Clonal Selection Algorithms

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***Abstract*-Inspired by Darwin's theory of natural selection to explain the diversity and adaptability of life, Burnet's clonal selection theory explains the diversity and learning properties of the acquired immune system of vertebrates. In a similar mirroring manner to the field of evolutionary computation that attempts to use the principles of the Darwinian theory and genetics to address practical engineering problems, a new field of study called 'Clonal Selection Algorithms' has emerged that attempts the same task by abstracting and applying the principles of Burnet's foundational immunological theory. This paper provides a summary of this new field of clonal selection algorithms and proposes an algorithm taxonomy, a standardized nomenclature, and a general model of such algorithms. Finally, the field is compared and contrasted to the field of evolutionary computation, and general research trends are discussed.**

Keywords- Clonal Selection Algorithm, CSA, Clonal Selection Theory, Clonal Selection Principle, Artificial Immune System, Algorithm Review, CLONALG, AIRS, BCA, MISA, IA

I. Introduction

Artificial Immune Systems (AIS) is the investigation of models and abstractions of the vertebrate (typically mammalian) immune system and the application of these models and algorithms to practical endeavours such computation problem domains in the fields of science, engineering, and information technology [88]. Although the source of inspiration for computational models in the immune system is near limitless, four main sub fields of research have emerged in AIS cantered on prominent immunological theories; negative selection algorithms (NSA), immune network algorithms (INA), danger theory algorithms (DTA), and clonal selection algorithms (CSA).

Like Darwin's theory of theory of accumulated blind variation in the face of natural selection that revolutionized the field of biology [19], Burnet's theory (inspired by Darwin's) of clonal selection suitably explains the laboratory observations of antibody diversity in the acquired immune system and transformed modern immunology [43-45]. A discussion of Burnet's theory is beyond the scope of this work (for a modern introduction see [13,112,153]), although it is not the theory that is relevant, but rather the computational principles that can be drawn. Thus, it is popular in the field of clonal selection algorithms to describe the inspiration as the 'clonal selection principle' as opposed to the 'clonal selection theory', as it is the principle that is being *applied* rather than the theory that is being *investigated*.

In brief, the principle of the theory is that the antigen (the foreign molecule that the immune system is defending against) selects those lymphocytes (B-cells or white blood cells that detect and stop antigens) with receptors capable of reacting with a part of the antigen. Selection results in the rapid proliferation of the selected cell to combat the invasion (clonal expansion and production of antibodies). During this cell duplication process coping errors occur (somatic hypermutation) which may result in an improved affinity of the progeny cells receptors for the triggering antigen.

This description clearly sounds like a selective and stochastic-based adaptive process. This general method has inspired the field of clonal selection algorithms which attempt to harness its potential in the application to primarily optimization and classification problem domains.

The paper is broken down as follows; Section II presents a general model of clonal selection algorithms which includes a standard definition, specification of algorithmic principles, and a standardized nomenclature. Also presented is a high-level algorithm taxonomy for interpreting the current state of the art in clonal selection algorithms. Section III applies the taxonomy from section II.C and reviews the field of clonal selection algorithms. This review is complete[1] and focuses on applications and general algorithmic principles. Section IV addresses the clear similarity between clonal selection algorithms and some evolutionary algorithms, contrasting the two related fields of research. Finally V general trends observed from the literature review are discussed, and some potential future areas for clonal selection algorithm design are suggested.

II. General Model

The clonal selection theory is the foundational principle of modern immunology, thus it is tightly interconnected with other immunological theories. This follows for the algorithms inspired by such theories. For example, negative selection algorithms model classification problems in the complement space although still rely on the clonal selection principle to iteratively improve exemplars. Immune network algorithms for clustering and optimization use the excitation and suppression properties of the network model though also use the clonal selection principle for

[1] To the authors knowledge at the date of publication and given the scattered nature of publications in this field and intense googling

iterative refinement of their models. A more complete review of the field would include a discussion of the clonal selection properties of other immunological algorithms such as immune network and negative selection algorithms, and this remains an exercise for future work.

Definition 1.0: *A clonal selection algorithm is primarily focused on mimicking the clonal selection principle which is composed of the mechanisms; clonal selection, clonal expansion, and affinity maturation via somatic hypermutation.*

A.*Nomenclature*

Given that inspiration is such a critical feature to this field of study, it is important to have a consistent nomenclature when describing clonal selection algorithms. This nomenclature is drawn from the biological inspiration and refers to the principles mimicked by inspired algorithms (see Table 1 for a listing of common CSA terms drawn from the literature).

General	Clonal Selection Algorithms
Candidate Solution, Exemplar	Antibody, B-Cell, Lymphocyte
Collection of New Samples, Progeny	Clone
Elitism, Memory	Memory Set, Memory Cell
Generalization	Cross-reactivity
Learning Principle	Clonal Selection Principle
Mutation, Variation	Hypermutation
Population, Collection of Samples	Repertoire
Re-sampling Principle, Improvement	Affinity Maturation
Re-sampling, Reproduction	Cloning, Clonal Expansion
Selection	Antigen-Antibody Matching
Solution Quality, Fitness	Affinity, Avidity

Table 1 - Clonal Selection Algorithms Common Nomenclature

B.*Archetype Algorithm*

Cutello and Nicosia [144] suggest clonal selection algorithms take two key features into account; the hypermutation and the clonal expansion mechanisms. They go on to describe hypermutation as a local search procedure that leads to fast maturation, and the clonal expansion phase triggers growth of a new population of useful B-cells focused on the triggering antigen. They also propose that the primary immune response may be taken as a training phase, whereas the improved secondary response may be taken as the testing phase.

de Castro and Timmis [88] also suggest the two key features of clonal selection algorithms are the mutation and cloning properties, and go on to outline more specific properties of these mechanisms ([88] page 80):

Principle 1.0: *The proliferation rate of each immune cell is proportional to its affinity with the selective antigen (higher the relative affinity, the more progeny)*

Principle 1.1: *The mutation suffered by each immune cell during reproduction is inversely proportional to the affinity of the cell receptor with the antigen (higher the relative affinity, the lower the mutation)*

They also suggest that selection plays a critical role in both the strong selective pressure during affinity maturation, and in the selection of long lived memory cells.

Thus a general clonal selection algorithm possesses the following mechanisms:

```
1. Randomly initialise pool of antibodies
2. Expose the pool to antigen
      a. Clonal Selection
      b. Clonal Expansion
      c. Somatic Hypermutation
```

Figure 1 - General algorithmic model of the clonal selection principle

Where the pool is exposed to ≥ 1 antigen, the operator's selection and expansion are affinity proportionate, and mutation is affinity inversely-proportionate.

C.*Taxonomy*

Before an algorithm taxonomy is presented, it is useful to present a brief taxonomy of the broader field of research. As stated in the introduction the term chosen for the field of study is 'Clonal Selection Algorithms' (CSA) inspired by the 'Clonal Selection Principle' (CSP) which is derived from the 'Clonal Selection Theory' (CST). The field belongs to the study of Artificial Immune Systems (AIS) which is commonly associated with Biologically-Inspired Computation (BIC) or Computational Intelligence (CI).

A taxonomy of clonal selection algorithms has not been presented before[2], and although obvious is expected to be useful in interpreting the current state of the field. A algorithmic-genealogical approach was taken similar to that used by Galeano, Veloza-Suan, et al. [64] in the comparative analysis of artificial immune network models. Here, the lineage is defined by the seminal algorithm names, as follows; the Artificial Immune Recognition System (AIRS), the B-Cell Algorithm (BCA), the Clonal Selection Algorithm (CLONALG), the Immunological Algorithm family (IA), Multi-objective Immune System Algorithm (MISA), and Other for unclassified works (see Table 2).

Lineage	Algorithms	Primary Application
AIRS	AIRS, AIRS2, Parallel AIRS	Classification
BCA	BCA	Optimization
CLONALG (CSA)	CSA, CLONALG, CLONALG (1,2), ACS, CLONCLAS, RCSA, MOCSA, IMCSA, AISMM, SACSA, ECA	Optimization
IA (SIA)	IA, SIA, I-PAES, CLIGA, CLIGA+, NC-IA, READ-Alg, opt-IA, opt-IMMALG, Par-IA, Dyn-IMMALG	Optimization
MISA	MISA	Multi-Objective Optimization
Other	*Too large to classify at this time*	Optimization

Table 2 – Basic algorithm genealogy

III. ALGORITHMS

This section presents a review of clonal selection algorithms applying the taxonomy presented in II.C. Sections A through to E present the five main algorithm lineages. Section F summarizes uncategorized works, and section G summarizes those works claimed or referred to be clonal selection algorithms which do not meet definition 1.0.

[2] To the best knowledge of the authors at the time of writing.

A.*Clonal Selection Algorithm (CLONALG)*

Hidden at the back of a technical report on the applications of artificial immune systems de Castro and Von Zuben [86] proposed the Clonal Selection Algorithm (CSA) as a computational realization of the clonal selection principle for pattern matching and optimization. This algorithm which has become perhaps the most popular in the field of AIS, was later published and represented [84], and again [85] where it was renamed to CLONALG (CLONal selection ALGorithm).

The general CLONALG model involves the selection of antibodies (candidate solutions) based on affinity either by matching against an antigen pattern or via evaluation of a pattern by a cost function. Selected antibodies are subjected to cloning proportional to affinity, and hypermutation of clones inversely-proportional to clone affinity. The resultant clonal-set competes with the antibody population for membership in the next generation, and finally low-affinity population members are replaced by randomly generated antibodies. The pattern recognition variation of the algorithm includes a maintenance memory solution set which in its entirety represents a solution. A binary-encoding scheme is employed for the binary-pattern recognition and continuous function optimization examples, and an integer permutation scheme is employed for the Travelling Salesman Problem (TSP) example.

CLONALG Description and Pseudocode

Parameter	Description
P	Repertoire of antibodies
N	The fixed antibody repertoire size
n	The number of antibodies to select for cloning
L	Bit string length for each antibody
Nc	Number of clones created by each selected antibody. Originally expressed as a function of the repertoire size (for optimization) $N_c = round(\beta \cdot N)$ (where β is a user parameter), although a direct integer specification of *Nc* is simpler. A rank-based (affinity proportionate) variation of the question is presented for pattern recognition.
d	Number of random antibodies to insert at the end of each generation. Random antibodies replace the d lowest affinity antibodies in the repertoire
Stop condition	Typically a specified number of generations or function evaluations.
affinity	Solution evaluation, typically the solution is decoded into a domain specific representation and assigned a quality costing
clone	Duplication of a bit string.
hypermutate	Modification of a bit string where the flipping of a bit is governed by an affinity proportionate probability distribution. Originally $p = \exp(-\rho \cdot f)$, although the opt-aiNET variant is also popular $p = \left(\frac{1}{\rho}\right) \cdot \exp(-f)$ (where ρ is a user parameter and f is the normalized affinity scoring).

Table 3 - CLONALG parameters

```
P <- rand(N, L)
While Not StopCondition Do
 ForEach p of P Do            // presentation
  affinity(p)
 EndFor
 P1 <- select(P, n)           // clonal selection
 ForEach p1 of P1 Do          // clonal expansion
  C <- clone(p1)
 EndFor
 ForEach c of C Do            // affinity maturation
  hypermutate(c)
 EndFor
 ForEach c of C Do            // presentation
  affinity(c)
 EndFor
 P <- insert(C, n)            // greedy selection
 Pr <- rand(d, L)
 P <- replace(P, d, Pr)       // random replacement
EndWhile
```

Figure 2 - CLONALG pseudocode listing

In an attempt to exploit the 'inherent distributedness' of the immune system, Watkins, Bi, et al. [12] propose that each antibody in the algorithms repertoire can be treated independently given the lack of inter-antibody interactions. The pattern recognition variation of the CLONALG was modified such that each memory cell is partitioned to different processes and evolved independently or in small groups, the results from which are collated at the end of the algorithm run and returned as the algorithm result[3]. White and Garret [54] also investigated the pattern recognition version of CLONALG and generalized the approach for the task of binary pattern classification renaming it Clonal Classification (CLONCLAS) where their approach was compared to a number of simple Hamming distance based heuristics.

Walker and Garrett [59] investigated CLONALG and Evolution Strategies (ES) on dynamic function optimization, showing that although CLONALG can achieve better results faster than ES on low dimensional dynamic functions, ES consistently outperforms CLONALG on the two high-dimensional problems tested. In an attempt to address concerns of algorithm efficiency, parameterization, and representation selection for continuous function optimization Garrett [122] proposes an updated version of CLONALG called Adaptive Clonal Selection (ACS). The mutation parameter, the number of antibodies selected for cloning, and the number of clones produced for each antibody were changed to automatic parameters, controlled in a similar way to those in Evolution Strategies (ES).

Cutello, Narzisi, e al. [141] proposed two modified versions called CLONALG1 and CLONALG2 with varying elitist strategies which were raced against the opt-IA algorithm. Dilettoso and Salerno [34] treated CLONALG as a niching technique and raced it against traditional EC niching approaches. Wang [157] proposed a CSA based on CLONALG with a static clone sized applied to power filter design observing niching like behaviours. Cruz-Cortes, Trejo-Perez, et al. [110] investigated CLONALG with binary and gray encoding schemes as well as a real-valued encoding scheme with a mutation scheme based on Gaussian and Cauchy random numbers.

[3] The choice of application is poor, given that the binary pattern recognition task was selected by de Castro and Von Zuben for demonstration purposes only.

Babayigit, Akdagli, et al. [14] applied CLONALG to locating good model parameters for the null synthesizing of linear antenna arrays by amplitude control. Given their reported success, the authors applied the algorithm to other antenna design problems [2,81]. Campelo, Guimaraes, et al. [36] proposed a Real-coded Clonal Selection Algorithm (RCSA) with Gaussian-based mutation applied to the electromagnetic design optimization problem (called the TEAM workshop problem 22). Campelo, Guimaraes, et al. [37] also proposed a multi-objective version of their algorithm called MOCSA. This variation was later applied to the same electromagnetic design problem in [38]. Another multi-objective application of CLONALG was proposed by Stevens, Das, et al. [22].

Dong, Shi, et al. [149] proposed the Immune Memory Clonal Selection Algorithm (IMCSA) applied to designing stack filters for noise suppression. This extension to CLONALG used dual-binary strings in each antibody, self-tuning mutation parameters, recombination parameters and inserted memory cells that were developed using alternative algorithms. Acan [1], proposed an extension called Artificial Immune System with Mutation Multiplicity (AISMM) that used multiple concurrent mutation operators in the application to continuous function optimization. Bian and Qiu [164] applied CLONALG to PMU placement, and Amaral, Amarak, et al. [63] applied CLONALG to parameter tuning in PID controller design.

CLONALG has also been hybridized with many other optimization procedures, some examples include the following: Zuo and Fan [168] proposed the Chaotic Search Immune Algorithm (CSIA) that integrated elements of the CLONALG algorithm and was applied to the tuning Radial-Basis Functions (RBF) in real-time controller design. Zhong, Zhang, et al. [171] proposed the Simulated Annealing Clonal Selection Algorithm (SACSA) which hybridizing CLONALG with SA in the application to classification. This approach was extended by Zhong, Zhang, et al. [170] and renamed to the Unsupervised Artificial Immune Classifier (UAIC). Wang, Wang, et al. [113] combined CLONALG with Particle Swarm Optimization (PSO) and applied it to function optimization. Karakasis and Stafylopatis [136] combined CLONALG with Gene Expression Programming (GEP) called Enhanced Clonal Algorithm (ECA) and applied the approach to data mining. Litvinenko, Bidyuk, et al. [135] created a similar hybrid algorithm and applied the approach to time series prediction.

B. *Artificial Immune Recognition System (AIRS)*

After CLONALG, the Artificial Immune Recognition System (AIRS) algorithm is perhaps the second most popular clonal selection algorithm, although the approach was designed for and has only been applied to the supervised classification problem domains. The earliest work on AIRS was in Watkins masters' thesis [4], although was later published in [6]. The approach is a supervised learning algorithm for classification that uses the idea of an Artificial Recognition Ball (ARB) introduced in earlier works on the Artificial Immune Network algorithm (AINE) to represent clones (groups) of identical B-cells. The AIRS is a clonal selection inspired procedure of cloning and somatic hypermutation for preparing a set of real-valued exemplars suitable for classifying unobserved cases and uses a single iteration over a set of training data. Watkins and Boggess [11] quickly went on to apply the AIRS to a suite of benchmark classification problems, and Goodman and Boggess problems [28] did the same, comparing the approach to the similar Learning Vector Quantization (LVQ) approach.

Given the rapid popularity of the approach Marwah and Boggess [46] investigated the algorithm seeking issues that affect the algorithms performance. The compared various variations of the algorithm with modified resource allocation schemes, tie-handling within the ARB pool and ARB pool organization. AIRS was again raced againt LVQ by Boggess and Hamaker [97] on datasets that contained irrelevant features to assess the algorithms ability to handle noise. Greensmith and Cayzer applied AIRS to hierarchal document classification [66] which culminated in Greensmith's masters work [65].

Watkins and Timmis [8] proposed a new version of the algorithm called AIRS2 which became the replacement for AIRS1. The updates reduced the complexity of the approach while maintaining the accuracy of the results. An investigation by Goodman, Boggess, et al. [29] into the source of the AIRS so called power indicating that perhaps the memory cell maintenance procedures played an important role. The approach was compared to some state of the art classification algorithms. A follow-up empirical investigation by Goodman and Boggess [27] supported the original finding indicating that the process by which new memory cells are admitted into the ARB pool is critical to the success of the approach.

Using work on parallelizing the CLONALG [12] as a basis, Watkins and Timmis [9] proposed a parallel version of AIRS permitting the division of training patterns and memory pool suitable to exploit parallel hardware. An empirical study of various non-Euclidean distance measures was performed by Hamaker and Boggess [53] assisting application to mixed-variable classification domains. Finally a large study of both version of AIRS was published by Watkins, Timmis, et al. [10], and culminated in Watkins dissertation [5].

Jin, Bie, et al. [166] extended AIRS and applied the approach to software quality classification. Meing, Putten, et al. [92] benchmarked AIRS determining that the classifier is quite stable. Xu, Chow, et al. [82,83] applied AIRS to power outage cause identification with an imbalance of training cases. Finally, Polat, Shan, et al. [78,79] extended AIRS to make use of fuzzy logic rules called FS-AIRS. The authors later applied the approach to ECG data [80], and later renamed the approach to Fuzzy-AIRS [77]. Garain, Chakroborty, et al. domain [128] propose a CSA inspired by AIRS and CLONALG for optical character recognition. This work was extended and applied to a more difficult multiple-class pattern recognition problem in characters [129].

C.*B-Cell Algorithm (BCA)*

Kelsey and Timmis [61] proposed the B-Cell Algorithm (BCA) as an AIS designed for continuous function optimization. The algorithm maintains a pool of B-cells (binary-encoded candidate solutions) that are subjected to cloning and mutation. An elitist replacement population maintenance scheme is applied that ensures only improved cells are admitted into the pool. The mutation operator, which is called 'contiguous somatic hypermutation' selects a random sub-string of a solution to probabilistically vary, what the authors claim as 'hot-spot' mutation. Kelsey, Timmis, et al. [60] applied the BCA to multimodal-dynamic chaotic test functions. Empirical algorithm tuning by the authors revealed small population sizes (3-5, 12) show better results.

In an investigation of AIS applied to optimization, Hone and Kelsey [7] provide a case study investigation of the BCA and show apparently fractal structures on the complex plain suggesting the potential usefulness of studying AIS as nonlinear dynamical systems. In a further empirical study, Timmis, Edmonds, et al. [62] compare the BCA to opt-aiNET[4] and the HGA attributing the partial success of BCA to the mutation scheme, speculating it results in the escaping of local-optima search behaviour.

BCA Description and Pseudocode

Parameter	Description
P	Repertoire of antibodies
N	Antibody population size
Nc	Number of clones to create of each antibody
nR	Number of random antibodies to create and insert each generation
Stop Condition	Typically if no progress is made for a number of generations
hypermutation	Uses a processes called contiguous hypermutation, a random location in the bit string is selected, and a random bub-string length is selected. Each bit in the substring is flipped with the probability ρ .
replace	A parent is replaced only if a member of its clone has a higher affinity (greedy replacement)

Table 4 - BCA parameters

```
P <- rand(N, L)
While Not StopCondition Do
 ForEach p of P Do             // presentation
  affinity(p)
 EndFor
 ForEach p of P Do             // clonal expansion
  C <- clone(p, Nc)
  C <- rand(nR, L)             // random insertion
  ForEach c of C Do            // affinity maturation
   hypermutate(c)
  EndFor
  ForEach c of C Do            // presentation
   affinity(c)
  EndFor
  C' <- best(C)
  P <- replace(c, p)           // clonal selection
 EndFor
EndWhile
```

Figure 3 - BCA pseudocode listing

A proof of convergence for the BCA is proposed by Clark, Hone, et al. [35] using a Markov chain model. The proof simplifies the algorithm to an elitist search with a single population member suggesting that the members of the population can be treated independently given the lack of interaction during the optimization procedure. Further, they speculate that the introduction of inter-solution interactions in the BCA will have a detrimental effect on the number of function evaluations during a search. Finally in a recent empirical study Bull, Knowles, et al. [111] the authors apply the BCA to what they refer to as less-smooth test problem instances (Diophantine equations) seeking empirical convergence heuristics. Four variants of the algorithm are compared, an approach that uses an elitist selection mechanism to introduce inter-solution interactions, and three of what the authors refer to as 'megamutation' schemes that attempt to introduce further diversity into the search. These less-greedy modifications of to the achieve better final results compared to the classical BCA on the test functions chosen, perhaps suggesting the use of diversity introduction approaches in further BCA applications.

D.*Immunological Algorithm Family (IA)*[5]

A simple clonal selection inspired algorithm was proposed by Cutello and Nicosia [142,143] called Immunological Algorithm (IA) later renamed to Simple Immunological Algorithm (SIA) [144]. The algorithm maintains a population of B-cells that are exposed to a clonal expansion process each generation. This expansion process involves the cloning of cells and the application of a hypermutation operator. The algorithm was demonstrated on the Minimum Hitting Set Problem (MHSP) and the 3-Satisifiability Problem (3-Sat).

The SIA was extended and an applied to the Graph Colouring Problem (GCP) [146]. The extensions involved the introduction of a local-search procedure that operated upon each B-cell after the clonal expansion phase. In addition, rather than an elitist selection method of maintain the population size after each expansion, an aging operator was introduced for the B-cells. B-cells are probabilistic deleted from the population using an equation inspired by the biological literature. Two variations of the aging operator were applied, an elitist version that ensured the best B-cell's were not deleted, and a pure strategy that probabilistically deleted irrespective of the elitist concerns. A birthing operator was also added to 'top-up' the population to the configured level as needed, and an information gain (a stabilization in the measure of information discovered by the algorithm) measure was used as the termination criteria for the algorithm.

The probabilistic aging operator was replaced with a simplified generational aging operator by Cutello, Nicosia, et al. [148] in an application to the 2DHP protein folding problem. In a more detailed study on different varieties of the same protein folding domain, the aging operator was further tweaked to facilitate

[4] (opt-aiNET) an immune network algorithm as specified in [87]

[5] The Immunological Algorithm (IA) is renamed and represented many times by its authors. Other names include Simple Immune Algorithm (SIA), Cloning Information Gain Aging (CLIGA), and Optimization Immune Algorithm (opt-IA, opt-IMMALG).

longer life spans on some B-cells deemed useful to the search process here [134]. The clonal expansion aspect of the algorithm (cloning and hypermutation) was grafted into to an existing evolutionary multiple-object optimization technique [140] and called I-PAES.

The transformed algorithm (generational aging, information gain stopping criteria) was reviewed and renamed to the 'Cloning, Information Gain, Aging' (CLIGA) algorithm [144]. A modified version called CLIGA+ was proposed in which each B-cell contains more than one receptor (pattern), permitting application of the algorithm to pattern recognition tasks. Also proposed in this work is a Noisy Channel variation of SIA (NC-IA), and a Reaction-Diffusion variation of SIA (READI-Alg) both of where were applied to instances of the GCP.

Cutello, Narzisi, et al. [139] again renamed the approach to Optimization Immunological Algorithm (opt-IA) and applied the approach to instances of binary trap functions. An additional fitness inversely-proportional hypermutation (referred to as 'hypermacromutation') schemes was proposed and compared to the traditional static approach. This algorithm was evaluated again in a larger study involving a number of machine learning domains [141], and again on a large number of continuous function optimization instances [131].

Cutello, Nicosia, et al. [147] investigate the hypermutation operators of opt-IA. Cutello, Morelli, et al. [138] apply opt-IA to the 3DHP protein folding problem. Cutello and Nicosia [145] apply opt-IA to graph colouring, MHSP, and satisfiability. Work by Anile, Cutello, et al. [3] hybridizes opt-IA with a direct search method. An extension of opt-IA called aligner was proposed by Cutello, Lee, et al. [137] applied to multiple sequence alignment of DNA.

SIA Description and Pseudocode

Parameter	Description
P	Antibody population
l	Length of binary string representation
d	Population (repertoire) size
dup	The number of clones created for each antibody
clone	Duplication of the bit string
hypermutation	Probabilistic modification of a bit string (bit flipping), requires the specification (ρ) of the probability of flipping each bit.

Table 5 - SIA parameters

```
P <- rand(d, l)
ForEach p of P Do              // presentation
  affinity(p)
 EndFor
While Not StopCondition Do
 ForEach p of P Do             // clonal expansion
  Pc <- clone(p, dup)
 EndFor
 ForEach c of Pc Do            // affinity maturation
  hypermutate(c)
 EndFor
 ForEach c of Pc Do            // presentation
  affinity(c)
 EndFor
 P <- select(Pc, P, d)         // clonal selection
EndWhile
```

Figure 4 - SIA pseudocode listing

An extension to opt-IA was proposed by Cutello, Nicosia, et al. [132] called parallel immune algorithm (Par-IA) which is a master-slave version of the algorithm applied to numerical function optimization. Cutello, Nicosia, et al. [133] again renamed the approach to Optimization Immune Algorithm (Opt-IMMALG), applying the approach to continuous function optimization using a real-valued representation as opposed to the binary representation used in previous works. Also stated in this work is the use of fitness inversely proportional hypermutation as the standard mutation operator for the approach. This algorithm is extended and renamed dynamic immune algorithm (dyn-IMMALG) by Cutello, Lee, et al. [130] who propose a dynamic rather than static clonal operator. The approach is applied to binary trap functions and compared to opt-IA and variations of CLONALG.

E.*Multi-objective Immune System Algorithm (MISA)*

Coello Coello and Cruz Cortes [18] introduce an AIS called the Multi-objective Immune System Algorithm (MISA), and as its name suggests was designed as a population-based approach for constrained and unconstrained multi-objective optimization. In the approach a repertoire of solutions is split into antigens (Pareto non-dominated and feasible solutions) and antibodies (Pareto dominated and infeasible solutions). A bit-string representation is used and antigens are selected at random and matched against antibodies (using Hamming distance). After selection, antibodies are cloned and mutated the population is unioned and reduced back to the configured size, culling the lower quality solutions. An external (elitist) memory repertoire is maintained of non-dominated feasible solutions. Solutions are added to the memory set if they are non-dominated by the current memory set population and sufficiently diverse as determined by a grid-based maintenance structure.

MISA was extended by the same authors [109] and further compared to state of the art evolutionary approaches for multi-objective optimization. An EC-AIS hybrid terminology was adopted and an EC-based crossover mechanism was adopted within the memory set. The main algorithm was simplified such that all population members were consider antibodies, and only the lower score solutions are selected for cloning and hypermutation. The modified algorithm was shown effective, although it demonstrated rapid convergence behaviours on benchmark problem instances. Finally, Villalobos-Arias, Coello Coello, et al. [104] proposed a convergence proof for the update MISA showing that the elitism within the algorithm was needed to guarantee convergence.

F.*Miscellaneous Works*

This section lists works that do not neatly fit into the above rough grouping of works. The works contained in this section are not canonical, are new, or are less frequently referenced. It should be noted that the majority are recent (within the last two years), application works (as opposed to new algorithms or theory), inspired or derived from CLONALG (with or without reference) and produced by non-western research groups (mainly from China). See Table 6 for a summary of these works arranged by general application domain[6].

General Application	References
Feature selection for model	[41,93,107,152,159-162]
Parameter tuning for model or controller	[26,39,55,95,105,127,163,167]
Parameter tuning for a PID controller	[30,31]
Anomaly and or intrusion detection	[40,67,99,108]
Pattern recognition	[52,89]
Multi-objective optimization	[16,20,90,102,150,156] [116,151]
Function optimization	[32,47-51,56,91,96,101,118,119,154,155,172,175,176,178,180,181]
General optimization	[15,17,21,42,94,117,121,165,179]
Multi-user detection	[57,57,98,100,103,173]
Hybridized with other algorithm(s)	[33,58,158,174]

Table 6 - Summary of uncategorized application CAS works

G. *Outliers*

This section pertains to algorithms and works which superficially appear to be clonal selection algorithms, theoretical investigations into the principle commonly sited as algorithms, and algorithms which have been labelled as such although do not meet the definition outlined in section II. They are listed here for completeness, although by no means is this a complete collection of ambiguous clonal selection algorithm works.

Forrest, Javornik, et al. [123] investigated the pattern recognition properties of the immune system. They used a binary coded genetic algorithm (GA) to model antibody-antigen matching in the immune system, which included the clonal selection mechanism, claiming "*The GA without crossover is a reasonable model of clonal selection, while the GA with crossover models genetic evolution*". Hightower, Forrest, e al. [115] use a Binary GA model of somatic hypermutation of clonal selection to investigate the Baldwin Effect and evolution. Weinand [114] propose a dynamical systems computational model of somatic mutation of B cells to evaluate the affect of somatic mutation of affinity maturation of the immune response. Fukuda, Mori, et al. [126] and Mori, Tsukiyama, et al. [76] use a GA to investigate clonal selection properties and immune network algorithms for scheduling and resource allocation.

Zhang and Hou propose a Niching Clonal Selection Algorithm (NCSA) [169] that combines negative selection and refinement using CSA applied to the pattern matching problem of anomaly detection. Yo and Hou [177] proposed an extension of CLONALG called CsAL (Clonal Selection Algorithm) to investigate the negative selection approach to virus detection. Kim, Bentley, et al. [68-74] have a body of work on a Dynamic Clonal Selection (DynamiCS) which is a T-cell inspired negative selection approach for intrusion detection that uses clonal selection mechanisms during detection generation.

IV. Relation to Evolutionary Computation

Evolutionary Computation (EC) is a field of study much like the field of AIS, although draws its inspiration for computation from Darwinian (theory of natural selection) and neo-Darwinian (findings of modern genetics also referred to as the new synthesis) theories of evolution. The field of EC is also more established, and clonal selection algorithms bear a superficial similarity to some EC algorithms such as the Genetic Algorithm (GA), and properties of modern Evolution Strategies (ES). See [23,24] for a classical treatment of EC and [124,125] for a modern treatment of the field of EC.

In their work on CLONALG, de Castro and Von Zuben [86] address the similarity between a GA and their approach, particularly in regard to the binary representation used and the stochastic-Darwinian processes employed by both. They go on to suggest the differences, include the vocabulary used (genetics and evolution verses the shape-space formalism and antibody-antigen cellular interactions), and the somatic mutation and receptor editing used to explore the shape space. The authors [85] later claim that CLONALG can be categorized as an 'evolutionary-like algorithm', although they maintain the same arguments of inspiration, vocabulary, and formalism and the primary differences.

In their book de Castro and Timmis [88] again acknowledge the similarity of CLONALG to an EA. They are quick to point out that a major difference between the inspirations of the two approaches is that mutation in evolution is random, whereas the hypermutation process of clonal selection is controlled and directed – proportional to the receptors affinity with the triggering antigen. They go on to suggest that work on EA's can be leveraged by CSA's indicating that research on selection operators (e.g. tournament, roulette wheel, etc.) may be exploited. The shape-space formalism is presented as a CSA representation abstraction and alternative representation schemes and corresponding mutation mechanisms are discussed, also leveraging from research from representation and mutation in EA's.

de Castro and Timmis provide a treatment of evolution and the clonal selection of the acquired immune system. They suggest an important difference between the two theories is the fact that in the clonal process expansion occurs through cell cloning, that there is no sex or genetic recombination, rather only affinity inversely-proportionate somatic hypermuatation.

In work on the MISA Coello Coello and Cruz Cortes [18] claim that their approach is not a genetic algorithm because it does not use recombination (crossover operator), they later [109] adopt a crossover procedure in their approach, as well as adopt a hybrid EC and AIS terminology.

[6] Many of these works could not be obtained by the author prior to the publication of this paper, thus general application domain was assumed in some cases from paper abstracts

In their work evaluating the BCA on function optimization Timmis, Edmonds, et al. [62] suggest that BCA is not a GA based on the empirical performance of the approach on a small suite of test problem instances, although they are very quick to point out the limitations of their small study and the requirement for further research.

The niching-like properties (an EA property inspired by theories of population genetics and ecology) were observed by de Castro and Von Zuben [85] with CLONALG on multimodal function optimization and empirically compared to the fitness sharing approach of Goldberg, et al. [24,25,75]. The niching search properties are conjectured to occur given the hill-climbing like behaviour of the independent and semi-independent evolution of B-cells of the various clonal selection algorithms. Thus, there may be a connection between CSA and greedy stochastic-based hill climbing algorithms such as the real-valued hill-climber used by Mahfoud [120] when evaluating niching EA's, and the binary hill climbers used to evaluate early GA's [106].

To summarize:

1. The primary difference between EA's and CSA's is the inspiration, resulting in differing abstractions and nomenclature.
2. The secondary difference between EA's and CSA's is the operators, the specific adaptive mechanisms employed by both approaches.
3. The principles inspiring the algorithms are very similar in terms of their general adaptive method, specifically; selection, reproduction, and variation.
4. Some CSA's (CLONALG, BCA, IA family) may be viewed as specialized EA's without crossover, meaning some research on EA's is likely to be applicable to work on CSA's.

V. Conclusions

This review of clonal selection algorithms revealed at least three interesting findings.

The first being the clear and recent popularity in the application of CLONALG derivatives, particularly from eastern (Chinese) works. The volume of works suggests that potential ease of implementation of the approach and the variety of application (primary engineering optimization and model refinement) suggests the potential generality of the approach. The second interesting trend is the hybridization of the algorithm into other algorithms and systems. In addition to using CSA's as the general iterative adaptive element in other artificial immune system algorithms, the CSA principle has been grafted into a variety of other algorithms including particle swarm optimization (PSO), gene expression programming (GEP), evolutionary algorithms and various other adaptive methods. The third interesting finding is the clear similarity of the clonal selection principle with Darwin's evolution principle, and the resultant strong similarity between evolutionary algorithms (the genetic algorithm in particular) and some clonal selection algorithms (CLONALG, BCA, IA family).

This work attempted to unify the field of clonal selection algorithms by presenting 1) a specific and reusable definition of clonal selection algorithms, 2) a general model for interpreting clonal selection algorithms, and 3) a general taxonomy for interpreting the current state of clonal selection algorithms research.

It appears from the literature review that clonal selection algorithms are suitable for optimization domains and for classification domains. It is important to note that CSA research is still in its infancy and these applications may be considered merely demonstrations of capability of the general method.

Finally, from an algorithm design perspective, there are likely many aspects of the clonal selection principle which have not been realized in the current state of the art clonal selection algorithms. A study of the immunological theory from a biological rather than algorithm vantage as well as associated physiology will likely reveal not only computationally interesting mechanisms and architectures, but may also suggest suitable general application domains. Some plausible areas for future clonal selection algorithm investigation may include the distributedness of the immune system physiology and the autonomy of the clonal response, the specific cellular and or genetic mechanisms employed during clonal expansion, and physiology and mechanisms of the antibody-antigen binding during the immune response.

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