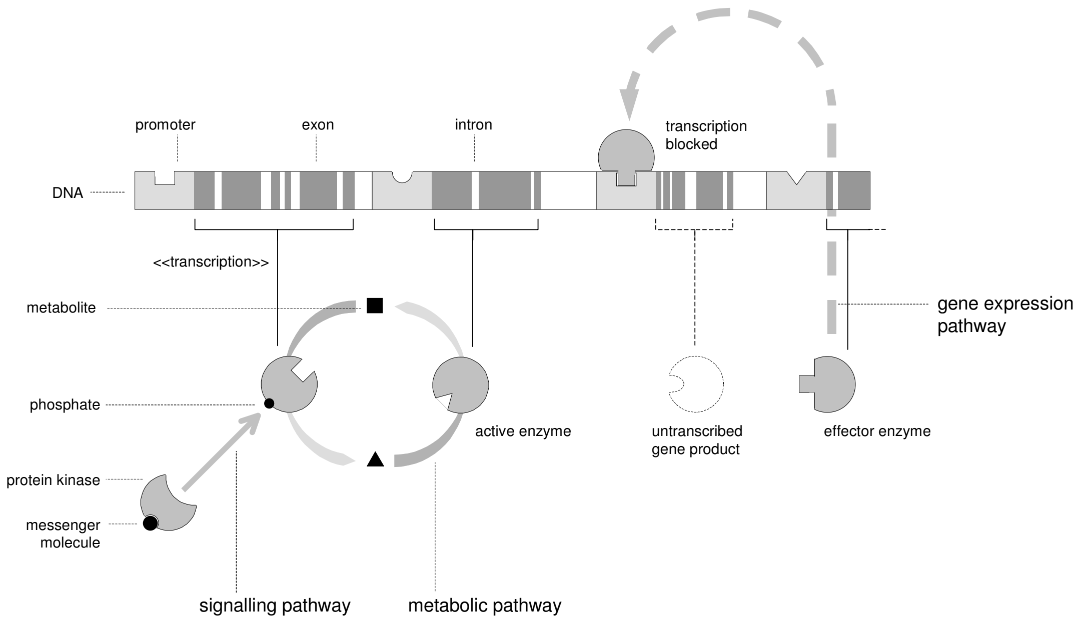


Figure 4.1. Biochemical Pathways

tion discusses the intra-cellular structures which emerge as a result of these interactions.

Figure 4.2 illustrates one such structure, the *citrate cycle*[1], a central part of the metabolism of both eukaryotes and prokaryotes (although not always used in the same way, see Forst and Schulten [1999]). The citrate cycle, in turn, fits into a larger structure, the *respiratory chain*, a sequence of reactions which eventually converts food into energy. Feeding the citrate cycle are other pathways, most notably *glycolysis*; which converts carbohydrates into pyruvate. Pyruvate is then converted into NADH by the citrate cycle, which feeds later stages of respiration. Pathways are highly evolved, conservative, structures which often carry out more than one task at once. For example, in addition to its role in respiration, the citrate cycle produces intermediates used in amino acid synthesis.

A metabolic pathway consists of two interdependent flows: *reaction* pathways and *control* feedbacks. Reaction pathways are composed of systems of enzymes with tightly linked specificities for one another's products and substrates. In many cases, these pathways are forked, with more than one enzyme having specificity for a given product. As demonstrated by the citrate cycle, pathways may also feed back into them-

[1]Also known as the Krebs (after its discoveror) cycle and the tricarboxylic acid cycle

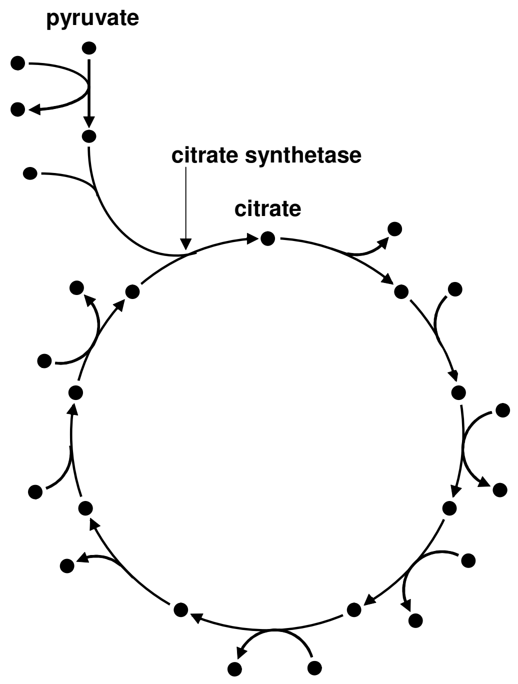


Figure 4.2. The citrate cycle. Nodes represent products and substrates. Arrows represent enzymes.

selves, producing an iterative structure. Control feedback may be positive or negative, internal to the pathway, or caused by external metabolic or signalling pathways. The citrate cycle is regulated by substrates and products within the cycle. Glycolysis is regulated by hormones, notably insulin. The functions of pathways are either *anabolic* (constructive), *catabolic* (destructive), or *amphibolic*. Amphibolic pathways are both anabolic and catabolic, and often link anabolic and catabolic pathways.

The sharing of reaction and control between pathways means that most pathways are not separate structures, but conventions which indicate one way of subdividing the metabolism into smaller systems. However, some pathways (or parts of pathways) are independent of others. These are *genetically independent* pathways [Schilling et al., 1999]: pathways where there exist no other pathways which use only a subset of their reactions[2]. Approximately 80% of metabolic intermediates have just one use in the cell [Marijuán, 1994]. However, the existence of regulatory networks makes it unlikely that genetically independent pathways will be long, since at some point a pathway is regulated by factors in another pathway. To make understanding of the pathway easier, convention defines pathways such that they largely contain a regulatory network.

[2]The term genetically independent stems from the fact that the enzymes in this pathway define an independent genotype.

Even though many key reaction pathways have been identified and charted, the metabolism is still not completely understood. As a result, known pathways tend to reflect incomplete knowledge, describing a subset of the operation of actual metabolisms. Factors such as re-use of reactions, multiple equivalent paths through the network, and variety between cell types and between individuals (since our genomes are not identical) add to the difficulty of understanding. Fortunately, with the genomes of a number of organisms now completely sequenced, the data required to fuel this understanding is becoming available. The difficult task now is in interpreting this data, a task undertaken by traditional mathematical techniques [Heinrich and Schuster, 1998], modelling [Reddy et al., 1993, 1996], and bioinformatics [Schilling et al., 1999]. A better understanding of the metabolism would have many uses, including those in bioprocess engineering (creation of novel metabolic pathways for use in chemical plants) and health-related (finding alternative paths through defective networks, design of drugs which intervene in the metabolism) areas [Karp and Mavrovouniotis, 1994]. Current understanding is expressed through charts and diagrams [Michal, 1999] (for which representation is a key concern [Michal, 1998, Karp and Paley, 1994]) and public databases [Karp, 1999, European Bioinformatics Institute, 2000].

Finally, understanding of the metabolism can be aided by an understanding of how it evolved. This topic has been approached from a number of areas, including biochemistry [Lyubarev and Kurganov, 1997, Wächtershäuser, 1990], biophysics [Igamberdiev, 1999] and molecular evolution [Page and Holmes, 1998, Forst and Schulten, 1999]. The molecular evolution approach uses the current form of genomes to infer properties of earlier forms. For example, in many cases enzymes proximal in a pathway are also proximal in the genome, since they must have had a high degree of genetic linkage in order to have survived recombination events during evolution.

4.2 Signalling Networks

Signalling between cells in an organism is a fairly well understood process. Cells produce signal proteins which, after being released through the cell's plasma membrane, spread throughout the organism via bodily fluids. Receptors on the surface of other cells then detect this signal and relay it to the appropriate components within the cell.

How this intra-cellular communication happens, by comparison, is only now beginning to be understood by molecular biologists.

In fact, research shows this process to be surprisingly complex — not simply a case of a receptor generating the right signal and transmitting this into the cytoplasm — but rather an extended series of events involving many different agents. Key amongst these agents are *protein kinases* and *phosphotases*, enzymes which modify the activity of other enzymes. Other players include *secondary messenger* molecules, protein *adapters* — which connect other proteins together — and *scaffold proteins* — which co-ordinate the activities of other molecules.

Under the classic model [Sutherland, 1972, Fisher et al., 1999], occupation of a receptor by an external signal molecule causes the activation of an internally-bound effector enzyme. This effector then generates secondary messenger molecules which spread the signal throughout the cell and activate target proteins. These signal sensitive protein kinases or phosphotases then, either directly or indirectly via the (in)activation of other protein kinases or phosphotases, modify proteins within the metabolic or gene expression networks of the cell. This brings about a change in cellular activity. Of particular note is the degree of amplification involved in the system: one primary signal molecule causes many secondary signal molecules which then activate a hierarchy of modifier proteins.

More recent research (summarised in [Scott and Pawson, 2000]) refines this understanding. Many receptors are in the family *receptor tyrosine kinase*. These enzymatic proteins work in pairs. When a pair of receptors bind signal hormones, their cytoplasmic tails (which protrude below the plasma membrane) bind phosphate molecules to one another's tyrosine amino acids. These altered residues then become bound, either directly, or indirectly through adapters, to signalling enzymes — activating the signalling enzymes, causing them to generate secondary messenger molecules (see figure 4.3). The key differences in this new interpretation are that: (i) signalling proteins typically consist of multiple domains; and (ii) these proteins are spatially co-ordinated. In more complicated signalling systems, scaffold proteins, which consist of multiple linker domains, provide this co-ordination. Indeed, they are particularly prevalent in hierarchical protein kinase/phosphotase systems. This is necessary because these enzymes often have broad specificity, meaning that if not co-ordinated, they can modify

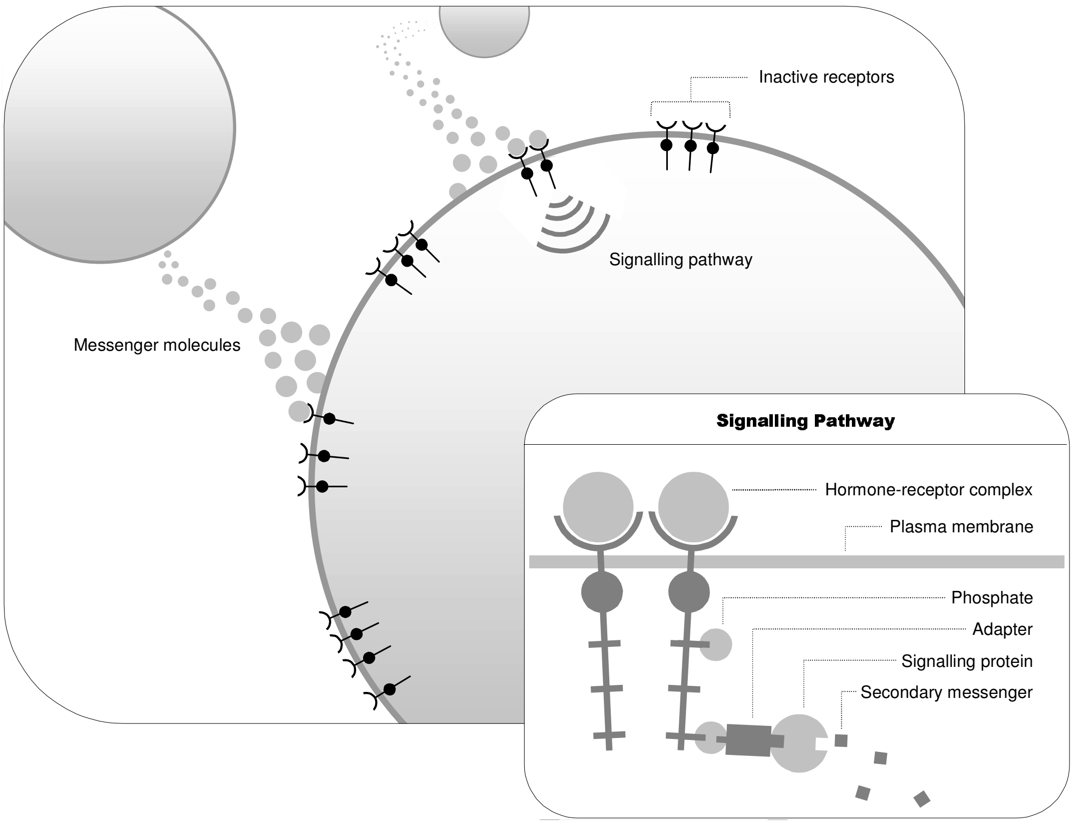


Figure 4.3. Initiation of a Signalling Pathway

the activity of a wide range of proteins — an effect not typically wanted. In addition, the modular make-up of signalling proteins is thought to improve the evolvability of these systems, since new systems can be formed by novel re-arrangements of existing, and newly created, modules.

Bray [Bray and Lay, 1994, Bray, 1995] has described computational aspects of signalling pathways. Enzymes involved in signalling pathways can be conceptually seen as having a number of inputs, each corresponding to a certain class of regulatory or phosphorylation events. The action (output state) of the enzyme is then some function of these inputs. For instance, enzymes exist which become active only after being phosphorylated by two protein kinases — an `AND` function; whereas some require the presence of only one of two possible regulatory molecules: an `OR` function. A more general pattern is that of amplification and switching i.e. if a signal (one molecule) activates an enzyme, the enzyme reacts with an amplified secondary signal (many molecules). Combining these behaviours — function application, switching and amplification — results in a system not unlike a neural network. In fact, signalling enzymes are more like McCulloch-Pitts neurons (perceptrons) than are real neurons. Taking this idea further, Bray has experimented with abstract models of these 'protein circuits', using simulated evolution (optimising reaction rates and binding constants) as a training system.

The switching behaviour of an enzyme depends upon a number of kinetic properties: properties which affect the speed and crispness of responses. However, the quantum mechanical behaviour of enzymatic reactions means that they do not always behave as ideal Boolean switches, but display varying degrees of fuzzy response. Bray suggests that this behaviour is caused by asymmetries and synergisms between inputs; and results in enzymes behaving like fuzzy logic elements, which may be more computationally powerful than Boolean logic units. Fisher et al. [1999], too, discuss the fuzzy properties of signalling enzymes, particularly protein kinases, comparing their behaviour to fuzzy classifier systems. Moreover, they describes the 'signalling ecology' as a "vast parallel distributed processing network of adaptable agents", conferring such cognitive properties as pattern recognition, handling fuzzy data, memory capacity and context-sensitivity to these agents.

4.3 Gene Expression

A cell's type is defined by the subset of genes which are typically expressed (transcribed) within the cell. Recall from section 3.2.2 that transcription of a particular gene depends upon the correct formation and activity of a transcription complex, a process which can be blocked by the binding of certain inhibitors to regulation sites associated with the gene. Inhibitors are proteins and therefore must be encoded by other genes. Each of these regulating genes, in turn, may be regulated by inhibitors encoded by other genes. Typically, a single regulating gene may regulate a small number of other genes, each of which may then, in turn, regulate a small number of other genes. By transitivity, a single gene may indirectly affect the regulation of a large number of other genes. A gene may also, either directly or indirectly, regulate its own transcription. This complex system of regulatory interactions is known variously as a gene expression network, a genomic regulatory network, or more concisely, a genetic network.

Genetic networks are not easy to understand and, like all discrete dynamical networks, are difficult to analyse using partial differential equations and other techniques from continuous mathematics. Hence, they are typically modelled with automata and analysed by simulation, a trend captured by Stuart Kauffman in the form of random boolean networks (RBN's) [Kauffman, 1969, Somogyi and Sniegoski, 1996]. These describe regulatory networks as a mapping from state t to state $t + 1$, employing directional links, binary on/off states, parallel updates and combinatorial logic on inputs. Whilst an idealised representation, these abstract networks still demonstrate behaviour similar to real networks. Interestingly, when simulated, the networks indicate the existence of attractors, which pull the network towards a small set of final states starting from a large number of initial states. In [Somogyi and Sniegoski, 1996, Wuensche, 1998], this behaviour is compared to specialisation in cells with an attractor comparable to a single cell type and paths between attractors equivalent to pathways of differentiation. Following from this, a cell type can be expressed as a set of closely related gene expression patterns, centered around a basin of attraction. It is also conjectured that the strength of this attractor must represent a balance between a cell's adaptiveness and a need not to cross to neighbouring states (which could, for instance, correspond to cancer cells).

As well as being dynamic and self-adaptive in their own right, networks of genetic expression are also directly subject to evolution. In [Shimeld, 1999], this evolution is discussed in terms of gene duplication events. In [Bornholdt and Sneppen, 1998, Bornholdt and Rohlf, 2000] artificial evolution is used to evolve connectivity in Boolean (and other dynamical) networks. In [Bignone et al., 1997], evolution of genetic networks is considered from a mathematical perspective.

Chiva and Tarroux [1995], too, have applied simulated evolution in order to gain a greater understanding of how biochemical networks develop. Their system includes both transcriptional (gene regulation) and post-translational (protein interactions) components, reflecting the coupling between genes and gene-products — and the influence of both in the gene regulation process. These 'protein regulation networks' are deterministic, recurrent and synchronous. The activation state (concentration) of a unit (protein) is a weighted sum of activations of other units. The weights are defined in a genome, where a gene represents each protein. Gene expression is defined by two sets: the set of states where this protein may be regulated by others, and the set of states where this protein may regulate others. The intent is that the model should mimic protein folding. The algorithm used is a genetic algorithm with uniform crossover, a degree of steady-state and a set (no duplicates) as the population structure. The last point is meant to reduce genetic drift. Gene duplication and new gene events take place population-wide at fixed intervals (keeping all solutions the same length). The system is intended to emulate differentiation, triggered by external stimuli. Hence, the fitness function rewards solutions which change state when given pertinent stimuli and punishes those which differentiate with false or vacant signals. Communication signals are implemented with 'clamped' units, whose concentration (activation) is externally dictated.

A key observation is that a gradual increase in solution size from N_0 to N_1 produced markedly superior results than fixing solution size at either N_0 or N_1. This suggests that gene networks evolve best by building upon existing, smaller, networks — an observation that explains why yeast and humans share similar pathways; the human pathways including the yeast pathways as subsets of their possible reactions. The explanation behind this phenomenon is that evolution in smaller networks is much more likely to find the local optimum, whereas evolution in a larger network is harder. For a larger network to evolve, it must go via stable intermediate states — which are provided explicitly by smaller networks.

Another observation is the development of 'command units', those for which fan-out is of much higher intensity than fan-in — amplification — and for whom input signals are heterogenous, whereas output signals are homogenous. This causes the formation of hierarchies, similar to those found in biological signalling pathways. Finally, the genome encoding used implicitly made the network fully-connected (although some of these connections may be ignored by a given unit). The authors speculate that sparsely-connected networks, corresponding to biological systems, might provide a better opportunity to develop clusters of specialised function within the network.

5 Biological Evolvability

Many definitions exist for the term ‘evolvability’. The most general of these is ”the capacity to evolve” [e.g. Smith et al., 2003] i.e. the capacity for some entity or group of entities to undergo change, or as Suzuki [2003] puts it, ”the possibility (potential ability) of evolving a variety of genotypes or phenotypes”. Most, however, agree on a more limited definition of evolvability: summarised by Nehaniv [2003] as ”the ability to reach ‘good’ solutions via evolution”, and implicitly appealing to a requirement for direction within evolution. Likewise, Altenberg [1994] offers ”the ability of a population to produce variants fitter than any yet existing”; Wagner and Altenberg [1996]: ”the genome’s ability to produce adaptive variants when acted on by the genetic system”; and Kirschner and Gerhart [1998]: ”the capacity to generate heritable selectable phenotypic variation”. A key issue addressed by these definitions is access to adaptation: the degree to which the evolving system is able to gain adaptive traits (termed ‘accessibility’ in Volkert [2003]) and the amount of evolution required to transform the existing system into a system which possesses these traits. Also important for evolvability, though implied rather than stated explicitly in these definitions, is the maintenance of existing traits: without which the gaining of new traits is largely academic. To use Kirschner and Gerhart’s own words, evolvability (in a biological context) requires a capacity ”(i) to reduce the potential lethality of mutations and (ii) to reduce the number of mutations needed to produce phenotypically novel traits” [Kirschner and Gerhart, 1998].

In part due to its unfortunate association with ideas of group selection, the study of evolvability is still in its relative infancy. Nevertheless, as understanding of biology, complex systems and, more recently, evolutionary computation has increased; it has become apparent that considerable insight can be made into evolvability phenomena. Research into evolvability follows three broad themes: (i) the characteristics of evolvable systems and the requirements for a system to exhibit evolvability; (ii) actual sources of evolvability within biological and non-biological systems; and (iii) the evolution of evolvability.

Some of the most significant insights into evolvability have been made by Michael Conrad [1979, 1985, 1990]. In particular, he speculates that evolvable systems are a very unique kind of system that reflects a balance between the need for phenotypic stability on the one hand and the pressure towards genetic exploration on the other. Following from studies of complex systems, it is known that the functioning of randomly-connected systems becomes more unstable as complexity increases yet more sensitive to (e.g. genetic) change as complexity decreases. According to Conrad [1990], these competing pressures can only be satisfied in systems that display compartmentalisation, component redundancy, and multiple weak interactions.

5.1 Compartmentalisation

Of these requirements, compartmentalisation is perhaps easiest to understand. A compartment is a group of components whose interactions are mostly internal to the group. Consequently, a change (e.g. due to genetic variation) within one of the group's components is most likely to have its effect limited to other members of the group rather than percolating to the entire system. Likewise, multiple changes to the system are likely to affect separate sub-systems rather than have a compound (and probably lethal) effect upon a single sub-system. In Kirschner and Gerhart [1998], the authors describe compartmentalisation as a significant source of de-constraint within biological organisation. Constraints upon evolutionary change occur where one part of a system in unable to change because of the un-welcome effects a change would have upon other parts of the system to which it has strong linkage. An example of constraint is where a gene codes for an enzyme which carries out different roles within more than one different pathway or the same pathway carrying out a different role within a different type of cell; and where a change to the gene would improve its function within one context but lead to a lethal change within the other. If, however, the enzymes within both contexts were coded by separate genes, then both enzymes could vary — and be selected for — independently. Following this logic, it would make evolutionary sense to have genetic independence between both pathways.

However, in Hansen [2003b] the author argues that modularisation is not always the best solution for evolvability. In actual biological systems, there exists a substantial level of pleiotropy between characters: with one gene having an influence (via use of the same protein) upon the function of more than one tissue, organ or trait. Hansen suggests that this is due to increased variational potential out-weighing the interference caused by pleiotropy. In particular, it would seem that pleiotropy should be encouraged in the early stages of adaptation, with an evolving sub-system making use of functional building blocks used elsewhere within the organism. Depending upon the selective pressure placed upon the two sub-systems, their sensitivity to change, and the role of the shared function, it might then make continued sense for the shared function to co-adapt within both systems via this pleiotropic link. Indeed, Hansen suggests that in some cases the evolution of modularity may not be a necessary condition for the evolution of evolvability.

One process in which compartmentalisation appears to play a crucial role is during the embryonic development of multi-cellular organisms [Kirschner and Gerhart, 1998]. Development is characterised by the differentiation of the organism into increasingly more specialised compartments. The initial segmentation of the embryo is dependent upon concentration biases in the fertilised egg. However, as development proceeds, separate compartments rapidly become independent of the activities — and therefore of the errors — occurring in other compartments. Hence, a failure caused by genetic change (or otherwise) in one compartment will not impede upon the development of the entire system. Likewise, evolution can carry out morphological exploration within one compartment without affecting other compartments: another example of de-constraint.

Compartmentalisation also appears within the spatial arrangement of genes within a genome. This phenomenon, called epistatic clustering, occurs in both prokaryotes and eukaryotes. In prokaryotes, it is particularly apparent in the form of operons: where a group of genes with tightly-linked products are located proximal in the genome and are transcribed within a single transcription event. Functionally, this is advantageous for prokaryotes because they save time and energy when expressing new pathways in response to changes in the environment. However, it also aids evolvability by improving the efficacy of horizontal gene transfer since, due to their proximal locations in the genome, it is likely that the genes in an operon would be transferred to other prokaryotes as a single unit. The other prokaryote would in effect receive an entire metabolic pathway, which is far more likely to improve its fitness than a group of unrelated genes [Poole et al., 2003]. Eukaryotes, by comparison, transfer genes during sexual recombination. After crossover, a pathway is more likely to be preserved if the genes which code for it are located close together within a chromosome. Evolvability might therefore be improved in a genome which expresses modularity in the form of epistatic clustering [Pepper, 2003].

5.2 Redundancy

Redundancy appears in many forms in biological systems. This section introduces functional redundancy, structural redundancy, and weak linkage.

5.2.1 Functional redundancy

Examples of functional redundancy in biology include: at the genomic level, gene families, pseudo-genes and polyploidy; and at the phenotypic level, allozymes (functionally equivalent enzymes) and homogenous tissues. In a sense, functional redundancy is another form of compartmentalisation where functionally similar, or equivalent, components conceptually form groups that limit the affect of perturbations from other kinds of component [Conrad, 1990]. This buffering occurs in response to both genetic change: where redundant copies help maintain the previous role of the component that has been changed; and phenotypic perturbation: by allowing multiple steady states in the space of phenotypic behaviour. Consequently, functional redundancy provides a means of overcoming the opposing requirements for phenotypic stability and the increased complexity (more components) needed to support genetic change.

Functional redundancy underlies Ohno's theory of 'evolution by gene duplication' [Ohno, 1970]. This theory proposes that the majority of molecular evolution has occurred through a process of gene duplication and divergence: whereby genes recursively duplicate (possibly through misaligned crossover) and evolve separately into genes that encode proteins with increasingly more specialised functions. (This process may also be involved in the evolution of modularity — see Wagner and Altenberg [1996].)

5.2.2 Structural redundancy

Structural redundancy occurs where biological components such as proteins, chromosomes, and pathways have higher complexity than is required to fulfill their phenotypic task. Structural redundancy improves evolvability by acting as a genetic buffering mechanism which limits or gradualises the effect of genetic change. An example is non-coding DNA, which effectively segregates genes, making it more likely that crossover junctions will form between, rather than within, genes: and therefore limiting the disruptiveness of recombination. Another example (see section 5.3) is the mutation buffering provided by redundant amino acids during the evolution of protein structures. Structural redundancy can also enable the formation of new evolutionary mechanisms. A good example is transposons, which make use of structural redundancy within the genome and may play a role in producing mutational hot-spots (where genetic change occurs faster than in other regions of the genome) in addition to their roles (described earlier) in gene duplication and gene formation.

5.2.3 Weak Linkage

Weak interactions are another form of redundancy, but one that occurs at the interconnection level. A weak interaction has a small informational effect: such as the bond made by an individual amino acid at an enzyme's binding site; whereas a strong interaction has a large informational effect: such as the binding of a substrate at a binding site. In the case of weak interactions, the net effect is one of integration — the summing of the effect of multiple weak interactions from many different sources. Removing or adding a single interaction will have little effect upon this sum, and hence the effect it produces. For strong interactions, by comparison, each interaction is capable of having a decisive effect: for example, the inputs to a logical AND function are strong signals since each can individually determine the output of the function. According to Conrad [1990], redundancy through multiple weak interactions is the best way of compromising genetic instability and phenotypic stability within a system, since it allows a system to have many components and interactions (and therefore a high degree of genetic control) whilst limiting the impact of any particular component or interaction (and therefore the effect of a phenotypic change).

A small genetic change to a weak interaction will typically lead to a small phenotypic change. This means that a system with weak interactions is highly controllable at the genetic level, and suggests why weak interactions are a key component of many evolvable structures seen in biology. The benefit of weak interactions can also be seen in results by Volkert and Conrad [1998] and Volkert [2003] in the context of enhancing evolvability in a non-biological system. In this work, the authors studied the behaviour of random and evolved dynamic network models (non-uniform cellular automata) with and without weak interactions; and found that weak interactions could improve the exploratory scope (access to behaviours), the performance of evolved networks, and the stability of evolved networks when exposed to random genetic mutation.

Weak interactions occur extensively in regulatory pathways. Regulatory pathways, in turn, are thought to have been of considerable importance to the evolution of complex multi-cellular organisms [Kirschner and Gerhart, 1998]. Examples of multiple weak interactions are the calcium ions whose concentration controls the secretion of neurotransmitters in the brain; and the interactions between the binding site, enzymes, enhancers, and control signals that lead to the formation of a transcription complex in eukaryotes. In each of these cases it is the net effect of all of the interactions that controls the activation level. Because of this, the strength of activation can be varied gradually through the addition and removal of components and interactions, and can respond flexibly to new sources of regulation.

5.3 Evolution through Redundancy

The effect of redundancy is to increase the tunability of evolution such that most mutations lead to small or neutral changes to an organism's fitness. Proteins, for example, exhibit all three forms of redundancy discussed above. Functional redundancy results from the presence of gene families and polyploidy and reduces the impact of deleterious variants by offering functional alternatives. Structural redundancy results from the presence of extra amino acids and allows a protein's shape (and therefore its activity) to be varied more gradually than a protein with no structural redundancy. Weak linkage occurs during protein folding where weak interactions such as hydrogen bonding, hydrophilic interaction and Van der Walls interactions produce the protein's functional shape: and allows small changes in the protein's shape and chemistry by adding and removing bonds. The shape of the protein, in effect, can evolve along either of these redundancy axes through a process of gradual change which Conrad [1985] calls mutation buffering to reflect the fact that a protein, or other structure, can experience a number of mutations with little or no change to its functionality. Evolution through redundancy, in this respect, is a clear example of how neutral evolution can lead to adaptation.

Conrad [1979, 1990] has attempted to explain the role of redundancy in evolution by appealing to the notion of an organism's adaptive landscape: a solution space which associates every possible phenotypic conformation of the organism with a fitness value and arranges phenotypes such that those which are proximal are separated by a single mutation. Adaptation, generally speaking, is only possible along upward running paths within this landscape i.e. those where a series of neutral or positive mutations link a lower-fitness phenotype with a higher-fitness phenotype. Adaptation is highly unlikely if more than one mutation is required in parallel or if the organism must move to a lower fitness level before a positive mutation is possible. Roughly speaking, the effect of redundancy is to introduce new dimensions to the adaptive landscape, presenting adaptive paths which were not present prior to the introduction of redundancy. Conrad [1990] calls this phenomenon extra-dimensional bypass.

5.4 Neutral Evolution

Neutrality is a form of redundancy which has attracted substantial interest in recent years. The theory of neutral evolution was originally postulated by Kimura [1983] in order to explain the high levels of polymorphism (multiple alleles for a gene) found within natural populations. According to the selectionist theory of evolution prevalent at the time, evolution occurs through gene substitution: where the selective advantage gained by infrequent positive mutations causes them to replace less-fit alleles within the population. From this, it follows that mutant alleles will either be removed immediately (due to a negative impact) or move quickly to fixation (due to a positive impact). Consequently polymorphism would only be expected to occur where there is balancing selection brought on by a heterozygotic advantage[1]. However, experimental measurement of genetic diversity has shown that polymorphism readily occurs when there is no heterozygotic advantage. Kimura's neutral theory of evolution, in response to this, proposed that the majority of evolutionary change occurs through the random fixation (through genetic drift) of neutral mutations: mutations which occur often and have no affect upon fitness. The implication of this is that, most of the time, evolution proceeds through a random walk of the fitness-equivalent solutions within genetic space; and only infrequently does a positive mutation lead this walk into higher fitness regions of the genetic space. The potential routes that such a random walk can follow form what is known as a neutral network: a graph of solutions, each of which has the same fitness, and each of which can be reached by a series of neutral mutations (a neutral walk) from any other member of the neutral network.

There are good reasons, and an increasing amount of evidence, to believe that neutral evolution benefits evolvability. Some of this evidence emanates from research into evolutionary computation and is discussed in section 7.4.2. However, the benefits of neutrality can also be seen directly within the evolution of RNA structures [Huynen et al., 1996, Huynen, 1996, Schuster, 2000]. The mapping between RNA sequence and RNA secondary structure has a number of interesting features. First, sequence space is very rugged. Mutating a small number of bases can result in a very different structure which, ordinarily, would suggest a fitness landscape that is difficult to traverse. However, there are a small number of possible RNA structures and these are represented by a relatively large number of RNA sequences: suggesting a high degree of neutrality. Test-tube experiments have shown that the neutral networks which correspond to different structures are well-connected: meaning a neutral walk within a

[1]Heterozygotic advantage, or *overdominance*, occurs when a heterozygote (an organism which has a different allele at a particular gene locus within its maternal and paternal chromosomes) has higher fitness than either of the homozygotes (two copies of the same allele). This leads to *balancing* (or *stabilising*) *selection*, resulting in a balanced polymorphism (more than one allele supported by the population) between the two alleles.

particular neutral network can eventually lead to other neutral networks that correspond to a considerable number of alternative RNA structures. This, in turn, supports a mode of evolution where a population diffuses within a particular neutral network until a chance mutation leads one member of the population to a higher-fitness neutral network; at which point selection pulls the rest of the population towards the fitter neutral network and the process begins again [Huynen, 1996]. In essence, neutrality overcomes the ruggedness of the RNA sequence landscape which, in the absence of neutrality, would make evolution very difficult. Huynen [1996] calls this phenomenon 'smoothness within ruggedness'.

Neutrality is enabled by redundancy in the form of both structural redundancy and multiple weak interactions. However, Toussaint and Igel [2002] offer a view that whilst sources of neutrality are redundant in a static sense, i.e. their current state does not contribute to an organism's current fitness; they are not redundant from an evolutionary perspective. Genotypes corresponding to different locations in a neutral network, in their own words: "can encode different exploration strategies and thus different information; a genotype encodes not only the information on the phenotype but also information on further explorations." According to this view, genetic information that is redundant within a generation serves to encode 'strategy parameters' that affect self-adaptation of the genotype between generations. An example of this occurs within HIV sequences, which appear to make use of the neutral properties of the genetic code in order to encourage or discourage mutation at particular gene loci. Each amino acid can be coded by more than one nucleic acid codon. Accordingly, the codons for a particular amino acid form a neutral network. Within this network, there are access points (via point mutations) to other neutral networks corresponding to other amino acids. However, some codons have more access points than others and are therefore more likely to undergo non-synonymous mutation. In HIV, codons with relatively many neutral neighbours are more likely to occur in functionally important areas of the genome whereas codons with relatively many non-neutral neighbours are more likely to occur in areas that tend to be recognised by a host's immune system [Stephens and Waelbroeck, 1999].

In a sense [Lones and Tyrrell, 2001b], the redundant components of the genome form an evolutionary scratch-pad that serves both to record previous avenues of search and to suggest future avenues of search, augmenting the static role played by non-redundant genetic components.

5.5 Other Sources of Evolvability

Whilst simple concepts like compartmentalisation and redundancy explain the underlying evolvability of biological systems, there are numerous other complex and adaptive mechanisms which also contribute to evolvability. Transfer of DNA, for example, allows genes to move from one environment to another. In eukaryotes, this occurs during recombination and leads to offspring with novel combinations of parental alleles: in effect, increasing the explorative power of evolution in its search for adaptation. In prokaryotes, 'horizontal' DNA transfer can occur between members of both the same and different species, and is an important factor behind the ability of bacteria to adapt rapidly to changing environmental conditions [Poole et al., 2003].

In Kirschner and Gerhart [1998], the authors discuss the flexible roles of 'exploratory mechanisms' such as epigenetic and developmental processes in supporting evolvability. These mechanisms make use of compartmentalisation and redundancy to de-constrain their roles within organism construction and maintenance from mutational change in the components and structures that they construct and maintain. The immune system, for instance, makes no prior assumptions about what constitutes 'self' and, therefore, evolution is free to change the constitution of 'self'. Likewise, during the development of the limb structures of complex multi-cellular organisms, growth of the nervous and vascular systems occurs relative to the growth of cartilage. Consequently, changes in limb size and shape can be achieved through mutation of the cartilage growth process without requiring (highly unlikely) corresponding mutations in the growth processes of the nervous and vascular systems. (Further insight into the implications of phenotypic plasticity upon evolvability can be found in Poole et al. [2003] and Dawkins [1989].)

In addition to the genetic and phenotypic levels, evolvability is also affected by processes which occur at epigenetic and ecological levels. Cytosine methylation is an example of a fairly low-level epigenetic mechanism where information is passed from parent to offspring via DNA patterning. Cytosine is a DNA base which when methylated becomes unstable and easily converted into thymine: producing mutational hotspots within the genome. Mutational biases, in theory, can lead to differential rates of evolution across the genome, which may be of benefit to evolvability (for more information see, for example, Bedau and Packard [2003]). DNA patterning may also affect evolvability through evolution of the 'epigenotype' [Poole et al., 2003]. Higher level forms of epigenetic inheritance such as transmission of learned information from parent to offspring and cultural interaction have an effect upon evolutionary direction through their affect upon mate choice and lifestyle. Therefore it seems likely that, by pushing populations in the direction of increased adaptation, these mechanisms might also have a significant bearing upon evolvability. Finally, differences between the adaptations required for species to occupy particular niches and pressure from competing species also tends to push the evolution of populations in certain directions and, again, these factors can form important sources of evolvability [Poole et al., 2003].

5.6 Evolution of Evolvability

The previous sections all give credence to the notion that biological representations possess evolvability. However, assuming that evolution is individually responsible for generating these biological representations, an outstanding question is: How did evolvability evolve? There is no universally accepted answer to this question. Nevertheless, there are two common answers: that (i) evolvability has hitch-hiked along with the selection of other traits; and that (ii) evolvability is actively selected for.

The first of these reflects the view that most mechanisms which improve evolvability originally evolved for some other purpose and that, therefore, it is not necessary to introduce any new evolutionary mechanisms to explain the evolution of evolvability. Poole et al. [2003] argue that hypermutation, horizontal transfer, sex and recombination, cell-cell interactions and cell adaptations all evolved as stress adaptations. Horizontal transfer, for example, occurs at an accelerated rate when prokaryotes experience stress as a result of low nutrient levels in their environment: their aim being to build new metabolic pathways that will allow them to process alternative nutrients. The role of horizontal transfer (and eventually recombination) in conferring evolvability may have hitch-hiked along with selection for this stress response. Furthermore, in Dawkins [1989], the author argues that sources of evolvability such as segmentation may even have inhibited the fitness of the organisms they originated in, but eventually proliferated due to their ability to support increased morphological exploration and lead their descendants to colonise new niches.

The alternative view is that, in most cases, evolvability has been implicitly selected for its role in improving the adaptability of entire lineages. This can be argued by asserting that any mutation which improves an organism's evolvability will improve the chance of its descendants undergoing adaptation, being selected for, having more offspring: and in the process, passing on their evolvability-enhancing mutation to a greater percentage of the population. In Dawkins' [1989] words: "Evolution has no foresight. But with hindsight, those evolutionary changes in embryology that look as though they were planned with foresight are the ones that dominate successful forms of life."

Nevertheless, it remains difficult to explain how the use of very basic mechanisms of evolvability, such as redundancy, might have evolved. This difficulty has prompted a third, partial, explanation for the evolution of evolvability: that evolvability is a 'frozen accident'; an innate property of the planet's biochemistry which might not have evolved within other possible systems of representation. According to this view, biological representations are evolvable because they always have been evolvable.

5.7 Summary

Evolvability is the relative capacity for organismal lineages to become better adapted to their environment as a consequence of natural selection acting upon essentially random genetic variation. Biological systems are believed to be organised in a way that promotes evolvability. Important sources of evolvability include redundancy, compartmentalisation, exploratory mechanisms, and epigenetic and ecological processes. Redundancy in particular is though to support neutral evolution: a conceptually powerful mode of evolutionary exploration. Whilst it is not known how these sources of evolvability evolved, it has been speculated that this is due both to re-use of mechanisms evolved for other purposes and to lineage selection.

6 Genetic Programming

Genetic programming is a computer algorithm which designs and optimises programs using a process modelled upon biological evolution. This chapter introduces the family of algorithms to which genetic programming belongs, introduces genetic programming, discusses its behaviour and limitations, and reviews derivative approaches.

6.1 Evolutionary Computation

Evolutionary computation (EC) is an approach to search, optimisation and design which uses a family of approaches called evolutionary algorithms (EAs) that use evolutionary processes to evolve any kind of entity which may be represented on a computer. Most evolutionary algorithms model the biological process of evolution. Using terms from Chapter 1, this kind of process is group-based and involves both competitive and co-operative mechanisms during the evolution of the group: and in this respect is related to other group-based search algorithms such as particle swarm, memetic, tabu, and ant algorithms.

Central to an evolutionary algorithm is the data structure which holds evolving entities: the *population*. At the start of an evolutionary run, this structure is *initialised* to contain a group of candidate solutions to some problem. Typically these solutions are randomly generated. Consequently most will be far from optimal, but nevertheless all are evaluated using some *fitness function* which determines their relative ability to solve the problem and assigns each candidate solution a respective *fitness* value. Following evaluation, the evolutionary algorithm applies a *selection* mechanism which removes the least fit candidate solutions from the population. After this, a breeding

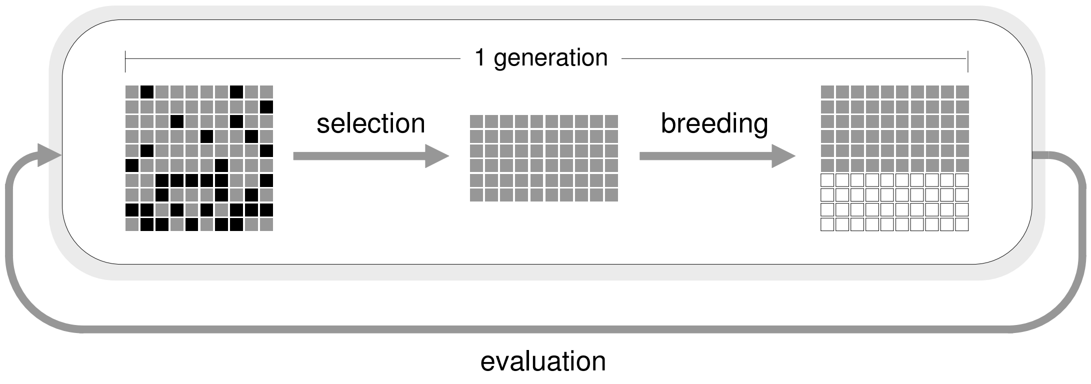


Figure 6.1. One generation of an evolutionary algorithm. Having evaluated the solutions within the population, selection removes the relatively poor solutions (shown black) and breeding generates new solutions (white) from the surviving, relatively good, solutions (grey).

process fills the vacated population slots with new candidate solutions which it derives from existing solutions. At this point the population consists only of relatively fit solutions from the initial population and their derivatives. Accordingly, it is expected that the average fitness of the population will have increased. The process of evaluation, selection, and breeding is repeated over and over again — with hopefully a higher average fitness after each iteration — until either the population contains an optimal solution, or the entire population *converges* upon sub-optimal solutions. Figure 6.1 illustrates this process.

Different classes of evolutionary algorithm differ in the way in which they represent solutions and the way in which they derive new solutions from existing solutions. Individual algorithms also differ markedly in the size of populations which they use, the way in which they carry out selection, and in the proportion of the population which they replace during each selection-breeding cycle. It is common to classify particular evolutionary algorithms as being either genetic algorithms [Holland, 1975], evolution strategies [Rechenberg, 1973], evolutionary programming [Fogel et al., 1966], or genetic programming [Koza, 1992]: although this form of classification arguably introduces artificial barriers to common issues. Whilst this thesis is concerned primarily with genetic programming, the following chapters also make significant mention of genetic algorithms; and for this reason they are briefly reviewed in the following section.

6.1.1 Genetic Algorithms

The genetic algorithm (GA) is an evolutionary algorithm which mimics both the representation and variation mechanisms of biological evolution. A GA candidate solution is represented using a linear string in analogy to a biological chromosome. Accordingly, GA practitioners use biological terms to describe the components of candidate solutions: whereby each position within a GA chromosome is known as a gene locus (or just a gene) and its value is an allele. Historically, GA chromosomes are fixed length binary strings (although some GAs use variable length strings and higher-cardinality alphabets — including real numbers). New solutions are constructed from existing solutions using operators whose effects resemble the action of mutation and recombination upon biological chromosomes. Mutation operators randomly change the allele of a particular gene locus whereas crossover recombines groups of contiguous genes from two or more existing chromosomes. The mechanics of individual GAs vary considerably. However, most GAs are *generational*: meaning that the entire population is replaced during each iteration; and most have a selection mechanism that allocates each solution's contribution to the next generation roughly in proportion to its relative fitness in the current generation. Consequently, the best solutions have their genes well represented in the next generation whilst the worst solutions tend to give no contribution to the next generation.

Crossover is traditionally considered the dominant search operator in GAs, and mutation is considered a background operator which replenishes genetic diversity lost during selection. Crossover proceeds as follows: two chromosomes are aligned, a number of crossover points are selected randomly along the chromosome lengths, and groups of genes between every other pair of crossover points are swapped between the two chromosomes. Genetic linkage is said to occur between alleles at different gene loci that remain together following recombination. Given the way that crossover works, genetic linkage is most likely to occur between alleles at gene loci which have proximal positions within the chromosome. This means that GAs must function as a result of propagating small groups of alleles found close together within chromosomes: groups that are known as *building blocks* within the GA literature [Goldberg, 1989]. However, this is only useful if chromosomal building blocks correspond to building blocks found within the problem domain. If this is not the case, or particularly if the problem's building blocks are represented by groups of highly spaced alleles, performance is likely to be impaired. Such problems can sometimes be solved by re-arranging gene loci within the chromosome. GAs which do this automatically are known as *linkage learning* GAs and are discussed in section 7.5.

6.2 Conventional Genetic Programming

Genetic programming (GP) is a generic term used to mean an evolutionary computation system which is used to evolve programs. Early forms of GP can be traced back to Friedberg [1958] and Cramer [1985]. The first GP system to bear the name 'Genetic Programming' was devised by Koza[1] [Koza, 1992]; and this, by virtue of being the first successfully applied and widely recognised form of GP, forms the basis of conventional GP systems.

Koza's genetic programming represents programs by their parse trees. A parse tree is a tree-structure which captures the executional ordering of the functional components within a program: such that a program output appears at the root node; functions are internal tree nodes; a function's arguments are given by its child nodes; and terminal arguments are found at leaf nodes. A parse tree is a particularly natural structure for representing programs in LISP; the language Koza first used for genetic programming. This is one reason why the parse tree was chosen as a representation for genetic programming. A problem, in GP, is specified by a fitness function, a function set, and a terminal set. The function and terminal sets determine from which components a program may be constructed; and the fitness function measures how close a particular program's outputs are to the problem's required outputs. The initial population is filled with programs constructed randomly from components in the function and terminal sets[2].

Conventional GP derives new programs from existing programs using three different methods. Point mutation randomly changes the functions or terminals found at a proportion of the nodes within a parse tree. The number of nodes to be mutated

[1]Hence the term genetic programming is also sometimes used to refer to versions of Koza's GP used to evolve entities other than programs: for example, engineering structures; some of which can be described with the same representation that Koza's GP uses to represent programs.

[2]Although in most implementations, the programs in the initial population are biased towards certain shapes and sizes in order to maximise search space coverage.

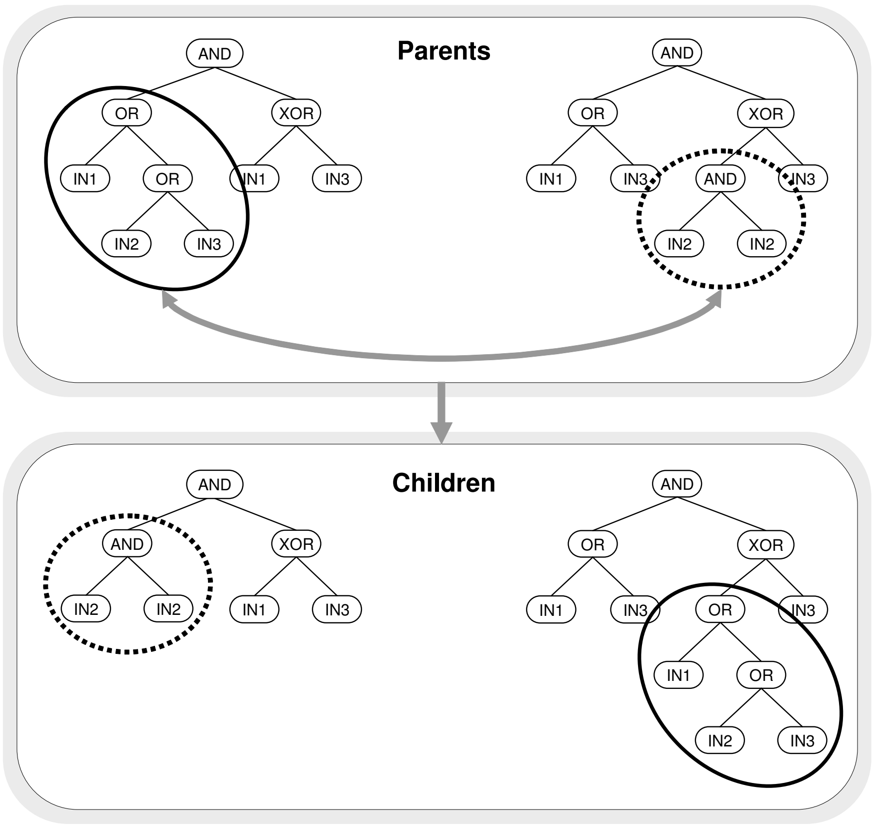


Figure 6.2. Sub-tree crossover creating new programs from existing programs. Sub-trees are selected randomly from two existing parse trees and are then swapped to produce child parse trees.

are determined by a probabilistic parameter called the mutation rate. Sub-tree mutation, by comparison, randomly changes entire sub-trees; building new sub-trees out of randomly chosen functions and terminals. Sub-tree crossover, which is traditionally considered the most important GP variation operator, constructs new program parse trees by swapping randomly chosen sub-trees between existing parse trees: an example of which is depicted in figure 6.2.

Genetic programming has been applied within a huge variety of problem domains. A number of these are used primarily for comparing the performance of particular GP approaches: algebraic symbolic regression, for example. In other domains, GP has been used to re-discover solutions which had previously been invented by humans; as well as discovering new solutions of comparable performance (see, for example, [Miller et al., 2000]). In yet other domains, GP has evolved solutions to problems which had not previously been solved by humans. This includes certain quantum computing algorithms and problems in biological understanding (e.g. [Koza, 2001]).

6.3 Problems with Recombination

Despite its successes, GP is known to have behavioural problems which limit its applicability and performance. Most significant of these is the manner in which parse trees are affected by sub-tree crossover. First, it has been argued that sub-tree crossover does not perform meaningful recombination and does not therefore aid search performance. This argument is reviewed in this section. Second, sub-tree crossover is thought instrumental in causing program size bloat; an issue which is discussed in the following section.

In [Koza, 1992] it is argued that sub-tree crossover is the dominant operator within genetic programming: responsible for exploiting existing genetic material in the search for fitter solutions. However, experimental evidence [Angeline, 1997, Luke and Spector, 1997, 1998] suggests otherwise. In [Angeline, 1997], the author compares the performance of sub-tree crossover against an operator — headless chicken crossover — which resembles crossover, but which actually carries out a behaviour more akin to sub-tree mutation. This operator works by performing a sub-tree exchange between an existing parse tree and a randomly generated parse tree of a similar size. Across three problem domains, the difference between the performance of sub-tree crossover alone and headless chicken crossover alone is statistically insignificant: suggesting that the behaviour of sub-tree crossover is no better than that of macro-mutation. However (despite what the author suggests) the behaviour of sub-tree crossover is not equivalent to headless chicken crossover; given that sub-tree crossover is only able to use genetic material which already exists within the population. It could be argued that sub-tree crossover performed badly in these experiments because of the lack of mutation, upon which it would ordinarily rely to introduce new genetic material and maintain diversity within the population.

However, more recent work by Luke and Spector [1997, 1998] also suggests that sub-tree crossover performs little better than macro-mutation. Luke and Spector compare runs with 90% sub-tree crossover and 10% sub-tree mutation with runs of 10% sub-tree crossover and 90% sub-tree mutation across a range of problem domains and parameter values. Their results indicate that whilst crossover does perform slightly better than sub-tree mutation overall, the benefit is slight and in most cases the difference in performance is statistically insignificant. The authors also note that for certain prob-

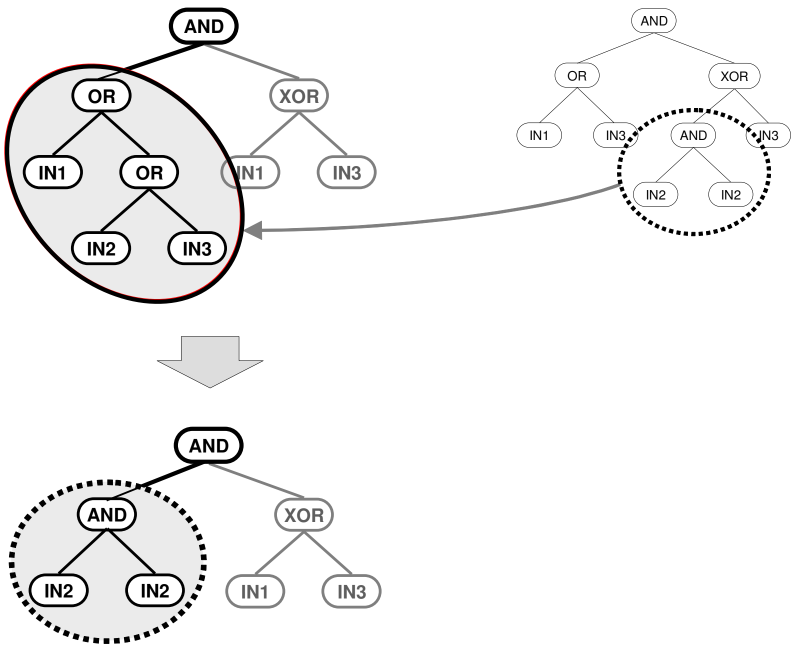


Figure 6.3. Loss of context following sub-tree crossover.

lems (including symbolic regression), crossover performs better for large populations and few generations whilst sub-tree mutation performs better for small populations and large numbers of generations. However, this does not hold for all problems.

This poor performance has perhaps less to do with crossover than it has to do with the parse tree representation. For GAs, it is fairly well accepted that crossover improves performance for problem domains with reasonably low levels of epistasis and with a reasonable arrangement of genes within a chromosome i.e. in situations where building blocks can be readily processed by crossover. After all, recombination is logically a useful operation — it enables co-operative evolution by allowing information exchange within a population. Furthermore, it appears to play a primary role within eukaryotic evolution.

Sub-tree crossover is a natural recombination operator for parse trees. However, by exchanging randomly chosen sub-trees between programs, it does not carry out a logically meaningful operation. This is illustrated in figure 6.3. In this example, a random sub-tree is selected in an existing parse tree and is replaced by a sub-tree which is randomly selected from another parse tree. These parent parse trees have significant shared behaviours: both apply an `AND` function to the outputs of `OR` and `XOR` functions, and both have a left-hand branch which calculates the `OR` of a number of input terminals; so in principal it would seem that they have compatible information to share. However, because the exchanged sub-trees are selected from different positions and have different size, shape and functionality, the behaviour of the resulting child solution bears little resemblance to either parent. The behaviour of each of these programs is determined by the output of the `AND` function at the top of the program. The output of a function depends upon both the function it applies and upon its *input context*: the inputs to which it applies the function. Consequently, if its input context changes considerably, then so does its output. Given that most possible programs will generate very poor solutions to a problem, and that the parent programs are presumably relatively good at solving the problem, a considerable change in output behaviour is likely to result in a program with low fitness. In the example, one of the `AND` function's inputs changes from being the `OR` of three inputs to the `AND` of a single input with itself: leading to a significant change in output behaviour.

Since it is unlikely that sub-tree crossover will exchange sub-trees with similar position, size, shape, or behaviour, most GP sub-tree crossovers will lead to child programs which are considerably less fit than their parents. In essence, this happens because a component's context is recorded in terms of its position within a parse tree; and because sub-tree crossover does not preserve the positions of components. Later in this thesis it will be argued that this failing is as much the fault of the program's representation as it is the fault of the sub-tree crossover operator.

6.4 Solution Size Evolution and Bloat

Parse trees are variable length structures and, in the absence of any mechanisms of constraint, may change size freely during the course of evolution. Unfortunately, in GP there is a tendency for parse trees to grow, rather than shrink, over time. This leads to a phenomenon called *bloat* whereby programs become larger and larger without significant improvement in function. In standard GP, program bloat has nearly quadratic complexity [Langdon, 2000a]. This causes a number of problems. First, it places a strain on both storage and executional resources. Second, it leads to programs which are large, complex, inefficient and hard to interpret. Third, bloat usually takes the form of an increase in non-functional code; and given that this code comprises most of the program, it becomes the target of most crossover and mutation events: protecting the functional code from change and ultimately reducing the effectiveness of evolution. The role of non-functional code in GP is discussed in more detail in section 7.4.1. Although the exact cause of bloat is not known, a number of mechanisms have been identified which appear to contribute to the effect. These are replication accuracy, removal bias, search space bias, and operator bias; and are discussed below.

The *replication accuracy* theory of bloat [Blickle and Thiele, 1994, McPhee and Miller, 1995, Nordin and Banzhaf, 1995] follows from the protective role of non-functional code outlined above. Large programs containing a lot of non-functional code are more likely to survive crossover or mutation with no change to their function than smaller programs or programs with less non-functional code. Therefore, these programs have a higher replication accuracy. Given that their behaviour is less likely to change as a result of crossover; and given that behavioural changes resulting from crossover tend to be negative; these programs are more likely to be the parents of viable children; and hence will become better represented in the next generation than smaller programs and programs with less non-functional code. Consequently, there is selective pressure for programs to become larger. Furthermore, child programs derived from programs with high replication accuracy are themselves likely to be good replicators (they have high effective fitness, to use Banzhaf et al.'s [1998] terminology) and will pass this trait on to their descendants.

The *removal bias* theory of bloat [Soule et al., 1996] also appeals to the disruptive effect of sub-tree crossover. Following crossover, the behaviour of a child program is more likely to be like its parent (and therefore more likely to be viable) if the sub-tree being replaced occurs near the bottom of the parent parse tree. This is because: (a) components lower in a parse tree have less influence upon the program's outputs; and (b) non-functional code tends to occur at the bottom of parse trees. Consequently, the sub-tree which is replaced is likely to have below average size. However, there are no similar constraints upon the size of the sub-tree with which it is replaced; meaning that the existing sub-tree is more likely to be replaced with a larger sub-tree. Accordingly, viable child programs are more likely to be larger than their parents.

The *search space bias* theory of bloat [Langdon and Poli, 1997] does not appeal to the behaviour of variation operators. To use Langdon and Poli's [2002] own words: "above a certain size threshold there are exponentially more longer programs of the same fitness as the current program than there are of the same length (or shorter).” Accordingly, it is more likely that evolutionary search will explore those programs which are longer than those which are of the same length or shorter. A similar argument is made by Miller [2001], who believes that bloat is caused by evolution exploring a program’s neutral variants: most of which will be larger than the existing program. The *operator bias* theory of bloat suggests that certain variation operators aggravate this effect through innate imbalances which cause them to sample larger programs (see, for example, [McPhee and Poli, 2001]).

6.5 Expressiveness

Expressiveness is the capacity for a representation to express appropriate programs. Evolvability is the capacity for a representation to evolve appropriate programs. For GP, these two issues are related: it is not possible to evolve a program which can not be expressed and it is not possible to express a program if it can not be evolved by the GP system. Clearly, both of these issues are important. For GP to be successful, it must be able to both search the appropriate region of the search space, i.e. express programs in that region; and be able to get to the appropriate region of the search space from those areas covered by an arbitrary starting population, i.e. evolve programs in that region. Furthermore (and certainly in the software engineering community), expressiveness is seen as a property which encourages evolvability; since if a program can be expressed, it can also be evolved by making a certain number of changes to an existing program. Nevertheless, expressiveness in itself is not sufficient to produce evolvability; since although it may make it possible to evolve a certain program, it does not necessarily make it easy to evolve the program.

Despite these relations, in GP research expressiveness and evolvability are often treated as different, sometimes conflicting, design goals. Improving expressiveness can increase the scope of GP by making it possible to evolve a greater range of programs or particular types of programs. However, in doing so it changes the search space of GP; and this can make it harder to evolve a program to solve a particular problem. Indeed, for a particular kind of problem, there is probably a trade-off between the expressiveness of the representation and its evolvability — even though in practice a knowledge of the problem domain would be required to make this trade-off.

Nonetheless, expressiveness is an important topic in GP and it does share a number of issues in common with the study of evolvability in GP. In recognition of these facts, this section provides a flavour of some of the approaches which have been taken to improve the expressiveness of GP. However, it does not attempt to be an exhaustive reference and, although the issue of evolvability is discussed at length in the next chapter, it does not attempt to artificially separate the concerns of expressive and evolvable representations.

So far the term *representation* has been used somewhat generically to refer to the way in which a program is presented to the evolutionary mechanism of the GP system. For the remainder of this chapter, the term is used in a more restricted sense to mean the format or structure of the program rather than the language it is written in. The term *representational language* (taken from Altenberg [1994]) is used to refer to the language within which a program is expressed. This section is organised into two parts; separating those approaches which are primarily motivated by a desire to change the representational language from those which are primarily motivated by a desire to change the representation of GP.

6.5.1 Linguistic Approaches

This section introduces a selection of GP approaches which use languages or linguistic elements not normally found in GP. The section is split into three parts. The first part introduces techniques which introduce a notion of type to GP. The second part discusses the relative merits of using memory and state within GP. The third part presents GP systems which use particular kinds of programming language.

Type Systems

The use of type systems to limit evolutionary and genetic behaviours was first explored by Koza [1992] in the form of constrained syntax structures. Most GP systems are based around the idea of closure: that all data within a program can be interchanged freely between nodes; constraining the data to be of one type. Introducing typed data involves re-writing tree generation and genetic operator routines such that generated and modified programs always obey the rules of the type system. Koza's ideas were extended in [Montana, 1994, 1995] by Strongly-Typed GP (STGP), a system allowing variables, constants, function argument and return values to be of any type, so long as the exact types are defined in advance. Generic functions were introduced as a means of avoiding re-writing functions for each data type. When used in a program, these are instantiated (and remain instantiated) with typed arguments and return values.

By introducing type constraints and limiting evolution to generating legal trees, STGP significantly reduces the search space. In Montana's experiments, STGP was shown to produce superior results to standard GP across a range of moderately hard problems. This form was reproduced in [Haynes et al., 1996], where STGP was applied to a difficult agent-cooperation problem. The programs evolved were significantly better than those produced by GP. In addition to being more effective, the STGP programs also demonstrated greater generality and readability. The reduced search space meant that they evolved significantly faster than standard GP programs. However, this reduced search space also suggests potential problems in domains where the optimal solution is outside of the constraints imposed by the type system. Here, STGP will not find the optimum, and it will not be obvious in advance whether the optimum can be found by STGP.

Another approach to introducing types to GP can be found in Spector's [Spector, 2001, Spector and Robinson, 2002] PushGP; a form of GP based upon Spector's custom-designed Push language[3]. Push is a stack-based language which maintains separate stacks for data of different types. Functions, whilst generic, operate upon arguments at the top of whichever stack is currently identified by the system's `TYPE` stack; a special stack which contains type references. Programs comprise a linear sequence of arguments and functions. Because the stack system de-couples arguments from the functions which use them, it is no longer possible to apply incorrectly-typed arguments to a function; and therefore there is no need to use special syntax-preserving recombination operators. PushGP performs better than GP upon even-n-parity prob-

[3]The Push language is actually designed to support auto-constructive evolution systems, such as Pushpop, in which programs describe and evolve their own reproduction operators. However, this work is outside the scope of this thesis.

lems where $n > 5$; and, more importantly, scales considerably better for increasing n that either standard GP or GP with ADFs (Automatically Defined Functions; which are introduced in section 7.3.1).

Memory and State

Conventional GP has no explicit notion of state. The problems it handles are functional or reactive, based upon simple mappings from input to output. Adding state allows GP to solve harder knowledge-based problems. The earliest attempt at state was Koza's `progn` statement, implicitly handling state via side-effecting terminals. State can be represented explicitly within programs using either abstract variables or indexed memory. Indexed memory, in particular, introduces Turing completeness: and is the motivation behind an approach described by Teller [1994, 1996].

Teller defines memory as an array of integer-holding locations, M-locations wide and holding numbers between 0 and M. The use of M for both limits prevents evolving programs from using out-of-range values, since a stored number might be used as an index elsewhere in the program (and vice versa). This is simpler, and more natural, than normalising out-of-range numbers. To handle memory-access, two extra non-terminals are placed into the function set. `READ(Y)` returns the value at address `Y` in the memory. `WRITE(X,Y)` places `X` at address `Y`, returning the previous value of `Y`. The low-level approach taken by this strategy means that no constraints are placed on how memory should be used, and in theory allows the emergence of more advanced memory models such as indirection. Teller found a 600% improvement in performance over conventional GP when he applied this system to a problem requiring state information. However, optimal performance is only achieved if the memory is the right size for the problem. If M is too small, then either there is too little state space or the state variables become too close together in memory[4]. If M is too large, then information is easily lost because there is little chance of a read and a write using the same memory location.

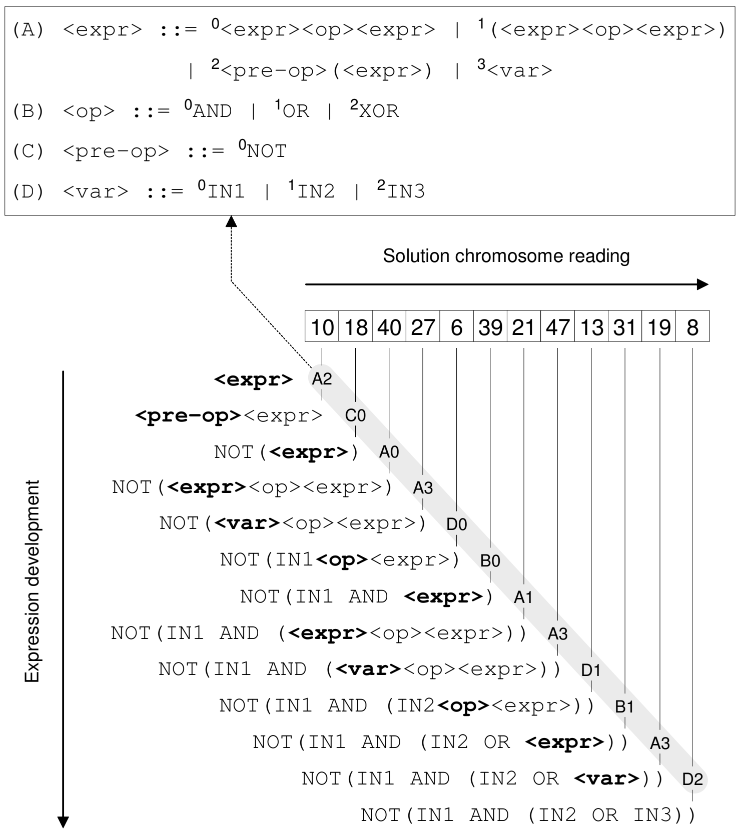
In [Langdon, 1995], Teller's scheme is used to evolve data structures. More recently,

[4]This is called the 'tight representation problem', usually found in codes when adjacent states have very different representations. For instance, in binary 7 (0111) is very different to 8 (1000). A similar problem occurs here when state components are forced too close together. Introducing redundancy, in both indexed memory and in codes, alleviates this problem.

Spector and Luke [1996] have taken Teller's indexed memory and used it to confer a notion of culture within an evolving GP system. Culture is the non-genetic transfer of information between individuals. In natural systems, this provides a means of communication, both within and across generations, which is faster and more open than normal genetic evolution. In this approach, culture is expressed as a common indexed memory which any member of any generation can access using Teller's standard functions. Spector found the use of culture to improve performance upon a range of reactive problems. In theory, culture should allow various co-operative or competitive strategies to evolve. Furthermore, it allows an individual to communicate with itself across generations and even across fitness cases. Spector also noted that, for all the reactive problems he tried, Teller's GP performed worse than standard GP without memory; suggesting that memory should only be used for problems which cannot be solved without it. Presumably this is due to the increased size of the search space caused by the presence of the extra `READ` and `WRITE` functions.

Language

A number of GP systems attempt to evolve programs in specific languages, or specific types of language. Yu [Yu and Clack, 1998, Yu, 1999], for instance, describes a GP system based upon a functional programming approach. The motivation behind this approach was to make use of the implicit structural abstraction available within functional languages. Structure abstraction is based upon the use of higher-order functions; a motif common in functional programming where a function is passed as an argument to another function. The function passed is defined as a λ-abstraction: an anonymous reusable module. By introducing a minimal type system, crossover is forced to preserve the bi-layer λ-abstraction/higher-order function motif. Structure abstraction occurs because genetic manipulation still allows the content of both layers to change. During evolution, λ-abstractions are generated dynamically. Higher-order functions typically apply a λ-abstraction recursively over a data structure; an effect called implicit recursion. This high-level behaviour, linked to controlled use of recursion, allows the complexity of some hierarchical problems to be reduced to a simple linear problem; though the success of this approach depends upon user-definition of appropriate higher-order functions.



```
(A) <expr> ::= ⁰<expr><op><expr> | ¹(<expr><op><expr>)
             | ²<pre-op>(<expr>) | ³<var>
(B) <op> ::= ⁰AND | ¹OR | ²XOR
(C) <pre-op> ::= ⁰NOT
(D) <var> ::= ⁰IN1 | ¹IN2 | ²IN3
```

Solution chromosome reading
10 18 40 27 6 39 21 47 13 31 19 8
Expression development
<expr> A2
<pre-op><expr> C0
NOT(<expr>) A0
NOT(<expr><op><expr>) A3
NOT(<var><op><expr>) D0
NOT(IN1<op><expr>) B0
NOT(IN1 AND <expr>) A1
NOT(IN1 AND (<expr><op><expr>)) A3
NOT(IN1 AND (<var><op><expr>)) D1
NOT(IN1 AND (IN2<op><expr>)) B1
NOT(IN1 AND (IN2 OR <expr>)) A3
NOT(IN1 AND (IN2 OR <var>)) D2
NOT(IN1 AND (IN2 OR IN3))

Figure 6.4. Grammatical evolution. A series of numeric values are translated into an expression. At each stage, the current grammar rule is determined by the left-most non-terminal (highlighted in bold) and the transition is given by the modulus of the current chromosome value divided by the number of transitions in the current rule. For example, at the beginning of translation; rule A is determined by `<expr>` and transition 2 (`<expr>::=<pre-op><expr>`) is given by the remainder of 10/4.

A more general approach to specifying the language in which programs are represented is taken by grammatical evolution [Ryan et al., 1998]; where the representation language is described by a Backus Naur Form grammar and programs are expressed as a series of grammar transitions. An example of a grammatical evolution solution chromosome, the language in which it is written, and the process by which it is translated into a program expression, is shown in figure 6.4. Note that if the program expression still contains non-terminals when the end of the solution chromosome is reached, translation returns to the beginning of the chromosome. This can presumably lead to very efficient solutions for a limited class of problems; although in the example, a chromosome of length 12 is needed to describe an expression containing 6 components. Nevertheless, grammatical evolution is a popular approach and has been shown to out-perform conventional GP upon certain problems.

6.5.2 Representational Approaches

This section describes three different, yet related, approaches to adapting the representation of evolving programs in GP. The first approach involves changing the architecture of the program. The second targets the executional structure of programs. The third uses developmental representations.

Program Architecture

Perhaps the simplest adaptation of the standard GP representation is to use a graph rather than a tree to express the connectivity of a program. PDGP (Parallel Distributed Genetic Programming) [Poli, 1997] and cartesian GP [Miller and Thomson, 2000] both take this approach: representing a program as a directed graph in which each node is either a function or a terminal. Both systems have significant commonality: both have mechanisms to prevent cycles (when appropriate) and both allow nodes to exist in the representation but not have any connections to other nodes (the significance of which is discussed in section 7.4.3). However, the motivation behind these systems is different. PDGP aimed to use a program model which reflects the kind of distributed processing that occurs in neural networks. Cartesian GP was originally designed to evolve both the functionality and routing of circuits on FPGAs: requiring a representation in which components were laid out on a grid — and which incidentally could be interpreted as a graph structure. Both methods show performance improvement within certain problem domains; and both tend to evolve smaller, more efficient, programs (a behaviour which is discussed in more detail in section 7.3.2).

A number of GP systems [Angeline, 1998a, Silva et al., 1999, Ferreira, 2001] take a two-layer approach to representation in which one layer describes a collection of parse trees and a higher layer describes how these parse trees interact to perform some unified processing. The earliest of these is Angeline's MIPs (Multiple Interacting Programs) [Angeline, 1998a] representation. A MIPs net (named to reflect its structural similarity to a neural network) can be interpreted as a graph in which each node corresponds to a parse tree. A number of nodes are designated output nodes; and the outputs of their corresponding parse trees determine the output behaviour of the program. Connections between nodes are realised by references to the outputs of other nodes appearing internal to parse trees. In theory, these connections may be feed-forward or recurrent and have synchronous or asynchronous updates; although Angeline limited his experiments to synchronous recurrent MIPs nets. Applied to a number of problems, his approach demonstrated better performance and better solution generality. Applied to a problem whose solution required memory, the system evolved a particularly efficient solution which made use of the representation's implicit ability to store state. Similar observations have been made by Silva et al. [1999] in the context of their Genetically Programmed Network approach; which uses a representation broadly similar to Angeline's MIPs representation. Ferreira's GEP (Gene Expression Programming) [Ferreira, 2001] also makes use of multiple parse trees; though the meaning and connectivity of these parse trees is determined by the fitness function and is not evolved by the system. Perhaps what is most interesting about GEP is the way in which parse trees are encoded: a pre-fix variant which the author believes to be particularly supportive of variation operators. GEP also shows significant performance gains over standard GP (although the author's 'marketing' style of writing makes it hard to work out exactly why this is the case): and is the only one of these approaches to have had a notable impact on the GP community; even though the other two approaches are perhaps more behaviourally interesting.

Executional Structure

Many of the GP systems introduced in section 6.5.2 use representations which implicitly change the manner in which a program's executional structure is represented. In conventional GP, the effect of a component upon execution is determined by its location within a parse tree. By comparison, in PushGP there is considerable decoupling between the location of an instruction or argument in the representation and its temporal role within the program's execution. This occurs because arguments and results can be stored within stacks and used later; or even not be used at all. A similar argument applies to other forms of GP which use linear representations; such as AIMGP[5] (Automatic Induction of Machine Code with Genetic Programming) [Nordin, 1994] which represents programs as a sequence of machine code instructions, each of which

[5]AIMGP and its predecessors were originally developed to make the evaluation phase of GP faster. Nevertheless, such approaches also have benefits for evolvability. These are discussed in proceeding chapters.

is able to save and load values from register locations. In this case the registers provide the means for decoupling instruction location from instruction behaviour. In fact, any form of memory or state within any kind of representation can have some effect upon the executional structure of a program: although in representations such as parse trees this effect is relatively small.

Whilst for most representations executional ordering emerges implicitly from the connectivity and behaviour of components, some GP systems use representations which express execution ordering explicitly. PADO (Parallel Algorithm Discovery and Orchestration) [Teller and Veloso, 1996] is a complex learning system based upon the principles of genetic programming. PADO uses a graph-based representation in which each node describes some processing behaviour and, depending on the result, carries out some judgement behaviour which decides which outgoing path execution will continue along. Unlike normal GP, which typically describes fixed expressions, PADO describes structures which are much more akin to computer programs: containing complex flows of execution which depend upon the results of internal calculations. PADO has been used for object recognition tasks, giving an impressive level of performance. GNP (Genetic Network Programming) [Katagiri et al., 2000, Hirasawa et al., 2001] is a GP approach with a similar representation to PADO; but which also expresses delays within and between program nodes. GNP is used to model complex dynamical systems; out-performing conventional GP on a complex ant-foraging problem [Hirasawa et al., 2001].

Developmental Representations

For most of the approaches described above, a program's representation directly describes a program. A developmental representation, by comparison, describes *how* a program or other artifact is constructed. It only indirectly describes *what* is constructed. In the long term, it would seem that development is key to overcoming the problems currently associated with scalability in evolutionary computation. For direct (non-developmental) GP encodings, representation length is proportional to program length. Typically this means that representation length grows in proportion to problem difficulty, and typically this means an above-linear rise in the time and space required for evolutionary search — not to mention the fact that the time required to evaluate solutions also often grows at an above-linear rate. With developmental encodings, however, representation length normally grows at a below-linear rate relative to program length: and consequently could lead to better scalability and better evolutionary performance. However, developmental representations for evolutionary computation are still in their relative infancy and are yet to show a demonstrable performance advantage. Nevertheless, research in this area has led to a number of interesting ideas and some promising insights.

Developmental representations are based around the idea of re-writing systems: starting from some initial configuration, a series of re-writing rules transforms this configuration through a number of steps which eventually lead to the developed artifact. Grammatical evolution is a simple example of this approach. However, many approaches are modelled upon biological growth processes [Boers and Kuiper, 1992, Gruau, 1994, Koza et al., 1999, Haddow et al., 2001, Downing, 2003, Miller and Thomson, 2003]. A number of these have been applied to genetic programming (especially circuit evolution) [Haddow et al., 2001, Downing, 2003, Koza et al., 1999, Miller and Thomson, 2003]. Miller and Thomson [2003] use a developmental model in which a single starting 'cell' is iteratively replicated to generate a pattern of interacting cells in which both the pattern of interaction and the behaviour of each cell is decided by a single evolved cartesian GP program. Following development, the cellular pattern is interpreted as a digital circuit where interactions represent wires and cellular behaviours represent gates. Whilst distinctly unsuccessful from a performance perspective, this system is apparently capable of evolving partially generalised solutions to the even-n-parity problem; where n is determined by the number of iterations allowed during circuit development.

Downing [2003] describes a developmental program representation based upon Spector's Push language (described in section 6.5.1). In Downing's approach, which is based upon a cellular colony metaphor, both development and execution are determined by a single Push program. Each cell has its own code and data stacks. The generation of new cells and interaction between cells is achieved through special language primitives. Inter-cell communication is achieved through primitives that redirect function outputs to stacks in other cells. Downing gives examples of how particular Push programs lead to emergent processing behaviours within the resulting cellular ecologies. Whilst intended to be used within an EC framework, results regarding evolutionary behaviour and performance have yet to be published.

6.6 Summary

Genetic programming (GP) is an evolutionary computation approach to automatic programming: using a computational model of evolution to design and optimise computer programs and other executable structures. GP is mechanistically similar to the genetic algorithm and other population based search algorithms. Whilst GP has been successfully applied within a wide range of problem domains, the method has certain behavioural problems which limit its performance and scalability. Perhaps the most significant of these is the failure of its recombination operator, sub-tree crossover, to carry out meaningful recombination; limiting the capacity for co-operative interactions between members of the population. Sub-tree crossover is also thought to play a substantial role in the un-controlled program size growth phenomenon known as bloat.

In addition to reviewing conventional GP, this chapter has introduced a selection of derivative GP approaches which attempt to improve the behaviour or scope of program evolution by increasing the expressiveness of the representation used to represent programs. The next chapter continues this look at derivative GP approaches by presenting a range of techniques which aim to improve the evolvability of the GP program representation.

7 Evolvability in Evolutionary Computation

This chapter is a review of research aimed at improving the evolvability of the artefacts which are evolved by evolutionary computation techniques. In particular, it attempts to address those issues which are of special relevance to genetic programming. Where appropriate, this includes research done in other fields of evolutionary computation.

7.1 Variation versus Representation

In Chapter 1, evolutionary change was described as the result of sources of variation acting upon the representation of an entity. From this it follows that the nature of evolutionary change might be improved by either (i) improving the ability of variation to enact appropriate change; or (ii) improving the ability of the representation to accept appropriate change. Both of these are valid. Nevertheless, in this thesis, emphasis is clearly placed upon the second of these approaches. This is for two reasons.

First, whilst variation mechanisms are an important part of biological evolution, their behaviours appear relatively simple when compared to the rich organisation, developmental mechanisms, and behavioural scope of biological representations. Even recombination, which is under evolutionary control, carries out a non-deterministic behaviour whose evolutionary effect is determined primarily by the response of the representation. In looking for biological guidance concerning evolvability it would seem, therefore, that more information could be gleaned by looking at biological representations rather than the sources of variation within biological evolution.

Secondly, it is common knowledge in computer science that if the same effect can be achieved by improving the way information is represented or by improving the way information is operated upon, better generality can be achieved by adapting the representation. For instance, if the information in a database is structured in a way that makes certain information difficult to manipulate, it would be considered better in the long run to improve the way the database is structured rather than improve the complexity of queries used to manipulate the information. Likewise, in the first instance it would seem better in the long run to change the way an evolving entity is represented rather than the way in which it is manipulated if both are capable of improving the way that it evolves.

Nevertheless, some interesting work has been done in adapting variation operators. This is briefly reviewed in the next section. The remaining sections of this chapter are concerned with existing approaches to improving the evolvability of representations. These are organised according to the manner in which they attempt to introduce evolvability: through pleiotropy, redundancy or removal of positional bias. In part this requires some familiarity with information from the previous chapter and from Chapter 5.

7.2 Adapting Variation

In the last chapter, the relative failure of sub-tree crossover in genetic programming was attributed to the unlikelihood of it carrying out meaningful recombinative behaviours. A number of researchers [Poli and Langdon, 1997, Langdon, 1999, 2000b, Francone et al., 1999, Hansen, 2003a] have looked at the possibility of constraining the behaviour of GP crossover in order to prevent inappropriate behaviours. This has led to a range of homologous crossover operators which attempt to limit genetic exchange to regions of genetic homology. One-point crossover [Poli and Langdon, 1997, 1998], which resembles GA one-point crossover, does this by identifying and using a crossover point which occurs in the same position within both parent parse trees. Uniform crossover [Poli and Langdon, 1998] models GA uniform crossover by identifying regions of common position and shape within both parents and uniformly recombining the nodes within these regions. However, neither of these operators lead to a significant increase in performance and both introduce a considerable processing overhead in identifying homologous regions. Size-fair crossover [Langdon, 1999] uses a different approach and only constrains sub-tree crossover to sub-trees of equal size, though again produces little increase in performance. More recently, Langdon [2000b] has extended this approach by using a formal definition of genetic distance based upon location and size to determine where crossover events may occur. This has produced more encouraging results, although requiring more computational overhead during crossover.

The only homologous recombination operator to produce a sizeable improvement in performance is Francone et al's [1999] sticky crossover which works on linear GP programs. Sticky crossover is a relatively simple homologous operator which limits recombination to groups of instructions with common offsets and common lengths. Francone et al. believe that sticky crossover leads to programs with better generality and higher robustness than standard linear GP programs. Hansen [2003a] shows that sticky crossover offers superior performance across a wide range of regression problems and that the resulting programs contain lower incidences of intronic code (see section 7.4.1 for a definition of intronic code). The relative failure and complexity of tree GP homologous crossover operators when compared to sticky crossover tends to suggest that the linear GP program representation is innately more amenable to meaningful recombination than the parse tree structure of standard GP.

7.3 Introducing Pleiotropy

Recall from section 5.1 that compartmentalisation is the limitation of interactions between different sub-systems. In the context of biological systems, it was suggested that compartmentalisation introduces de-constraint: allowing sub-systems to evolve independently. Nevertheless, it is also believed that pleiotropy — the sharing of genes between sub-systems; conceptually the opposite of compartmentalisation — plays an important role by way of reducing the need to re-evolve the same functionality in different sub-systems. Tree-structured GP representations, by default, confer complete compartmentalisation to the programs they represent: since every function and terminal instance is involved in exactly one sub-expression. However, given limited availability of time and space, many researchers believe there is virtue in introducing pleiotropy to GP systems: reducing the time requirement by preventing the need to re-discover functionality; and reducing the space requirement by preventing the need to store the same sub-expression at multiple locations in the same program. This section introduces two general approaches to introducing pleiotropy to GP: modularity and implicit reuse.

7.3.1 Modularity

Much of the work on modularity in GP has been carried out by Koza [1992, 1994, 1995]. His earliest work took the form of a 'define building block' operator which named sub-trees and allowed them to be referenced elsewhere in the program as zero-argument functions [Koza, 1992]. Later, this idea was extended to the notion of automatically-defined functions (ADFs): argument-taking functions stored in trees which co-evolve with the main routine [Koza, 1994]. The architecture of the program — the number, argument-signatures, and hierarchical limits of these modules — has to be chosen before evolution begins, either by prospective analysis, which requires knowledge of problem-decomposition; over-specification, sufficient modules for any possible needs; affordable capacity, since more modules entail more processing; retrospective analysis, from feedback of previous runs; or by evolutionary selection, which uses an initial population seeded with many different architectures. Results reported in [Koza, 1992] and [Koza, 1994] suggest that use of ADFs can lead to a considerable decrease in the time required to solve certain problems. This is especially true for problems, like parity checkers, whose solutions require a high level of functional duplication. ADFs have also been shown to decrease the size of evolved solutions.

Nevertheless, from an evolutionary perspective, ADFs have distinct limitations. First, it is not possible for a program's architecture to evolve. This places a limit upon modularity and, if the initial architecture is not appropriate, may hinder evolution. Second, there is no obvious mechanism for introducing de-constraint. Change to an ADF will affect the behaviour of the program at each calling instance. Whilst this may sometimes be appropriate, sometimes it will not. For example, suppose an ADF is called from two different sub-trees in a program and, so far, the functionality of the ADF has been beneficial to the behaviour of both sub-trees. Now suppose that in order

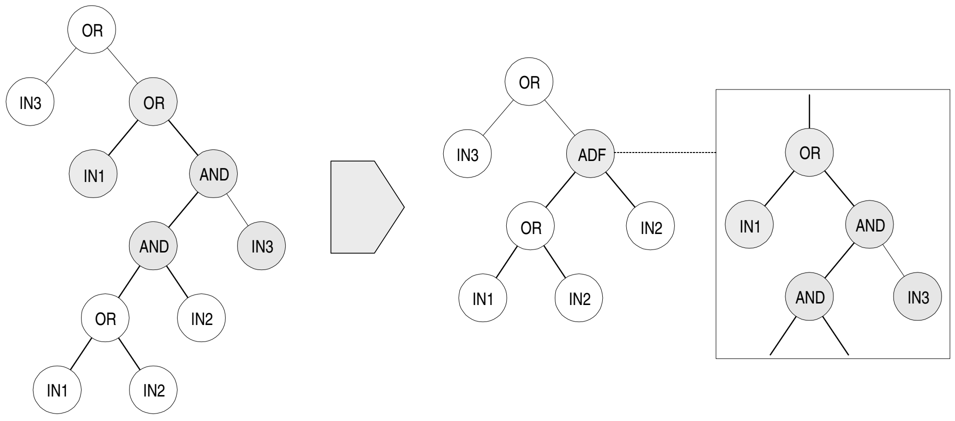


Figure 7.1. Introducing a capacity for pleiotropy using Koza's branch creation operator.

to progress further, the behaviour of the sub-trees must diverge. In this situation, pleiotropy between the two sub-trees in their shared use of the ADF is constraining further evolution since changes to the ADF which would benefit one sub-tree would not benefit the other. The only way of removing this constraint would be for the variation operators to replace at least one of the calls to the ADF with a copy of the code from the ADF: which would require a highly unlikely sequence of matings and crossovers.

To overcome these limitations, Koza [1995] proposed a collection of architecture altering operators inspired in part by the biological process of gene duplication. Gene duplication removes de-constraint by duplicating a pleiotropic gene, allowing the two versions to evolve in different directions. Koza's branch duplication operator does the same by duplicating ADFs. After duplication, some of the calls to the original ADF are randomly replaced by calls to the duplicate ADF. Koza calls this procedure case-splitting to reflect the fact that it can lead to functional specialisation: from one general ADF to multiple more specialised copies of the ADF. Functional specialisation can also be achieved through argument duplication: whereby extra arguments are presented to an ADF by duplicating existing arguments. Following argument duplication, references within the ADF to the existing parameter are updated randomly so that some of them now refer to the new duplicate parameter. Thereafter, the duplicated argument sub-trees below an ADF call will undergo separate evolution: another form of case splitting. Koza also describes operators which attempt to introduce pleiotropy. Branch creation transforms a randomly selected region of code into an ADF: replacing the code at its original position with an ADF function call and preserving the code below the removed code as arguments to the function call (see figure 7.1 for an example). Code elsewhere in the program may then call the ADF, thus introducing pleiotropy. Branch and argument deletion operators attempt to do the opposite to the duplication operators by generalising existing ADFs and arguments and reversing the move towards larger more specialised programs. However, without knowing what the code does, there is little chance that these operators will produce meaningful code, let alone a generalisation.

Other approaches to modularity in GP derive from an engineering viewpoint. In software engineering environments, modules are stored in libraries that are shared between programs. Over time new modules are added to libraries and existing modules are improved or possibly subsumed by new modules. The earliest example of a library approach in GP is Module Acquisition (MA) [Angeline, 1994]. In MA, a compress operator randomly selects blocks of code to place in a global library where they may be referenced by any member of the population. However, since there is no selection for modules with useful (or even any) functionality, MA's library often only succeeds in propagating poor or non-functional blocks of code from one program to another. A more successful library-based approach to GP modularity is Rosca and Ballard's Adaptive Representation through Learning (ARL) [Rosca and Ballard, 1996] (and to a lesser extent, the earlier Adaptive Representation [Rosca and Ballard, 1994]). Central to their approach is the idea that the use of subroutines reduces the size of the search space by forcing the evolutionary mechanism towards productive regions. By steadily increasing the level of complexity within elements of the representational language (i.e. building programs out of high-level functions rather than primitives), the search space can be divided and conquered. However, this requires that building blocks be of high quality, since high-level functionality depends upon low-level functionality [Rosca and Ballard, 1995]. ARL attempts to identify high-quality blocks of code using two criteria: differential fitness and block activation. Differential fitness is used to identify which programs to extract code segments from, and block activation is used to identify which code segments to extract. Differential fitness is a measure of how much fitter a solution is than its least fit parent. If a program has high differential fitness, then it is likely that it contains a new fit block of code which was not present in its parents. Within a program, some blocks of code are more active than others, and presumably more useful. The most active blocks from the most differentially-fit parents are called salient blocks, and these are the targets for re-use. Once programs with the highest differential fitnesses have been identified, salient blocks are detected by logging the frequency of activation of the root nodes of blocks. Before these are stored separately as modules, they are generalised by replacing random subsets of their terminals with variables, which are provided by arguments in function invocations. Once they are stored, they enter competition with other subroutines. Subroutines have utility value, the average fitness of all programs which have invoked the subroutine over a number of generations. Invocation is either direct, by programs, or indirect, by other subroutines. In the latter case, the lower-level subroutines receive a reward each time the higher-level subroutine is called, meaning that essential low-level routines have a good chance of survival. Subroutines with low utility value are periodically removed from storage, textually replacing each of their function invocations in calling programs.

7.3.2 Implicit Reuse

Implicit reuse it an example of how a degree of reuse may be achieved purely through a change in representation. Unlike modularity, implicit reuse is not an intentional approach to reuse; but rather a natural by-product of representations which allow multiple references to a single sub-structure. The best examples of these are graphical representations where nodes can have more than one output connection. Obviously this is not possible with a tree representation, since by definition each node in a tree has exactly one parent node. Both Poli [1997], in the context of PDGP, and Miller and Thomson [2000], in the context of cartesian GP, describe a tendency for the evolutionary process to take advantage of implicit reuse. Given the absence of any variational pressure in this direction, this suggests that a certain degree of pleiotropy is beneficial to evolution: since those programs that exhibit pleiotropy have evidently out-competed programs with no pleiotropy.

7.4 Evolvability through Redundancy

There is considerable interest in the research community in the role that redundancy plays within the representations of evolutionary algorithms. This interest can be classified according to three themes: structural redundancy, coding redundancy (particularly the role of neutrality), and functional redundancy. The organisation of this section reflects these three themes.

7.4.1 Structural Redundancy

In section 5.2.2 structural redundancy was defined as the occurrence of complexity higher than that required to fulfill a phenotypic task. Within biological systems, structural redundancy has been theorised as playing an important role in increasing the evolvability of biological components and structures: either by enabling gradual change or by shielding existing components from disruption by sources of variation. In evolutionary computation, most of the interest in structural redundancy has concentrated on the second of these roles: in particular, the role of non-coding components in providing protection against crossover.

Non-coding inter-genic regions within biological chromosomes are thought responsible for segregating genes and thereby making it more likely that crossover junctions will form between, rather than within, genes. Likewise, according to the exon shuffling hypothesis of gene evolution [Gilbert, 1978], inter-genic non-coding regions (introns) segregate the coding parts of genes, making them more likely to be re-arranged to form new genes rather than be disrupted by crossover events. Within the EC literature, non-coding components of evolving solutions are generally termed introns; even though in most cases EA introns correspond more closely to intra-genic non-coding regions than inter-genic regions.

Introns in Genetic Algorithms.

Some of the earliest interest in introns in evolutionary algorithms came with the introduction of explicit introns into the candidate solution strings of genetic algorithms. Ordinarily, introns do not occur within the candidate solutions of canonical GAs;

prompting a number of researchers [Levenick, 1991, Forrest and Mitchell, 1993, Wu and Lindsay, 1995, 1996a,b] to suggest that introns within GAs could play similar beneficial roles to those which they are hypothesised to play within biological systems. Indeed, results by Levenick [1991] upon a simple model of a biological adaption problem showed that performance improved by a factor of ten when introns were introduced between pairs of genes. However, later results by Forrest and Mitchell [1993] on a problem with explicit hierarchically-defined building blocks showed a slight decrease in performance when introns were introduced.

A more thorough investigation of the benefits of introducing introns to GAs has been carried out by Wu and Lindsay [1995, 1996a]. In [Wu and Lindsay, 1995], the authors confirm the findings of both Levenick [1991] and Forrest and Mitchell [1993]: demonstrating that the benefits of using introns does depend upon the fitness landscape of the problem being solved. Notably, the authors found that introns tended to increase the stability of existing building blocks within solutions whilst reducing the rate of discovery of new building blocks. This suggests that introns improve exploitation during evolutionary search but at the expense of exploration: behaviour which proved more effective upon versions of Forrest and Mitchell's functions with more levels (i.e. harder versions) and with larger fitness gaps between levels. In [Wu and Lindsay, 1996a], the authors extend their investigation to a fixed-length GA representation with 'floating' building blocks, observing that performance improves — and soon surpasses the non-floating representation — as the proportion of introns increases. The authors suggest that this improvement is due to the role of introns in segregating building blocks and supporting linkage learning: a view which is also expressed by Harik [1997] and Lobo et al. [1997] in the context of linkage learning GAs (see section 7.5.1 for more information about these algorithms).

Introns in Genetic Programming.

In genetic programming, almost all representations and representation languages have the potential to express code segments which have no (or very little) influence upon a program's outputs. These 'introns' can be divided into two general classes[1]: syntactic and semantic. Syntactic introns are non-behavioural due to their context within a

[1]Note that this terminology is not standard and conflicts with taxonomies offered by other authors.

program, typically occurring below what Luke [2000] calls an 'invalidator': structures such as `OR(TRUE,X)` and `MULTIPLY(0,X)` where the value of one argument has no influence upon the output of the function due to the value of another argument. Semantic introns, by comparison, are non-behavioural due to their content. Examples of semantic introns are `NOT(NOT(...))` and `ADD(SUBTRACT(...,1),1)`. Introns are sometimes also classified by whether or not they are executed [Angeline, 1998b]. For example, the syntactic intron `X` would be executed in the expression `MULT(0,X)` but would not be executed in the expression `IF(FALSE,X)`. Semantic introns are always executed. Finally, it is possible for programs to contain effective introns: code segments which have very little effect upon a program. For example, in `DIVIDE(X, RAISE(10,100))`, most reasonable values of the effective intron `X` have a negligible effect upon the output.

In [Nordin and Banzhaf, 1995], the authors describe two roles of introns in GP: structural protection and global protection. Structural protection occurs when introns develop around a code segment, segregating it from other blocks of code and offering protection from crossover in much the same way as explicit introns in GAs. Global protection results from introns that offer neutral crossover sites and thereby discourage change to the program at a global level. Structural protection can only be offered by introns that exist at the interior of programs, since they must be placed around other code segments. This is only possible with semantic introns. Neutral crossover sites, however, can only occur below the program's functional code. Syntactic introns, which (in tree GP) are non-functional sub-trees, are therefore the principal source of global protection.

Nordin et al. [Nordin and Banzhaf, 1995, Nordin et al., 1996, Banzhaf et al., 1998] have investigated the benefits of introns in linear GP (see section 6.5.2 for an overview of linear GP). Both semantic and syntactic introns occur readily in linear GP. However, Nordin at al. wished to test whether the behaviour of the system could be improved through the use of explicit introns — which are easily introduced and varied by the system's genetic operators — and found that these, in concert with naturally occurring (implicit) introns, improved both the performance and generalisation abilities of the system. In tree-based GP, by comparison, it is widely believed [McPhee and Miller, 1995, Andre and Teller, 1996, Smith and Harries, 1998, Iba and Terao, 2000] that perfor-

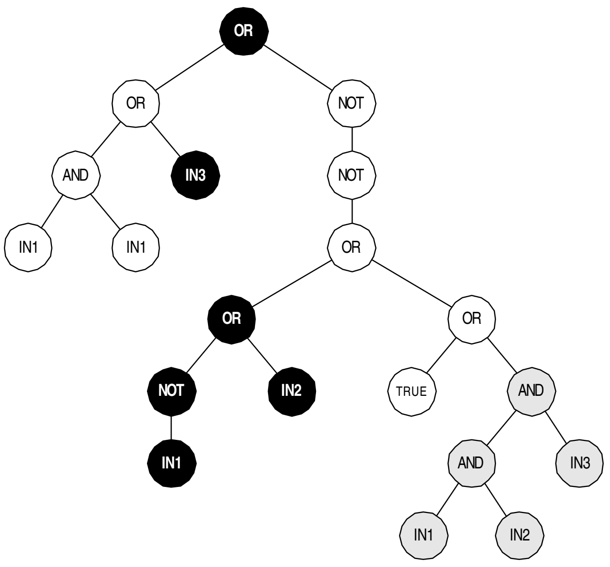


Figure 7.2. A GP expression tree containing introns. White nodes are semantic introns; grey nodes are syntactic introns. Expressed nodes, shown in black, represent the expression `OR(in3,OR(NOT(in1),in2))`. Note how semantic introns can segregate coding areas.

mance is almost always impeded by the presence of introns. For instance, McPhee and Miller [1995] maintain that introns are a major cause of bloat. Andre and Teller [1996] have shown that introns impair search by competing against functional code when size limits are in place. Smith and Harries [1998] found that explicit syntactic introns reduced the performance of GP, and Iba and Terao [2000] found, correspondingly, that removing syntactic introns improved performance.

Apparently, whilst introns are beneficial for linear GP (and GAs), they are detrimental for conventional tree-based GP (see figure 7.2 for an example of introns in a GP expression tree). Both Nordin et al. [1996] and Smith and Harries [1998] believe that this disparity lies within the different roles played by introns in the two different systems. In linear GP, introns convey benefit through their role in structural protection. In conventional GP, introns impair performance through their role in global protection. GP parse trees are recombined by swapping sub-trees. Syntactic introns, which are usually sub-trees, have a natural relationship with sub-tree crossover and are readily built, preserved and transmitted by this operator (a fact observed by Smith and Harries [1998] when trying to prevent the occurrence of introns). Semantic introns, by comparison, usually occur internally within sub-trees; and are more likely to be disrupted rather than constructed by sub-tree crossover. This means that within conventional GP there is a substantial bias towards construction and propagation of syntactic introns over semantic introns: and therefore a substantial bias towards global protection over structural protection. In effect, conventional GP suffers from too much global protection from crossover without gaining any benefits from structural protection. However, global protection can be reduced by limiting the growth of syntactic introns. Successful approaches include the removal of introns (the identification of which can be computationally expensive [Iba and Terao, 2000]) and limiting the behaviour of the crossover operator [e.g. Blickle and Thiele, 1994].

7.4.2 Coding Redundancy and Neutrality

A redundant code is one for which there are more possible representations than there are entities to represent. Accordingly, some entities have more than one representation. Recently, a number of studies have investigated whether or not redundant codes can confer an evolutionary advantage over non-redundant codes in the context of genetic algorithms [Shipman, 1999, Shipman et al., 2000, Shackleton et al., 2000, Ebner et al., 2001, Knowles and Watson, 2002, Rothlauf and Goldberg, 2002, Barreau, 2002].

Work by Shipman et al. [Shipman, 1999, Shipman et al., 2000, Shackleton et al., 2000, Ebner et al., 2001], in particular, has looked at the role of neutrality during the evolution of entities represented by redundant codes. This work has made use of a variety of representations with differing levels of redundancy. These include a direct mapping, where each solution is represented by exactly one binary string; random mappings, where each solution is represented by many un-related binary strings; voting mappings, where binary solution traits are encoded by more than one bit in the binary string and where the trait is determined by voting between these bits; and more complex mappings where binary strings describe state machines whose operation determines the configuration of the solution. Apart from the direct mapping, all of these exhibit a high level of redundancy. However, analysis of the connectivity of their search spaces (where connections are determined by single point mutations) shows that these mappings differ considerably in their patterns of neutrality [Shackleton et al., 2000, Ebner et al., 2001]. Random mappings show very little neutrality, which is to be expected since there is no logical relationship between different encodings of the same solution. Where there is no epistasis (sharing of bits between building blocks), voting mappings exhibit no neutrality. Where there is epistasis, voting mappings exhibit large neutral networks with considerable connectivity between networks. However, some of the neutral networks are relatively isolated. Of the complex mappings, the random Boolean network (RBN) mapping (based upon Kauffman's [1969] model of gene expression) demonstrates the highest level of neutrality: exhibiting large neutral networks with very high connectivity between networks. In one configuration, 58% of mutations are neutral and each encoding has on average 21 non-neutral neighbours accessible through single point mutations.

In [Ebner et al., 2001], these mappings are applied to a number of optimisation problems: a random landscape search, a function with many local optima, and a dynamic fitness function. For all of these problems, performance on mutation-only search correlates with the connectivity of the mappings' neutral networks. The direct mapping is unable to solve the first two problems; in part due to insufficient maintenance of diversity. The non-epistatic voting representation exhibits behaviour which is almost identical to the direct mapping (an observation which is also made in [Rothlauf and Goldberg, 2002]). For the redundant mappings, diversity increases over time. These results have lead the authors to conclude that redundancy can be used to increase the performance of genetic algorithms: so long as the redundancy is organised in such a way that leads to neutral networks that percolate the search space.

However, Knowles and Watson [2002] were unable to reproduce these findings when they compared the performance of direct and RBN mappings upon a variety of more familiar EC problems. Indeed, aggregated across all the problems they tried, RBN mappings lead to worse solution times than direct mappings. Nevertheless, they did find that mappings with high neutrality showed far less sensitivity to mutation rate than non-redundant mappings. The authors speculate that the slower performance of RBN mappings may be due to the time overhead involved in random walks across neutral networks. Whilst these results do not support the conclusions of Ebner et al., they do not preclude the possibility that other redundant mappings might be more effective than the RBN mapping or that neutral networks might be important in solving larger or more rugged problems than GAs with non-redundant encodings are able to solve. Further criticism of the redundant mappings used by Shipman et al. can

Symbol	Non-redundant	Redundant code	
A	000	0 000	1 110
B	001	0 001	1 011
C	010	0 010	1 010
D	011	0 011	1 000
E	100	0 100	1 100
F	101	0 101	1 111
G	110	0 110	1 001
H	111	0 111	1 101

Table 7.1. An example redundant code of the type described in [Barreau, 2002] with one added redundant bit (left) which permutes the symbolic mapping of the coding bits when it is set. Notice the neutrality in the encoding of symbols C and E in the redundant code.

be found in [Rothlauf and Goldberg, 2002]: where the authors argue that complex mappings between representation and solution can lead to low locality; meaning that offspring will tend not to resemble their parents and evolution will tend to be ineffective. However, whilst the results presented in [Ebner et al., 2001] tend to refute this assertion, it does seem likely that the best use of redundancy can not be made through arbitrary mappings with no clear relationship between solution and representation.

Barreau [2002] describes another approach to coding redundancy which introduces redundant coding bits that permute the existing encoding of a solution's building blocks. An example of this kind of redundant code is shown in table 7.1. The emphasis of Barreau's work lies in reducing the number of local optima which can be found during evolution: and thereby improving the adaptive performance of GAs. The best codes reduce the number of local optima by nearly a third on average across a range of symbolic mappings. Application of these codes to problems which have naturally non-redundant encodings shows that there is high correlation between a code's ability to remove local optima and its ability to improve evolutionary performance. On average, across three very different classes of problem, the best codes lead to an improvement in solution time of between two- and four-fold both with and without crossover. Interestingly, almost all redundant codings of this form reduce the presence of local optima (and therefore tend to improve performance) when their behaviour is averaged across a large number of problem instances. One group of codes in particular (whose mappings are based around rotation and symmetry) are guaranteed never to increase the number of local optima on any problem yet exhibit a marginal reduction in the number of local optima across all problems.

Barreau has also investigated the relationship between the neutrality found within his class of redundancy codes and their ability to reduce the number of local optima. However, the relationship is not linear; but rather there is a positive correlation up to a certain level (about 50% of maximum) after which increased neutrality tends to be associated with decreased reduction of local optima. The highest levels of neutrality are found in those codes which offer no or marginal reduction of local optima. Given the correlation between reduction of local optima and improvement in performance, these results would tend to support Knowles and Watson's view that too much redundancy can lead to reduced performance.

According to the terminology defined in [Rothlauf and Goldberg, 2002], the codes discussed above all exhibit more or less uniform redundancy: whereby every solution has roughly the same number of representations. However, it is also possible to define redundant codes in which certain solutions are over- or under-represented. This, according to Rothlauf and Goldberg [2002], leads to search biases which then reduce or increase performance depending upon whether optimal building blocks are over- or under-represented: and should therefore be taken into account when designing redundant codes or introducing redundancy to existing codes.

7.4.3 Functional Redundancy

Functional redundancy occurs when a representation contains more functional information than is necessary to construct the entity that it represents. However, this extra functional information may still have significant evolutionary roles: for instance; (i) it may have been expressed in previous solutions and therefore represents a potential source of backtracking; (ii) it may be passed on to future solutions where it may become expressed; (iii) it is still subject to variation and may therefore evolve into new functionality; and more generally, (iv) it allows a population to maintain genetic diversity even when solutions have converged; and (v) it enables neutral evolution.

In many representations, sources of structural redundancy are also sources of functional redundancy. GP syntactic introns, for instance, consist of code. Whilst this code's meaning is currently irrelevant from a behavioural perspective, it still has a functional meaning and could be involved in any of the evolutionary roles outlined in the previous paragraph. Haynes [1996] has investigated the evolutionary advantage of functional redundancy in GP by constructing a problem in which each sub-tree's role is independent of its position within a parse tree. Sub-trees are not expressed in cases where they describe incomplete, invalid, duplicate or subsumed structures. Haynes found that removing these redundant sub-trees during evolution led to a reduction in performance (the opposite effect to that found by Iba and Terao [2000]): and attributed this to both loss of diversity and loss of protection from crossover. Haynes, however, was particularly interested in the impact of the loss of 'protective backup' caused by the removal of duplicates of expressed structures; and therefore measured the change in performance caused by duplicating a solution's expressed sub-trees after all non-expressed sub-trees had been removed. Haynes found that more duplication of a solution's expressed sub-trees (duplicated up to seven times) led to faster solution times: suggesting that this kind of functional redundancy, at least, is beneficial to evolution. He also speculated that syntactic introns could be replaced by duplicated coding regions in non-positionally independent problem domains to achieve the same effect.

Angeline [1994] suggests that intronic structures like `IF FALSE THEN X ELSE Y` represent a form of emergent diploidy and dominance in GP: where sub-tree `X` corresponds to a recessive trait and sub-tree `Y` corresponds to a dominant trait. Changing the condition from `FALSE` to `TRUE` would then amount to a dominance shift. The concepts of diploidy and dominance have gained a lot of interest in the GA community [e.g. Goldberg, 1989, Smith and Goldberg, 1992, Dasgupta and McGregor, 1993, Collingwood et al., 1996, Levenick, 1999, Weicker and Weicker, 2001] as a way of handling non-stationary problems: problems where the search space changes over the course of time. Goldberg et al. [Goldberg, 1989, Smith and Goldberg, 1992] have developed a number of diploid representations for GAs. These use two chromosomes to encode each solution so that for each gene locus one chromosome contains a dominant allele and the other chromosome contains a recessive allele. Only the dominant allele is expressed in the solution. The most interesting of these is the triallelic scheme:

where each allele has a value of either 1, 0, or 1_0; where 1 is dominant over 0 and 0 is dominant over 1_0. Mutation effectively has two roles under this scheme: it can change the value of an allele by changing a 1 into a 0 or vice versa, but it can also change the dominance of an allele by changing 1 into 1_0 or vice versa. In [Smith and Goldberg, 1992], the authors present results that show this diploid representation to be more effective than a haploid (single chromosome) representation upon a cyclic non-stationary problem: finding past optima both faster and with higher fidelity. In their own words: "diploidy embodies a form of temporal memory that is distributed across the population...this added diversity is more effective than that induced by mutation, because of its sensitivity to function history". Collingwood et al. [1996] have investigated the utility of higher levels of polyploidy in GAs for solving a range of test problems; finding that solutions with up to nine chromosomes can out-perform haploid representations.

Dasgupta's structured GA [Dasgupta and McGregor, 1992a,b, 1993] uses a more complex dominance mechanism which uses analogues of regulatory genes to control the expression of other genes. The structured GA has a tree-like structure where genes at a higher level control groups of genes at lower levels. Genes at the lowest level, which may or may not be expressed depending upon the state of higher level genes, encode components of the solution. Dominance is enforced by limiting the number of regulatory genes which may be turned on at a given level. Dasgupta believes that the structured GA is more suitable for non-stationary functions than diploid GAs since whole blocks of genes may be turned on and off through a single regulatory gene mutation; and in [Dasgupta and McGregor, 1992b] presents results which show the structured GA achieving higher performance on the problem described in [Smith and Goldberg, 1992]. The structured GA also performs well on stationary problems. Results presented in [Dasgupta and McGregor, 1992a] show that the structured GA performs better than a conventional GA on a difficult engineering optimisation problem. Dasgupta believes that this is due to the structured GA's ability to retain greater genetic diversity.

In conventional GP, the level of functional redundancy is determined in part by the problem domain: since functional redundancy can only occur if the function and terminal sets can be used to construct introns. In cartesian GP, by comparison, functional

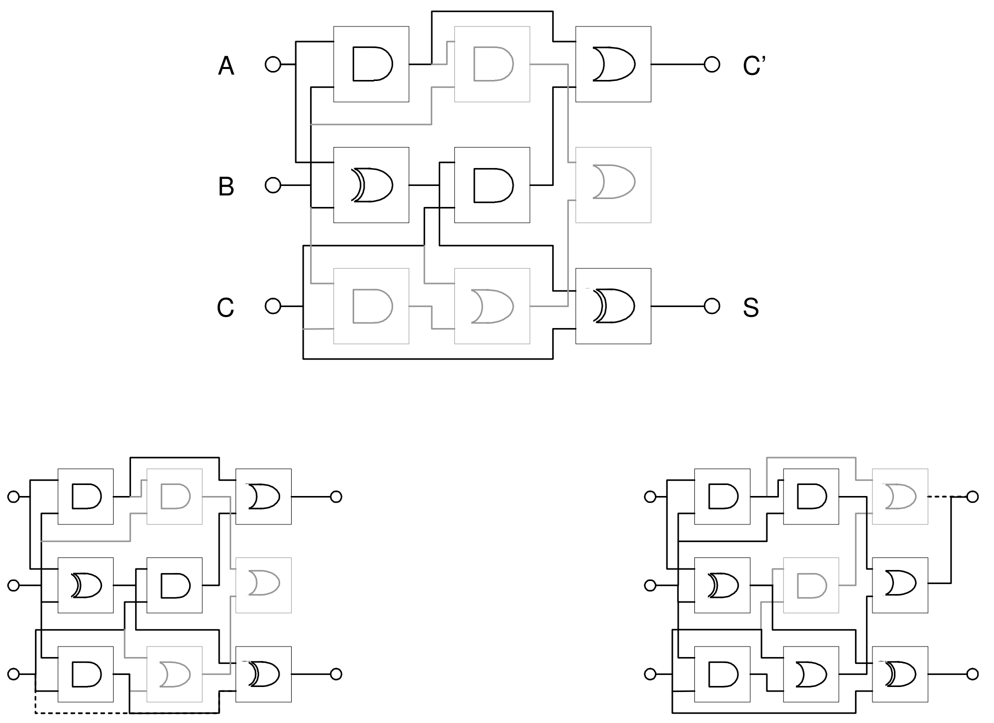


Figure 7.3. [top] A graphical example of a Cartesian GP circuit with functional redundancy. Components and connections shown in grey will not be expressed when the circuit is executed, [bottom left] but could become expressed if one of the expressed connections (shown in black) were to be re-routed following a mutation. [bottom right] A mutation could also result in behaviour akin to a dominance shift (see text).

redundancy occurs as a consequence of the way in which programs are represented: since the representation may define program components which are never referenced by coding components (see figure 7.3 for an example). This redundancy occurs irrespective of, and in addition to, redundancy allowed by the problem domain. Introns in both conventional and Cartesian GP have the potential to become expressed in descendant programs. In conventional GP, this is most likely to happen following a sub-tree exchange which moves a sub-tree from a non-coding position (syntactic intron) in one program into a coding position in another program. A non-coding sub-tree could also become expressed following a mutation which nullifies the invalidator of a syntactic intron: although in general this would only occur near the bottom of a program's parse tree and — especially in the later stages of search — would most likely be disruptive. In Cartesian GP, mutation plays a substantially different role since it is able to target the connectivity of program components in addition to their function. This means that mutation can cause un-expressed components to become expressed or expressed components to become un-expressed. It may also result in behaviours akin to dominance shift: with a dominant (expressed) sub-expression effectively being replaced by a recessive (un-expressed) sub-expression in the program. An example of this behaviour is shown in the bottom-right of figure 7.3.

Functional redundancy in Cartesian GP program representations provides an overt source of neutrality. From an evolutionary perspective, the components and inter-connections defined in a Cartesian GP program's representation describe not just the currently expressed program but also capture the programs which can be accessed through single changes to the input connections of expressed components. Changing the functions and inter-connections of functionally redundant components does not change the program that is currently expressed, but does change the programs that are available through single point mutations. In [Vassilev and Miller, 2000], the authors find that when these neutral mutations are not allowed, the best fitness attained when evolving three-bit multiplier circuits is significantly lower than that achieved when neutral mutations are allowed. Furthermore, results reported in [Yu and Milller, 2001] and [Yu and Miller, 2002] suggest that even large neutral changes (equivalent to hundreds of point mutations) play a significant role in improving search performance.

A related view of the kind of functional redundancy seen in Cartesian GP is that it provides a form of multiplicity: where, in a sense, a program's representation describes more than one potential program (this view of functional redundancy is discussed in Harik [1997] and Lones and Tyrrell [2001b] in the context of other EAs). Given that the components in the representation have common ancestory, it seems likely that these potential programs would have related functionality. This idea is taken further by Oltean and Dumitrescu [2002]; who describe a GP system — multiple expression programming — that resembles Cartesian GP but which measures a program representation's fitness according to all the programs that it could potentially express through single changes to the input connections of the output nodes. In effect, fitness captures the level of adaptation in the local neighbourhood of the search space. The authors report good performance across a range of standard GP problems: suggesting that there is a benefit to this approach; although there is inevitably a performance overhead. Presumably there is also the potential for search being disrupted in more rugged landscapes: where the variance of the fitness of the individual programs described by a program representation may be high. A recent paper by Hornby [2003] introduces another approach to encoding multiple solutions within a single representation, using it to evolve parameterised design families.

7.5 Positional Independence

It is perhaps taken for granted by biologists; but from the perspective of evolutionary computation, independence between the behaviour of a gene product and the position of its gene locus is a significant source of de-constraint within biological representations. Within most EC representations the meaning of a genetic component is determined by its absolute or relative position. This inevitably leads to problems during recombination. In GAs it may not be possible to find an optimal solution if components of optimal building blocks are assigned positions that are too far apart in the solution chromosome. In most forms of GP a component's context is determined by its position within the program representation. Given that crossover does not typically preserve a component's position, it is quite likely that its context, and therefore its function, will be lost following recombination. This section discusses existing approaches to removing positional dependence from EAs.

7.5.1 Linkage Learning

Linkage learning is the GA analogue of epistatic clustering. Linkage learning is motivated by the desire that all the genetic members of a building block should be inherited together during recombination in order to prevent their destruction. According to Smith [2002]: "for a problem composed of a number of separable components, the genes in the building blocks coding for the component solutions will ideally exhibit high intra-block linkage but low inter-block linkage [to encourage exploration]". The simplest approach to linkage learning involves limiting crossover so that it is less likely or unable to fall between genes whose alleles are considered to belong to the same building block. This is typically achieved by using crossover templates (successful approaches include those by Rosenberg [1967] and Schaffer and Morishima [1987]), though it may also be encouraged with explicit introns (see section 7.4.1). However, these approaches do not target the underlying cause of the linkage problem: positional dependence. Rather, they cause a kind of implicit epistatic clustering which is unlikely to benefit linked genes located far apart in the solution chromosome. Such a situation can only be remedied by moving the genes closer together within the chromosome. However, for most problems the optimal ordering of genes is not known in advance. Furthermore, it is generally not desirable for a genetic algorithm to rely upon domain knowledge.

7.5.2 Floating Representations

An obvious solution to this problem is to allow the ordering of genes within a chromosome to evolve. This requires that a gene can occupy any position within the chromosome without losing its original context. Typically this is achieved by associating each gene allele with some kind of identifier which — in the absence of positional information — shows the gene locus that it corresponds to. A prominent early example of this approach is Bagley's [1967] inversion operator. However early approaches such as Bagley's had little success, primarily due to competition between selection for fit solutions and selection for fit orderings; not to mention the problem of designing crossover operators which can appropriately recombine solution chromosomes with different orderings and the associated problems of under- and over- specification of gene alleles. Nevertheless, these so-called 'floating representation' approaches have proven successful in domains where under- and over- specification is not an issue [Raich and Ghaboussi, 1997, Wu and Lindsay, 1996a].

The messy GA [Goldberg et al., 1993] was the first broadly successful approach to use a floating representation to achieve linkage learning. The messy GA is an iterative algorithm where each iteration consists of a primordial phase: where building block identification takes place; and a juxtapositional phase: where building blocks are assembled into complete solutions. During each iteration, the algorithm attempts to identify and assemble higher level building blocks. Candidate solutions are represented by variable length chromosomes consisting of $< locus, allele >$ pairs. Each gene locus may be associated with any number of alleles. Where a locus is associated with more than one allele, the one which is defined nearest the left of the chromosome will be used during the solution's evaluation. If a solution has no alleles defined for some of its gene loci, values are taken from a template chromosome. The best solution

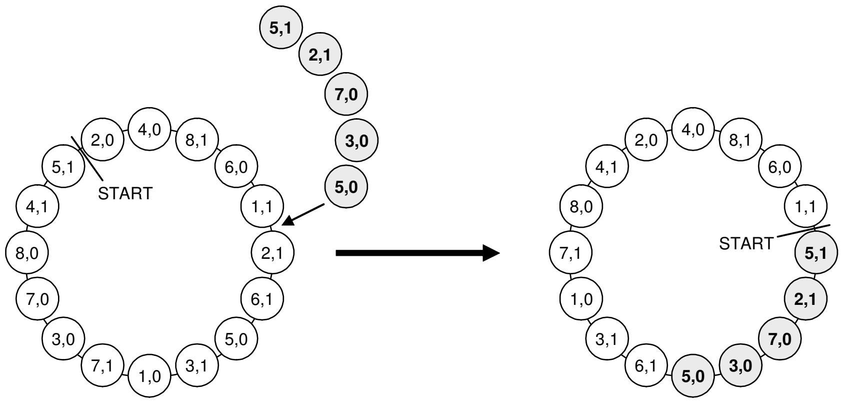


Figure 7.4. Recombination in Harik's Linkage Learning GA.

found within the juxtapositional phase of a particular iteration is used as the template chromosome for the next iteration. The template chromosome for the first iteration is randomly generated. The aim of the algorithm is for the template chromosome to contain optimal building blocks up to the current level and form the basis for the discovery of higher level building blocks in subsequent iterations.

The messy GA offers superior performance to simple GAs on problems with high levels of epistasis; and it does this by overcoming the problems which limited the applicability of earlier linkage learning approaches. Significantly, by separating building block identification from the assembly of building blocks to form solutions, the messy GA avoids competition between finding fit solutions and fit orderings. However, the algorithm is complex to implement and sensitive to parameter values, making it difficult to tune for a given problem domain. For these reasons, Harik [1997] proposed a linkage learning GA (the LLGA) based upon a conventional GA framework but with a representation and crossover operator derived in part from the messy GA. The LLGA, like the messy GA, uses chromosomes consisting of $< locus, allele >$ pairs. Unlike the messy GA, these chromosomes are circular and contain one copy of every allele of every gene locus. Both the position at which interpretation starts and the ordering of the alleles determines how the chromosome is interpreted. Different starting locations can lead to a chromosome being interpreted in different ways. Crossover takes the form of copying a contiguous sequence of $< locus, allele >$ pairs from a donor chromosome and then grafting it into a recipient chromosome, removing existing copies of the newly grafted $< locus, allele >$ pairs from the recipient chromosome (see figure

7.4 for an example). The effect of crossover is to re-arrange the ordering of both alleles and gene loci within a chromosome: changing both its interpretation and the linkage between its gene loci. Whilst unlike the messy GA the LLGA does not separate building block identification from building block assembly, it does avoid the problems with crossover and under- and over-specification found with earlier approaches and does avoid the complexities of the messy GA.

Floating representation has also been used within GP; though with limited success. In a biologically-inspired system described by Luke et al. [1999], a finite state automata is represented by a sequence of 'genes'; each of which is identified by a pattern, describes a state, and declares its connections in terms of the identity patterns of other genes. During a development process, each state attempts to connect to states whose patterns most closely match its input patterns. Whilst able to solve a range of string classification problems, this method shows little improvement over conventional GP.

7.5.3 Gene Expression

An altogether different approach to positional independence can be seen in Wu and Garibay's [2002] proportional GA and Ryan et al's [2002] Chorus GP system; where both sets of authors have taken inspiration from the role of protein concentration within gene expression. The proportional GA uses variable-length chromosomes comprised of symbols taken from a parameter alphabet; where each symbol corresponds to a particular parameter. The value of a parameter is determined by the proportion of its corresponding symbol within a chromosome — in much the same way that certain phenotypic traits are determined by the concentration, rather than just the presence, of a particular gene product. The precision with which each parameter is described depends upon the length of the chromosome: a factor which, the authors believe, leads to competition between solution length and precision. Across a range of problems, the proportional GA offers at least as good performance as the simple GA; with significantly better performance upon certain problems. The authors attribute this improvement to the proportional GA's ability to reduce the size of the search space by sacrificing unnecessary precision.

Ryan et al's [2002] Chorus system is based upon grammatical evolution. In GE, the meaning of a gene is calculated respective to the current grammar transition. In Chorus, by comparison, each gene refers to a specific rule within the grammar. As for GE, a Chorus program is interpreted from left to right. However, a gene only causes a grammar rule to be fired if it refers to a transition which is currently applicable: and only if there are no other relevant rules waiting to be expressed. If a gene refers to a rule which cannot currently be applied, the rule's entry in a 'concentration table' is incremented; showing that it is waiting to be expressed. Accordingly, a particular gene might have either an immediate or a delayed effect; meaning that its position within the program is not necessarily indicative of when it will be executed. However, possibly due to the greater fragility of its representation towards the effects of mutation, Chorus programs appear not to evolve as well as GE programs [Azad and Ryan, 2003].

7.6 Summary

This chapter has introduced four different approaches to improving the evolvability of the artefacts which are evolved by evolutionary computation techniques: homologous recombination, pleiotropy, redundancy, and positional independence. Whilst this review is biased towards techniques which adapt representation rather than those which adapt variation, it is interesting to note that homologous crossover can lead to an improvement in evolutionary performance. However, this performance gain is only significant for linear GP: which has a representation which easily supports homologous recombination. For conventional tree-based GP, the difficulty of implementing homologous recombination is reflected by a high computational overhead and little improvement in performance. By comparison, the introduction of pleiotropy (genetic re-use) into tree-based genetic programming has proved a very successful approach. This tends to reflect the biological viewpoint that a degree of pleiotropy helps evolution by preventing the need to re-evolve identical sub-structures more than once. The tendency for evolving programs to make use of implicit re-use within graph-based representations also supports this point of view.

Redundancy plays a range of interesting roles in evolutionary computation. Its capacity to provide structural protection from change has been the subject of a number of investigations. There appears to be some benefit to introducing structural redundancy into GA representations, particularly floating representations. Tree-based GP exhibits a high level of natural structural redundancy. However, this redundancy is generated by syntactic introns which accumulate at the bottom of programs; providing global protection to change which degrades performance and causes bloat. Nevertheless, results from linear GP suggest that appropriate forms of non-coding components can lead to better performance and better solution generality: though unfortunately this kind of redundancy is inherently unstable within tree-based GP.

Research into coding redundancy in GAs also suggests that performance gains should only be expected when redundancy is suitably organised. For example, codes which use redundancy to remove local optima generate a proportional increase in performance. However, there is some debate over the utility of neutrality within codes; though it appears that a degree of neutrality can benefit search by maintaining higher diversity within a population; although too much neutrality appears to reduce performance, possibly by reducing solution locality and introducing extra search overheads.

The functional role of redundancy is particularly interesting, though perhaps least understood. Functional redundancy plays a particularly important role when solving non-stationary problems, where it helps to buffer previous solutions. However, it is also known to improve performance upon stationary problems in both GA and GP: though again the organisation of redundancy appears to be an important determining factor. The value of functional redundancy is perhaps best seen within approaches like multiple expression programming which make explicit use of non-coding components in evaluating a solution.

From the perspective of evolutionary computation, positional independence in biology seems like an important source of evolvability. Linkage learning GAs show how positional independence can be successfully introduced into EC representations. Positional independence can also be introduced to GP, but so far only within non-tree based systems and without any significant increase in performance.

7.7 Perspectives

On the whole, the research reviewed in this chapter supports the notion that biological concepts can be used within evolutionary computation in order to improve evolvability. What is perhaps less clear is that this research also impacts upon our understanding of biology, where current understanding of evolvability is mostly at a theoretical rather than experimental level. For instance, pleiotropy is evidently a powerful source of evolvability within EC: and this supports the idea that pleiotropy is also important within biological evolution — and future EC research could give more insight into what is an appropriate balance between pleiotropy and compartmentalisation. EC research also supports biological theories of the role of non-coding DNA in affirming structural protection. However, in other regards biological theories of redundancy are more advanced than EC practice. The role of redundancy structures in supporting gradual molecular evolution, for instance, could be an interesting inspiration for future EC research. Furthermore, future research directions could be measured more by the topics which are not covered in this chapter rather than those that are. For example: multiple weak interactions, exploratory mechanisms, epigenetic inheritance, and ecological interactions are all thought important in the evolution of biological systems.

8 Enzyme Genetic Programming

Enzyme genetic programming [Lones and Tyrrell, 2001c,b,a, 2002b,a, 2003b,a] is a genetic programming system that uses a program representation modelled upon the organisation and behaviour of biological enzyme systems. This chapter introduces enzyme GP and discusses the motivation behind the approach.

8.1 Introduction

A metabolic network is a group of enzymes which interact through product-substrate sharing to achieve some form of computation. In a sense, a metabolic network is a program where the enzymes are the functional units and the interactions between enzymes are the flow of execution. Enzyme GP represents programs as structures akin to metabolic networks. These structures are composed of simple computational elements modelled upon enzymes. The elements available to a program are recorded as analogues of genes in an artificial genome. These genomes are then evolved with the aim of optimising both the function and connectivity of the elements they contain. The mapping between genome and program is conceptually depicted in figure 8.1.

From a non-biological perspective, enzyme GP represents a program as a collection of components where each component carries out a function and interacts with other components according to its own locally-defined interaction preferences. A program component is a terminal or function instance wrapped in an interface which determines both how the component appears to other components and, if the component requires input, which components it would like to receive input from.

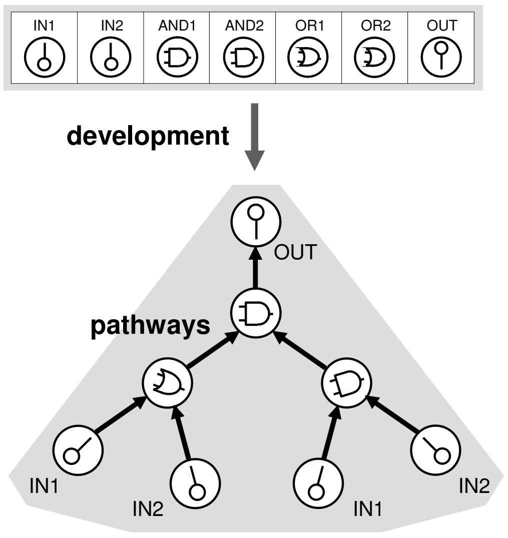


Figure 8.1. A program in enzyme GP is represented by a linear genome which is mapped into a program via a process analogous to the development of metabolic pathways.

8.2 Representing Programs in Genetic Programming

Program evolution within GP is a consequence of processes of change, such as mutation and crossover, acting upon the program's representation. In the absence of intelligent variation operators, program evolvability is determined by the ability of the representation to respond to change: in particular its ability to promote meaningful change whilst preventing the expression of inappropriate change. Chapter 6 recounts how the standard GP program representation, the parse tree, fails to support recombination — a conceptually meaningful evolutionary behaviour — whilst promoting program size bloat, a generally inappropriate behaviour. Parse trees lack evolvability because they have no nascent ability to filter change; and even when the representation languages of particular problem domains enable 'emergent' filtering mechanisms, such as the global resistance to semantic change offered by syntactic introns, the resulting bloating behaviour is inappropriate.

Chapter 7 reviews ways in which potential sources of evolvability can be introduced to the representations of genetic programming and other evolutionary algorithms, and how this approach generally leads to improved evolutionary behaviours and computational performance. Many of these sources of evolvability were identified by looking at the representations of biological organisms, and this seems to vindicate the notion that biological modelling can be used to improve the behaviour and performance of evolutionary computation — and forms part of the motivation for the development of enzyme genetic programming. The program representation used by enzyme GP is modelled both upon the way in which the function of biochemical pathways emerges from the sum of the behaviours of individual proteins and enzymes, and upon the way in which these systems respond to genetic change. Enzyme GP possesses many of the characteristics identified within the previous chapter as being sources of evolvability: including positional independence, functional and structural redundancy, neutrality, and implicit reuse.

The role of context within program representation is perhaps central to an understanding of enzyme GP and how it differs from other genetic programming approaches. According to the definition given in Section 6.3, a program component's context is determined by where it receives its inputs from: since this determines the arguments to which its function will be applied and therefore its outputs and hence its role within the program.

8.2.1 Explicit context

Within a parse tree, the context of a program component is determined by its position within the structure. For the remainder of this manuscript, this form of context is called *explicit context*, reflecting the fact that a component's context is recorded explicitly by its position within the representation relative to other components. Other GP approaches which use explicit context representations include linear GP [e.g. Nordin, 1994] and grammatical evolution [e.g. Ryan et al., 1998]. Explicit context representations have two properties which limit their ability to be evolved. The first, that a component's context is determined by position, that crossover operators do not preserve this position, and that therefore contextual information is easily lost, has already been discussed at length. Second, explicit context usually enforces a one-to-one mapping between representation and program, such that changes to the representation lead directly to changes within the program. The variation operators therefore act directly upon the program, implying that evolution is determined solely by processes of variation and selection. The representation, by comparison, has no dynamic role to play within the evolutionary process.

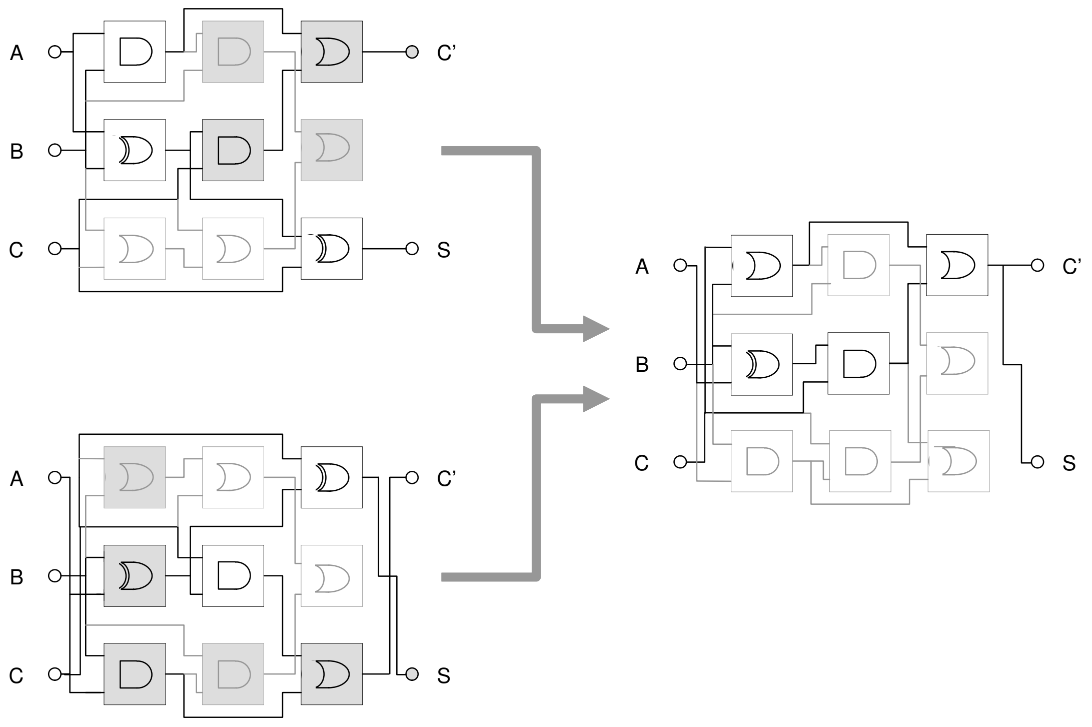


Figure 8.2. Recombination can cause loss of context when indirect context is used. A cartesian GP circuit is recombined with a flipped version of itself, but due to the same components occupying different locations in the two circuits, context (and consequently behaviour) is not preserved in the recombined circuit. Recombined parts are shaded grey.

8.2.2 Indirect context

In some other GP representations [e.g. Poli, 1997, Miller and Thomson, 2000], connections between components are specified using indirection. Typically each component is assigned a reference (which may be a location, a number or an arbitrary code) and other components specify their input connections using these references. A good example of this is Cartesian GP [Miller and Thomson, 2000], where components are assigned to locations in a cartesian co-ordinate system and input connections are expressed in terms of the co-ordinates of components they wish to receive inputs from. Context within these representations is specified indirectly, hence this form of context is termed *indirect context*.

Indirect context representations support a number of interesting evolutionary behaviours. Perhaps most significantly, a component only becomes active in a program if another component expresses a connection to it. Otherwise it is recessive. This has some important implications. If a new component is added to the representation during recombination, it will only become active in the program if its reference is addressed by an existing component or it is an output node. This effect is termed *variation filtering*, since the representation only expresses certain variation events in the program whilst filtering out others.

Indirect context representations usually assign references arbitrarily: such that there is no correlation between component reference and component behaviour. Indirect context, therefore, does not declare any behavioural information. Consequently, it expresses no real meaning other than the connectivity of the current program. This leads to similar problems to those seen with explicit context representations. Most significantly, indirect context has no meaning between different programs since components with different behaviours can have the same reference and components with the same behaviour can have different references in different programs. This implies that recombination is unlikely to preserve context (see figure 8.2). Furthermore, if a component's input connection is mutated, there will be no correlation between the degree of mutation and the degree of change to the component's input context: meaning that the component's context cannot be varied gradually, unless by accident.

However, it is conceivable that the population might be able to evolve a correlation between component reference and component behaviour over the course of time, especially as the population becomes more homogenous. In this sense, the meaning of indirect context is evolvable. Furthermore, indirect context representations support both structural and functional modes of redundancy in addition to a capacity for implicit reuse.

8.3 Implicit Context Representation

By comparison to the explicit and indirect contexts used by GP, biology expresses component interactions with what could be called *implicit context*. With implicit context, a component's context is declared implicitly within the component's definition rather than being imposed by external factors such as its relative position within a representation. For example, the behaviour of a bio-chemical is dependent upon its physical shape and chemical properties. Enzymes, which conceptually receive their input in the form of bio-chemicals, express their preference for these inputs by the shape and chemical properties of their binding sites. Since the bio-chemicals that they bind have physical shape and chemical properties complementary to the binding sites, these binding sites are implicitly describing the enzyme's context in terms of the behaviour of the substrates they expect to bind.

8.3.1 An Illustrative Example

Figure 8.3 illustrates an example of an abstract system whose behaviour and evolution is determined by implicit context. The system is represented by three components: each of which has a shape, which identifies it to other components; and an implicit context, which declares the shape of the component it would prefer to interact with. If the system is allowed to develop, interactions occur according to the implicit contexts declared by each component; whereby each component attempts to interact with a component whose shape most closely matches its own implicit context. In essence, the system self-organises according to the properties of the components from which it is comprised. Because of this property of self-organisation, there is no external requirement for a component to be expressed in the developed system. In the example, a component is added to the representation which does not match any of the implicit contexts defined by the existing components and is consequently not 'expressed' in the developed structure of the system. Conversely, if a component is added to the representation which has a better match with one of the existing implicit contexts of the system, then it does become expressed in the system.

This is another example of a variation filtering process of the kind seen where an indirect context representation is used. In an indirect context representation, the lack of correlation between indirect context and behaviour causes variation filtering to be an arbitrary process. In an implicit context representation, by comparison, variation filtering is a process which filters out change which does not fit into the current system context whilst promoting change which improves the internal cohesion of the system. From an evolutionary perspective, this would seem like a useful function since it tends to preserve the existing evolved behaviour of the system by lessening the impact of change and without actually preventing change to the representation.

The bottom two panes in figure 8.3 show the benefits of recessive components within an implicit context representation. In the first of these, a component which was added

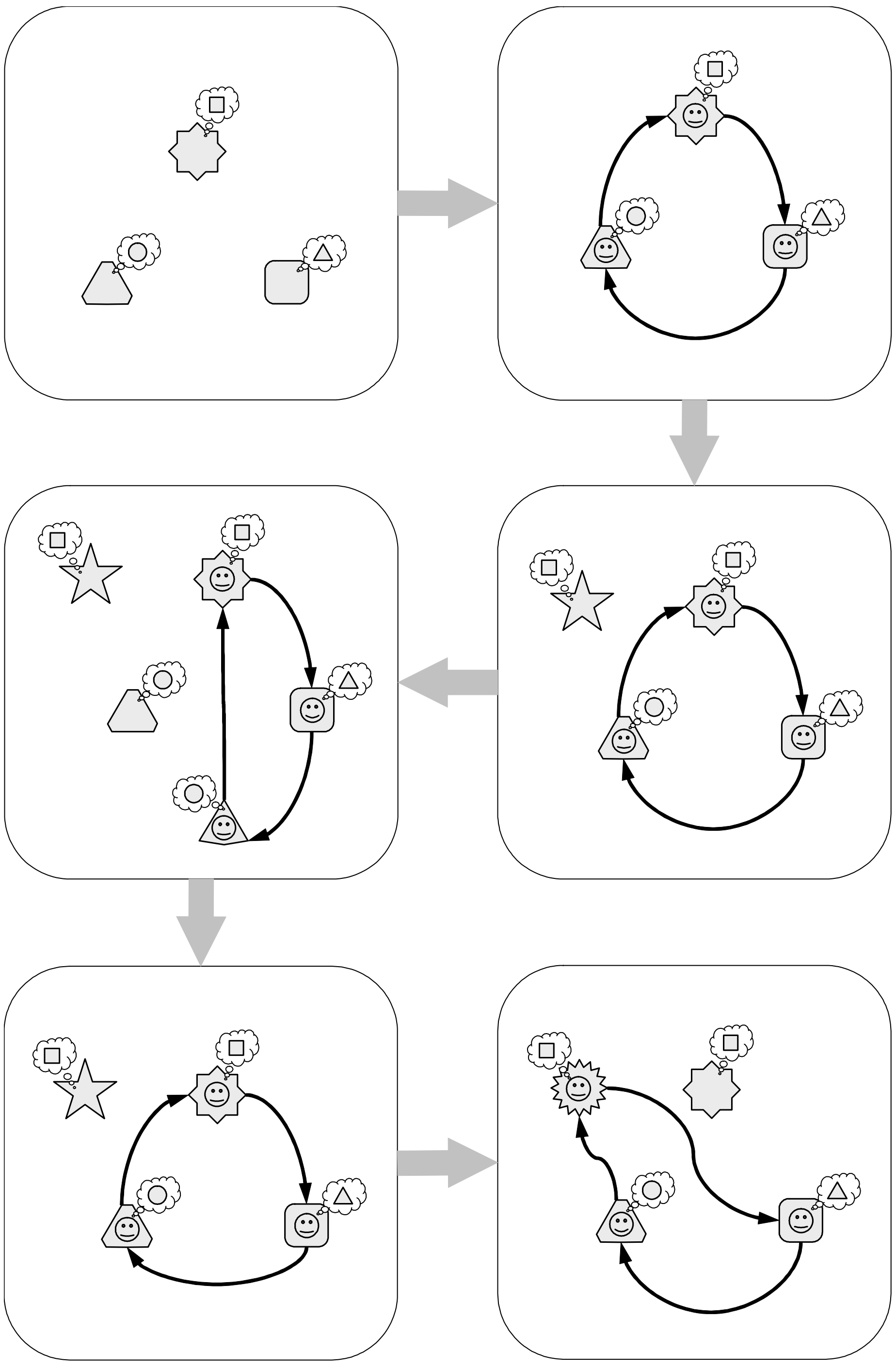


Figure 8.3. Evolution of an abstract implicit context system. [top-left] The system comprises three components. [top-right] The system self-organises according to each component's implicit context. [middle-right] A newly added component is not expressed because it does not match the system's existing contexts. [middle-left] A new component subsumes the role of an existing component. [bottom-left] The system backtracks to a previous state when a new component is lost. [bottom-right] Mutation leads to expression of a recessive component.

to the system has now been lost; but because the added component had only subsumed the role of an earlier component, rather than replacing it, the earlier component is able to resume its role. This demonstrates a capacity for backtracking, showing how functional redundancy can reduce the impact of the loss of a component upon the behaviour of the system. In fact, this is another example of variation filtering, but filtering the effect of removing a component rather than the effect of adding a component. The final pane of figure 8.3 shows that recessive components are also able to undergo evolution. In this case, the mutation of a recessive component allows it to fit into the context of the system and become expressed.

8.3.2 Representing Programs with Implicit Context

Implicit context does not seem like an obvious approach to representing programs, yet its pervasiveness in biology and the behaviours described above suggest that it is a good way of representing an evolving system. Indeed, implicit context representation seems to fulfill at least the first of Kirschner and Gerhart's principles of evolvability: the capacity to reduce the potential lethality of mutations — which it achieves through the variation filtering process described above, making it less likely that change to a representation will result in substantial change to the entity that it represents. This in turn makes it more likely that Kirschner and Gerhart's second principle will be met: a capacity to reduce the number of mutations needed to produce phenotypically novel traits; since there is more chance of the entity surviving a series of changes. Moreover, the presence of functional redundancy brings with it the potential modes of evolution described in sections 5.2.1 and 7.4.3; each of which tend to increase the explorative potential of evolution and hence the likelihood of a series of changes leading to an improved entity.

It is hoped that implicit context can be used to introduce variation filtering to program representations, leading to an improvement in the behaviour and success rate of conventional GP variation operators, and in particular enabling meaningful recombination. However, there are certain pre-conditions for implicit context to be able to enable useful variation filtering. These were originally identified in Lones and Tyrrell [2002a] and concern the relationship between implied context (the context declared in the representation) and actual context (the context which occurs in the program). Precision is the generality of the implied context: the degree to which it suggests an actual context. If implicit context is too general, then the behaviour of the program will not be obvious from the representation, making the mapping between representation and program unstable and therefore easily disrupted by the application of variation operators. In turn, this will make meaningful recombination unlikely. Related to precision is the issue of specificity: how well an implied context is able to identify an actual context. If a component's implied context is too unspecific, it is likely to form different actual contexts within different programs, meaning that variation filtering will tend to carry out arbitrary behaviours. Finally, there is the issue of accuracy: the ability of implicit context to match actual context given the availability of components within the representation and any constraints upon connections between components that are placed upon the behaviour of the program. Given that these limitations are unavoidable, there is little that implicit context can do to overcome them. Nevertheless, it is important that when the preferred context is not available, the implied context should match the nearest available actual context. In turn, this requires that a distance metric can be defined between implied and actual contexts, such that the greater the distance between contexts, the greater is the difference in component behaviour.

8.4 Implicit Context in Enzyme Genetic Programming

The enzyme GP implementation of implicit context is modelled upon biological systems in which the behavioural context of a component is both described and determined by its shape. As depicted in figure 8.4, program components in enzyme GP are loosely modelled upon biological enzymes. Each program component has a shape. This describes the behaviour of the component and also functions as an identifier which can be referred to by other components. Most program components also have a set of binding sites. Each binding site has a shape and this shape identifies the component it would expect to bind during a development process. Accordingly, shape determines where each component will be bound: giving its expected context within a developed program.

Each program component also has an activity. This activity is either a function, an input terminal, or an output terminal; and determines what the program component

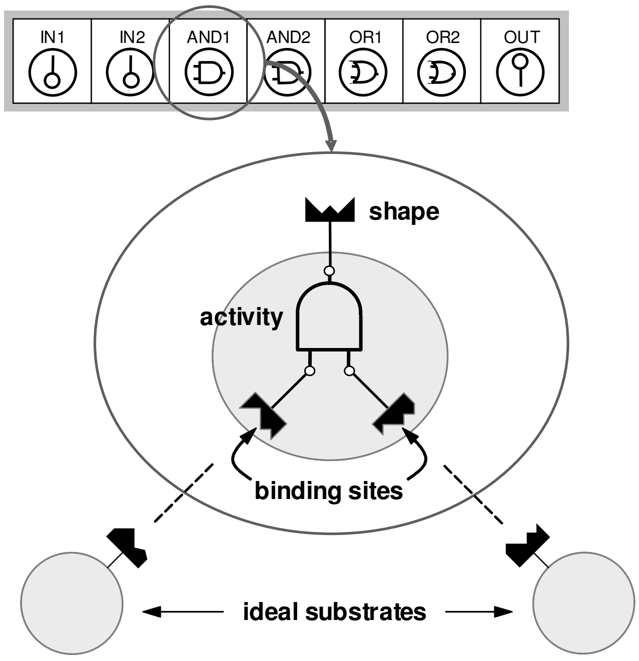


Figure 8.4. Enzyme model. A program component consists of a shape, an activity and a set of binding sites. Shape describes how the enzyme is seen by other program components. The shape of a binding site determines which component (or 'substrate') will be bound at a particular input.

will do within a developed program. Only components with functional and output terminal activities have binding sites. Following development, the function or output terminal's input(s) will be provided by the output of the components which are bound to the binding sites. Input terminal components provide program inputs at their outputs.

8.4.1 Functionality

A shape is not just an identifier. Shape also describes the behaviour of a program component. It would be insufficient for shape to merely express the activity of a program component since there will in general be many instances of only a few different functions and terminals within each program. Nevertheless, each of these instances will be carrying out a different role within each program. The aim of shape within enzyme GP is to capture this role.

The role of a program component depends not only upon itself and the activity it carries out but also upon the components it interacts with and the activities they carry

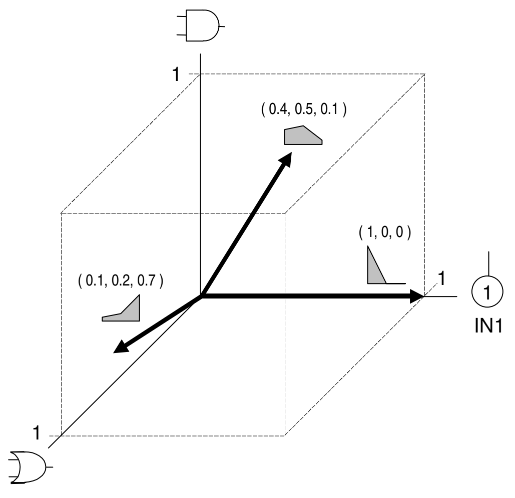


Figure 8.5. Functionality space for function set {AND, OR} and terminal set {IN1} showing example functionalities. Two-dimensional vector plots of functionalities, such as those shown in this figure, are used for illustrative purposes throughout this chapter.

out. In particular, the outputs of a functional activity depends upon its inputs, and this depends upon the components it receives its inputs from, whose outputs, in turn, depend upon the components they receive their inputs from, and so on. In fact, for parse trees, the outputs of a program component — its behaviour — are dependent upon all the activities of all the components which occur below it within a program. These activities are the information which a shape attempts to capture.

In essence, a program component's shape describes a profile of the activities which are expected to occur within the sub-tree of which the component is the root. This profile is called a *functionality* and is derived solely from the component's activity and binding sites. Information regarding the activities at and below the binding sites is inferred from the shapes of the binding sites: since these shapes give the functionalities of the components which are expected to be bound during development.

Formally, a functionality is a vector which describes the component's position within an activity reference space. This reference space has one dimension of unit length for each member of the GP function and terminal sets (see figure 8.5 for an example). The functionality, F, of a program component is a weighted vector sum of the functionality of its activity and the functionality of its binding sites, defined as follows:

$$F(component) = (1 - inputbias) \cdot F(activity) + inputbias \cdot F(binding\_sites) \quad (8.1)$$

where $inputbias$ is a constant that biases the functionality towards either the component's activity or the component's binding sites; $F(activity)$, the functionality of the component's activity, is a unit vector situated in the dimension corresponding to the enzyme's function; and $F(binding\_sites)$, the functionality of the component's binding sites, is defined:

$$F(binding\_sites) = \frac{\sum_{i=1}^{n} F(site_i) \cdot strength(site_i)}{\sum_{i=1}^{n} strength(site_i)} \tag{8.2}$$

i.e. the average of the functionalities corresponding to its binding sites weighted by the strength (a value between 0 and 1) of each binding site. Strengths are used to determine which binding sites are active when there are more binding sites than there are inputs to the activity. For instance, if a component has a two-input activity and three binding sites, only the two binding sites with the highest strengths will bind components during development.

An illustrative example of equations 8.1 and 8.2 is shown in figure 8.6, showing how a derived functionality captures the activity profile of a component's expected sub-tree.

In effect, a component's functionality declares an expected activity profile of the components that occur in the program fragment of which it is the root, weighted by depth and biased by the strength of binding sites. Functionality space itself is continuous and the distance between functionalities is calculated using vector subtraction. This reflects the difference between their activity profiles, meeting the requirement (outlined in the previous section) that the greater the distance between contexts, the greater is the difference in component behaviour.

However, the functionality approach has two inherent limitations. First, a functionality only gives a profile of the activities within an expected sub-tree. It does not describe where they occur within the sub-tree and how they are inter-connected. Second, a functionality only gives an expected profile. During development, it may not be possible for a component to bind the exact components described by its binding sites: either because they are not available within the program's representation or because there are constraints upon development (see following section).

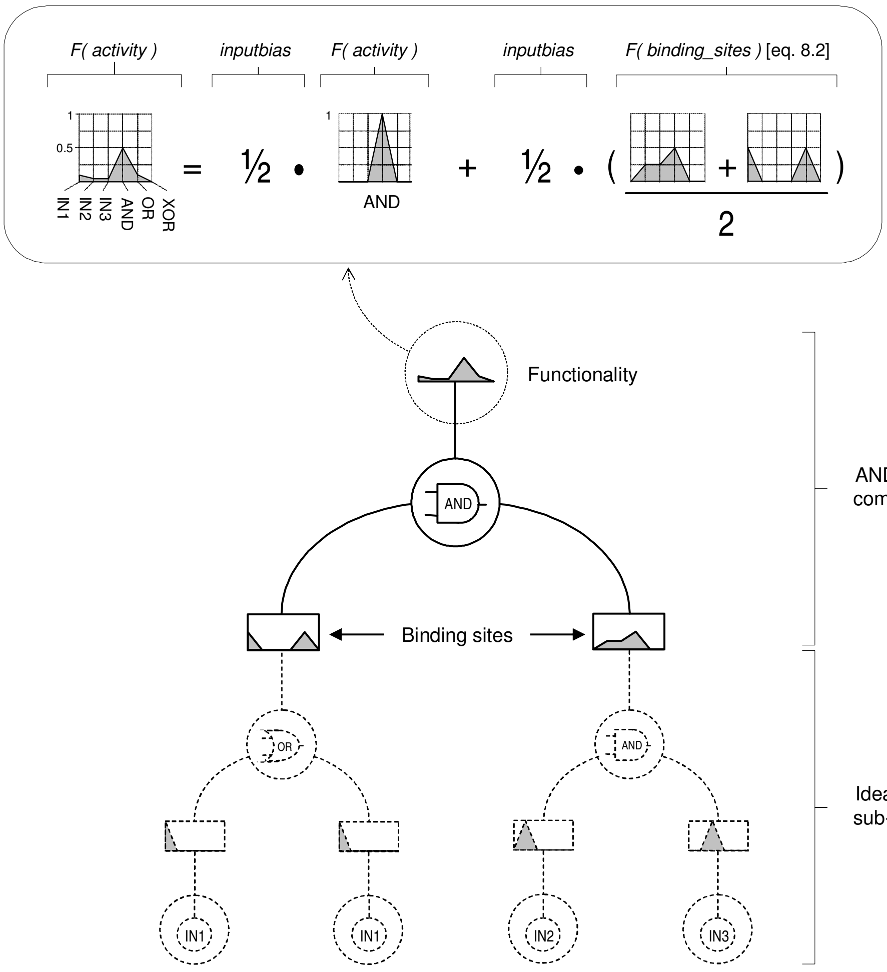


Figure 8.6. Derivation of functionality. An AND component's functionality is derived from the functionality of the AND function and the functionalities declared by its binding sites using equations 8.1 and 8.2 with $inputbias = \frac{1}{2}$ and assuming both binding sites have a strength of 1. The component's functionality captures a profile of the function and terminal content, weighted by depth, of itself and its ideal subtrees i.e. a high proportion of AND functions, a significant proportion of OR functions and IN1 terminals, a low proportion of IN2 and IN3 terminals, and no XOR content.

8.5 Program Development

An enzyme GP program consists of three types of component: input terminals, functional elements, and output terminals. A program's representation is the enzyme GP analogue of a biological genome: stored as a linear array of program components; the format of which is shown in figure 8.7. This program representation records the components which are available to the program and that may be expressed within the program following a process of development.

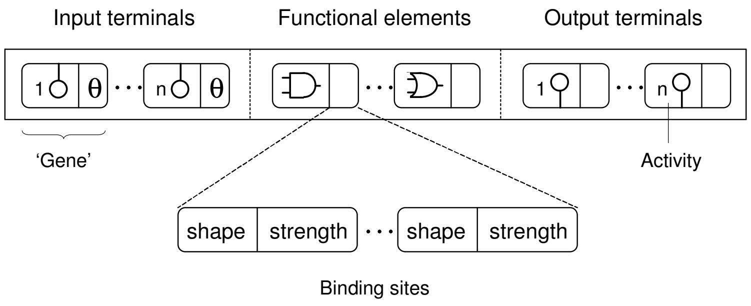


Figure 8.7. Format of a program representation, showing its division into input terminal, functional element and output terminal components. Every program representation contains a full set of input and output terminals components. Note that input terminal components do not have binding sites, for they receive no input from other components. Also note that component shapes are generated dynamically and do not therefore appear in the program representation.

The objective of the development process is to map the program representation into a program in such a way that each active input of each active component will be connected to the output of the component for whose shape its corresponding binding site has the highest specificity i.e. the shortest distance between functionalities. Two different development processes have been used in this research, although others are possible. The first, which could be called *top-down development*, begins with expression of the output terminals, which then choose substrates whose shapes are most similar to the shapes of their strongest binding sites. These substrates are now considered expressed and, if they require inputs, attempt to satisfy them by binding their own substrates. This process continues in hierarchical fashion until all expressed program components have satisfied all of their inputs. This development process is illustrated in figure 8.8 by way of an example.

The alternative development process involves transforming the program representation into a network random key representation of the kind described by Rothlauf and Goldberg [2002]. In essence, this means that connections between components — and hence the components involved in the connections — are expressed in order of strength: where the strength is the vector difference between a binding site and a shape. The strongest connections are expressed first and connections continue to be expressed until a complete structure has developed where every expressed component has all its inputs satisfied. This development process is called *strongest-first development*.

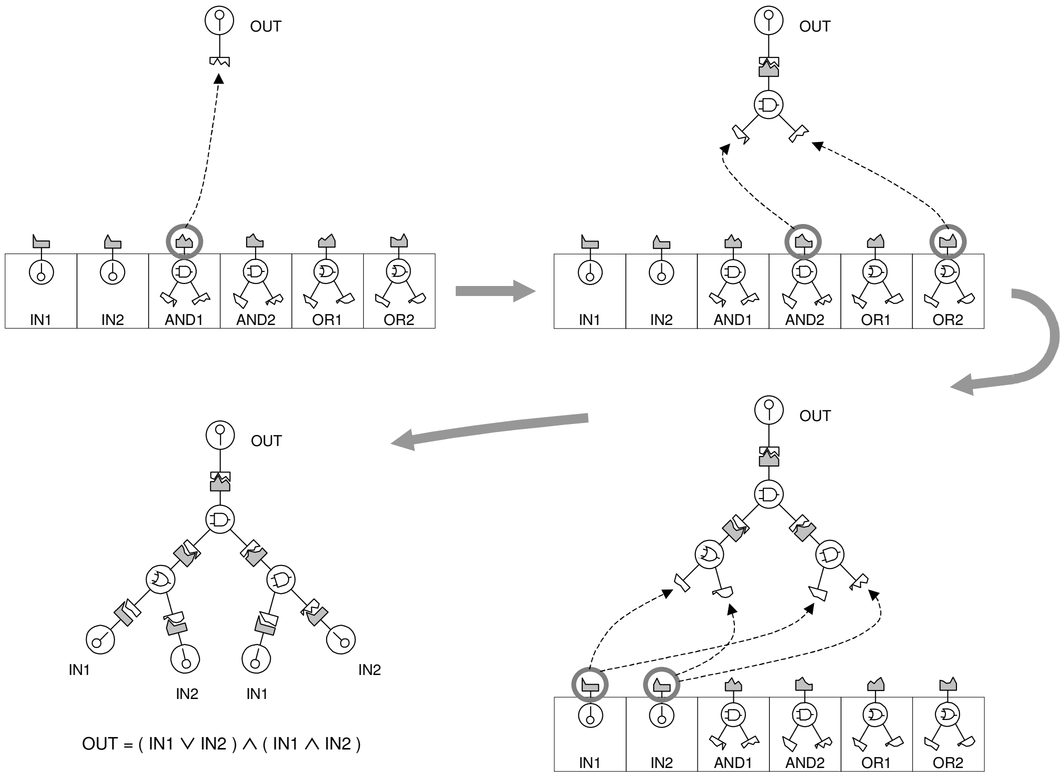


Figure 8.8. Top-down development of a simple Boolean expression. The first component to be expressed is the output terminal receptor. This then binds as a substrate the component whose shape is most similar to its binding site; the AND1 component. The AND1 component now chooses its own substrates and the process of substrate binding continues until the inputs of all expressed components have been satisfied. Note that OR1 is never expressed and that IN1 and IN2 are both bound twice.

For both development processes, each output terminal is expressed exactly once, whilst input terminals and functional elements can be expressed once or not at all. Where more than one component chooses the same substrate, the output of the substrate is shared between them: introducing a capacity for implicit re-use as described in section 7.3.2. In problem domains where there are no constraints on component interaction, both of these development processes should produce identical mappings between program representation and program — except that strongest-first development might lead to extra expressed components and connections which do not contribute to the program outputs by virtue of output terminal components being able to choose inputs internal to expressed structures (see figure 8.9).

However, where the problem domain introduces constraints on development, different development processes can lead to different mappings. For the problem domains

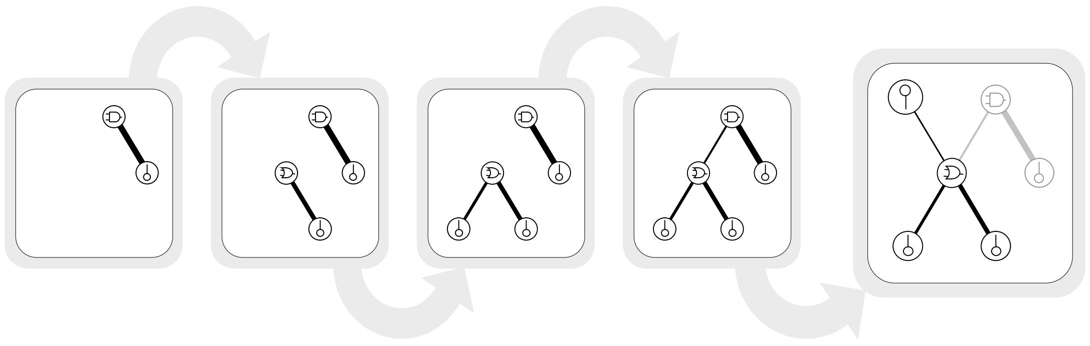


Figure 8.9. An example of strongest-first development. Line thickness shows the relative strength of a bond. Note that the components coloured grey in the developed circuit do not contribute to the circuit's output even though they are expressed during development.

used in this research, programs are constrained to have tree-structures and therefore must contain no cycles. This constraint is handled within both development processes by checking for the presence of cycles before a new connection is made. If a connection to a substrate would result in a cycle, then an alternative (less preferred) connection must be made. Where cycle prevention is used, development becomes sensitive to the order in which connections are expressed. During top-down development, cycles are prevented by stopping components from making connections to those components which already appear above them in the program tree. The further down a component appears in a program, the higher is the degree of constraint upon which components it can choose to bind and therefore the lower is the likely match between the components it wishes to bind and the components it actually binds. Accordingly, linkage will tend to be relatively high near the top of developed programs and relatively low near the bottom of developed programs. For strongest-first development, by comparison, high linkage connections would be distributed around the program. Because this development process promotes the expression of high linkage connections, it would also be expected that connections would be stronger on average than those in programs resulting from top-down development.

8.6 Evolution of Program Representations

Evolution of program representations occurs within the framework of a diffusion model distributed genetic algorithm called the *Network GA* [Lones, 1999] (depicted

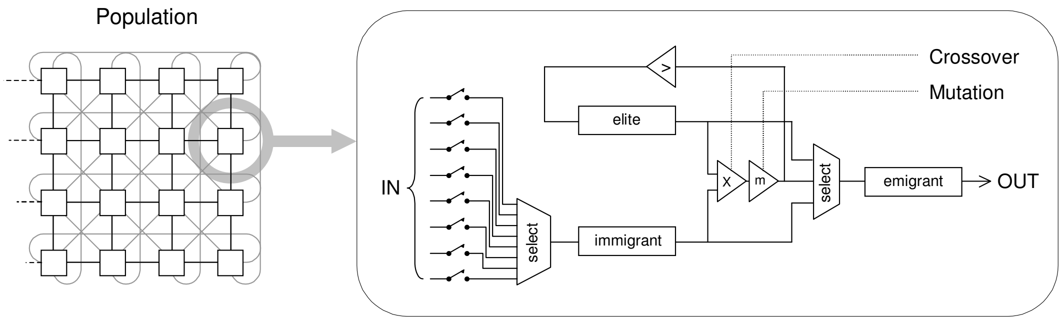


Figure 8.10. Structure of the network genetic algorithm, showing the organisation of the population and the processing which occurs in each cell of the population during each generation.

in figure 8.10). The population is organised into a spatially-distributed network of cells, each of which carries out an evolution strategy upon local state and inputs from surrounding cells. The network topology determines the processing behaviour of the population. For all experiments reported in this thesis, the network is a two dimensional edge-connected matrix (toroidal). A cell's evolution strategy selects the fittest individual from the emigrants of those cells designated as inputs by the network. This immigrant then undergoes recombination with the local *elite*; the fittest individual created so far within this cell. If the fittest child is fitter than the elite, then the elite is replaced with this child. The cell's emigrant is the fittest individual out of the parents and the children. By implementing elitism, the algorithm retains fit solutions. By making this elitism local to each cell, diversity is preserved and new solutions are encouraged. Diversity is also encouraged by the spatially-distributed structure of the population and the accurate sampling enabled by local selection. Whilst each cell contains three individuals, only the elite is considered resident and only the children are evaluated during each generation. The network GA was chosen both for its diversity-preserving behaviour — which allows the effects of neutral evolution to be more easily studied — and more generally for its use of a spatially-distributed population structure, which allows evolution to be easily visualised.

8.6.1 Initialisation and Variation

At the start of an evolutionary run, the population is filled with randomly generated program representations: each of which has a preset number of input and output terminal components and a randomly chosen assortment of functional components.

The number of functional components within a program representation is initially bounded but is allowed to vary freely during evolution. The activities of functional components are chosen non-deterministically. The dimensions of binding site functionalities are also chosen randomly, though not necessarily from a uniform distribution.

Enzyme GP uses both mutation and recombination (both separately and in concert) to generate new program representations from existing program representations. Mutation is able to target both activities and binding sites. Activity mutation is only applied to components with functional roles and works by replacing the current function with a new function chosen at random from the problem's function set. Binding site mutation targets each dimension of the binding site's functionality with equal probability; replacing the current value with a new value chosen at random according to the same probability distribution that was used during initialisation.

The experiments reported in the following chapter use two different kinds of recombination. *Uniform crossover* intentionally generalises the uniform crossover operator used by genetic algorithms and loosely models biological recombination. Uniform crossover is a two-stage process of gene recombination followed by gene shuffling. Gene recombination resembles meiosis, the biological process whereby maternal and paternal DNA is recombined to produce germ cells, and involves selecting and recombining a number of pairs of similar components from two parent program representations. Pairs of components are selected according to the similarity of their shapes and standard GA uniform crossover is used to recombine their binding sites. Gene shuffling then divides the recombined components uniformly between two child program representations. Figure 8.11 illustrates the resemblance between enzyme GP uniform crossover and meiosis.

Uniform crossover is a disruptive recombination operator which can be used to measure how program representations react both to high levels of change and to conventional evolutionary computation search operators. The second kind of recombination used by enzyme GP, termed *transfer and remove*, is used to observe how program representations react to lower levels of specific kinds of change. Transfer and remove recombination uses two complementary operators — transfer and remove — and takes advantage of the fact that components which are added to a program representation

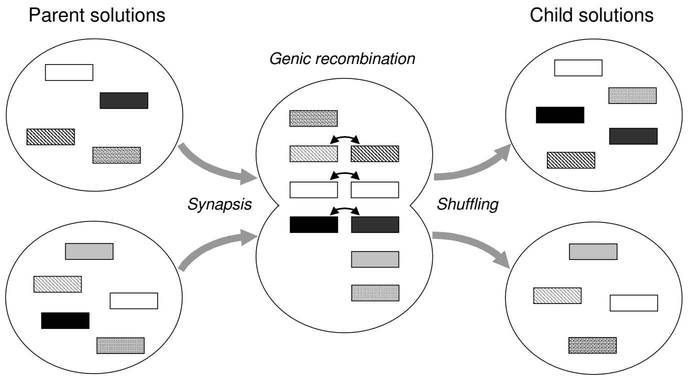


Figure 8.11. A conceptual view of enzyme GP uniform crossover. Components are shown as rectangles. Shade indicates shape.

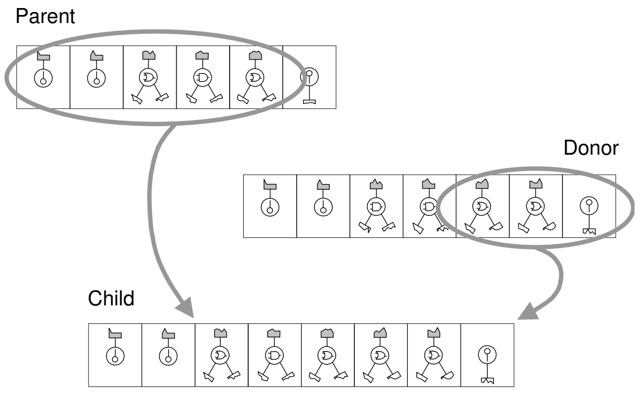


Figure 8.12. Recombination using transfer and remove. Note that the number of output terminal components in a program representation is fixed, so any that are transferred from the donor replace those copied from the parent.

need not replace existing components. The transfer operator forms a child program representation by copying a contiguous sequence of components from one program representation (the donor) to another (the parent) without removing any existing components (with the exception of output terminals, whose numbers remain constant — see figure 8.12). The remove operator forms a child program representation by removing a contiguous sequence of components from a parent program representation. Each of these operations is used, non-deterministically, for 50% of crossover events. The effect of the remove operation is to balance solution sizes so that recombination has an overall neutral effect upon solution size within a population. For both transfer and remove operations, the number of components targeted is chosen randomly within an upper limit.

8.7 Summary

This chapter has introduced a form of genetic programming based upon an implicit context program representation in which interactions between program components are specified via behavioural descriptions rather than by position or other arbitrary references. Implicit context representation is expected to lead to a process of meaningful variation filtering whereby inappropriate change induced by variation operators can be wholly or partially ignored as a consequence of program behaviours emerging from the self-organisation of program components — ignoring those components which do not fit the contexts declared by the other components within the program.

9 Experimental Results and Analysis

This chapter presents the results of a series of experiments designed to give insight into the performance, behaviour, and scope of enzyme genetic programming. In particular, this chapter aims to document:

- The efficacy of functionality as an implementation of implicit context.
- The performance and behaviour of recombination.
- The evolution of program size and structure.
- The role and evolution of redundancy.
- The evolution of compartmentalisation.
- The complexity and consequences of development.
- Comparative performance against other GP approaches.

9.1 Experimental Method

The implementation of enzyme GP used for this study uses a number of metrics to measure performance and behaviour. Table 9.1 lists those which are referred to in this chapter. Table 9.2 lists the parameters of the system, along with their default values. Where no parameter value is given for a particular experiment, the default value is assumed. Fitness values and run lengths are typically not normally distributed and

Metric	Range	Description
Computational effort	0+	Number of evaluations required to produce a 99% probability of finding an optimal solution
Distance	0%-100%	Average distance, as a proportion of a dimension, between the functionality of a binding site and its substrate
Expression	0%–100%	Proportion of functional components which are currently expressed
Fitness	–0	Highest fitness found within a population, measured by number of incorrect output bits during simulation
Genetic linkage	0%–100%	Genetic distance between interacting components as a proportion of genome length
Output distance	0%–100%	*Distance* between an output terminal's binding site and its substrate
Program size	0+	Number of functional components expressed within a program
Representation length	0+	Number of functional components within a representation
Reuse	0+	Number of times a single component is bound during program development
Solution time	0+	Number of generations required to find an optimal solution
Success rate	0%–100%	Proportion of runs which found an optimal solution

Table 9.1. Metrics used to measure performance and behaviour of program evolution.

where statistical significance is given, these are the results of non-parametric Mann-Whitney or Kruskal-Wallis tests. Variances and actual values reported by statistical tests are generally not given to avoid clutter. A confidence level of 95% is used to determine statistical significance.

9.1.1 Symbolic Regression

All the experiments reported in this chapter use symbolic regression as a problem domain. Application is limited to discrete regression problems involving Boolean logic. Whilst this might limit the generality of the results, these problems were chosen for their relative difficulty with regard to recombinative search.

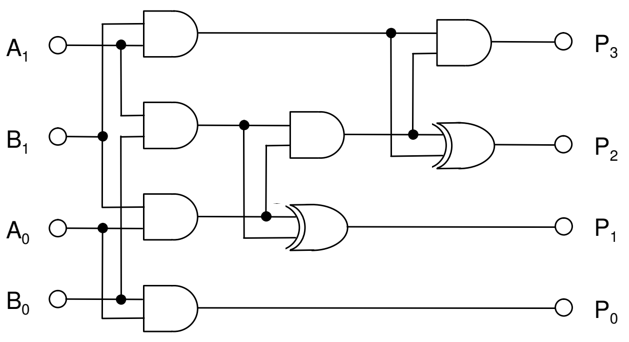
Symbolic regression involves the inference of a symbolic expression from a representative set of $< input, output >$ data points. For Boolean regression problems, these data points can be interpreted as a conventional truth table of the kind used in combinational logic design. All the problems used in this study are specified by complete truth tables: providing output test cases for every possible combination of inputs. For a particular problem, expressions can be built from members of a pre-defined non-terminal set, which specifies the available Boolean logic functions; and a terminal set, which specifies the available inputs. Test problems are listed in Table 9.3. A standard

Parameter Name	Label	Default value
Crossover type		transfer and remove
Development strategy		top-down
Distance limit for gene alignment in uniform crossover		1
Functionality dimension initialisation power	i	3
Generation limit	l	200
Number of binding sites per input component	bs	3
Number of runs per data point	r	50
Phenotypic linkage learning rate	ll_r	0%
Population dimensions	p_d	18 x 18
Problem		2-bit multiplier
Proportion of gene pairs recombined in uniform crossover		15%
Rate of activity mutation	m_a	1.5%
Rate of binding site strength mutation	m_s	2%
Rate of functionality dimension mutation	m_f	2%
Shape input bias (from equation 8.1)	k	0.3
Transfer size upper limit for TR crossover	t_u	5

Table 9.2. Behavioural parameters and their default settings.

solution for the two-bit multiplier problem is shown in figure 9.1.

Similar Boolean regression problems have also been addressed by Miller et al. [2000], Coello et al. [2002], and Koza [1992] using various forms of GP. Vassilev et al. [1999] have carried out an analysis of various multiplier landscapes and have found them to be typified by large planes of equal-valued solutions and little fitness gradient information. This would appear to be typical of Boolean regression landscapes and implies that such problems are difficult to solve using recombination; a view which is also expressed in [Miller et al., 2000].



A0	A1	B0	B1	P0	P1	P2	P3
0	0	0	0	0	0	0	0
0	0	0	1	0	0	0	0
0	0	1	0	0	0	0	0
0	0	1	1	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	1	0	0	0	1
0	1	1	0	0	0	1	0
0	1	1	1	0	0	1	1
1	0	0	0	0	0	0	0
1	0	0	1	0	0	1	0
1	0	1	0	0	1	0	0
1	0	1	1	0	1	1	0
1	1	0	0	0	0	0	0
1	1	0	1	0	0	1	1
1	1	1	0	0	1	1	0
1	1	1	1	1	0	0	1

Figure 9.1. Two-bit multiplier problem. Truth table and standard solution.

Name	Inputs	Outputs	Function set
1-bit full adder	3	2	`AND,OR,XOR`
2-bit full adder	5	3	`XOR,MUX`
2-bit multiplier	4	4	`AND,XOR`
3-bit multiplier	6	6	`AND,XOR`
even-3-parity	3	1	`AND,OR,NAND,NOR`
even-4-parity	4	1	`AND,OR,NAND,NOR`

Table 9.3. Boolean regression test problems.

2-bit Multiplier, bounds 12–16, pop. 324

Operator	Average	Success	CE
Uniform	118	77%	136,080
TR	76	75%	169,128
Mutation	94	56%	334,368

2-bit Adder, bounds 10–20, pop. 324

Operator	Average	Success	CE
Uniform	113	74%	244,620
TR	107	57%	340,200
Mutation	114	53%	392,364

Even-3-parity, bounds 5–10, pop. 100

Operator	Average	Success	CE
Uniform	54	43%	79,000
TR	47	32%	96,000
Mutation	40	7%	250,800

Even-4-parity, bounds 10–25, pop. 625

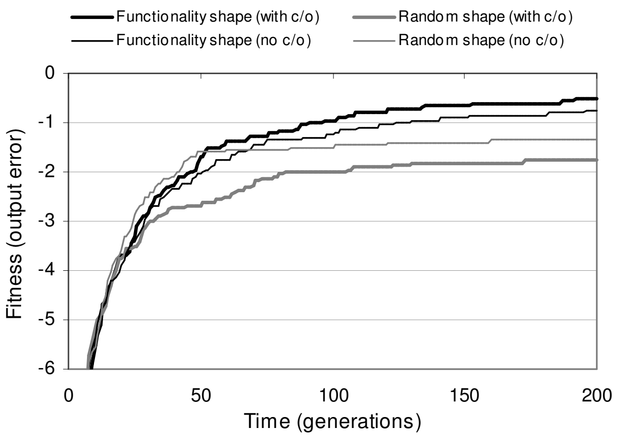
Operator	Average	Success	CE
Uniform	150	25%	2,588,750
TR	165	24%	2,703,125
Mutation	154	36%	1,830,000

Table 9.4. Performance of enzyme GP with different operators, recording average solution time, success rate, and computational effort (CE).

9.2 Comparative Performance

Table 9.4 shows the performance of enzyme GP upon a selection of problems. The adder, multiplier and even-4-parity problems have been solved by Miller et al. [2000] using Cartesian GP. Results from Koza [Koza, 1992, 1994], using tree-based GP, are available for both parity problems. Koza [1992] has also attempted the 2-bit adder problem, but quantitative results are not available. Miller records minimum computational effort[1] of between 210,015 and 585,045 for the 2-bit multiplier problem. Enzyme GP, requiring a minimum computational effort of 136,080 for a population of

[1]Computational effort is a measure defined by Koza [1992], giving the number of solution evaluations required to achieve a 99% confidence of finding an optimal solution to a problem.

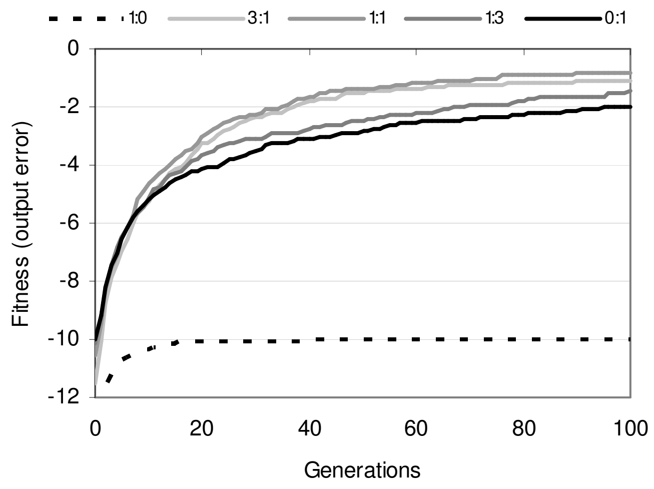


Random	C/o	Success	Average
No	Yes	70%	98
No	No	55%	79
Yes	Yes	26%	69
Yes	No	30%	64

Figure 9.2. Comparing mean number of output bit errors when evolving two-bit multipliers for functionality shapes and random shapes with and without TR recombination (c/o).

324, compares favourably with these results. For the 2-bit adder problem, Miller cites a minimum computational effort of 385,110. For enzyme GP, using the same functions as Miller, mimimum effort is 244,620: also a favourable comparison.

Koza has evolved even-n-parity circuits using populations of size 4,000 [Koza, 1992] and 16,000 [Koza, 1994]. For the even-3-parity problem (and without using ADFs), this gives minimum computational efforts of 80,000 and 96,000 respectively. For the even-4-parity problem, minimum computational efforts are 1,276,000 and 384,000 respectively. For enzyme GP, minimum computational effort has been calculated at 79,000 for the even-3-parity problem with a population of 100. For the even-4-parity problem with a population of 625, minimum computational effort is 2,703,000 with crossover and 1,830,000 without. This suggests that enzyme GP cannot easily evolve even-n-parity circuits where $n > 3$, at least for these (relatively small) population sizes and especially when crossover is used. This agrees with Miller's findings, where only 15 correct even-4-parity circuits were found in the course of 400 million evaluations. Langdon and Poli [1998] have suggested that parity circuits are unsuitable benchmarks for GP. Furthermore, parity circuits involve a high-degree of structure re-use and it seems plausible that sub-tree crossover, which is able to transfer sub-structures independently of their original context, may be more able to develop this sort of pattern than enzyme GP.



Ratio	Success	Average
1 : 0	0%	—
3 : 1	33%	51
1 : 1	50%	50
1 : 3	35%	69
0 : 1	15%	76

Figure 9.3. Comparing fitness evolution and performance for different ratios of activity to binding sites during shape calculation.

9.3 Functionality

The results outlined above suggest that enzyme GP is able to compete favourably against GPs which use indirect context representations. However, given the differences in evolutionary frameworks and other implementation details, it is difficult to compare indirect and implicit context by comparing the performance of different GP systems. A more direct comparison between indirect and implicit context representations can be made by comparing the performance of enzyme GP with functionality shapes against enzyme GP with randomly generated shapes. These random shapes effectively specify an indirect context, where there is no relationship between pattern and behaviour. Figure 9.2 shows that fitness for enzyme GP with random shapes initially grows at a high rate, but falls to a relatively low rate once a certain fitness level is reached. This suggests a high level of disruptive variation, which initially benefits search but later becomes a hindrance to effective exploitation. Enzyme GP with functionality shapes, by comparison, demonstrates a steady rate of decay in fitness growth, indicating a more structured search which continues until the optimum is found. The performance statistics listed in figure 9.2 indicate that performance is considerably better with functionality shape than with random shape[2]. This supports the notion that implicit context captures more meaningful context than indirect context.

[2]Note that it is considerably harder to find a solution with no output errors than it is to find a solution with one output error.

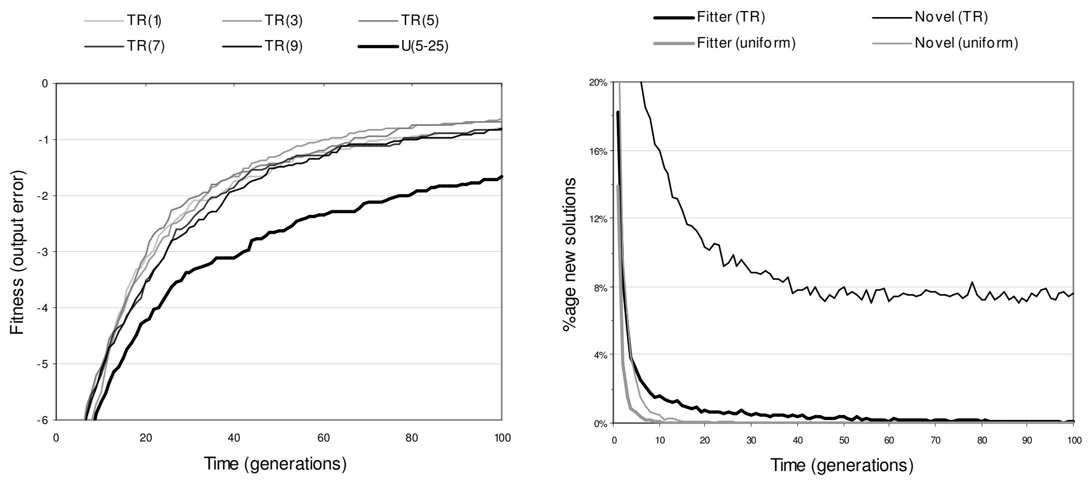


Figure 9.4. Comparing uniform and TR recombination. [Left] Fitness evolution for different transfer limits (TR) and size bounds (uniform). [Right] Ability to generate fitter programs and explore novel programs.

According to equation 8.1, a component's shape is a weighted sum of the functionality of its activity and the functionalities declared by its binding sites. Figure 9.3 shows the effect of this ratio upon fitness and performance: indicating that the best performance is attained when shape is calculated in an equal ratio from activity and binding sites. If shape calculation is weighted too far towards either activity or binding sites, then search becomes impaired. If the binding sites contribution is removed from shape calculation, then search becomes ineffective. If the activity contribution is removed, then performance becomes substantially degraded. These observations are not surprising. Weighting shape calculation too far towards the binding sites causes activity information, and therefore context information, to be lost. Weighting shape calculation too far towards activity causes the component's behavioural information to be lost; making it difficult to distinguish between the roles of components which have the same activity.

9.4 Recombinative Behaviour

9.4.1 Effect of crossover type

Section 8.6.1 described two types of recombination: uniform crossover and transfer and remove (TR). Table 9.4 shows that with the exception of the even-4-parity problem, the computational effort using uniform crossover is less than using TR crossover. However, this comparison is misleading since uniform crossover is constrained by

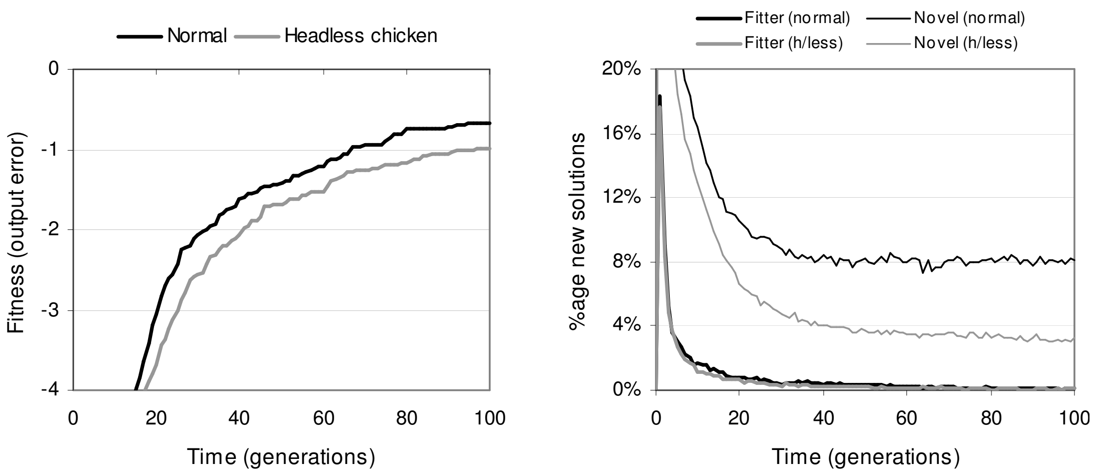


Figure 9.5. Comparing TR recombination against headless chicken TR recombination.

size bounds whereas TR recombination is not. Uniform crossover, therefore, explores a smaller area of the search space; an area which, in these cases, is known to contain an optimal solution. Figure 9.4 shows more meaningful comparisons between these two kinds of recombination. The graph on the left of the figure plots fitness evolution for different operator parameter settings. It can be seen that whilst uniform crossover appears to compete favourably for the size bounds used in table 9.4, its performance becomes considerably impaired when size bounds are used which more accurately reflect the region explored by TR recombination. The graph on the right of figure 9.4 plots the evolution of recombination's ability to generate neutral and fitter solution variants. For both measures, the performance of TR recombination is significantly higher than uniform crossover. Notably, uniform crossover is far less able to explore neutral variants than TR crossover — suggesting that uniform crossover is too disruptive to search in the neighbourhood of existing solutions. This is unsurprising given that uniform crossover targets multiple sections of the representation and always causes components to be replaced rather than appended. TR recombination is used for most of the remaining experiments documented in this chapter: both for the above reasons and because it is computationally less expensive, behaviourally more interesting, and fairly insensitive to initial representation size and transfer size (as indicated by figure 9.4).

9.4.2 Crossover versus Mutation

According to the arguments described in [Vassilev et al., 1999], recombination would be expected to offer relatively poor performance upon Boolean symbolic regression problems. For this reason, recombination was not used in Miller's experiments on digital circuit evolution [Miller et al., 2000]. However, results from experiments using enzyme GP indicate that recombination can play an important role in digital circuit evolution and, significantly, offers better search performance than mutation operators. Table 9.4 shows that, in all but the even-4-parity problem, enzyme GP with recombination performs considerably better than enzyme GP with mutation alone. In previous GP studies, headless chicken crossover operators, which recombine existing solutions with randomly generated solutions, have been used to show that crossover performs no better than macro-mutation. Results depicted in figure 9.5 show that for enzyme GP, TR recombination offers better performance than a headless chicken operator based upon TR recombination. This suggests that recombination is transferring useful information between programs. However, even the headless variant offers reasonable performance.

A more direct comparison between the search performance of recombination and mutation has been carried out by configuring enzyme GP's evolutionary framework to generate one child via recombination and another via mutation for every reproduction event and by measuring the relative fitness of the children produced by each operator. This was done for both functionality and random shapes. Figure 9.6 shows that when functionality shapes are used, recombination is responsible for generating the fittest child during a substantially greater proportion of reproduction events than mutation. This suggests that recombination has considerably more influence upon search than mutation. However, when random shapes are used, recombination is no longer the dominant operator with (especially for the multiplier problem) mutation generating the greater proportion of fitter children during reproduction events. This lends weight to the argument that implicit context improves the behaviour of recombination with respect to indirect context. Figure 9.6 also shows that transfer operations have a slightly higher success rate than remove operations during TR recombination. This reflects the fact that solutions are more likely to be disrupted by removing components than they are by gaining components.

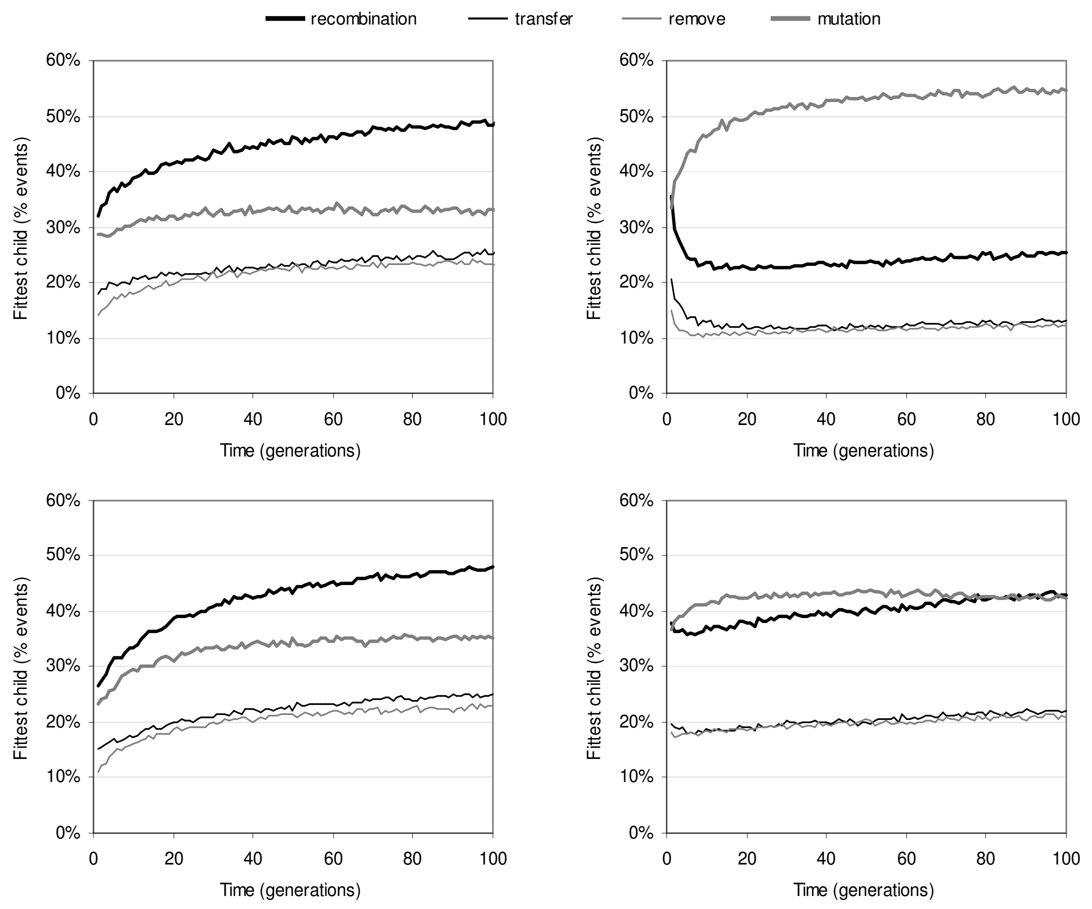


Figure 9.6. Comparing relative ability of recombination and mutation operators to generate fitter children during the evolution of [top] two-bit multipliers and [bottom] two-bit adders using [left] functionality shapes and [right] random shapes.

9.4.3 Microscopic Behaviours

The implementation of enzyme GP used for this study allows evolutionary behaviours to be observed at the level of individual solutions and individual variation events. Whilst these observations do not have the statistical significance of the macroscopic measures used elsewhere in this chapter, they provide an interesting insight into how evolution occurs at a microscopic level.

There are many kinds of behaviours which can occur as a consequence of applying variation operators. Nevertheless, many of these are built upon a selection of fairly simple behaviours which are seen to occur frequently within evolving populations. Figures 9.7 and 9.8 show examples of such behaviours that occur when transfer and remove operations are applied during recombination. The transfer operation cannot

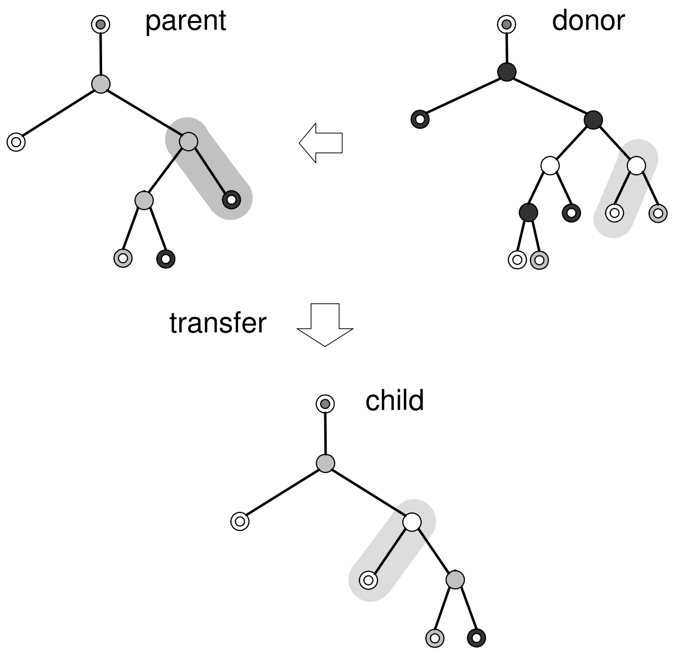


Figure 9.7. A simple example of subsumption resulting from a transfer operation. Different node and terminal shades represent different members of the function and terminal sets.

directly replace any components within a program representation (other than outputs). However, as figure 9.7 illustrates, it can still lead to behaviours at the program level that look like replacement. This happens because the new component has subsumed the role of the former component, offering a closer match to the input context declared by the parent node. Nevertheless, the former component is still present within the program representation and, if the new component were to be removed, could resume its former role in the program. Figure 9.7 also shows how subsumption is able to preserve the behaviour of the program below the component that has been replaced, indicating that the new component has a functionality similar to that of the former component, and illustrating the context preserving nature of recombination in enzyme GP.

Figure 9.8 shows two other behaviours which often occur during recombination: insertion and deletion. In the example on the left of the figure, a transfer operation leads to a new sub-tree being inserted between two existing components, something which is not possible using sub-tree swapping recombination in standard GP. Again, the existing sub-tree below the root of the inserted sub-tree is preserved, and from the perspective of the component (the output terminal) above the inserted sub-tree,

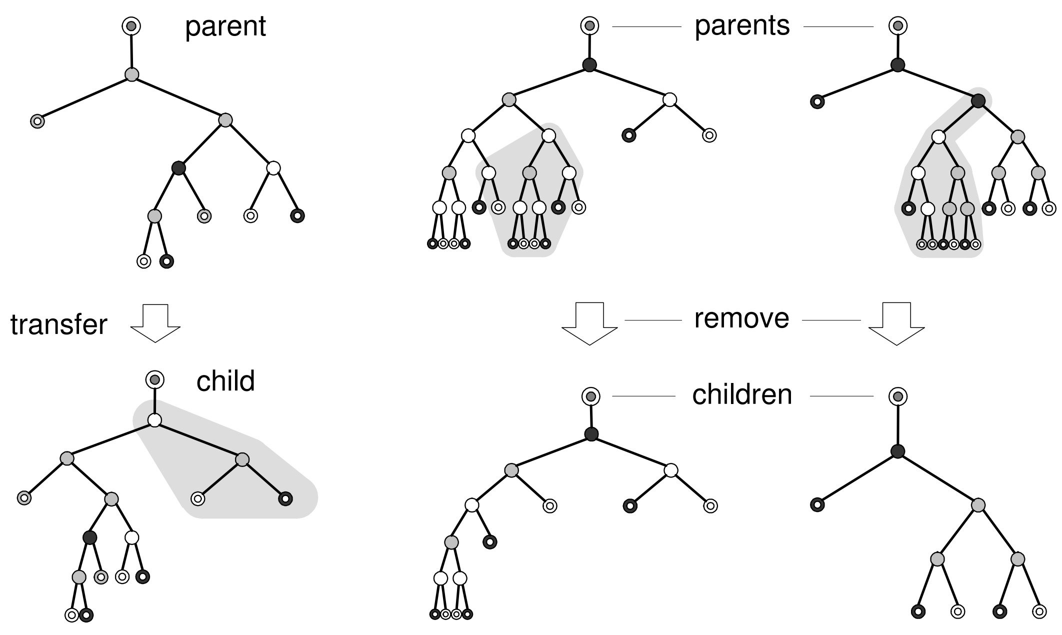


Figure 9.8. Behaviours resulting from transfer and remove operations.

the new context is related to the former context: and presumably a closer fit to the implicit context declared by its binding site. In fact, insertion is a special case of subsumption where the subsuming component happens to declare an input context which matches the role of the component that it subsumed. In the other two example in figure 9.8, removal operations lead to parts of programs being deleted. In the example in the centre, two sub-trees are affected by a single removal operation. This shows how recombination operators in enzyme GP operate upon groups of components at the representation level rather than structures (in this case sub-trees) at the program level: a behaviour which is presumably more disruptive, but also more expressive, than conventional sub-tree crossover. In the example on the right of the figure, an entire sub-tree is removed from between two nodes. This is the complement of the behaviour which occurs in the transfer example on the left of the figure, and shows how a subsumption operation might be reversed. In both of these removal examples, the program below the deletion remains unaffected, showing how the remove operation also encourages context preservation.

Conceptually, all the components defined in a representation occupy some position in a subsumption hierarchy. At the top are the expressed components: those which appear in the program. Below these are any redundant copies of the expressed components. Below these are components that have been subsumed by the expressed components; and further down, components that were subsumed by components further up the hierarchy which have since themselves also been subsumed. At the bottom are components which have never been expressed but which could in principle be expressed if all the components above them in the subsumption hierarchy were removed. All the behaviours that occur in enzyme GP are a result of variation operators modifying this subsumption hierarchy: either by adding new entries, by removing entries or by re-ordering existing entries (which is what mutation operators are essentially doing). Nevertheless, the operators are not aware of this subsumption hierarchy. They blindly add, remove and re-order entries — only causing change in the program when they happen to add, remove or re-order entries at the top of the hierarchy. All other changes are absorbed into the lower echelons of the hierarchy. Subsumption supports the idea that the program representation used by enzyme GP promotes meaningful variation filtering: since it is clearly the way in which the representation describes the program, rather than the action of the variation operators, that allows subsumptive behaviours to occur.

9.5 Size Evolution

In general, enzyme GP produces little or no bloat in both representation and program size. Figure 9.9 shows the size evolution of two-bit multipliers for both recombination operators and for different initial representation sizes. Size evolution under TR recombination is of particular interest, since in principal there is no upper bound to solution length. Nevertheless, there appears to be little pressure for the recombination operators to explore representation lengths much larger than the initial representation length. What little amount of growth there is for an initial representation length of 15 components can readily be accounted for either by the differential performance of the transfer and remove operators[3], by an initial representation length insufficient to easily express optimal solutions, or by there being many more solution representations of greater length than the initial representation length (or shorter). However, for an initial representation length of 30 components, even these factors appear to have no effect upon representation length.

[3]This is akin to the removal bias cause of bloat seen in tree-based GP.

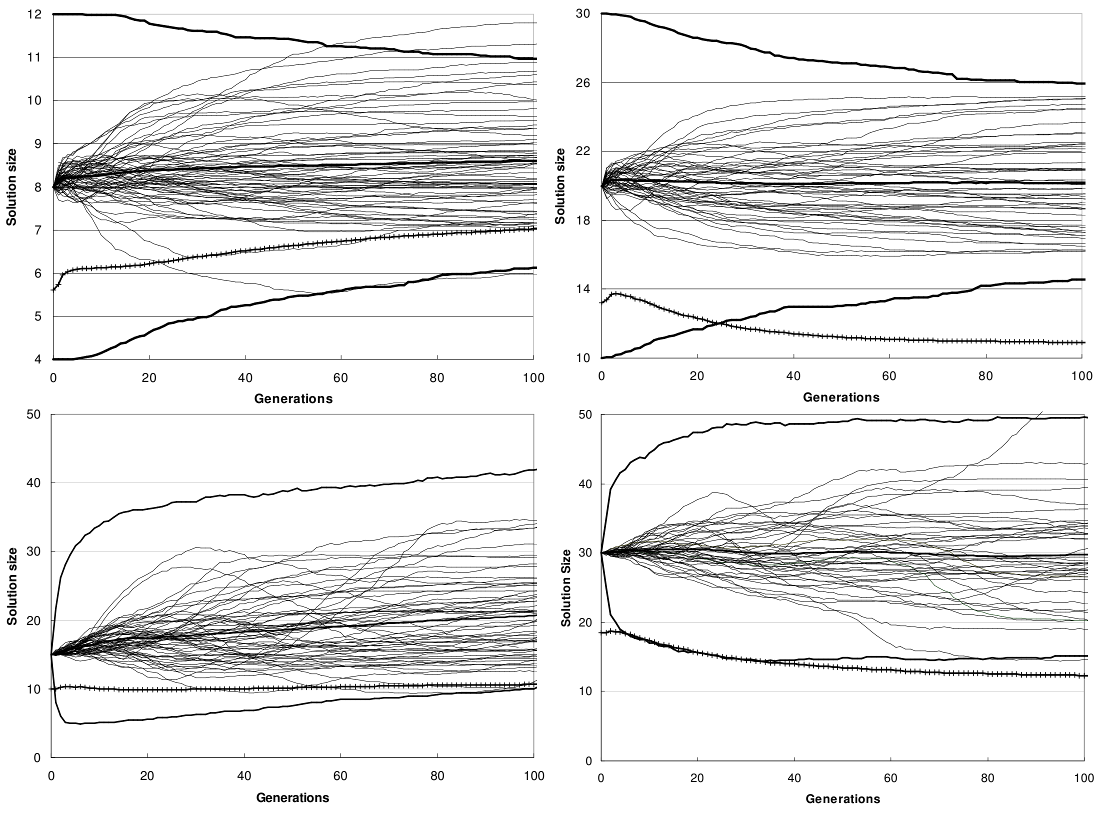


Figure 9.9. Two-bit multiplier size evolution using [top] uniform crossover and [bottom] TR recombination. Faint lines show average representation sizes for each run. Heavy un-crossed lines show average minimum, average and maximum representation sizes across all runs. Heavy crossed line shows average program size across all runs. Minimum optimal program size for this problem is 7 gates.

Figure 9.9 also shows that program size evolution is not proportional to representation length evolution. For both forms of recombination, change in average program size does not reflect change in average representation length. For TR recombination: with an initial representation length of 15 components, whilst representation length grows on average over the course of a run, program size remains fairly stable. For an initial representation length of 30, average program size falls whereas representation length remains stable. This behaviour reflects a decoupling between program and representation; and is an expected consequence of using an implicit context representation in which there is no necessity for components present in the representation to be used within the program. Nevertheless, given that large programs can only be expressed by sufficiently long representations, there is some dependence between representation length and program size.

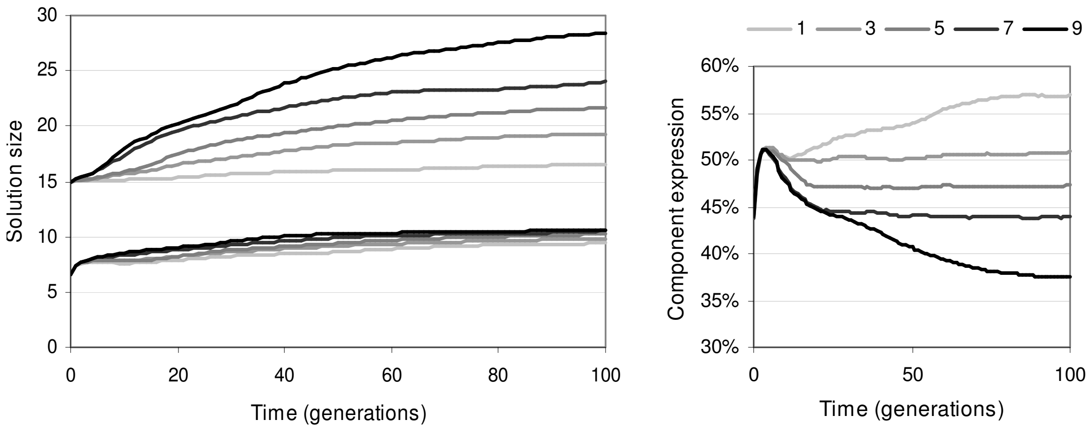


Figure 9.10. Effect of TR recombination transfer limit upon evolution of [left-upper] representation and [left-lower] program size and [right] component expression.

This decoupling characteristic allows program size evolution to follow a different pattern to representation length evolution. Figure 9.10 shows that the number of components transferred or removed during TR recombination has a significant effect upon the evolution of representation length for an initial length of 15 components. This is presumably because (for this initial length) greater transfer lengths allow exploration of a greater number of larger representation lengths without a similar increase in the number of shorter lengths which can be sampled. The trend for program size, by comparison, is far less pronounced. Indeed, it appears that program size is attracted towards a certain level regardless of representation length. This behaviour can also be seen in figure 9.11, in which initial representation length, whilst having a significant effect upon initial program size, has a relatively small effect upon the final average program size within a population. Consequently, for larger initial representation lengths, program size tends to evolve towards smaller solutions. In general, this would seem to be a beneficial behaviour; and certainly favourable to the bloating behaviour found in conventional GP. However, it could conceivably lead to evolution preferring a smaller sub-optimal solution over a larger optimal solution: although this behaviour was not observed in the test problems and recovery from this situation is made more likely given that representation length does not follow a similar trend.

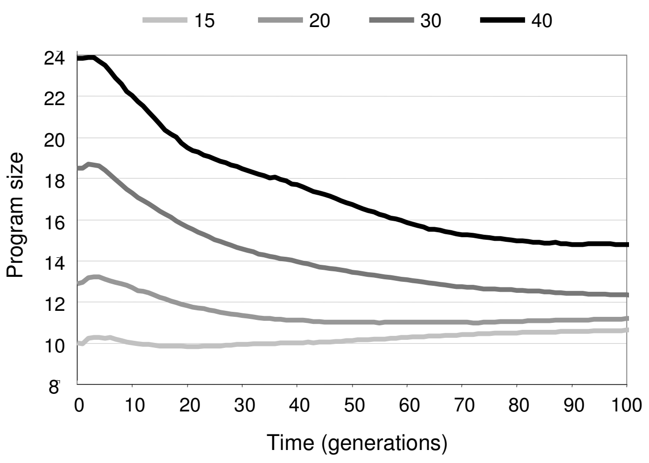


Figure 9.11. Evolution of program size with different initial representation lengths.

9.6 Redundancy

Before attempting to explain why program size evolution follows the pattern described above, this section addresses a related question: Why does the proportion of non-coding components within a representation increase over time? This trend can be seen in both figure 9.9[4] and figure 9.10. In part, this question can be answered by comparison to Miller's assertion that neutral growth in cartesian GP is due to the exploration of neutral variants within a problem's search space; most of which have more rather than less redundant components than existing program representations [Miller, 2001]. However, a more general answer to this question is that growth in the number of non-coding components is due to variation filtering.

The effect of variation filtering upon neutral growth can be seen in figure 9.12; which shows the pattern of growth in a population which is not undergoing fitness-based selection. Consequently, any problem-specific size information is removed. Again, program size growth is considerably lower than representation size growth, implying that the proportion of un-expressed components in a program representation, on average, increases over time. This effect can be accounted for by a process of variation filtering, where the un-expressed portion of the representation contains those components which have been inserted into the representation but not propagated to the program.

[4]Ignoring uniform crossover, which is assumed not to have a significant effect upon size evolution.

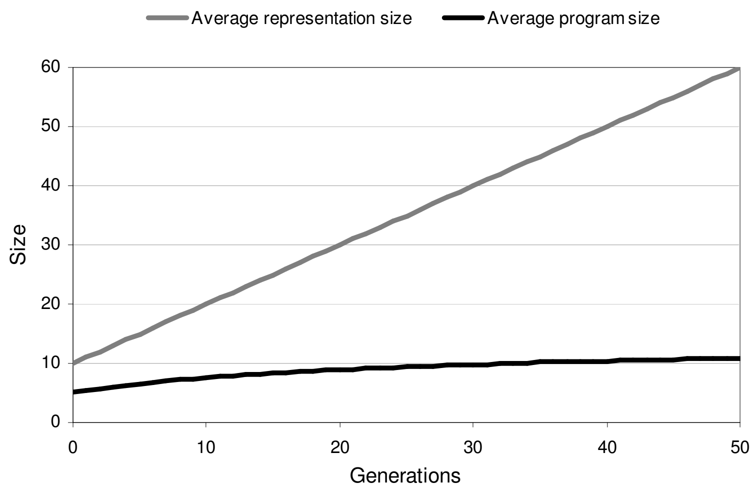


Figure 9.12. Comparing program size growth against forced representation growth in a population of size 100 with no selection pressure, no removal operation and no mutation.

This un-expressed portion of the program representation constitutes the recessive part of the subsumption hierarchy described in section 9.4.3. Although it would not normally grow at the rate seen in this example, it is interesting to consider whether it has a role other than filtering out components that do not fit into the context of a program. Figure 9.13 shows that when recessive components are removed from representations following program development, fitness evolution is substantially impaired. In fact, in this experiment enzyme GP was not able to evolve any 100% correct solutions when non-coding material was removed. This suggests that recessive components do play an important role in evolution. One of these roles is likely to be maintenance of diversity: making components which are not currently used within programs available for use within future solutions. However, it also seems plausible that recessive components enable evolutionary back-tracking; since if the population were to evolve towards a local optimum, these recessive subsumption hierarchies contain information that could be used as a means of escape to some previous point before the population converged upon the local optimum.

Figure 9.14 shows the effect of another source of redundancy, recessive binding sites (see section 8.4.1), upon fitness evolution and performance. Whilst the effect is fairly small, there is a statistically significant ($U = 1255.5, p < .05$) performance benefit to having a single recessive binding site for every functional component. However, the benefit becomes insignificant when too many recessive binding sites are used (com-

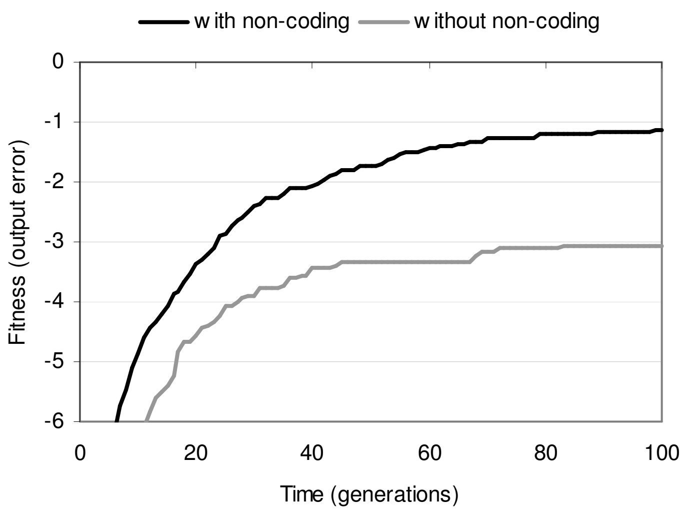
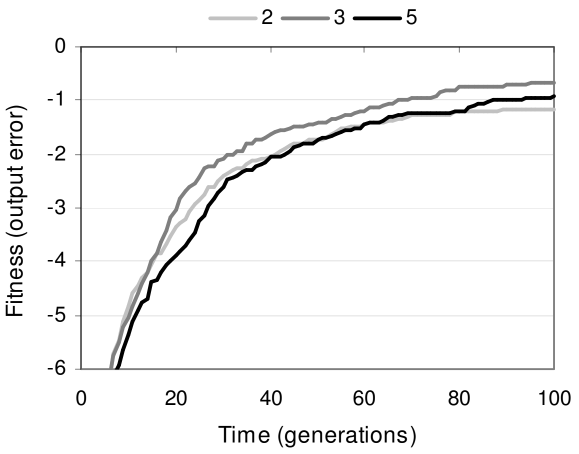


Figure 9.13. Effect of removing non-coding components upon fitness evolution ($bs = 2$).



bs	Success	Average
2	38%	55
3	49%	57
5	47%	64

Figure 9.14. Comparing fitness evolution and performance for different numbers of binding sites per component. All functions used are two-input, meaning that recessive binding sites are present for $bs > 2$.

paring $bs = 2$ to $bs = 5$: $U = 914, p = 0.2$). Again, the benefit to having recessive binding sites probably lies in the extra diversity that they confer. However, too many recessive binding sites presumably interfere with pattern calculation; and can encourage macro-mutation.

9.7 Phenotypic Linkage

The phenotypic linkage of a program is determined by the average Hamming distance between binding sites' functionalities and the functionality shapes of the substrates they bind during development. Phenotypic linkage is a measure of the internal co-

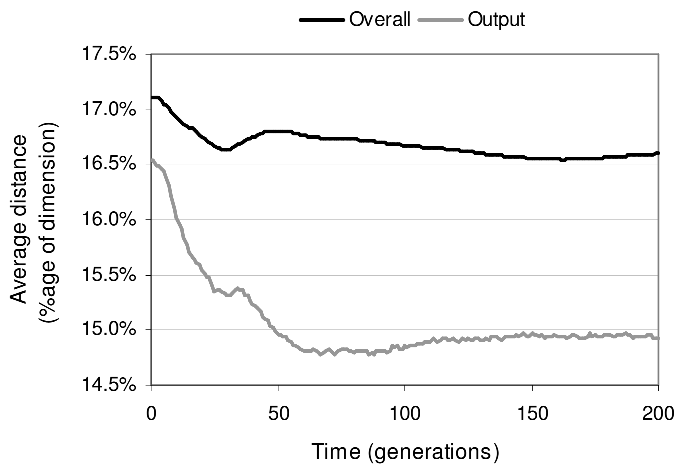


Figure 9.15. Evolution of phenotypic linkage.

hesion of a developed program; and therefore a measure of its relative fragility when exposed to evolution.

As figure 9.15 shows, the distance between binding sites and their substrates falls over the course of evolution. This implies that phenotypic linkage increases during evolution. This effect is fairly small for the average distance within the entire program. However, it is more pronounced for the average output distance. This is presumably for two reasons. First, components near the outputs of a program have the most impact upon the program's behaviour and are therefore likely to benefit most from the increased protection from change offered by tighter linkage. Second, variation filtering is more pronounced for the components near the outputs since they have less developmental constraint and are therefore more able to choose substrates which more closely match their binding sites.

However, the effect shown in figure 9.15 is not entirely due to evolution searching for tighter linkage. As figure 9.16 illustrates, tighter linkage is an automatic by-product of larger representation length. This is not surprising, since larger representations offer more choice during development: such that each binding site both has more choice of potential substrates and is more likely to be able to select a given substrate. Given that representation length does, on average, increase during evolution, a proportion of the growth in phenotypic linkage seen in figure 9.15 can be attributed to this increase in representation length. Nevertheless, as figure 9.16 shows, a substantial amount of the growth in phenotypic linkage does appear to be due to evolution searching for tighter

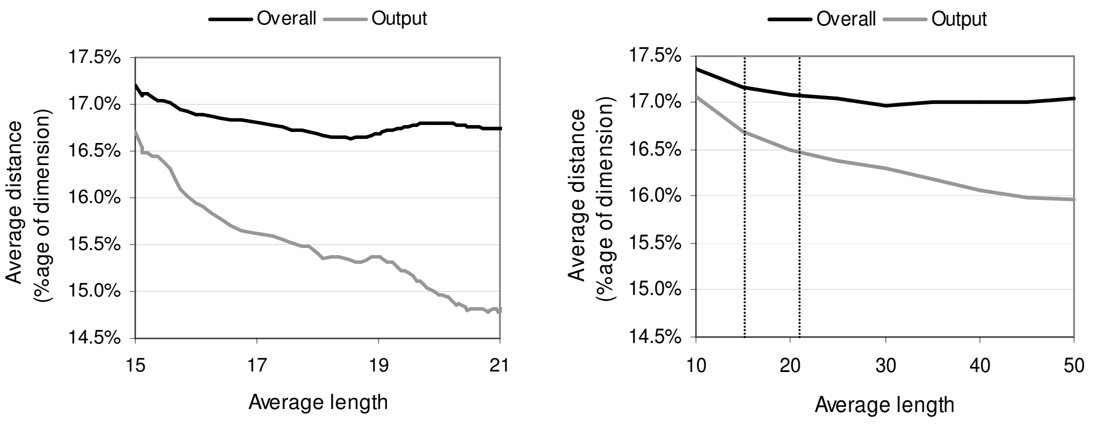
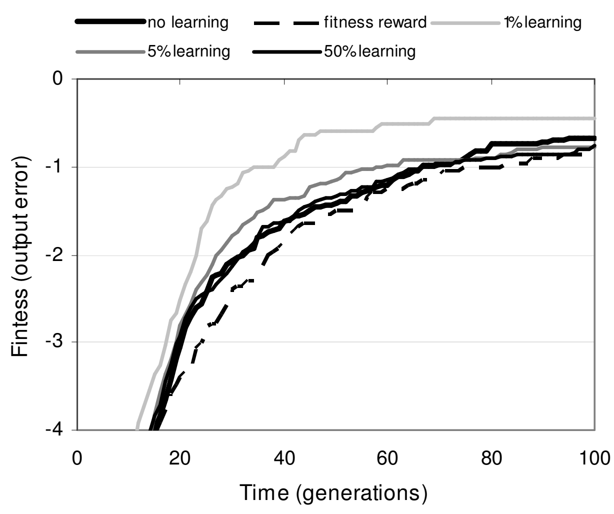


Figure 9.16. Relationship between average phenotypic linkage and representation length [left] during fitness-based evolution and [right] for random solutions. Broken lines indicate common region of representation length between graphs.

linkage. It could even be argued that evolution tends to search longer representations in order to improve phenotypic linkage.

9.7.1 Phenotypic Linkage Learning

Even without taking the effect of representation growth into account, the average increase in phenotypic linkage during the course of a run is not large. This raises the question: can evolutionary search be improved by making an explicit attempt to evolve tighter phenotypic linkage? Two strategies were used to answer this question. The first used an altered fitness function which rewards programs with tighter linkage. The second uses Lamarckian reinforcement learning: whereby following development, binding sites are changed (from the bottom of the program upwards) so that they more closely match the substrates which they have bound. Figure 9.17 shows the effect of these two approaches upon fitness evolution and performance. Where a fitness reward is used, performance is slightly impaired. This suggests that the phenotypic linkage component of the fitness function is interfering with the behavioural component; presumably because programs with tight linkage are not necessarily those with the highest behavioural evolvability. Reinforcement learning, by comparison, can lead to a considerable improvement in evolutionary performance. However, this improvement is dependent upon an appropriate learning rate. If the learning rate is set too high, then there is no improvement in performance. Whilst tighter linkage does



Condition	Success	Average
No learning	49%	57
Fitness penalty	48%	57
1% learning	75%	40
5% learning	56%	45
50% learning	50%	51

Figure 9.17. Effect of phenotypic linkage learning upon performance. Learning rate refers to percentage change in distance per functionality dimension during Lamarckian reinforcement learning.

both increase the fidelity of development and decrease the disruptiveness of variation operators by encouraging phenotypic building blocks, it must also reduce the scope of search by reducing exploration of new phenotypic building blocks — and hence the number of programs which can be sampled by variation operators. It seems, therefore, that in this case a learning rate of 1% per dimension represents an appropriate balance between phenotypic stability and phenotypic exploration.

9.7.2 Stability and Replication Fidelity

Figure 9.18 shows the effect of reinforcement learning upon phenotypic linkage and program size. Not surprisingly, higher levels of reinforcement learning lead to greater phenotypic linkage. However, higher levels of reinforcement learning also lead to larger program size and representation length. Presumably this happens as a consequence of increased phenotypic linkage; suggesting that higher phenotypic stability supports the evolution of larger programs — and that ordinarily it would be more difficult to evolve larger programs[5]. This observation helps to explain why enzyme GP tends to evolve small programs. Small programs are better replicators than large programs since they have fewer connections between components and are therefore less

[5]This does not suggest that large programs are impossible to evolve, just that smaller programs are more likely to be propagated by the evolutionary mechanism; and therefore preferred over larger programs with equivalent functionality.

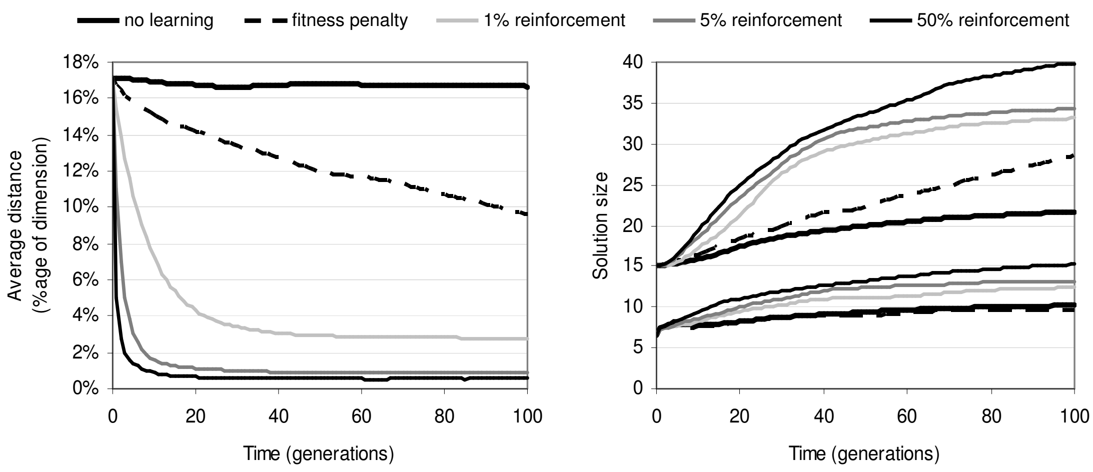


Figure 9.18. Effect of phenotypic linkage learning upon [left] phenotypic linkage, [right-upper] representation length and [right-lower] program size.

likely to be disrupted by variation operators. Small programs and their sub-structures are also more likely to be copied by transfer operations.

Figure 9.19 illustrates that the size of the function and terminal sets affect the behaviour of evolution even when a population is not exposed to selective pressure; indicating that program evolution is biased by the constitution of the activity set in a way which is independent of the problem's search space. This is one of the less desirable properties resulting from the use of functionality as an implementation of implicit context. Specifically, increasing numbers of functions and decreasing numbers of input terminals both lead to larger program size and higher phenotypic linkage. In part, this happens due to an implicit bias towards expressing preferences for input terminals over functional activities within random functionalities. Each function and input terminal activity is allocated one dimension in functionality space. However, whereas there are many copies of each functional component within a representation, there is only one instance of each input terminal. Consequently, there is a disproportionately high likelihood of a random functionality expressing a strong preference for an input terminal activity: although during selective evolution (where functionalities do not remain random) this is unlikely to be a problem unless a strong sub-optimal solution has a high proportion of input terminals close to its outputs. Nevertheless, this implicit bias may be another reason why enzyme GP tends to evolve short programs; and, as figure 9.19 shows, is a behaviour which can be altered by changing the ratio

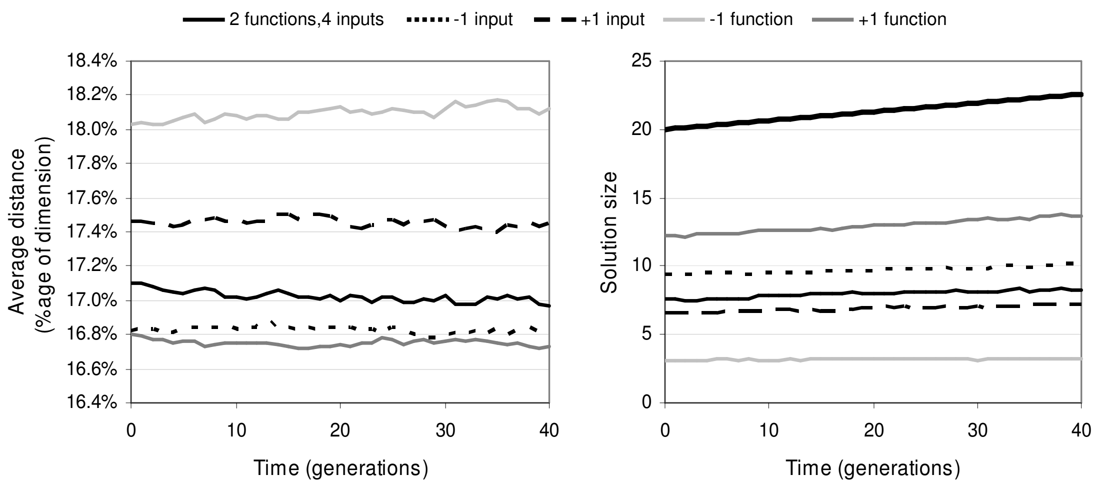


Figure 9.19. Effect of size of function and input terminal sets upon [left] phenotypic linkage and [right] program size (thick black line shows average representation length) for evolution without selective pressure.

between input terminal activities and functional activities.

A further explanation for the effect of function set size upon program size and phenotypic linkage may lie in the degree to which a function set can express large solutions. A component's functionality describes an expected profile of the functions which will occur in the sub-program of which it is the root. If a lot of different functions are used in a program, then functionality has a relatively large amount of detail with which to describe a sub-program. If there are fewer functions, then functionality has less detail with which to describe a sub-program and consequently less scope with which to distinguish between components. Accordingly, programs with fewer functions may have a tendency to display less internal cohesion and be more sensitive to variation, tending towards smaller sizes in order to gain sufficient replication accuracy.

9.8 Genetic Linkage

Figure 9.20 shows the pattern of genetic linkage evolution within enzyme GP. As with phenotypic linkage, larger representation lengths automatically generate tighter genetic linkage. This occurs because larger representations tend to have lower levels of component expression, implying that the expressed components can on average cover a smaller portion of the representation. Compensating for this trend, genetic linkage

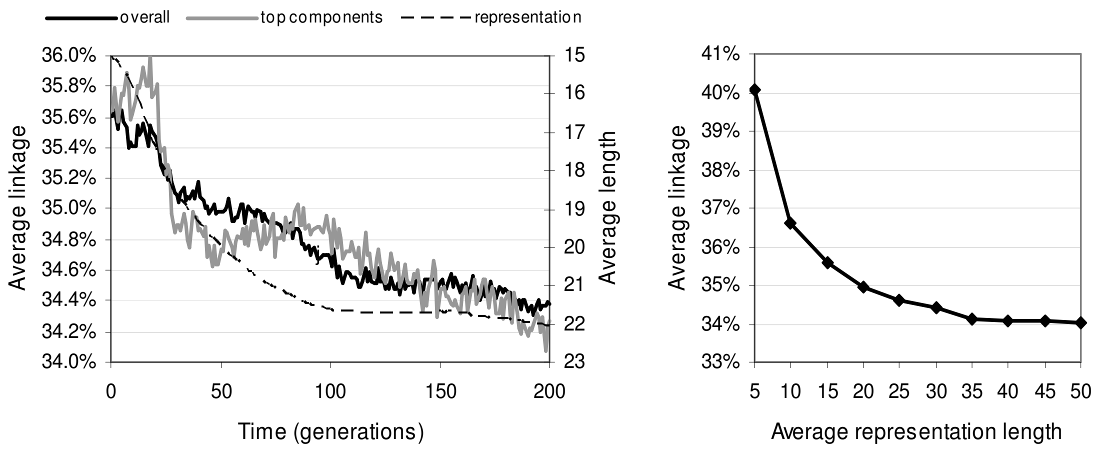


Figure 9.20. Average genetic linkage between components as a percentage of representation length. [Left] Evolution of genetic linkage for all components ('overall') and for components bound to outputs ('top components'), showing average representation length. [Right] Relationship between representation length and average genetic linkage without evolution.

does appear to evolve in enzyme GP, but at a very low rate (a few tenths of a per cent over the course of two hundred generations). The genetic linkage learning rate is slightly higher for components located proximal to the program outputs. Again, this would be expected given the greater value of building block formation nearer to the program outputs. In figure 9.20, the output linkage continues to improve following the convergence of representation length: though given the variance suggested by the noisy plot, this may not be a representative trend. In general, these results suggest that genetic linkage is not encouraged by enzyme GP. Accordingly, it might be interesting to investigate the merit of genetic linkage reinforcement considering the apparent benefit of phenotypic linkage reinforcement. Whilst it might not be possible to improve the genetic linkage between all pairs of interacting components, it certainly seems possible that genetic linkage could be improved on average, for components near program outputs, or for the most strongly interacting components in a program.

9.9 Component Reuse

Component reuse is the number of times a single component instance is bound during development. Accordingly, average component reuse measures how many times, on average, sub-expressions are reused within programs. Figure 9.21 shows how the

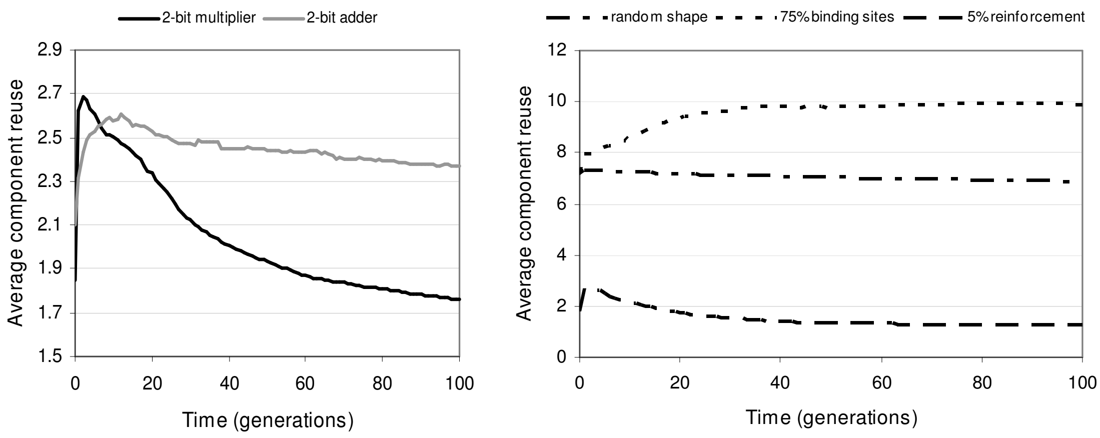


Figure 9.21. [Left] Evolution of functional component reuse for two-bit multipliers and adders. [Right] Some factors which affect component reuse during the evolution of two-bit multipliers.

average functional[6] component reuse changes during the course of evolution. These graphs display a number of trends: (i) the pattern of reuse is problem independent; (ii) reuse generally falls during evolution; and (iii) components are typically used more than once during program development. Implicit context is expected to promote a degree of component reuse; since, according to the definition of implicit context, behavioural reuse should require component reuse. It is therefore to be expected that the degree of reuse will depend upon the problem's search space — and presumably for both of these problems, behavioural reuse becomes less appropriate as search approaches the optimal program behaviour. Figure 9.21 also shows that reuse is affected by both reinforcement learning and the manner in which component shape is derived. For reinforcement learning, it is more likely that component reuse will reflect behavioural reuse, given that distances between components are likely to be smaller. This tends to suggest that without reinforcement learning, there is more reuse than is strictly necessary to express solutions. Where shape is generated randomly or heavily biased towards binding sites, reuse rises considerably. This reflects a decreased bias towards input terminal components, making it more likely that functional components will be bound during development.

These results indicate that evolution can take place using a wide range of degrees of component reuse. However, no attempt has been made to measure the relationship, if any, between reuse and evolutionary performance. Given the current debate

[6]Input terminal component reuse is ignored since there is only one instance of each input terminal and therefore an un-representative amount of reuse of these components.

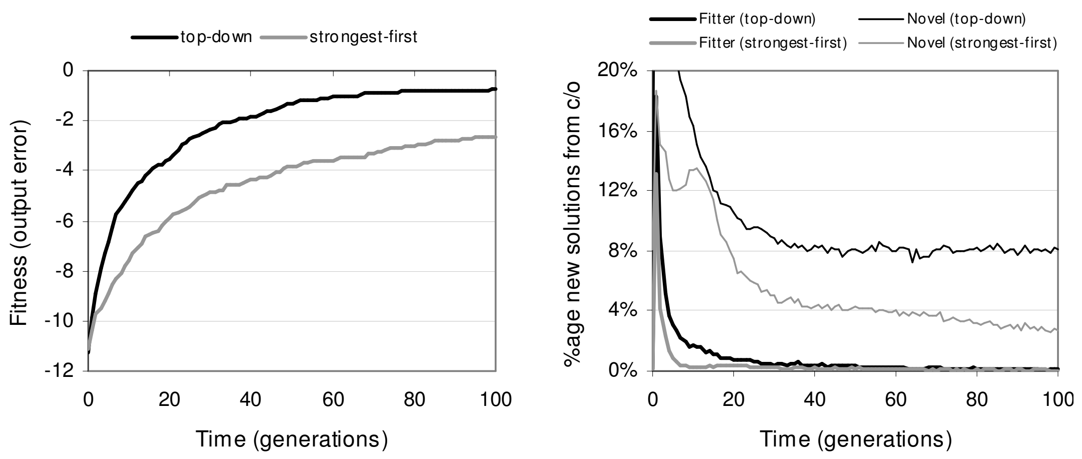


Figure 9.22. [Left] Fitness evolution and [right] recombinative behaviour of development strategies.

amongst evolutionary biologists over the relative merits of compartmentalisation and pleiotropy, this would be an interesting investigation for future work.

9.10 Development

Two different development strategies were outlined in section 8.5. Top-down development constructs a program from the outputs to the inputs, whereas strongest-first development constructs a program from the most strongly interacting components to the least strongly interacting components. Accordingly: (i) strongest-first development leads to higher average phenotypic linkage; (ii) top-down development leads to higher phenotypic linkage nearer to the program outputs; and (iii) strongest-first development is able to construct connections between components which do not contribute to the program outputs. Figures 9.22 and 9.23 show the consequences of these behaviours upon evolutionary performance, recombination, and development time. Top-down development supports better evolutionary search than strongest-first development. Figure 9.22 suggests that the relatively poor performance of strongest-first development may be due, at least in part, to lower recombinative success and lower neutral exploration through crossover. It is not entirely clear why this is the case. However, it might be speculated that this is due to lower phenotypic linkage between components near the program outputs; leading to lower correspondence between the expected behaviour and the actual behaviour of these behaviourally important components. This, in turn, could lead variation operators to more easily disrupt

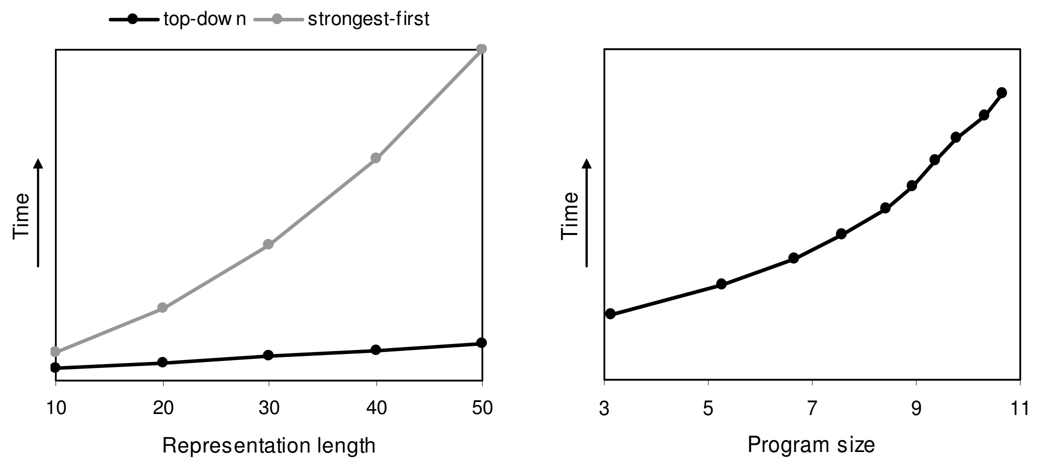


Figure 9.23. Relationship between development time and solution lengths.

the behaviour at the program outputs.

Figure 9.23 shows that top-down development also offers better time complexity than strongest-first development. This follows from point (iii) above. For top-down development, the fact that program size growth is a lot lower than representation length growth means that development time only rises at a near linear rate with respect to representation length; despite the fact that the development process has above-linear time complexity with respect to program size (see rightmost graph in figure 9.23). For strongest-first development, connections are made which are not part of the developed program; and since the number of connections made rises in line with representation length growth, the rate of development time growth is much higher than linear with respect to representation length growth.

9.11 Discussion

Implicit context representation improves a program's response to variation

It seems clear that, in principle at least, meaningful variation filtering is a key ingredient in the hunt for an evolvable representation. Perhaps the most persuasive evidence that implicit context leads to meaningful variation filtering is that search performance (figure 9.2) and the relative capacity for recombination to generate fitter children (figure 9.6) both decrease considerably when implicit context is replaced with a form of indirect context. Hence, it follows that these beneficial behaviours are a consequence of program components choosing their interactions according to behavioural descriptions of other components rather than arbitrary patterns. To a lesser extent, this argument is also supported by performance comparison between enzyme GP and cartesian GP (section 9.2); although this comparison is made unreliable by the many other differences between the two methods.

The argument that implicit context representations react in a meaningful way to change is also supported by the recombinative behaviours outlined in section 9.4.3 which occur as a result of the addition and removal of components. For each of these behaviours — subsumption, insertion, and removal — the child program 'attempts' to preserve the behaviours of the parent despite changes to the program's representation: yet still allows change to occur. Nevertheless, there has been no quantitative study of how often, and how effectively, these behaviours occur during program evolution; and whilst they are seen to occur frequently, they are rarely as pure as in these examples. Furthermore, many of the behaviours which are seen during evolution do not have such evidently beneficial characteristics. Therefore, whilst implicit context does lead to improved variation filtering behaviours when compared to indirect context, it seems fair to contend that this does not happen for all variation events. However, this is generally the nature of evolutionary search.

Implicit context preserves the meaning of recombined program fragments

This is an extension to the previous point. As well as improving the capacity for a representation to receive new components, implicit context also improves the likelihood of components maintaining their meaning when transferred between programs; and hence the capacity for a population to carry out co-operative evolution. This follows from the observation that recombination between pairs of existing representations leads to better evolutionary performance than headless chicken recombination between existing representations and randomly constructed representations (figure 9.5). Presumably this performance advantage is due to relatively fit program fragments being transferred between existing representations. Nevertheless, whilst there is a significant difference between the performance of recombination and headless chicken recombination, the performance of headless chicken recombination is still relatively high. That a macro-mutation operator can apparently carry out useful search supports the notion that implicit context representation improves response to variation. However, it also gives some concern that response to variation is dominant over transfer of information in generating recombinative performance. Consequently, in future work it might be interesting to take a closer look at how well information is transferred between programs and whether there are mechanisms which might improve the fidelity of information transfer. Genetic linkage reinforcement may be one such mechanism; since interacting groups of components are more likely to be transferred as a unit if they are located proximal in the representation. Without genetic linkage between components, there is some danger that transfer operations are more likely to transfer a group of small, non-interacting, program fragments which may either lose their behaviours or disrupt multiple sub-structures within the recipient program. Whilst some authors [e.g. Keijzer et al., 2001] believe that it is beneficial to change a program at multiple locations during recombination owing to increased search potential, it also seems that this sort of operation is more likely to disrupt the evolved behaviour of the program and lead to inviable offspring.

Functionality is a meaningful implementation of implicit context

This follows from the previous two points which show that functionality leads to the kinds of behaviours that would be expected from a meaningful implementation of implicit context. However, it appears that functionality is only meaningful when its derivation reflects an appropriate balance between a component's activity and its binding sites (figure 9.3). Otherwise, functionality fails to capture a sufficient description of a component's behaviour: either by not sufficiently describing how a component interacts with other components, or by not sufficiently describing the components it interacts with.

Despite its ability to describe implicit context, and the ease with which it can be calculated, functionality is not an ideal implementation of implicit context. Functionality is limited to describing contexts in terms of a functional profile. It can not describe the ordering or interactions between the functions in this profile. Whilst this is evidently sufficient to describe solutions to the problems used in this chapter, it apparently struggles to describe the kind of structural reuse seen in solutions to parity problems (section 9.2), and it is conceivable that it is not sufficient to describe all types of structure. Consequently, an important future avenue of research would be to investigate the applicability of functionality and, if necessary, consider other implementations of implicit context.

Enzyme GP does not suffer from bloat

Whilst, in some circumstances, enzyme GP structures experience a degree of growth; enzyme GP does not experience conventional GP bloating behaviour (figure 9.9). Recall from section 6.4 that there are a number of hypothesised causes of bloat within tree-based GP: replication accuracy, removal bias, search space bias, and operator bias. The replication accuracy theory contends that bloat is needed to protect programs from the disruptive effects of recombination. It seems that whilst the recombination operators of enzyme GP do not always carry out meaningful behaviour, TR recombination in enzyme GP is less disruptive than sub-tree crossover in tree-based GP. Partly this is a result of variation filtering at the representation level. However, disruption is also reduced by the decoupling between transfer and remove operations. Whereas in conventional GP, one group of components always replace another; in enzyme GP transfer does not physically replace components, and remove operations operate independently to transfer operations. Furthermore, as with linear GP (see section 7.4.1), non-coding components within enzyme GP representations are able to provide a structural protection role which can, in principle, increase reproductive fidelity without the need for the kind of global protection behaviour provided by bloating in tree-based GP.

Removal bias can still be caused by the disparity between the success rate of transfer and remove operators; but does not have the potential to drive bloat at anything like the levels seen in tree-based GP. Search space bias is a property of the problem domain rather than the search process, so presumably is still a factor in enzyme GP. There is no operator imbalance in enzyme GP, since recombination — at least mechanistically — has a size neutral effect. In summary, it seems that the lack of bloat in enzyme GP can in part be explained by a lessening of the behaviours hypothesised to cause bloat in conventional GP. However, it seems that the remaining behaviours, particularly search space bias, should have the capacity to drive a certain amount of size growth: yet this growth is not seen in practice.

Program size is decoupled from representation length

This occurs because components present in the representation need not be expressed in the program. However, the representation length does place an upper limit upon the program size, even after component reuse has been taken into account. The advantage of this decoupling is that program size evolution is not directly linked to the action of the recombination operators and is therefore free to vary within the upper bound set by the representation length. In practice it appears that evolution is biased towards searching smaller program sizes: which, from a practical viewpoint, is advantageous since it leads to small, efficient solutions. It also helps to explain why representation length does not bloat, since there is little search pressure towards higher upper limits on program size.

There appear to be two reasons for this behaviour (section 9.7.2). First, functionalities with a disproportionately high degree of input terminal activities are over-represented in functionality space; giving functionality space an implicit bias towards short solutions. This bias is particularly apparent when the activity set contains many input activities and few functional activities (figure 9.19). Nevertheless, the bias only applies to random functionalities; and consequently dissipates as functionalities become non-random during the course of evolution. Second, small programs presumably have higher replication fidelity since they have less internal connections to be disrupted when exposed to variation operators and, having shorter defining component sequences, are more likely to be propagated during transfer operations.

In part, the trend towards smaller program size compensates for the higher time complexity resulting from the development process (figure 9.23). It also leads to lower space complexity. However, there is some danger that enzyme GP will find it harder to solve problems with large solutions; particularly if sub-optimal solutions are short. Some useful directions for further research will be to look at ways of removing functionality bias, possibly by selecting more representative initial generation functionalities, and ways of reducing the complexity of development. Perhaps the most obvious way of reducing complexity would be to allow recurrent solutions; since most of the development time is involved with preventing recurrency.

Redundancy improves the performance of evolutionary search

This follows from the observation that when redundant components are removed from program representations following development, evolutionary search is substantially impaired (figure 9.13). The beneficial effect of non-coding components could either be due to a structural or functional role. Although a structural role can not be discounted, it seems relatively difficult for non-coding components to carry out a structural protection role in enzyme GP given that (i) there is little genetic linkage between interacting components, and therefore little scope for the construction of linear sequences of non-coding components between coding sequences; (ii) non-coding components do not necessarily remain non-coding following transfer, and therefore do not substantially decrease recombinative disruption; and (iii) there is relatively little scope for the construction of syntactic introns. However, there are good reasons to believe that redundancy provides a beneficial effect through its functional role. Considering that program size tends towards small solutions, it would be easy for a population to lose functional diversity if it were not for the substantial proportion of non-coding components found within representations. Furthermore, it seems that this redundancy must be organised in the form of a subsumption hierarchy (section 9.4.3); where the components at the top of the hierarchy may play a key role in enabling back-tracking behaviours in response to disruptive variation events. This apparently beneficial functional role of redundancy also agrees with the findings of much of the research reviewed in section 7.4.3.

Lamarckian reinforcement learning can significantly improve performance

A reinforcement learning rate of 1% of the difference between a binding site and the shape of its bound component leads to a 50% improvement in success rate and a significant reduction in the average number of generations required to evolve a two-bit multiplier (figure 9.17). Presumably this is due to the stabilising effect that reinforcement learning has upon the building blocks of evolving programs. Given that interactions are reinforced following each variation event, reinforcement learning will give most stability to those building blocks which have remained in the same program throughout a number of variation events or have passed through a number of programs via transfer operations. Therefore, reinforcement learning implicitly strengthens those building blocks which have a high effective fitness; and in effect increases their effective fitness over time by making them easier to propagate between programs. The benefits of Lamarckian reinforcement learning within enzyme GP mirrors its benefits within other GP systems [Teller, 1999, Downing, 2001]. The trade-off between exploration and exploitation in choosing an appropriate learning rate in enzyme GP also mirrors the balance between insufficient learning and over-learning when choosing a learning rate for the neural network back-propagation algorithm.

10 Summary and Conclusions

This chapter summarises the work reported in this thesis and the rationale behind it; presents conclusions; discusses limitations of the experimental method; and speculates about further work.

10.1 Rationale and Work Done

This thesis began with the goal of mining biological knowledge to improve the behaviour and performance of genetic programming. Biology has served as an inspiration to computer science throughout its history. Many fields of modern computer science, such as machine vision, robotics, and neural networks, place an implicit emphasis upon the mimicry of biological systems in both their goals and their methods. Indeed, biology possesses many of the attributes which many people would one day like to see in computer systems, including: fault tolerance, self repair, autonomous behaviour, self-replication, intelligence, learning, reconfigurability and environmental interaction. Yet, according to Charles Darwin's theory of evolution, all these attributes came about through an iterative process of selection acting upon random change to some initially very simple organism — and herein lies the motivation behind evolutionary computation.

Nevertheless, both our understanding of biology and our understanding of change within non-biological systems points to the realisation that a complex artifact can only be evolved if the artifact is internally organised in a suitable way. For example, it is very difficult to derive a complex software system from a basic software system if the basic software system does not have a meaningful architecture or is not written in legible code — and this is true even if the changes are being made by an experienced and intelligent programmer. Within biological systems, genetic change is essentially random: yet biological systems are still considered to be highly evolvable. This is because biological systems are internally organised in a way that, to an extent, prevents inappropriate change and promotes meaningful change. The sources of evolvability within biological systems exist at many levels and include: redundancy, compartmentalisation, exploratory mechanisms, and epigenetic and ecological processes. However, perhaps one of the most important sources of evolvability in biology is that behaviour emerges bottom-up from interactions between biological components which *implicitly* know what they want to do and what they want to do it to. This characteristic has been termed 'implicit context' within this thesis.

By comparison, most genetic programming systems use what could be termed 'explicit context' representations: where the interactions between components are determined *explicitly* by their position within the representation. However, such positionally dependent representations have important limitations: (i) a component loses its context, and hence changes its behaviour, if its relative position is changed; and (ii) particular positions can have different meanings within different programs. This implies that recombination operators, which move components between programs and typically change their position, rarely preserve the behaviour of the components they recombine; with the consequence that co-operative evolution — a conceptually powerful form of evolution — can not easily occur within genetic programming populations.

A number of non-standard GP systems [Poli, 1997, Luke et al., 1999, Miller and Thomson, 2000, Oltean and Dumitrescu, 2002] use an alternative form of representation which, in this thesis, is termed 'indirect context'. In an indirect context representation, each component is assigned a reference and each component specifies its interactions with other components according to these references. Explicit context can be seen as a special case of indirect context in which a component's reference is its position within a program representation and in which components can only occupy positions which are referred to by other components. In an indirect context representation, by comparison, components may be assigned references that are not referred to by other components within the representation. Consequently, these components are not used within the program described by the representation but can be used to support modes of evolution believed to be significant sources of evolvability in biological systems: such as neutral evolution and analogues of evolution be gene duplication. It is also possible for a component to be referred to by more than one other component, a condition comparable to pleiotropy in biological systems. Importantly, a component's reference need not be related to its position within the representation, and hence components can be moved within a representation without changing their behaviour. However, particular references can still have different meanings within different programs: and consequently indirect context does not prevent the loss of a component's meaning following recombination.

The work reported in this thesis concerns the development of an implicit context representation for genetic programming. The potential benefits of implicit context for evolutionary computation are very significant. Within biological systems, the behaviour of a biological component — both what it does and what it interacts with — is determined solely by its chemical constitution and physical shape: both of which are a consequence of its genetic definition. Loosely speaking, if during recombination a biological component's genetic definition is moved from the genome of one organism to the genome of another and the component becomes expressed, it will implicitly attempt to carry out the same behaviour in this new organism that it did in the previous organism i.e. its meaning will be preserved following recombination. This happens because biological components interact with other biological components according to recognition of one another's shape, which describes their behaviour, rather than one another's genomic position or other arbitrary reference. For example, the shape of an enzyme's binding site is complementary to that of its substrate; so the enzyme is effectively describing (in part) the behaviour of the component it would like to interact with.

The notion of an implicit context representation for genetic programming is based upon this biological concept of implicit context. Rather than program components specifying their context via explicit position or indirect reference, in an implicit context representation components specify their interactions in terms of the behaviour of the components they would like to interact with. However, in order for this to be possible, components must be able to interrogate other components to determine their behaviour. Assume for the moment that there is a perfect mechanism whereby components can determine the behaviour of others. Following recombination, a component would be able to inspect other components and determine whether or not there are any components it should interact with in order to achieve its pre-defined behaviour. Note that there is no requirement for a component to become involved in a program if there are no suitable interactions. In this situation the component would become recessive. However, any behaviour which a component does carry out will be consistent across programs.

Variation operators can alter a program representation in four different ways. They can add components, remove components, re-order components, or change (mutate) the behaviour of components: either by changing how they should interact with other components (their function) or by changing which components they should interact with. The use of implicit context leads to a phenomenon which is termed 'variation filtering' within this thesis; whereby particular variation events can be wholly or partially ignored. For example, if a component is added to a program representation, then it will only affect the program's outputs if it interacts with existing components that are expressed in the program i.e. only if it fits into the existing contexts declared by the program. If an expressed program component is removed from a program representation, then it might be possible for the other expressed components to compensate for its absence by interacting with a previously recessive component with a similar behaviour. This could also happen if an expressed component lost its previous behaviour as a result of a mutation event; or conversely a mutation event might cause a previously recessive component to offer a better match to an existing component's interaction preference than a currently expressed component. In effect, there is a tendency for variation events to be ignored or partially compensated for if they cause change which does not fit the contexts currently declared by the program. This, in turn, promotes gradual change in program behaviour: something which is conceptually desirable from the perspective of evolvability.

Enzyme genetic programming is a form of genetic programming based upon an implementation of implicit context representation. In enzyme GP, a program is a collection of inter-connected functions, program inputs, and program outputs. A program is represented by a linear array of program components, each of which has: an activity; a behavioural description; and — if it processes input — a set of input preferences, which describe the behaviour of the components whose outputs it would most like to receive inputs from. A program representation is mapped into a program via a development process which attempts to connect the inputs of every component to the outputs of those components which most closely match their input preferences.

Unlike in biology, it would be insufficiently precise to describe a program component by its activity alone, since both within a single program and within a population of programs there will be many program components with the same activity but with different roles. To overcome this problem, a program component, in enzyme GP, is described by both its own activity and the activities of the components which develop below its inputs. However, the exact components which develop below a component's inputs can not be known until after the development process is complete. Consequently, enzyme GP must describe a component's behaviour in terms of its expected inputs; those components which would be connected to its inputs if its behavioural preferences were matched precisely during development. This description is called a functionality and, in effect, declares a component's behaviour as an expected activity profile, weighted by depth, of the components that occur in the program fragment of which it is the root.

10.2 Conclusions

Enzyme genetic programming has been applied to a range of discrete symbolic regression problems. Analysis of the performance and behaviour of the evolutionary process has led to a number of conclusions.

Implicit context leads to meaningful variation filtering

Meaningful variation filtering is defined as the capacity for an evolutionary system to filter out inappropriate change caused by the action of variation operators. Theoretically (see above), the use of implicit context representation should allow an evolutionary system to carry out meaningful variation filtering. This is supported by a significant amount of experimental evidence indicating that enzyme genetic programming does carry out meaningful variation filtering.

Meaningful variation filtering promotes meaningful recombination

The main experimental evidence that enzyme GP carries out meaningful variation filtering lies in the ability of enzyme GP to carry out meaningful recombination. When compared to indirect context, enzyme GP's implicit context representation leads to a substantial improvement in recombinative performance: both in the capacity for a program representation to receive components transferred from another program representation, and in its capacity to preserve the meaning of the transferred components. These quantitative results are supported by the identification of context-preserving behaviours during qualitative analysis of the effect of recombination upon individual programs.

Meaningful variation filtering is supported by redundancy

It has been hypothesised that the redundant portions of implicit context program representations are organised into a subsumption hierarchy; and that this subsumption hierarchy supports meaningful variation filtering by absorbing inappropriate change and saving subsumed program components in case they are needed for back-tracking. The utility of this structure can be seen in the observation that the non-coding portion of representations grows in response to the addition of components; filtering out components which do not fit into the contexts defined by programs. Evolutionary performance is substantially degraded when redundancy is stripped from program representations following program development. This supports the views of other researchers that functional redundancy is an important source of evolvability within evolutionary representations [e.g. Smith and Goldberg, 1992, Dasgupta and McGregor, 1993, Haynes, 1996, Levenick, 1999, Yu and Miller, 2002].

Meaningful variation filtering gradualises change

Output terminal components have an important role in program development for they uniquely determine the program's output context and therefore which components will contribute to the program behaviour following development. Furthermore, by attempting to make the same input connections, they attempt to implement the same output behaviour irrespective of which components are actually present within the

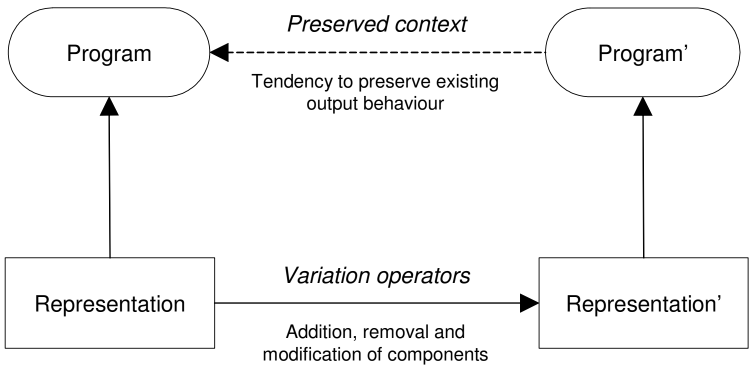

Preserved context
Program
Program'
Tendency to preserve existing output behaviour
Representation
Variation operators
Representation'
Addition, removal and modification of components

Figure 10.1. The combination of implicit context and variation filtering causes a tendency to preserve existing context and program output behaviour.

program representation. Consequently, so long as the output terminal components remain the same, they should function as an attractor, tending to preserve the existing program output behaviour irrespective of changes that occur within the program representation as a result of the application of variation operators (this idea is depicted in figure 10.1). This, within enzyme GP, should be the ultimate effect of the variation filtering process enabled by implicit context representation. This effect should also occur where recombination leads to a child program containing output terminal components from more than one parent program. In this case, there will be a tendency to preserve the output behaviour from each parent for the corresponding output terminal: which, in many cases, is exactly the behaviour that is wanted from recombination.

Gradualised change can improve evolutionary search

This is suggested by the considerable positive effect of a low level of Lamarckian reinforcement learning; where program components' input preferences are changed so that they more accurately reflect the input connections they have made during development. The effect of this is to strengthen the internal cohesion of a program over time, increasing the effect of variation filtering and thereby making it less likely that large changes will occur as a result of variation events. This supports both previous results on the utility of Lamarckian reinforcement learning [Teller, 1999, Downing, 2001], and the view that compartmentalisation can be an important source of evolvability [Conrad, 1990, Kirschner and Gerhart, 1998].

Implicit context leads to improved size evolution characteristics

It is difficult to make general conclusions regarding the effect of implicit context representation upon the evolution of program size, since program size within enzyme GP appears to be significantly affected by inherent biases within the functionality implementation of implicit context. However, it can be speculatively suggested that GP with implicit context representation should suffer significantly less from bloat than GP with explicit context representation, given that: (i) recombination is less disruptive; (ii) the recombination mechanism does not promote the development of protective syntactic introns; (iii) the effect of removal bias is far smaller; and (iv) program size is decoupled from representation length. This argument is somewhat supported by the observation that there is little or no bloat in enzyme GP. It has also been hypothesised that small programs are better replicators than large programs, since they have less internal connections and are therefore less likely to be disrupted by variation events. This is also supported by the tendency towards the evolution of small programs in enzyme GP. However, there is some concern that this might make it harder to solve problems which have large optimal solutions and relatively short sub-optimal solutions — although this concern is somewhat allayed by the diversity preservation mechanism that is inherent in implicit context representations.

These conclusions support the hypothesis that models of biological representations can be used to represent computer programs and other artificial executable structures within genetic programming, thereby improving the evolvability of these structures.

10.3 Limitations of This Study

Whilst considerable effort has been made to verify these conclusions through both experimental investigation and theoretical understanding, there are limitations of the experimental method which might reduce their generality. The most significant limitation is that the performance of enzyme genetic programming has not been vigorously analysed upon a wider class of problems; and whilst discrete symbolic regression was chosen for its relative difficulty with regard to recombination, it can not be representative of all other problem domains. Partly this limitation reflects a need to generalise the functionality implementation of implicit context to handle so-called ephemeral random constants and structural behaviours in addition to functional behaviours. Suggestions as to how this might be done are given in the further work section. Furthermore, there has been little direct comparison between the performance of enzyme genetic programming and conventional genetic programming. This is due both to the lack of existing results applying conventional GP to Boolean regression problems, and to the difficulty of direct performance comparison caused by the use of a non-standard evolutionary framework within enzyme GP. However, it is assumed that explicit context representations have worse performance than indirect context representations upon recombinative search (for reasons given elsewhere in this thesis); and that therefore the performance of explicit and implicit context are being compared by transitivity. Nevertheless, it is hoped that these limitations will be addressed in future research.

10.4 Further Work

Section 9.7.2 discussed how biases within functionality space may lead to size and structural biases during search. An important avenue for future work will be to look into ways of removing this bias. Bias can be reduced by warping functionality space so that changes within over-represented regions have less influence upon the evolutionary process. However, early work concerned with variable dimension lengths had led to little success. Perhaps a more effective approach, in the short term, will be to look at ways of biasing the initialisation and mutation mechanisms in order to counteract the biases in fuctionality space; although a more long term strategy should be to look at alternative reference spaces which do not have the same kinds of biases which are seen in functionality space.

Perhaps a more important short term goal should be to reduce the time complexity of development. The most obvious way of doing this would be to remove the non-recurrency constraint during development. Without this constraint, development will simply be a process of comparing the input preferences and behavioural descriptions of each pair of components; a process which will have far less complexity than maintaining and interrogating connection information at each node in order to determine

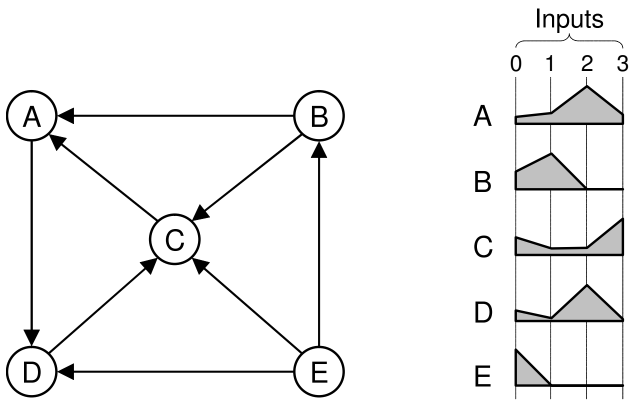


Figure 10.2. Implicit structural context. Shapes (right) describe the structural profile, weighted by distance, of each node in the structure on the left in terms of the degree of input connectivity within its local sub-graph.

whether or not a future connection will lead to recurrency. It will also allow the expression of recurrent structures: an important motif in many problem domains, including programming. If non-recurrent structures are still required, this constraint can be handled during execution by only propagating the first argument that arrives at a component output. However, it will be possible to evolve invalid structures in which there are missing paths between outputs and inputs; though if infrequent, these structures can be filtered out during selection. Furthermore, using the current approach to calculating functionalities, it may not be possible to represent recurrent structures exactly, since it may no longer be meaningful to give a profile of the sub-structure which develops below a component, given that the component may occur within this sub-structure via a recurrent connection. Nevertheless (as figure 10.2, discussed below, shows), it is still possible to give a profile of the activities which occur within the neighbourhood of a component. In any case, this will make little difference to program evolution, since actual evolved functionalities are unlikely to exactly describe components anyway.

In the long term, one of the most interesting avenues of research will be to look at forms of implicit context representation which are able to represent a far wider selection of structures. However, it will also be interesting to look at the potential of the current approach to implicit context. Within enzyme GP, functionalities attempt to describe profiles of the functional activities which occur within evolved structures. This approach can be generalised by describing profiles of 'behavioural properties' within structures, which could include both functional and non-functional properties of their components. Figure 10.2, for example, shows how descriptive shapes can be used to represent an arbitrary digraph. Rather than describing the functions of the nodes within the structure, these shapes describe nodes by the number of incoming connections they have from other nodes. In theory, this approach could be used for any kind of structure; although in practice it would require that structures have sufficient heterogeneity in the connectivity of their nodes and the distribution of connectivity within the structure. However, as problems such as the two-bit multiplier show, the behavioural properties (e.g. activity types) within a structure do not have to be very diverse in order for it to be expressed and evolved by this method. Furthermore, there is no reason why a descriptive shape could not describe both functional and non-functional properties together. For example, the behaviours of components within digital circuits could be described by profiles of both the functional and structural properties of their expected sub-trees. There is also scope for describing continuous parameters. For example, ephemeral random constants have two functional properties: they are a constant input source and they provide a particular value. One functionality dimension could be used to describe the relative occurrence of constants within a program fragment and one could could be used to describe the relative value of the constants.

Recently, there has been some interest in using implicit context[1] within manual programming environments. In an approach described by Walker and Murphy [2000], components analyse their call history in order to learn more about the behaviour they are expected to provide to other components. Because of this, components are able to request behaviour from one another via fewer function calls and fewer parameters; simplifying component interaction and leading to communication along narrow, well-defined paths. Due to cleaner interfaces and less complex connectivity, this form of implicit context, in principle, makes it easier for components to be re-used within other programs. Whilst only partially related to the idea of implicit context introduced in this thesis, this idea of a component learning its own context could be used within an EC implicit context representation. Lamarckian reinforcement learning is an existing mechanism whereby context learning can take place in the functionality model of implicit context. However, this form of learning is currently carried out at a program

[1]This use of the term *implicit context*, whilst related, was coined independently.

level and can only learn simple information about those activities which have dimensions within functionality space. A more complex form of learnt implicit context can be imagined in which a program consists of software agents which can flexibly learn about their environment and preserve this information when transferred between programs; gradually building up knowledge about the space of possible component interactions and their expected behaviour within this space. At the start of evolution, these agents would only have a general idea of the role they should fulfill — making behavioural exploration easy — but, during the course of evolution, they would become more specialised — improving behavioural exploitation.

Such behaviourally complex forms of implicit context representation could also be used within software engineering environments. Rather than programmers scripting the interactions between program components; implicit context would allow them to focus on writing components. When these components are placed in a program together, the program behaviour would emerge from implicit interactions between components. This would amount to applying biological principles of organisation to the realm of human design. However, this vision is currently rather far-fetched (and perhaps even impractical!). Perhaps a more productive goal in the meantime would be to apply more of the principles of biological organisation to the development of evolutionary computation representations. Thus far, in this thesis, this approach has led to the development of a representation modelled upon the interactions within metabolic pathways. It seems conceivable that this model could be extended to include the interactions between metabolic pathways and signalling and gene expression pathways. Gene expression pathways, in biology, are evidently the source of many of the more complex behaviours seen within biological systems. Signalling pathways are the predominant source of distributed processing within biological systems; and distributed processing appears to be an important factor both behaviourally and as a source of evolvability within biological representations. Certainly it is conceivable that the enzyme GP model could be extended to allow regulation of component expression by currently expressed components (a behaviour which could be particularly useful for solving dynamic problems) and to allow communication between 'cellular' groups of components (which might themselves result from differential component expression). However, whilst making the system far more expressive, this will also make it harder to interpret by a human.

In addition to using enzyme GP as a mechanism for applying current biological understanding, it seems that enzyme GP, and other EC models of biology, could be used to discover biological knowledge. Certainly this has proved a productive approach for neuro-computing; which has helped add to biological understanding by testing the validity of neural theories, by allowing observation of animated neural models, by posing questions in response to implementation problems, and by testing the generality of neural processing through application to non-biological problems. Biological evolution is difficult to study using conventional data-centric bioinformatics techniques due to the sparseness of the fossil record and the slow pace of evolution. Evolutionary computation, by comparison, is relatively fast, can provide a complete 'fossil record' and, in principle, could be used to to model, observe, pose questions about and study the generality of biological evolution. Perhaps the most beneficial use of this technique would be in understanding biological sources of evolvability; many of which can be modelled without reference to biological information. Existing EC research has already given some insight into the roles of redundancy and compartmentalisation — and there are still plenty of biological motifs, mechanisms, and structures which are not well understood in the context of evolvability. In particular, it would be interesting to consider whether enzyme GP might have a role in understanding biological evolution; particularly the early stages of biological evolution. It seems evident that variation filtering behaviours do occur in biological systems, although the relatively simple behaviours of the kind described in this thesis may only have had an influence before active forms of genetic and enzymatic regulation evolved. Likewise, it seems plausible that the non-coding portions of DNA have a role similar to the recessive subsumption hierarchy described in this thesis — providing a source of error recovery and evolutionary back-tracking.

A The Activity Model

The activity model [Lones and Tyrrell, 2001c,b,a, 2002a] is an earlier model of implicit context which predates the functionality model described in Chapter 8.

For the activity model, the shape of a component is its activity and the activity of a component is an instance of a function; not the function itself. This allows there to be multiple identifiable instances of a function, each recognised as a separate activity. Since shape is defined upon activity, so too are binding sites. Moreover, each component which receives input has a binding specificity defined for every outputting activity (input terminals and function instances) present within the program representation. An activity model program representation can be visualised as a fully-connected weighted network where the weight of a particular edge (the strength of a particular binding specificity) defines a relative preference for this edge being realised as a connection within the program. This idea is depicted in figure A.1. Evolution and program development proceed in the same manner as enzyme GP with the functionality model. Program representations are recombined using a uniform crossover operator. More details about the implementation of the activity model can be found in Lones and Tyrrell [2001c].

Population	Average (generations)	Success rate	Computational effort
196	69	35%	213,248
324	70	55%	252,720
400	56	60%	179,200

Table A.1. Performance of activity model upon two-bit multiplier problem.

Performance metrics for activity model enzyme GP upon the two-bit multiplier problem are listed in Table A for various population sizes. More detailed performance

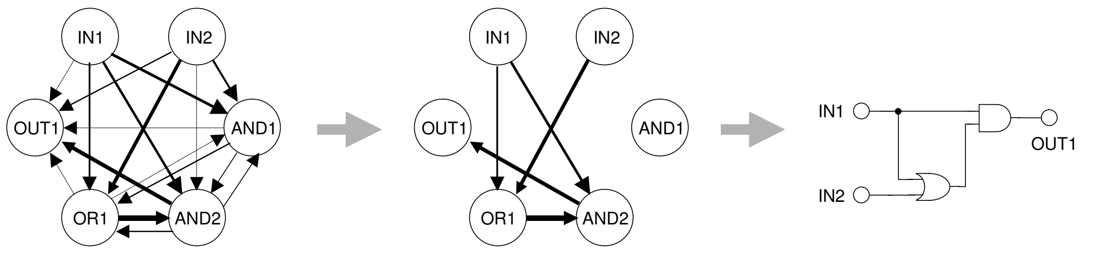


Figure A.1. Visualising the activity model. Shape is equivalent to activity. Connections show the specificity of one activity for input from another. Specificity strengths are shown by line weight. During development, the strongest specificities are realised as connections (within the bounds of the non-recurrency constraint).

analysis, and comparison with the functionality model, can be found in Lones and Tyrrell [2002a]. Figure A.2 shows an example of a full adder being evolved with activity model enzyme GP. Note that whilst the behaviour of recombination is quite disruptive, recombination events still appear to play a significant role during evolution.

Programs evolved by the activity model are fixed-length and contain only pre-defined instances of components. Concern that the activity model contains excessive redundancy [Lones and Tyrrell, 2001c] and that it can not easily be extended to support variable-length solutions lead to the development of the functionality model.

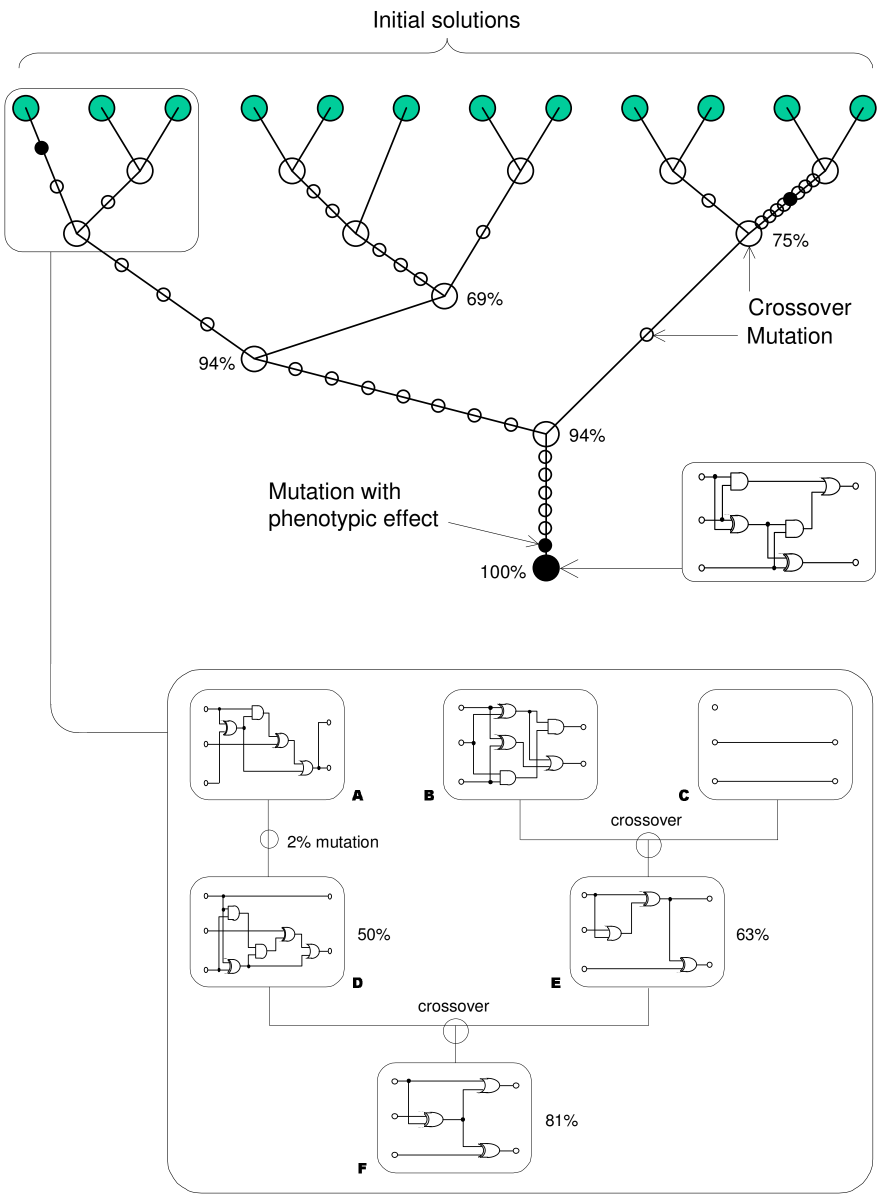


Figure A.2. Evolution of a full adder with the activity model. Both crossover and mutation are used to evolve an optimal solution. Most mutations are neutral. Note the neutral walk that leads to the optimum after the final recombination.

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