A Generational Population-Based Clonal Selection Algorithm and Extensions

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***Abstract*-Host organisms with acquired immune systems reproduce, perpetuating their population. The creation of progeny hosts by a parental population introduces a generational relationship, which may be reduced to a lock-step population in which the present population is replaced by a created progeny population. This work extends the previously defined host-based population-based algorithm by introducing the generational principle. Extension of a minimal generational algorithm facilitates inter-generational information sharing inspired by maternal immunity and deo-Darwinian evolution.**

Keywords-Clonal Selection, Artificial Immune System, Natural Selection, Generational, Evolution, Maternal Immunity

I. Introduction

Host organisms in a population reproduce such that a generational structure may be defined between hosts where progenitor-hosts produce progeny-hosts. This generational principle provides an extension to a previously proposed population-based clonal selection algorithm [6] in which a population of acquired immune systems interact with each other and a pathogenic environment. This work proposes a minimal generational population-based clonal selection algorithm and the generational-based extensions of maternal immunity and natural selection, as proposed in previous works [2,3]. Section II introduces the generational extension to the population-based clonal selection algorithm in a minimal generational algorithm. Section III extends the minimal generational algorithm by introducing inter-generational sharing, first explicitly in a maternal immunity inspired algorithm, and implicitly via selection and genetic variation under reproduction in a neo-Darwinian inspired inherited-immunity algorithm.

II. A Generational Population-Based Algorithm

The minimal population-based clonal selection algorithm consist of a collection of independent immune systems, each responding in their own way to pathogenic exposures from the environment. This algorithm, and the proposed extensions that facilitate intra-population interactions, may be extended further by introducing a generational mechanism. In this mechanism, the population of immune systems (the present generation) are responsible for creating a new set of immune systems (the next generation), which replace the present generation.

Generational Principle*: A generational principle is one in which the present set of hosts are responsible for creating the next generation of hosts that replace the present generation.*

Hosts may use an asexual reproduction mechanism where one host contributes a variation of itself to the next generation. Alternatively, hosts may collaborate in their contributions to successive generations (sexual reproduction). Further, the contributions of various hosts to successive generations may not be homogenous, such that more successful hosts (by some measure of success) may contribute more than less successful hosts.

Generational Operators*: A generational population structure may use a sexual or asexual reproduction strategy. The contributions of hosts may or may not be uniform to successive generations.*

One may consider a minimal generational population-based clonal selection algorithm in which reproduction is asexual and host contribution to successive generations is uniform. This minimal configuration highlights the core characteristics of the generational algorithm which focus on multiple restarts (or attempts) for a given host system (host system lineage) to acquire information about a given pathogenic environment.

Minimal Generational Algorithm*: An extension of the population-based clonal selection algorithm in which the present population is replaced by a new population, although not before the present population is given time to acquire information about the environment. Each host in the present generation contributes a single progeny to the next generation*

The premise of the generational mechanism is that a given instance of a host immune system may acquire different information in successive trials (generations). The minimal generational algorithm does not allow one generation of hosts to convey information to progeny, rather it provides a clean slate for each system to repeat a trial. Thus, the minimal generational algorithm (in essence) 'resets' each host to initial conditions at the beginning of each new generation.

Restart Principle*: The minimal generational algorithm allows each host system a retrial of the pathogenic environment with each successive generation.*

Step1: *Initialise* all immune systems in the population
Step2: *Stimulate* the systems according to the pathogenic environment
Step3: *Respond* to any exposures according to each systems principles
Step4: *Interaction* between systems in the population
Step5: *Repeat* Step2-Step4, until generation condition is triggered
Step6: *Construct* the next generation from the present generation
Step7: *Repeat* Step1-Step6, until stop condition is triggered

Figure 1 - Summary of the generational modification to the minimal population-based clonal selection algorithm

The principle components of the generational algorithm are the reproductive scheme, and the mechanism that triggers the generational change.

Reproductive Scheme: The mechanism by which one generation contributes to and prepares the successive generation. Examples include sexual and asexual reproduction where hosts cooperate or stand alone in their contributions to the next generation. Further, the contributions of any one host to the next generation may or may not be homogeneous with respect to the other hosts of the present generation.
Generational Trigger: The condition, that once satisfied requires the application of the reproductive scheme to the present generation to create the next generation of immune systems. An example is a time trigger in which immune systems are given a representative exposure to the pathogenic environment.

Figure 2 - Summary of the principle components of the generational algorithm

The restart principle gives a population of immune systems, each with their unique and ongoing perspective of the environment, successive chances of learning a perspective of the environment. The inability of the systems to share acquired information between generations, means that each generation the population must re-learn (start from scratch) those things learned in the previous generation. If a generational-accumulative model is desired, it must be implemented as a mechanism at a higher scale than the generational model. Such a mechanism is responsible for explicitly integrating information across generations. The hope, of the generational model is that each fresh-start and subsequent run (trial with the environment) results in a varied perspective, and thus varied acquired information perhaps at the individual system-level, and more importantly at the population-level.

Varied Perspective Principle*: The restart-principle (fresh start) suggests that the population is able to acquire different information about the environment with the same general principle components, in different runs*

III. EXTENSIONS: GENERATIONAL SHARING

The concern of the minimal generational population-based clonal selection algorithm is that operating with a fresh-start is too computationally intensive (inefficient) with regard to the information acquired and explicit integration. More importantly, there is little guarantee that such the varied perspective principle will hold for a given environment. This section extends the minimal generational population-based algorithm by proposing two different mechanisms by which populations can share information between generations of the a algorithm.

Generational-Sharing Principle*: (Vertical Sharing) The sharing of acquired information (explicitly or implicitly) from a population of hosts in one generation with a population of hosts in a subsequent generation*

The intent of sharing information between generations is that subsequent generations can learn from the success and failures of the previous generation, and the generations that came before it. Such mechanisms allow the generational-population (species) to implicitly integrate information about the environment over generational time (rather than explicitly by an external mechanism). Further, such mechanisms do not restrict subsequent generations to the limitations of the past, rather integrating generational knowledge into the 'fresh-start' systems facilitating the desired trait of the minimal generational algorithm of acquiring a varied perspective (if such a variation in possible).

A. *Maternal Immunity*

A previous work highlighted a type of immunity passed from mother to child called maternal immunity [2]. In this type of immunity, the child receives antibodies and immune cells (mature effectors and memory cells) from the mother, both across the placenta, and in breast milk (mucosal immunity). This type of immunity is referred to as natural-passive immunity because the conferred acquired immune information is passed between the hosts without eliciting an immune response (active immunity). Previously a model was proposed that employed this sharing mechanism, called 'vertical sharing' [3].

Maternal Immunity*: The sharing of acquired immune information from a host system in the present population with progeny host systems in the subsequent generation*

The minimal generational population-based algorithm may be augmented to facilitate maternal immunity between generations, as follows:

Step6a: *Construct* the next generation from the present generation
Step6b: *Sample* acquire immune cells from the present generation
Step6c: *Transmit* sampled immune cells to the hosts of the next generation

Figure 3 - Maternal Immunity Generational Algorithm

The maternal immunity generational algorithm is similar in mechanism to the pathogen transmission and vaccination population-based algorithms in that both sampling and transmission are required [6].

Cell Sampling Scheme: The selection of mature acquired immune cells (effectors and memory cells) from host systems to be removed and transmitted to host systems of the subsequent generation. The selection scheme should draw a representative sample of the information acquired by the system over the course of its lifetime (trial period)
Host Transmission Scheme: The selection of instantiated host systems of the subsequent generation by hosts of the present generation to which sample acquired immune systems cells will be transmitted. A simple host selection scheme is the selection of progeny host systems.

Figure 4 - Principle components of the maternal immunity algorithm

The concerns of cell sampling are predominantly similar to the concerns highlighted in the vaccination/inoculation population-based algorithm. It is important to highlight the trade-off of the sampled cells and their effect on freshly instantiated host systems. A selection of a sample that is too large or contains many dominant (with respect to clonal selection) pieces of acquired information (memory cells) will cause the recipient systems to (in effect) represent continuances of the transmitting host. The sample should be diverse and representative, and likely contain many effector cells.

Sample Effectors: *The sample of cells selected for transmission from hosts of one generation to the next should consist of a diverse and representative sample, made up predominantly of effector cells.*

The selection of effector cells for transmission is useful for a number of reasons. Firstly, the biological inspiration (maternal, and more importantly mucosal immunity) confers mostly this type of acquired immunity in the form of antibodies. Effector cells, if not used in a reasonable about of time are removed form the system via attrition (die). This effect holds (is expected to hold) for proposed fundamental clonal selection algorithms and their principle components (such as the elaborated clonal selection algorithm [4]). Further, if a random sampling technique is used to select the sample, given that effectors are the most common cell type in the repertoire (expected to be the case), they will naturally be the dominant cell type of the random sample. The host transmission scheme requires the selection of hosts in the subsequent generation to receive the sampled cells. A natural implementation of this scheme is the selection of progeny hosts. Specifically, the selection of hosts in the subsequent generation by hosts in the present generation, to which they are responsible for instantiating.

Parent-Child Transmission: *The transmission of sampled cells from hosts in the present generation to hosts in the subsequent generation to which they are responsible for creating*

The parent-child transmission scheme may result in the formation of independent generational host-lines given the asexual basis of the minimal generational algorithm. The concern of this effect is that if a given host system is lost (in some way), then the information acquired by that host's generational line is also lost.

Concern: *The restriction of inter-generational cell transmission from parent to child causes the formation of generational cell lines, such that if a given host in the present generation is lost, then the host's cell line is lost*

This concern may be addressed by relaxing the parent-child transmission constraint, and allowing parent-hosts to potentially transmit to any host in the child generation. A biological basis for this configuration may be the use of manufactured formulae, or the use of a wet-nurse. A sample decoupled transmission scheme is random host selection, with reselection. The reselection allows a given host in the child generation to potentially receive acquired immune information from more than one parent host system.

Decoupled Transmission: *The selection of hosts in the child generation by hosts in the parent generation that is not restricted to the parent-child constraint. A child system may receive the acquired immune information from more than one parent host system*

The transmission of cells to non-child hosts provides redundancy between host lines, if there is a relationship between parent-child that may affect host-loss (such as reproduction in a spatial environment). A one-to-many transmission scheme between the generations will also foster redundancy of acquired information between the generations. The concern in a host system receiving acquired immune information from more than one host, is that the child system may become overly biased by the previous generation. A parent-child (one-to-one) transmission scheme limits the scope of received acquired immune information to a single host of the previous generation's perspective.

B. *Inherited Immunity*

Another inter-generational sharing scheme is evolution by natural selection [2]. Unlike maternal immunity, evolution does not share acquired immune information directly in the form of cells, rather it shares it indirectly through selection and inheritance of the mechanisms that create and utilise those cells.

Inherited Immunity: *The sharing of information between generations of immune systems that defines the creation and utilisation of acquired immune information, shaped by natural selection*

Sharing acquired immune models inspired by natural selection were proposed previously, called evolved immunity [3]. This section proposes an extension to the generational population-based clonal selection algorithm to incorporate inherited immunity.

Step6a: *Select* the parent host systems to contribute to the next generation
Step6b: *Reproduce* selected parents to create the next generation

Figure 5 - Inherited immunity generational algorithm

The inherited generational population-based algorithm requires a selection and reproduction mechanisms for hosts, as in the minimal generational algorithm. The important differences in this specialisation of the algorithm is that a given host may contribute more or less than the other hosts in its generation. This is a realisation of natural selection, where a measure of the hosts in the population discriminates reproductive fitness and genetic contribution to the next generation. The principle difference of this specialisation is the use of a genetic-basis for traits that effect hosts acquired immune system.

Selective Scheme: A specialisation of the host selection scheme of the minimal generational algorithm that realises the principles of natural selection. A given hosts contribution to the subsequent generation is differentiated based on assessed fitness against an inherited trait that effects a hosts acquired immune system.
Genetic Basis: A genetic code (genome) is used to define a trait of a hosts acquired immune system. This genetic code provides the basis of natural selection (differentiated reproductive success), and the medium for reproduction (genetic inheritance)
Reproductive Scheme: The reproductive scheme of the minimal generational population-based algorithm, that may take into account the broader considerations of asexual and sexual reproduction. Reproduction provides the basis for inheritance with regard to the genetic basis of the trait or traits that effect a hosts acquired immune system, and manipulations to that genetic representation in the form of genetic mutation and or genetic recombination.

Figure 6 - Summary of the principle components of the inherited generational algorithm

The reproductive scheme provides the mechanism for inheritance of the genetic basis of an acquired immune system trait. Reproduction provides a duplication of the parents genetic material which may be modified in minor ways by genetic mutation (lower rate of mutation than that of hypermutation in the immune response). This introduces variations of the trait for natural selection to differentiate reproductive success. A property of the host populations acquired immune system is defined by a parameter or set of parameters, which is encoded in a genome. The genome is the basis for inheritance, and the expressed trait is the basis for host selection. An example trait, and minimal natural-selection generational algorithm is the biasing of the generation of naïve immune cells.

***Minimal Natural Selection Algorithm**: The minimal natural selection algorithm encodes information that defines the generation of naïve immune cells in a hosts acquired immune system*

Unlike the maternal sharing scheme that directly reinforces the receptor configurations that are useful, the minimal natural selection algorithm indirectly reinforces receptor configurations in the generation of a hosts base repertoire, and ongoing naïve cells. This is a broader form of sharing that provides the flexibility for the selection mechanism and scope of genetic basis for the trait to define the regions of 'receptor configuration space' that are beneficial for a hosts untested acquired immune system to sample. The algorithm provides an interesting example that combines both genetic-based learning over generational time and somatic-based learning over a hosts lifetime.

***Learning at Two Scales**: The minimal natural selection algorithm provides learning at the host-lifetime scale in somatic adaptations via clonal selection, and learning at the population-generation scale in genetic adaptations via natural selection*

Examples of other traits that may be subjected to the pressures of evolution by natural selection include (1) the sensitivity of matching in the clonal selection algorithm (2) and the organisation and connectivity of tissue types in the lymphoid tissue algorithm. In addition to opening up parameterised models in the framework to the process of evolution via natural selection (generational learning), the minimal natural selection algorithm provides a connection of the host-level of the acquired immune system framework ([5]) with the field of genetic algorithms [1].

IV. Discussion

This work extended the minimal population-based clonal selection algorithm by introducing the principle of generational turnover of the population. This minimal general algorithm was extended further with inter-generational sharing, both directly via maternal immunity, and indirectly via inherited immunity. Where the incorporation of the host-population model opened the door for the integration of immunology and population ecology, the incorporation of evolution into the model framework opens the door further, to the integration of immunology and population genetics.

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