# Models, Algorithms, and the Hierarchal Acquired Immune System Framework

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***Abstract*-A series of adaptive models inspired by abstractions of the acquired immune system provided the basis for the proposal of a series of acquired-immune inspired algorithms. This work attempts to unite the adaptive models with the proposed series of algorithms in the context of a hierarchal framework of the immune system. This work reviews the adaptive models and algorithms, and explicitly highlights the relationships between these two, until now, implicitly related areas of work. The seminal information processing property of each algorithm is reiterated, outlining a series of studies verifying the capabilities of the algorithms.**

***Keywords-Algorithms, Artificial Immune Systems, Acquired Immune System, Hierarchal Framework, Clonal Selection***

## I. INTRODUCTION

A series of adaptive models were proposed based on the information processing properties of the immune system at the cellular level, between tissues, and between immune systems in a population. At all three of these scales, the information processing in these models is concerned with the interactions between the principle components of the model with each other, and their interactions with stimulation by exogenous antigen (pathogen). This realisation lead to the proposal of a stimulus-response based 'pathogenic exposure' paradigm [5], and a hierarchical acquired immune system framework in which to relate the adaptive models at the three scales [15]. Based on the proposed immune-inspired adaptive models, a number of algorithms were proposed to realise the information processing properties of the models at each scale of the framework. This work summarises the models and algorithms in the context of the hierarchical framework, and attempts to reconcile their relationship from a number of perspectives, resulting in a plan for future work.

Section II summarises the adaptive models and realised information-processing algorithms in the context of the hierarchal framework of the acquired immune system. Section III considers the relationship between the models and algorithms from a number of perspectives, attempting to both reconcile their relationship, and provide a foundation for their cohesion in a broader context. Section IV exploits the various perspectives on the relationship between the models and the algorithms, and suggests the core information processing concern of each algorithm requiring verification against its related adaptive model. Finally, Section V, highlights future work, not limited to the elaboration of the integrated framework and pathogenic exposure paradigm, and the elaboration of an abstracted model of distributed immune-inspired information processing.

## II. MODELS AND ALGORITHMS

The foundation for the series of acquired immune system adaptive models was laid [2], which lead to the later elaboration of the models, proposal of inspired algorithms, and proposal of a broader contextual hierarchical framework. This section summarise the adaptive models and the algorithms that they inspired. The models and algorithms are retrospectively presented in the three tiers of the hierarchical framework [15].

### A. *Cell-in-Tissue Algorithms*

The principle concern with models and algorithms in the cell-in-tissue level is the interaction of immune cells with (1) other immune cells and with (2) pathogen. The early work [2] proposed 'principle components' as the clonal selection and related principles that operate on cells at this level, and 'base models' that employ those principles. These principles were considered in more depth in a later work that discussed design principles and behavioural expectations for algorithms realised at this level [7]. Also proposed in the early work were so called 'extended models' that included a memory model that contributed to a later realised elaborated clonal selection algorithm, and B and T cell model that contributed to a later realised T-cell mediated algorithm.

| Model | Summary |
|---|---|
| *Principle Components* | Clonal selection principles such as selection, expansion, mutation and population principles such as management, diversity and memory |
| *Base Models* | Clonal selection models including selection, mutation, and expansion |
| *Extended Models* | Broder scoped clonal selection models including memory, negative selection, dynamic antigen, and T-cell mediation |

Table 1 - Summary of the adaptive models proposed at the cellular level

A minimal clonal selection algorithm was later proposed that employed a winner take all principle. This most basic algorithm was expanded to incorporate the principles discussed in the base models, in what was referred to as the elaborated clonal selection algorithm

[10]. The elaborated algorithm paved the way for a number of extension algorithms that considered other intra-tissue cellular interactions in addition basic stimulus-response of clonal selection. A T-cell mediated clonal selection algorithm was proposed where pathogen interact with a population of B-cells, which in turn interact with a population of T-cells [13]. An intra-repertoire recognition algorithm was proposed based on the immune network theory, where cells recognise and respond to other cells in addition to pathogen [11]. Finally, a spatial-based clonal selection algorithm was proposed, where cell-pathogen interactions are confined to a spatial projection [12].

| Algorithm | Summary |
|---|---|
| *Minimal Clonal Selection* | Simple stimulus response clonal selection principles |
| *Elaborated Clonal Selection* | Elaborated clonal selection, providing more flexibility |
| *T-Cell Mediated* | Population of B-cells interacting with a population of T cells |
| *Intra-Repertoire Recognition* | Inter-population recognition based on network theory |
| *Spatial Clonal Selection* | Clonal selection in a spatial projection |

Table 2 - Summary of the algorithms at the cellular level

B. ***Tissue-in-Host Algorithms***

The principle concern with models and algorithms in the tissue-in-host level is the interaction of tissues with (1) other tissues in the host, and with (2) pathogen. The early work [2] proposed simple 'discretised models' that considered cell recirculation between tissues, and different lymphoid tissue types. These models were elaborated in a later work, where the class of model was relabelled 'discretised repertoire models' [4]. This elaboration was inspired by a review of lymphocyte migration research and an overview of the lymphatic system [3]. The elaboration discussed the principle components of the discrete repertoire models including tissue types, cell types, and cell migration behaviours. These principle components were employed in a series of models including a recirculation model, a cell-type model and a tissue type model. The design principles and behavioural expectations of general distributed tissue models was considered in the context of pathogen exposures [8]. That work laid the foundation for later tissue-based algorithms, referring to them as 'multiple repertoire algorithms'. Models included a recirculation, germinal centre, inflammation, homing, and homeostasis.

| Model | Summary |
|---|---|
| *Discrete Models* | A recirculating population model between tissues, and a differentiated lymphoid tissue model |
| *Discrete Repertoire* | Recirculation model, tissue model, cell-type model |
| *Multiple Repertoire* | More specific tissue behaviours such as recirculation, homing, germinal centre, and inflammation |

Table 3 - Summary of the pre-cursor tissue models

A minimal cell recirculation algorithm was proposed as a base tissue-level algorithm on which to incorporate other tissue-based interactions [17]. Also proposed in that work was a tissue-homing algorithm where cells express preferential residence in tissues. A lymphoid tissue architecture was proposed in which varied tissue types provide varied information processing mechanisms such as streaming, clonal selection, and cell generation [18]. Also proposed in this work was homing and recirculation as information recruitment strategies, and the proposal of a more directed information recruitment strategy called the inflammation algorithm. The lymphoid tissue architecture was elaborated in a later work in which the specific information properties of each tissue type were clearly specified, and employed in a series of information processing models [16]. These architectures included a filtering model, a lymphoid node model, and a complete host model, all of which were specialisation of the general architecture.

| Algorithm | Summary |
|---|---|
| *Minimal Recirculation* | Base-level tissue algorithm where tissue interact with each other by exchanging cells |
| *Tissue Homing* | Preferential residence of cells in tissues (preferential transmission of cells that do not exhibit a preference) |
| *Tissue Inflammation* | Directed information recruitment |
| *Lymphoid Tissue Architecture* | Information processing properties of different tissues, and tissue organisations |

Table 4 - Summary of the algorithms at the tissue level

C. ***Host-in-Population Algorithms***

The principle concern with models and algorithms in the host-in-population level is the interaction of hosts with (1) other hosts in the population, and with (2) pathogen. The early work [2] proposed simple multiple system models that proposed populations of immune systems exposed to vaccination and evolution. These models were elaborated in the context of interactions in populations with immunity and evolutionary concerns reviewed in [6]. A series of multiple system models was proposed including control of pathogenic exposures, inter-population and inter-generational sharing of acquired immunity and traits of the acquired immune system shaped by evolution [9]. These principle components were combined in various ways to propose general population, sharing, and evolutionary models.

| Model | Summary |
|---|---|
| *Multiple System* | Populations of acquired immune systems exposed to vaccination and evolution |
| *Multiple Immune Systems* | Principle components of inter-population and inter-generational sharing of acquired immunity, controlled and uncontrolled exposures and evolution |

Table 5 - Summary of pre-cursor host models

A minimal population-based algorithm was proposed as a base-level host algorithm without any intra-population interaction between hosts [19]. This algorithm was extended to include two-types of interaction within the population. The first was a pathogen transmission algorithm which may be specialised to facilitate pathogen-controlled and host-controlled (vaccination) transmission. The second interaction is the sharing of acquired immune information between hosts in the population (transplantation). The minimal population algorithm was extended to a minimal generational algorithm where the present population creates progeny that replace the present generation [14]. This minimal generational

algorithm was extended to allow the inter-generational sharing of acquired immunity (inspired by maternal and mucosal immunity). The minimal algorithm was also extended to incorporate evolution by natural selection. A minimal natural selection algorithm was proposed in which the parameters used to generate naïve cells in the initial repertoire and ongoing are influenced by the pressures of evolution.

| Algorithm | Summary |
|---|---|
| *Minimal Population* | Population of non-interacting host systems |
| *Pathogen Transmission* | Intra-population transmission of pathogen including pathogen-controlled and host-controlled (vaccination) |
| *Shared Acquired Immunity* | Intra-population sharing of acquired immune cells (transplantation) |
| *Minimal Generational* | Generational population of non-interacting host immune systems |
| *Maternal Immunity* | Inter-generation sharing of acquired immune cells (maternal and mucosal immunity) |
| *Minimal Natural Selection* | Inter-generational implicit sharing of acquired immune traits evolved by natural selection |

Table 6 - Summary of the algorithms at the host level

## III. PERSPECTIVES

The previous section summarised the models and the algorithms in the context of the hieratical framework, although it did not reconcile their relationship (other than superficially). This section assesses the relationship between the proposed adaptive models and information-processing algorithms from a number of perspectives, and attempts to retrospectively reconcile their proposal and development.

### A. *Motivations and a Developmental Perspective*

The models and the algorithms may be united from the perspective of motivation, specifically the motivation for investigating biologically inspired distributed information processing of the acquired immune system.

***Motivation**: The investigation of distributed information processing inspired by the acquired immune system*

From this perspective, the tissue models are concerned with the information processing properties of inter-tissue interactions (trafficking lymphocytes for example), and populations of immune systems are concerned with the information processing properties of inter-host interactions (vaccination and evolution for example). Further, this perspective suggests that the cellular-level models provide the basis (zeroth level models) for embedding in the more complex models.

***Inspired Information Processing**: Adaptive models represent abstractions of the (biological) acquired immune system that embody information processing characteristics at different scales of the biological system*

Motivations suggest that the cellular-level algorithms demonstrate base-level information processing, whereas the tissue-level and host-level algorithms demonstrate distributed information processing. Further, these motivations suggest that the adaptive models propose the information processing properties that the inspired algorithms are required to demonstrate. Thus, the adaptive models provide the abstraction and the link from the observations of the biological system to computational realisations.

***Developmental Perspective**: Adaptive models abstract observations of the biological acquired immune system, suggesting the information processing properties to be verified in realised algorithms*

### B. *Framework Perspective*

From the developmental perspective, the information processing is the central theme, and the hierarchical framework provides a background abstraction that links the models and algorithms together. An alternative perspective is to make the framework itself the central theme, and consider the models and algorithms in its context. From this perspective, the framework represents the acquired immune system as an information processing system that may be partitioned into three scales of observations: cellular, tissue, and host.

***Framework**: A holistic abstraction of the acquired immune system as an inspiration (abstraction) for information processing*

From this perspective, the adaptive models are phrased as pieces in the context of the holistic abstraction. They represent a strict adoption of the three scales of the hierarchy; more specifically, they are opportunistic abstract information processing models from the framework (so called 'low hanging fruit'). Rather than being biologically accurate (theoretical immunological models), they provide the basis for the realisation of algorithms, which, as specified in the developmental perspective, must be verified against the information processing properties of their related models.

***Algorithm Verification**: The algorithms must be verified against the information processing characteristics of the adaptive models from which they were derived*

The difference from the motivated/developmental perspective is that the framework suggests a relationship between the models, and thus the algorithms at different scales. Further, it may suggest subsumption of models and algorithms in the ascension of the framework (bottom-to-top), and a reductionist causal relationship in the decomposition of the framework (top-to-bottom).

***Hierarchal Relationship**: The framework perspective suggests vertical relationships between the models and algorithms, both subsumptive (bottom-up) and reductionist (top-down) in nature*

## IV. A SERIES OF STUDIES

The commonality between the perspectives in uniting the models and algorithms is the required verification of the algorithms information processing characteristics as outlined in their development and related adaptive models. This section proposes a series of verification studies of each algorithms information processing properties, by highlighting the seminal (single distinct) information processing characteristics of each proposed algorithm.

A. ***Cellular Algorithms***

The hypothesis of the algorithms at the cellular tier is that cells can perform information processing within the scope of a tissue. This information-processing hypothesis is proposed initially for cells and their interaction with pathogen and the principle of adaptation outlined by the clonal selection theory. The elaboration of this simple algorithm facilitates more control over this interaction. These simple clonal selection-inspired algorithms are then augmented in three different ways to facilitate cell-cell interactions. The first interaction facilitates the development of higher-order structures through the T-cell mediation principle. The second interaction facilitates the development of higher-order structures through the network-theory principle. Finally, the third interaction fosters intra-tissue organisation through spatial pressures.

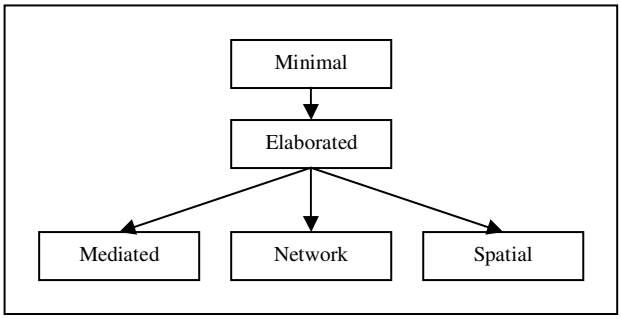


Figure 1 - Depiction of the relationship between cellular-level algorithms

The base algorithm is the minimal clonal selection algorithm, the elaborated algorithm is the same algorithm with augmentations that facilitate more control over the adaptation process. This flexible algorithm provides the basis for three additional augmentations. The changes in functionality may be compared to the base-level (minimal) clonal selection algorithm.

| **Algorithm** | **Information Processing Hypothesis** |
|---|---|
| *Minimal Clonal Selection* | Multiple perspectives |
| *Elaborated Clonal Selection* | Develops cell casts |
| *T-Cell Mediated* | Develops higher-order structures |
| *Intra-Repertoire Recognition* | Develops higher-order structures |
| *Spatial Clonal Selection* | Develops spatial organisation |

Table 7 - Summary of the principle information processing characteristics of cellular-level algorithms

B. ***Tissue Algorithms***

The hypothesis of algorithms at the tissue tier is that tissues are able to perform information processing through the employment of multiple instances of the clonal selection principle. The focus of the information processing by the algorithms at this tier is the interactions between tissues and pathogen, and tissues with each other. Specifically, different tissues constrain the information processing that may occur within them, thus, the base-level of algorithms at this tier is a tissue systems architecture. The systems architecture proposes a filter arrangement that represents a re-phrasing of the minimal clonal selection algorithm (and descendants). A networked lymph node architecture is proposed, and a culminating host-tissue configuration that contains instances of both of the previous models. This systems architecture and the specialisations proposed provide the basis for tissue-interaction algorithms. Three tissue-interaction algorithms are proposed, the first is the recirculation of information between tissues. The second is an augmentation of recirculation that facilitates the homing (preferential residence) of information in tissues. Finally, the third augmentation is the inflammation at sites of exposure in an effort to recruit resources.

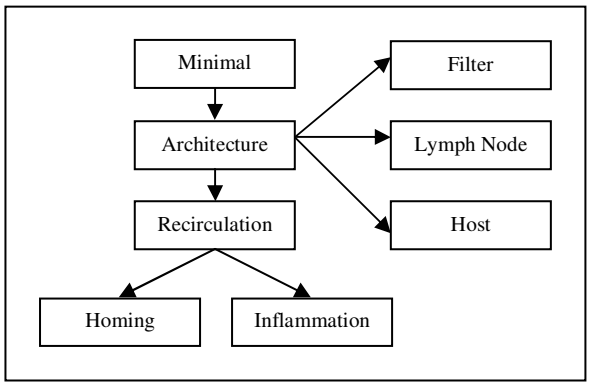


Figure 2 - Depiction of the relationships between tissue-level algorithms

The architecture provides a context for tissue-tissue interaction, although does not define algorithms. Thus, the algorithms stand-alone with regard to testing, although may be embedded within the architecture for evaluation. A base-line algorithm that was not proposed, and is required for comparison, thus, one may propose a isolated tissues algorithm (a minimal tissue algorithm). In this model, the tissues only interact with pathogen, and not with each other, much like the minimal population algorithm, and the minimal clonal selection algorithm. It provides a level of comparison to evaluate the effects of recirculation and augmentations that facilitate information sharing and recruitment. Further, the minimal tissue algorithm may provide sufficient context, to consider the proposed systems architecture an elaboration of the minimal algorithm.

| **Algorithm** | **Information Processing Hypothesis** |
|---|---|
| *Minimal Tissues* | Different perspectives of pathogenic exposures |
| *Minimal Recirculation* | Share acquired information between the tissues of the host |
| *Tissue Homing* | Preferential residence to improve the probability of information being used |
| *Tissue Inflammation* | Recruit more useful resources to a point of stimulation |
| *Filter Tissue Architecture* | Filter a data stream |
| *Lymph Node Architecture* | Networked coverage system |
| *Host Architecture* | Cohesive combination |

Table 8 - summary of the seminal information processing characteristics of tissue-level algorithms

C. ***Host Algorithms***

The hypothesis of the algorithms at this tier is that hosts are able to perform information processing though the employment of multiple instances of the host-abstraction (multiple tissues) of the minimal clonal selection algorithm. The minimal population-based algorithm is different from that of the minimal tissue algorithm in that a single host contains multiple instances of the minimal clonal selection algorithm (or extensions), whereas the population consists of multiple hosts, each with (potentially) many instances of the

minimal clonal selection algorithm (or extensions). The focus of the information processing at this tier is the interactions of hosts with pathogen and with each other. The minimal population algorithm provides a base-line of comparison with no intra-population interactions between hosts. Three augmentations of the algorithm provide three different mechanisms for hosts in the population to share information. The first through the transmission of pathogen (controlled or uncontrolled). The second through the sharing of acquired immune information (result of the maturation process following exposure). The third method introduces a base generational mechanism that does not directly share information between hosts, although does facilitate inter-generational sharing though two extension. The first in the inter-generational sharing of acquired immunity (result of the maturation process following exposure), and the second indirectly through the process of Darwinian evolution.

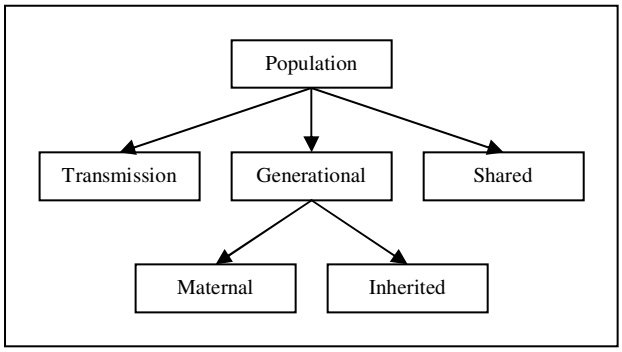


Figure 3 - Depiction of the relationships between host-level algorithms

The population-based algorithms are well structured. There minimal algorithm provides a baseline for inter-population sharing, and the minimal generational algorithm provides a baseline for inter-generational sharing.

| Algorithm | Information Processing Hypothesis |
|---|---|
| *Minimal Population* | Different perspectives on an environment |
| *Pathogen Transmission* | Share acquired information (triggers for maturation) between the hosts in the population |
| *Shared Acquired Immunity* | Share acquired information (results of maturation) between the hosts in the population |
| *Minimal Generational* | Multiple trials at achieving different perspectives |
| *Maternal Immunity* | Shared acquired information (direct result of maturation) between trials |
| *Minimal Natural Selection* | Shared acquired information (indirect generation of the basis for maturation) between trials |

Table 9 - Summary of the principle information processing characteristics of host-level algorithms

## V. DISCUSSION

This work reviewed the series of adaptive models and immune-inspired algorithms in the context of the hierarchical acquired immune system framework. Implicit relationships between the algorithms and models were made explicit by phrasing them at the same level of detail (scope) in the framework. This revealed the role of the adaptive models as abstractions of the biological system and prescriptions for expected information processing characteristics in related algorithms. In addition to the verification work required of the algorithms, two other areas of work were highlighted.

***Framework and Pathogen***: The proposed hierarchal framework ([15]) provides a cohesive abstraction of the acquired immune system at different levels of detail. One important part of that work was the connections made to the stimulus-response pathogenic environment. This connection needs to be strengthened, particularly from the perspective of 'levels-of-detail' in which the acquired immune system at different scopes may be delineated to address pathogen at different scopes. This provides a subsumptive perspective of pathogenic exposures that complements both the hierarchical framework and the stimulus-response 'pathogenic exposure' paradigm.

***Abstract Model***: A second important property that the framework and the summary of algorithms and models in this work highlighted is the commonality between the levels of the framework. Particularly how common processes are constrained in different ways by the abstractions of the acquired immune systems at each of the three scales. This observation requires elaboration, as it is expected to both strengthen the differences between the abstractions and algorithms of the framework, and to provide a general computational model for information processing, likely a general case of the IIDLE platform [1].


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